

VOLUME 21
NUMBER 1
JANUARY 2008

Journal
of the
Bangladesh
Society of
Anaesthesiologists



JOURNAL OF THE BANGLADESH SOCIETY OF ANAESTHESIOLOGISTS

VOLUME - 21

NUMBER - 1

JANUARY 2008

CONTENTS

Editorial

- Anaesthesia in laparoscopic Bariatric Surgery- Is it some thing special in all respect ? 1

Original Articles

- A Study of Priming Technique of Rocuronium in Facilitating Intubation 3
Md. Liaquatunnoor, Rubina Yasmin, UH Shahera Khatun
- Study On Role Of Oral Clonidine In Laparoscopic Cholecystectomy Surgery – 12
A Comparative Study
Amirul Islam, Mozaffer Hossain, AKM Akhtaruzzaman, UH Shahera khatun
- Effect of Low Concentration Isoflurane with Thiopental Sodium for Craniotomies of 21
Intracranial Space Occupying Lesion
*Md. Rafayet Ullah Siddique, Md. Mustafa Kamal, Nezamuddin Ahmed
Lutful Aziz, KM Iqbal*
- Prophylactic Use of Ketamine Hydrochloride For Prevention of Post Operative Shivering 29
*Rabeya Begum, Rezaul Islam, Paresh Chandra Sarker, Kamal Krishna Karmakar,
ABM Muksudul Alam*
- A Comparative Study on Haemodynamic and Recovery Status in 36
Day-Case Anaesthesia Between Infusion of Propofol, Midazolam, Nalbuphine and
Ketamine, Diazepam, Tramadol
*M Masudul Haque, Md Rabiul Alam, Md Al Mamun, Md. Mozaffer Hossain,
Md Zahurul Islam*
- Comparison of Ondansetron And Ondansetron Plus Alprazolam for Prevention of 43
Nausea and Vomiting Following Elective Caesarean Section
Md. Rafiqul Hasan Khan, S.N. Samad Choudhury

Article of Speical Interest

- Anaesthetic Management for Hand Assisted Laparoscopic Enucleation of 50
Pancreatic Insulinoma
*AKM Akhtaruzzaman, Satyajit Dhar, AKM Asaduzzaman, Md Abdus Samad,
Manzoorul Haq Laskar, Mustafa Kamal, Md A Hye*

Case Reports

- Neuropathies in Sepsis: a Difficult Situation to Wean from Ventilator 53
*Md. Mozaffer Hossain, SMA Alim, Muslema Begum, Nasiruddin Ahmed,
UH Shahera Khatun*
- Supraventricular Tachycardia during Regional Anaesthesia (Spinal Anaesthesia) 56
Tahmina Banu, Wahiuddin Mahmood

Editorial

ANAESTHESIA IN LAPAROSCOPIC BARIATRIC SURGERY- IS IT SOME THING SPECIAL IN ALL RESPECT ?

Obesity, derived from the Latin word "Obesus" which means "fattened by eating" has already become a health problem and has reached epidemic proportions in the western countries. The prevalence of obesity in the USA has reached to 19 percent in 1999, and now a days certainly it has been increased to a much higher level.

Obesity is a major health problem with clearly established health implications, including an increased risk of coronary artery disease, hypertension, hyperlipidaemia, diabetes mellitus, gall bladder disease, degenerative joint disease, obstructive sleep apnoea, socioeconomic and psychological impairment. Evidence shows that obesity is associated with increased morbidity and mortality.

"Bariatric", comes from the Greek word "weight treatment" is the only surgery which provides significant and sustained weight loss option for the morbidly obese patients.

For surgery these group of patients are regarded as very high risk patients. Are these patients also fall in high risk group for Anesthesia? These patients are obese and sometimes morbid obese. The Federal guidelines for obesity state three important parameters to assess over weight. (1) Body mass index (BMI), (2) Waist circumference and waist hip ratio, (3) Patients risk factors for diseases associated with Obesity. The world Health organization has endorsed the body mass index as a measure of obesity.

Over weight – BMI > 25-29.9 kg/m²

Obesity t BMI, > 30-34.9 kg/m²

Morbid obese- BMI > 35 kg/m²

The patients who have metabolic syndrome at least three or more of the following criteria must be present

1. Waist circumference > 102 cm for man and > 85 cm for woman
2. Serum triglyceride > 100 mg/dl
3. High density lipoprotein < 40 mg/dl for man and < 50 mg/dl for woman.

4. Systolic Blood pressure > 130 mmHg or diastolic Blood pressure > 85 mmHg
5. fasting blood sugar > 110 mg/dl. /

What procedure the surgeon does in Bariatric Surgery? The surgeon goes for Malabsorptive or restrictive procedures like vertical banded gastroplasty or gastric banding .

In addition to gross physiological changes in Cardio Vascular Respiratory, Renal and Hepatic, the main changes that occurs in this speciality is the effect of carboperitoneum or venous circulation. Morbid obesity is a major independent risk factor for sudden death from acute postoperative pulmonary embolism.

Increased intra abdominal pressure reverse trendelenburg position high fatty acid level, hypercoesteremia, diabetes accelerated fibrin formation and increased platelet function all promote venous stasis. Increased intra¹abdominal pressure (IAP) during laparoscopic gastric banding results in reduced peak femoral systolic velocity by 43% and increase in the femoral cross sectional area by 52% Nguyea reported that by combining Carboperitoneum to reverse trendelenburg position, peak systolic velocity is decreased to 57% of base line value.

The sequential compression device (SCD) has been only partially effective in augmenting the femoral peak systolic velocity and the ineffectiveness is attributed to the larger calves and thighs of these individuals.

Special pre-operative evaluation is made regarding CVS specially systemic or pulmonary hypertension, left or right heart failure and Ischemic heart disease. Sites for peripheral or central venous access and for arterial cannulation should be secured before operation.

Another major problem is obstructive sleep apnoea or bronchitic disease. So extreme caution is the rule when administering any pre or postoperative medication that may have a depressant effect on respiratory function. Main goal for several of the

patient should be a rapid return to a fully alert co-operative state in which the patient can protect the airway. Intensive Care support is a mandatory to maintain the airway either by invasive or non invasive (Bi pap/Cpap) ventilation after operation.

Morbid obese patients of Bariatric Surgery needs induction agents and which are extremely costly. For example propofol is the best and safest induction agents. Likewise desflurane or sevoflurane which are costly and needs special machine as well. Specially designed operation table are required having a maximum weight limit of approximately 205. Special table capable of holding upto 455 kg with extra width are available but needs huge cost.

In addition to standard monitoring, these group of patients need some special monitoring like Intra abdominal pressure monitoring (IAP), invasive arterial pressure monitoring, and arterial blood gases. In respiratory monitoring needs the information regarding compliance peak and plateau airway pressure, work of breathing etc. which helps for ventilatory setting. Another special monitor which is called bi spectral index monitor to ascertain

intra operative awareness is necessary for these patients.

Immediately after operation all most all patients of this group needs ICU support for atleast 24 hrs. So to establish this surgical speciality will need adjacent ICU support .

Though bariatric Surgery in morbidly obese patients is associated with higher morbidity and mortality, associated with highest technology needing extraordinary cost, associated with skilled and increased number of man power is still in progress for establishing the field. If special effort is provided, some private sector may come in front and invest huge cogt for developing this specialty. In near future this group of morbidly obese patients will get benefit from the surgery and will be able to maintain more better life.

Dr. Qumrul Huda

Assistant Professor of Anaesthesia Analgesia & Intensive Care Medicine, BSMMU, Shahbag, Dhaka-1000.

Original Article

A STUDY OF PRIMING TECHNIQUE OF ROCURONIUM IN FACILITATING INTUBATION

Md. Liaquatunnoor¹, Rubina Yasmin², UH Shahera Khatun³

SUMMARY:

Tracheal intubation is usually performed after induction of anaesthesia followed by relaxation of skeletal muscle with depolarizing or non-depolarizing Neuro Muscular Block Agent (NMBA). The ability to intubate the trachea rapidly and safely is still paramount in all clinical situations. Suxamethonium is still the drug of choice for this purpose. This short-acting depolarizing NMBA is probably the most popular drug used for making intubation quick, easy and atraumatic. But this drug has many side effects like post operative muscle pain, hyperkalemia, malignant hyperthermia, masseter rigidity etc. For these reasons, researchers have concentrated to develop an alternative drug to suxamethonium or an alternative method of using non-depolarizing NMBA (Neuromuscular Blocking Agent) for rapid sequence induction to intubation technique.

Rocuronium bromide, an aminosteroid non-depolarizing NMBA, the onset time of which is significantly shorter than equivalent doses of other non-depolarizing NMBA. Priming technique with rocuronium has been investigated by several authors in an attempt to reduce the onset time and also to optimize its efficacy and reduce the incidence of side-effects.

This study was performed to investigate the influence of priming technique on the intubating time and intubation conditions with standard intubating dose of rocuronium (0.6 mg/kg), which may be comparable with standard intubation dose of suxamethonium (1.5 mg/kg). Thus using priming technique Rocuronium with standard intubating dose (0.6 mg/kg) may be suitable alternative to suxamethonium for rapid sequence induction of anaesthesia.

So, we can avoid many life-threatening side-effects associated with suxamethonium like, hyperkalemia, masseter spasm, malignant hyperthermia and we can also avoid mega-dose of rocuronium (0.9-1.2

mg/kg) used for same purpose.

A total number of 90 adult subjects, aged 18-45 yr, ASA I-II, undergoing elective surgery were studied. The selected patients were equally divided into three groups, 30 patients in each group. Following induction with thiopentone (5mg/kg) and Fentanyl (2µg/kg), patients in group-I (n=30) received suxamethonium 1.5 mg/kg, group-II (n=30) received a priming dose of rocuronium 0.06 mg/kg followed 3 minutes later by an intubating dose of 0.54 mg/kg and group-III (n=30) received rocuronium 0.6 mg/kg in single bolus injection. Neuromuscular function was assessed at the wrist using acceleration transducer (TOF-watch). In priming group any unpleasant symptoms during priming like visual disturbance, feeling of dyspnoea, difficulty in controlling tongue were closely observed. Intubating conditions were assessed using the intubation criteria of Cooper et al. as excellent, good, fair or poor, based on jaw relaxation, position of the vocal cords and response of the diaphragm to intubation. The main outcome variables were intubating time and intubating conditions. Timing at intubation showed that all of the patients of suxamethonium group (group-I), 86.7% of the priming group (group-II) and nearly three quarter (73.3%) of the single dose rocuronium group (group-III) were feasible to be intubated within 60 second. The difference between the priming and the single dose rocuronium group was not statistically significant in terms of timing of intubation (p=0.329). While evaluating intubating conditions, no significant difference was also observed between priming group (group-II) and single dose rocuronium group (group-III) in jaw relaxation (p=0.698), vocal cords movement (p=0.646) and response to intubation (p=0.514). The suxamethonium group allowed much earlier intubation compared to other two groups (p=0.039) and in terms of intubating conditions, smooth intubation was significantly higher in suxamethonium group (Group-I) compared to other two groups (p=0.043).

1. MO, OSD, DGHS, Dhaka

2. Assistant Professor, Department of Anaesthesiology & ICU, Dhaka Medical College Hospital

3. Professor & Head, Department of Anaesthesiology & ICU, Dhaka Medical College Hospital

In terms of unpleasant effects of priming it was observed that 1.1% of the patients of priming group had visual disturbances, 3.3% dyspnoea, 1.1% difficulty in controlling tongue and 2.2% difficulty in swallowing during the priming interval and remaining 92.7% was free of any unwanted side-effects. Haemodynamic state at intubation and just after intubation demonstrateds that the haemodynamic variables like pulse rate, systolic blood pressure, diastolic blood pressure, oxygen saturation (SpO₂) all were within physiological range and almost homogeneously distributed among the three groups and no adverse outcome was noticed.

Using priming technique with standard intubating dose of rocuronium 0.6 mg/kg has no beneficial effects on reducing intubation time and providing better intubating conditions over single bolus injection of rocuronium 0.6 mg/kg .So Rocuronium 0.6 mg/kg in single bolus injection can replace suxamethonium for quick endotracheal intubation in surgical procedures of short and medium duration.

INTRODUCTION

Ability to intubate the trachea rapidly and safely is still very important in all clinical situations including emergency anaesthesia where there is possibility of regurgitation and aspiration of gastric contents. For making intubation quick, easy and atraumatic, suxamethonium is still the drug of choice. This short-acting depolarizing NMBA is probably the most popular drug used . But this drug has many side effects, some of which are minor and can be prevented (e.g. muscle pain can be prevented by pretreatment of small dose of non-depolarizing NMBA). However, it cannot be used safely in severely burned patient, patients with plasma cholinesterase deficiency, patients with myotonia or in patients susceptible to malignant hyperthermia. It is also relatively contraindicated in patients with severe liver disease, penetrating eye injuries or on patients with raised intracranial pressure.

Rocuronium bromide, an aminosteroid non-depolarizing NMBA is newly introduced in our country, the onset times of which is significantly shorter than equivalent doses of other non-depolarizing NMBA . In the majority of the patients, clinically acceptable intubating conditions are obtained within 60 to 90 seconds after a 0.6 mg/kg dose of rocuronium with a clinical duration of action

of 30 to 40 minutes under balanced anaesthesia¹. Based on onset of action, Magorian et al². suggested that 0.9 to 1.2 mg/kg rocuronium may be necessary as an alternative to suxamethonium, but this mega-dose correspondingly increases the clinical duration of action³. Clinical durations were shown to be 50 minutes following a 0.9 mg/kg dose and around 80 minutes following a 1.2 mg/kg dose of rocuronium^{1,2}. So in order to achieve the onset of action closer to the onset of suxamethonium, using mega-dose of rocuronium is not desirable for the short and medium duration of surgical procedures. For this reason, various alternative methods were studied with standard intubating dose of rocuronium (0.6 mg/kg) in a view to achieve comparable onset time and intubating conditions following suxamethonium like, timing⁴ or priming principle. Timing is potentially unpleasant and dangerous for the patient.

'The priming principle' has been described by Foldes⁵ consists of administering a small dose of non-depolarizing NMBA 3 to 6 minutes prior to induction allowing sufficient time for relaxant to reach the receptors and than administering a second larger dose to facilitate rapid intubation after induction. Priming technique with rocuronium has been investigated by several authors in an attempt to reduce the onset time and also to optimize it's efficacy and reduce the incidence of side-effects Griffithetal⁶ Jaochimet. al⁷ used a priming dose of 0.06 mg/kg and after priming interval of 3 minutes, intubating dose of 0.54 mg/kg were administered to compare onset times and intubating conditions with the patients receiving rocuronium 0.6 mg/kg in bolus dose.

In the present study, a priming dose of rocuronium 0.06 mg/kg and a priming interval of 3 minutes were chosen to compare the influence of priming technique on the onset times and intubating conditions with standard intubating dose (0.6 mg/kg) and outcome was also compared with a control group receiving suxamethonium (1.5 mg/kg). Previous studies of the priming principle of rocuronium have been investigated by using propofol as induction agent ⁶ or Naguib ⁷ some used additional TPS 2mg/kg immediately prior to tracheal intubation. All the intubations were done by principle investigator himself to avoid subjective variation. The first attempt was made at 30 second

after administration of intubating dose of relaxant (rocuronium or suxamethonium). Intubating conditions were assessed using the criteria described by Cooper et al.¹ as excellent, good, fair or poor based on jaw relaxation, position of vocal cords and response to intubation. Any unpleasant effects of priming like visual disturbance, feeling of dyspnoea etc. were closely observed. If the first attempt was designated to be sign of unacceptable intubation conditions, subsequent intubation attempt was made at every 30 second interval until intubation can be achieved with good to excellent intubation condition.

This study was performed to investigate the effects of priming rocuronium on the intubation time and intubation conditions, to find out whether tracheal intubation is possible within 60 sec. with standard intubating dose of rocuronium using priming technique. Also to avoid side-effects associated with the use of suxamethonium like, post operative muscle pain, hyperkalemia, malignant hyperthermia, masseter rigidity etc. and to observe whether priming technique is associated with any unpleasant symptoms like, visual disturbance, feeling of dyspnoea etc.

MATERIALS AND METHODS

This prospective, randomized study was carried out in the department of Anaesthesiology and ICU, Dhaka Medical College Hospital, during the period of July, 2006 to June, 2008.90 (Ninety) patients, aged between 18-45 years, ASA I & II, Mallampati class I & II admitted in Surgery, Gynae&Obs. and ENT departments of Dhaka Medical College Hospital, undergoing elective surgery, requiring general anaesthesia and endotracheal intubation were selected for the study. Patients who had anticipated difficult intubation or history of difficult intubation (Mallampati class III & IV), patients having medications affecting neuromuscular function, history of drug allergy or any hypersensitivity, patients with hepatic or renal impairment, morbidly obese patients were excluded from the study. After recruitment, patients were divided into three groups, 30 patients in each group. Group-I patients (n=30) received Thiopentone (5mg/kg) and Fentanyl (2?gm/kg), followed by intubating dose of Suxamethonium (1.5mg/kg). Group-II patients (n=30) received priming dose of Rocuronium (0.06mg/kg), 3 minutes later, anaesthesia was induced with Thiopentone (5mg/kg) and Fentanyl (2?gm/kg), followed by intubating dose of Rocuronium (.54mg/kg). Group-III patients (n=30) received Thiopentone (5mg/kg) and Fentanyl (2?gm/

kg), followed by intubating dose of Rocuronium 0.6mg/kg in single dose. Patients data were collected in prescribed forms containing patient's particulars, Pre-induction variables (Pulse, Blood pressure, SpO₂) 3 minutes after priming (Pulse, Blood pressure, SpO₂, Visual disturbance, Feeling of dyspnoea, Difficulty in controlling tongue, Difficulty in swallowing, TOF ratio) Post-induction variables (Pulse rate, Blood pressure, SpO₂, TOF ratio) Time interval between administration of NMBA (Suxamethonium or Rocuronium) and completion of intubation in seconds, Scoring of intubating conditions. After arrival of the patient in operation theatre intravenous access was secured with a wide-bore cannula, i.v infusion was started with Hartmann's solution at a rate of 2 ml/kg/hr. Acceleration transducer (TOF- Watch) was connected to the thumb and the electrodes were placed over the ulnar nerve on the medial side of the wrist, so that the distal electrode was setting where the proximal bending line crosses the radial side of flexor carpi ulnaris muscle. The proximal electrode was placed 2.5 cm above the distal one. The test hand was immobilized in a supinated position. All the patients were pre-oxygenated for 3 minutes.

After pre-oxygenation, anaesthesia was induced in every patient with Fentanyl (2 ?g/kg) and Thiopentone (5mg/kg) and TOF ratio was started to measure at every 10s interval.

In group-I (control group), the patients received suxamethonium (1.5 mg/kg). **In group-II**, patients received priming dose of rocuronium 0.06 mg/kg. After 3 minutes of priming interval, patients were enquired about any unpleasant symptom and then anaesthesia was induced with fentanyl and thiopentone in usual doses. After loss of consciousness, intubating dose of rocuronium 0.54 mg/kg was given. **In group-III**, after induction of anaesthesia, patients received standard intubating dose of rocuronium 0.6 mg/kg in single dose. All drugs were given into a rapidly running infusion of Hartmann's solution. Injection times were 10s for thiopentone and less than 5s for rocuronium, diluted to a volume of 5 ml. After induction of anaesthesia, mask ventilation was not done till tracheal intubation unless the oxygen saturation goes to <95%.

The head of the patient was placed in the 'sniffing position' before intubation procedure started. The first intubation attempt was made 30s after administration of intubating dose of relaxant

(suxamethonium or rocuronium) with an appropriate sized Macintosh blade by the principal investigator himself. Intubating conditions were assessed using the criteria of Cooper et al.1 as excellent, good, fair or poor based on jaw relaxation, position of the vocal cords and response of the diaphragm to intubation.

If first attempt was designated to be sign of unacceptable intubation conditions, subsequent intubation attempts were made at every 30s intervals until intubation was achieved with acceptable conditions. If endotracheal tube was not passed successfully within 90s after use of relaxant, this was recorded as a failed intubation. Intubation time was recorded as the number of seconds from the end of administration of intubating dose of relaxant to the insertion of the tube in the trachea, as measured by a stop-watch with the help of a trained assistant and TOF ratio, 3 minutes after priming and at the time of intubation were also recorded.

Statistical Analysis

Summary statistics (sample size, mean) were calculated for all quantitative variables of each group. TOF ratio and haemodynamic variables were compared between the groups using ANOVA test. Intubating conditions were compared among the

groups using chi-square test . P-value of less than 0.05 was considered statistically significant.

RESULTS

Table I shows the distribution of demographic characteristics among the three groups. The mean age of Group-I was higher (35.4 ± 8.0 years) than that of Group-II (30.4 ± 9.0 years) and Group-III (31.5 ± 10.5 years) although the difference did not reach the level of significance (p = 0.099). The weight of the subjects in three groups was almost homogenous. The groups were also homogeneous in terms of sex distribution (p = 0.241). (Table-I).

Haemodynamic state 3 minutes after priming:

Table II shows the haemodynamic state 3 minutes after priming in Group-II. The mean heart rate was 81 ± 9 /minute, mean systolic blood pressure 113.9 ± 10.7 mmHg, mean diastolic blood pressure 72.3 ± 6.9 mmHg, mean SpO₂ 100 ± 00 (%) and mean TOF ratio 87 ± 5.8 (%) (Table-II). All the haemodynamic variables were in stable condition 3 minutes after priming.

Side-effects 3 minutes after priming in Group II:

Figure 1 shows that 1.1% of the patients of Group-II had visual disturbance, 3.3% dyspnoea, 1.1% difficulty in controlling tongue and 2.2% difficulty in swallowing 3 minutes after priming (Figure-1).

Table I
Demographic characteristics among the three groups

	Groups			
	Group - I (n = 30)	Group - II (n = 30)	Group - III (n = 30)	
Age (yrs) [#]	35.4 + 8.0	30.4 + 9.0	31.5 + 10.5	0.099
Weight (kg) [#]	52.5 + 6.9	47.6 + 8.7	49.6 + 8.8	0.073
Sex [¶]	7/23	13/17	9/21	0.241

Data were analysed using ANOVA statistics and are presented as mean + SD; ¶ data pertaining to sex were analyzed with the help of χ^2 Test and are expressed as male-female ratio.

Table II
Haemodynamic state 3 minutes after priming in Group-II

Haemodynamic variables	Mean	SD
Heart rate (/minute)	81	09
Systolic BP (mmHg)	113.9	10.7
Diastolic BP (mmHg)	72.3	6.9
SpO ₂ (%)	100.0	00
TOF ratio (%)	87.0	5.8

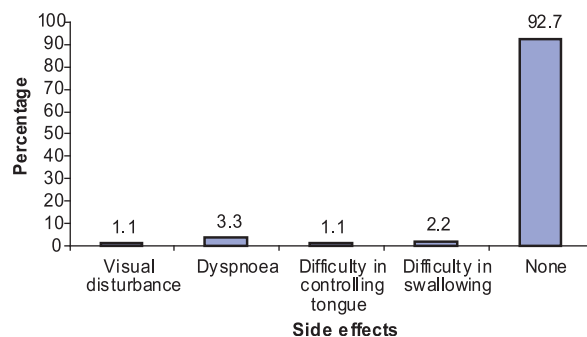


Fig.-1: Side-effects encountered by the patients 3 minutes after priming

Timing of intubation:

Timing at intubation shows that 30% of the patients of Group-I, 20% of Group-II and 10% of Group-III were successfully intubated at 30 sec following induction. The rest of Group-I (70%), 66.7% of Group-II and 60% of Group-III were effectively intubated at 60 sec. The entire suxamethonium group (Group-I), 86.7% of the priming rocuronium group (Group-II) and nearly three quarter (73.3%) of the single dose rocuronium group (Group-III) were feasible to be intubated within 60 seconds. The suxamethonium group allowed much earlier intubation compared to other two groups ($p = 0.039$). However, the difference between the priming and the single dose rocuronium group was not statistically significant in terms of timing of intubation ($p = 0.329$).

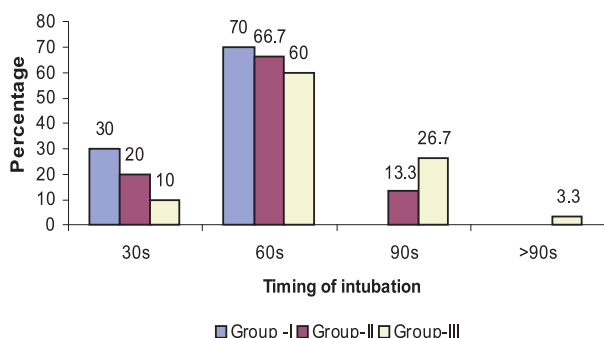


Fig-2: Comparison of timing of intubation among the groups

INTUBATING CONDITIONS:

Jaw relaxation:

Table III shows that 60% of the subjects of Group-I and Group-II and 53.4% of Group-III exhibited good relaxation of jaw relaxation at the time of intubation. The moderate relaxations were 40%, 40% and 43.3% in Group-I, Group-II and Group-III respectively. No significant difference was observed among the three groups in terms jaw relaxation ($p = 0.698$) (Table-III).

Table III

Comparison of jaw relaxation among the three groups

	Group			
	Group I (n = 30)	Group II (n = 30)	Group III (n = 30)	
Minimal	00	00	1(3.3)	
Moderate	12(40.0)	12(40.0)	13(43.3)	0.698 ^{NS}
Good	18(60.0)	18(60.0)	16(53.4)	

#Data were analysed using χ^2 Test.

*Figure in the parentheses denotes corresponding percentage

Table V illustrates the response to intubation among the three groups. Over 56% of Group-I, 33.3% of Group-II and 36.7% of Group-III did response at all to intubation, 43.3% of Group – I, 66.7% of Group – II and 56.7% of Group-III responded to intubation by slight diaphragmatic movement. Only 2(6.6%) cases of Group-III responded by mild coughing. The smooth intubation was significantly higher in Group-I compared to other two groups ($p = 0.043$), while Group-II and Group-III were almost identical in terms of smooth intubation ($p = 0.514$) (Table-V).

Vocal cords:

Two-third of Group-I and 60% of Group-II and 56.7% of Group-III showed completely open vocal cord ($p = 0.646$), a condition need for successful intubation (Table IV).

Table IV

Comparison of state of vocal cords at intubation among the groups

	Group			
	Group I (n = 30)	Group II (n = 30)	Group III (n = 30)	
Closing	00	00	1(3.3)	
Moving	10(33.3)	12(40.0)	12(40.0)	0.646 ^{NS}
Open	20(66.7)	18(60.0)	17(56.7)	

#Data were analysed using χ^2 Test.

*Figure in the parentheses denotes corresponding percentage

Response to intubation:

Table V

Response to intubation among the three groups

	Group			
	Group-I (n = 30)	Group-II (n = 30)	Group-III (n = 30)	
Mild coughing	00	00	2(6.6)	
Slight diaphragmatic movement	13(43.3)	20(66.7)	17(56.7)	0.043
None	17(56.7)	10(33.3)	11(36.7)	

#Data were analysed using χ^2 Test.

*Figure in the parentheses denotes corresponding percentage

COMPARISON OF INTUBATION SCORE:

Based on intubation score 63.3% of Group-I, 53.3% of Group-II and 43.3% of Group-III were categorized as having excellent outcome. The rest of the respective groups, except 1(3.3%) subject of Group-III had good outcome (Table-VI). The mean intubation score in three groups were not statistically different ($p = 0.286$).

Table VI

Comparison of intubation score among the three groups.

	Group			
	Group I (n = 30)	Group II (n = 30)	Group III (n = 30)	
0 – 2 (Poor)	00	00	00	
3 – 5 (Fair)	00	00	00	
6 – 7 (Good)	11(36.7)	14(46.7)	16(53.3)	
8 – 9 (Excellent)	19(63.3)	16(53.3)	13(43.3)	
Mean + SD	7.8 + 1.2	7.6 + 1.2	7.2 + 1.6	0.286 ^{NS}

#Data were analysed using χ^2 Test.

*Figure in the parentheses denotes corresponding percentage

TOF ratio at different stages of intubation in Group II & III:

Comparison of TOF ratio at different stages of intubation in Group II and III showed no significant differences ($p = 0.644$ and $p = 0.457$ respectively) (Table VII)

Table VII

Comparison of TOF ratio at different stages of intubation in Group II & III

	Group		
	Group II (n = 30)	Group III (n = 30)	
3 minutes after priming	87.0 + 5.8	Not done	
At intubation	57.4 + 8.4	54.5 + 7.8	0.644 ^{NS}
Just after intubation	39.7 + 13.8	36.4 + 14.6	0.457 ^{NS}

Data were analysed using unpaired t-Test and presented as mean + SD.

DISCUSSION

Various techniques are used to reduce intubation time of non-depolarizing NMBA like timing, administration of mega-dose or 'priming principle'. However, timing (administration of neuromuscular blocking drugs 20 sec. before induction agent) is potentially unpleasant and dangerous for the patient (e.g. due to intravenous line precipitate) resulting in a conscious but paralyzed patient. While application of mega-dose of rocuronium may be suitable for rapid-sequence induction and intubation, but at the cost of much longer duration of action², which is not desirable in the surgical procedures of short and medium duration.

'The priming principle' has been described by Foldes⁵ consists of administering a small dose of non-depolarizing NMBA 3 to 6 minutes prior to induction allowing sufficient time for relaxant to reach the receptors and then administering a second larger dose to facilitate rapid intubation after induction. A suitable Priming dose would allow the patient to maintain adequate respiration, protect his airway and be well tolerated. Priming technique with rocuronium has been investigated by several authors in an attempt to reduce the onset time and also to optimize its efficacy and reduce the incidence of side-effects.

Griffith et al.⁶ used a priming dose of 0.06 mg/kg and after priming interval of 3 minutes, intubating dose of 0.54 mg/kg were administered to compare onset times and intubating conditions with the patients receiving rocuronium 0.6 mg/kg in bolus dose. They found that the onset times with priming rocuronium (34±6sec) were significantly shorter ($p < 0.01$) than those without priming (59±14sec).

Yavascaoglu et al.⁹ studied 75 adult patients (17–67yr.) using different priming interval (two and three minutes) and priming doses (priming dose: rocuronium 0.06 or 0.1 mg/kg, intubating dose 0.54 or 0.5 mg/kg). They found that priming with three minutes interval shortened the onset time of rocuronium, while a two-minute interval did not significantly decrease the onset time.

Naguib⁸ reported significant acceleration of the onset times of rocuronium in the priming group using same priming dose and priming interval. However, he administered additional thiopental sodium 2 mg/kg immediately prior to tracheal intubation.

In the present study, timing at intubation showed that 30% of the patients of group-I, 20% and 10% of the patients of group-II and group-III respectively were successfully intubated at 30 second following induction. All of the patients of suxamethonium group (group-I), 86.7% of the priming group (group-II) and nearly three quarter (73.3%) of the single dose rocuronium group (group-III) were feasible to be intubated within 60 second. The suxamethonium group allowed much earlier intubation compared to other two groups ($p = 0.039$). However, the difference between the priming and the single dose rocuronium group was not statistically significant in terms of timing of intubation ($p = 0.329$). This result correlate poorly with the findings of Griffith et al.⁶, Yavascaoglu et al.⁹ and Naguib⁸ who all observed significant acceleration of onset time of rocuronium using same priming dose and priming interval.

The reason for these disparities was due to differences in anaesthetic technique. Intubating conditions depend not only on the degree of neuromuscular blockade but also on the depth of anaesthesia. Satisfactory intubating conditions had been reported without muscle relaxant following a propofol-alfentanil induction¹⁰. In addition, propofol was reported to produce significant depression of laryngeal reflexes¹¹. In the previous studies, Griffith et al.⁶ and Yavascaoglu et al.⁹ induced anaesthesia with midazolam, fentanyl and propofol and also used 60% N₂O in oxygen until tracheal intubation and additional doses of thiopentone⁸ or propofol⁹ were used as needed prior to tracheal intubation. On the other hand, in this study, we used thiopental sodium, the commonly used induction agent in our country and neither additional dose of TPS nor any inhalational agent except oxygen was used prior to tracheal intubation.

The other reason for the differences was due to the use of different modes of nerve stimulation. Rocuronium induced neuromuscular block develops faster at the adductor muscles of larynx than at the adductor pollicis muscle, so it appears that intubation may be performed before complete block is achieved as measured at the thumb¹². In a study conducted by¹³ observed that, at the time of intubation, the neuromuscular block achieved at the adductor pollicis muscle was incomplete in most patients. They expressed their opinion that, when conducting studies of intubating conditions, only

frequent-interval intubation attempts begun sufficiently early can development of optimum laryngeal conditions. This is particularly true for fast-acting muscle relaxants, such as rocuronium, where peripherally assessed onset of neuromuscular block can give no exact indication of moment when optimum laryngeal relaxation has first been achieved⁷. The use of repetitive intubation attempts to evaluate tracheal intubating conditions has been reported previously¹⁴. AP Dobson et al.¹⁵ used predetermined time interval of 30 sec. in their study to evaluate effective time to satisfactory intubating conditions using rocuronium 0.6 mg/kg to 120 adult patients anaesthetized with propofol or thiopentone. Sparr et al.¹⁶ also used predetermined time interval of 45 sec. to evaluate onset time and intubating conditions following rocuronium 0.6 mg/kg in adults patients anaesthetized with either propofol or thiopentone. The observation of Jaochim et al.⁷ correlated well with the present study in terms of TOF-ratio, which was around 0.57 and 0.54 at the time of successful intubation in group-II and group-III respectively.

In terms of intubating conditions, no significant difference was observed between priming group (group-II) and single dose rocuronium group (group-III) in jaw relaxation ($p=0.698$), vocal cords movement ($p=0.646$) and response to intubation ($p=0.514$). This result agrees with the findings of Griffith et al.⁶ who observed good to excellent intubating conditions in the majority of the patients in priming group compared with single dose rocuronium group, but this finding did not reach statistical significance.

In this study it was found that about three-quarter (73%) of the patients of group-III, were feasible to be intubated within 60 seconds following single bolus dose of rocuronium 0.6 mg/kg. This result agrees with the findings of Scheiber et al.¹³, who observed good to excellent intubating conditions after rocuronium 0.6 mg/kg can be obtained within 30-60 seconds in young children.

This study also showed that the suxamethonium group allowed much earlier intubation compared to other two groups ($p = 0.039$) and in terms of intubating conditions, smooth intubation was significantly higher in suxamethonium group (Group-I) compared to other two groups ($p = 0.043$). This finding correlated well with the study of Cheng

et al.¹⁷ who found superior intubating conditions with suxamethonium (1.5 mg/kg) in comparison with rocuronium (0.6 mg/kg) during modified rapid-sequence induction using alfentanil and thiopentone in children. In another study Tryba et al.⁴ found same intubation conditions following a single bolus dose of rocuronium (0.6 mg/kg) and suxamethonium (1.5 mg/kg) but they used thiopentone 6 mg/kg and rocuronium was administered immediately prior to thiopentone. Based on intubation score as described by Cooper et al. (1992), 63.3% of Group-I, 53.3% of Group-II and 43.3% of Group-III were categorized as having excellent outcome. The rest of the respective groups, except 1 (3.3%) subject of Group-III had good outcome. The mean intubation scores in three groups were not statistically different ($p = 0.286$) (Table VI).

In terms of unpleasant effects of priming we observed that 1.1% of the patients of priming group had visual disturbances, 3.3% dyspnoea, 1.1% difficulty in controlling tongue and 2.2% difficulty in swallowing during the priming interval and remaining 92.7% was free of any unwanted side-effects. TOF-ratio, 3 minutes after priming was around 0.87, this observation correlates well with the findings of Aziz et al.¹⁸ who reported TOF-ratio of around 0.89 in young rocuronium group in a study to investigate the effect of priming with vecuronium and rocuronium on young and elderly patients.

Haemodynamic state at intubation and just after intubation demonstrated that the haemodynamic variables like pulse rate, systolic blood pressure, diastolic blood pressure, oxygen saturation (SpO_2) all were within physiological range and almost homogeneously distributed among the three groups and no adverse outcome was noticed. All the haemodynamic variables were also stable at three minutes after priming in the patients of group-II (Table-II).

From the above description, it is clear that for fast-acting non-depolarizing NMBA, like rocuronium, using 'priming principle' has no significant beneficial effects on reducing the onset time and ensuring better intubating conditions. On the contrary priming technique is not completely devoid of harmful effects to the patients. From the result of this study, we also observed that suxamethonium group allowed much earlier intubation compared to other two groups and in terms of intubating

conditions, smooth intubation was significantly higher in suxamethonium group. We also found that more than 75% of the patients of the remaining two groups were feasible to be intubated within 60 seconds with good to excellent intubating conditions and the mean intubation scores among the three groups were not statistically different ($p = 0.286$). So, rocuronium 0.6 mg/kg in single bolus dose following induction with thiopental sodium can be suitable alternative to suxamethonium for rapid tracheal intubation for surgical procedures of short and medium duration.

CONCLUSION

Using priming technique with standard intubating dose of rocuronium 0.6 mg/kg has no beneficial effects on reducing intubation time and providing better intubating conditions over single bolus injection of rocuronium 0.6 mg/kg and this technique is not completely devoid of harmful effects to the patients. So Rocuronium 0.6 mg/kg in single bolus injection can replace suxamethonium for quick endotracheal intubation in surgical procedures of short and medium duration and thus protecting the patients from its side-effects.

REFERENCES

1. Cooper R, Mirakhur RK, Clarke RSJ, Boules Z. Comparison of intubating conditions after administration of Org 9426 (rocuronium) and suxamethonium. *Br J Anaesth* 1992;69:269-73.
2. Magorian T, Flannery KB, Miller RD: Comparison of rocuronium, succinylcholine and vecuronium for rapid-sequence induction of anaesthesia in adult patients. *Anaesthesiology* 1993; 79:913-8.
3. De Mey JC, Debrock M, Rolly G. Evaluation of the onset and intubation conditions of rocuronium bromide. *Eur J Anaesthesiol* 1994;11(Suppl 9):37-40.
4. Tryba M, Zorn A, Thole H, Zenz H. Rapid-sequence orotracheal intubation with rocuronium: a randomized double-blind comparison with suxamethonium –preliminary communication. *Eur. J. Anaesth.* 1994; 11(9): 44-48.
5. Foldes F. Rapid tracheal intubation with non-depolarizing neuromuscular blocking drugs:the priming principle(Letter). *Br J Anaesth* 1984; 56:663.

6. Griffith KE, Joshi GP, Whitman PF, Garg SA. Priming with rocuronium accelerates the onset of neuromuscular blockade. *J Clin Anaesth* 1997; 9:204-7.
7. Jaochim Schmidt MD, Andrea Iroushek, Tino Muenster MD, Thomas M. A priming technique accelerates onset of neuromuscular blockade at the laryngeal adductor muscles. *Can J Anesth.* 2005;52(1):50-54.
8. Naguib M. Different priming techniques including mivacurium accelerate the onset of rocuronium. *Can J Anaesth* 1994;41:902-7
9. Yavascaoglu B, Cebelli V, Kelebek N, Uckunkaya N, Kutlay O. Comparison of different priming techniques on the onset time and intubating conditions of rocuronium. *Eur J Anaesthesiol* 2002; 19:517-21.
10. Scheller MS, Zornow MH, Saidman LJ. Tracheal intubation without use of muscle relaxant: a technique using propofol and varying doses of alfentanil. *Anaesth Analg* 1992;75:788-93.
11. McKeating K, Bali IM, Dundee JW. The effects of thiopentone and propofol on upper airway integrity. *Anaesthesia* 1998;43:638-40.
12. Meistelman C, Plaud B, Donati F. Rocuronium (Org 9426) neuromuscular blockade at the adductor muscles of the larynx and adductor pollicis in humans. *Can J Anaesth* 1992;39:665-9.
13. Scheiber G, Ribeiro FC, Marichal A, Bredendiek M, Renzing K. Intubating conditions and onset of action after rocuronium, vecuronium, and atracurium in young children. *Anesth Analg.* 1996 Aug; 83(2):320-4.
14. Schiller DJ, Feldman SA. Comparison of intubating conditions with atracurium, vecuronium and pancuronium. *Anaesthesia* 1984;39:1188-91
15. A.P. Dobson, A. McCluskey, G. Meakin, R. D. Baker. Effective time to satisfactory intubation conditions after administration of rocuronium in adults, comparison of propofol and thiopentone for rapid sequence induction of anaesthesia. *Anaesthesia* 1999;54:172-97.
16. Sparr HJ, Luger TJ, Heidegger T, Putensen-Himmer G. Comparison of intubating conditions after rocuronium and suxamethonium following 'rapid-sequence induction' with thiopentone in elective cases. *Acta Anaesthesiol Scand* 1996;40:425-30.
17. Cheng CA, Aun CS, Gin T. Comparison of rocuronium and suxamethonium for rapid tracheal intubation in children. *Paediatric Anaesth.* 2002 Feb;12(2): 140-45.
18. Aziz L, Jahangir SM, Choudhury SN, Rahman K, Hirakawa M. The effect of priming with vecuronium and rocuronium on young and elderly patients. *Anesth Analg* 1997; 85:663-6.

Original Article

STUDY ON ROLE OF ORAL CLONIDINE IN LAPAROSCOPIC CHOLECYSTECTOMY SURGERY – A COMPARATIVE STUDY

Amirul Islam¹, Mozaffer Hossain², AKM Akhtaruzzaman³, UH Shahera khatun⁴

SUMMARY

Laparoscopic surgical techniques have been rapidly accepted by the surgeon worldwide e.g. especially laparoscopic cholecystectomy, with published reports describing the benefits of less postoperative pain, reduced hospital stay and an earlier return to work. The hall mark of laparoscopic surgery is the creation of pneumoperitoneum with pressurized CO₂. The high solubility of CO₂ increases systemic absorption by the vasculature of the peritoneum. This, combined with smaller tidal volumes because of poor lung compliance, leads to increased arterial CO₂ levels which is known as hypercarbia. If hypercarbia allowed to develop, will stimulate the sympathetic nervous system and thus increase heart rate, blood pressure, and the risk of dysrhythmias. These effects can prove especially challenging in patients with restrictive lung disease, impaired cardiac function, or intravascular volume depletion¹.

The present study was to evaluate the role of oral clonidine and atenolol in controlling tachycardia and hypertension associated with pneumoperitoneum with CO₂ during laparoscopic cholecystectomy under general anaesthesia and also to find out the best premedicant in controlling haemodynamic instability in laparoscopic cholecystectomy. 75 patients scheduled for laparoscopic cholecystectomy were randomly selected by blind envelope method. Patients were divided equally into three groups, which were Group-I: Oral clonidine(150µg), Group-II: oral atenolol(25mg) and Group-III: placebo (vitamin-c tablet), twenty five patients were in each group.

The mean difference of pulse rate at different times was significant ($p < 0.05$), however just before induction, just after skin incision and just after insufflations CO₂ were not significant ($p > 0.05$). The mean differences of systolic, diastolic BP at different times were not significant ($p > 0.05$), however BP was almost stable just before induction to the end of the operation in group I patients. The mean difference of SPO₂ at different times was not significant ($p > 0.05$) but just after intubations (99.6%±0.5% in group I, 99.3%±0.5% in group II and 98.7%±1.1% in group III) and just after skin incision (99.5%±0.6% in group I, 98.9%±0.6% in group II and 98.3%±0.9% in group III) was significant ($p < 0.05$). The mean difference of ET/CO₂ at different times was not significant ($p > 0.05$) however after 5 minutes insufflations (35.8±0.8 mmHg in group I, 36.5±0.5 mmHg in group II and 35.5±0.8 mmHg in group III) was significant ($p < 0.05$). The mean (±SD) halothane intake of group I patients was 0.49±0.06%, 0.56±0.10% in group II and 0.66±0.09% in group III. The mean (±SD) duration of first analgesic demand of the patients was 90.8±8.5 minutes in group I, 74.0±8.5 minutes in group II and 72.2±8.7 minutes in group III. The mean difference of halothane requirement & duration of first analgesic demand were significant ($p < 0.05$). The Aldrete recovery status of original criteria were almost similar in three groups ($p > 0.05$).

We can conclude that oral clonidine and atenolol to control heart rate & haemodynamic instability in laparoscopic cholecystectomy under general anaesthesia is better than placebo.

-
1. Assistant Register (Anaesthesiology), Department of Anaesthesia, NICVD, Dhaka
 2. Junior consultant, Department of Anaesthesiology and ICU, DMCH, Dhaka
 3. Associate Professor, Department of Anaesthesia, and ICU, BSMMU, Dhaka
 4. Professor and Head, Department of Anaesthesiology and ICU, DMCH, Dhaka

INTRODUCTION

Laparoscopic surgery, also called minimally invasive surgery (MIS), bandaid surgery, keyhole surgery, or pinhole surgery is a modern surgical technique in which operations in the abdomen are performed through small incisions (usually 0.5-1.5cm) as compared to larger incisions needed in traditional surgical procedures. Laparoscopic surgery includes operations within the abdominal or pelvic cavities, whereas keyhole surgery performed on the thoracic or chest cavity is called thoracoscopic surgery. Laparoscopic and thoracoscopic surgery belong to the broader field of endoscopy².

Laparoscopy (or peritoneoscopy) procedure allowing endoscopic access to the peritoneal cavity after insufflation of a gas (CO₂) to create space between the anterior abdominal wall & the viscera. The space is necessary for the safe manipulation of instruments and organ. Laparoscopic surgery can also be extraperitoneal. It can also be gasless with abdominal wall retraction, and, more recently it may be hand assisted³. The choice of anaesthetic technique for upper abdominal laparoscopic surgery is mostly limited to GA because of patients discomfort associated with creation of pneumoperitoneum and the extent of position changes associated with the procedure. Cuffed endotracheal tube placement will minimize the risk of acid aspiration if reflux occurs. Controlled ventilation is recommended because several factors may induce hypercarbia. In general, local or regional anaesthetic techniques have not been advocated for laparoscopic cholecystectomy or other upper abdominal laparoscopic procedures⁴.

Today, as equipment and techniques improved and a greater number as well as more involved types of surgery are performed using laparoscopy. As a result of the frequency and complexity of much of this surgery, it is imperative that the anaesthesiologist has a clear understanding of the procedure, the physiologic changes and the potential complications. Clonidine is an imidazole compound and a selective α_2 adrenoceptor agonist. It is currently the only drug in this group available for use in anaesthetic practice. Clonidine is lipid soluble and is absorbed rapidly and almost completely after oral administration with peak plasma concentrations occurring 60-90 minutes.

The cardiovascular effects of clonidine probably involve both α_2 - adrenoceptors & imidazole receptors, administration leads to a decreased HR and arterial pressure. Clonidine decreases the requirements for both IV and volatile anaesthetics. Clonidine produces sedation and anxiolysis.

Atenolol is a β -adrenoceptor blocking agent with a cardioselective action i.e. β_1 selective, on CVS- It produces negative inotropic effect i.e. decrease force of contraction and negative chronotropic effect i.e. decrease heart rate, as a result decrease blood pressure. It also decreases myocardial O₂ consumption. It has no sympathomimetic action and no membrane stabilizing effect on cardiac muscle. patients were selected for laparoscopic cholecystectomy, age 30 to 60 years and weight 50-60 kg of either sex. Patients who had bronchial asthma, COPD, diabetes mellitus, hypertension, IHD and who had H/O hypersensitivity reaction to study drugs were excluded from the study. After taking informed written consent, patients were randomly divided into three groups, twenty five patients were in each group. A total number of 75 cards, 25 in each group was prepared in a white envelop by another person who is not involved in the study. Each patient selected for study was allowed to draw one card and grouped accordingly. Group-I: received oral clonidine 150µgm, Group-II: received oral atenolol 25mg, Group-III: received placebo i.e. oral vitamin-c tablet 1hr before induction of anaesthesia.

On arrival of the patients in the operation theatre an IV line was inserted and heart rate, blood pressure and respiratory rate were recorded. Before induction of anaesthesia 10ml/kg body weight of Lactate Ringer's solution was infused. Oxygen saturation was observed by pulse oxymeter. One hour before induction group-I got oral clonidine 150µgm, group-II got oral atenolol 25mg and group-III got placebo i.e. oral vitamin-c tablet. Patient pre-oxygenated with 100% O₂ for 5 minutes, receiving Inj. Fentanyl (1.5µg/kg body weight) then given IV induction agent Inj. thiopental sodium (3-5mg/kg/body weight). Endotracheal intubation was facilitated by Inj. Succinylcholine (1-1.5 mg/kg/body weight). Anaesthesia was maintained by Halothane 0.5% and Nitrous oxide 66% in oxygen. Controlled mechanical ventilation was maintained for all study patients. Muscle relaxation was achieved by Inj. Vecuronium (0.1mg/kg body weight). Intra operative proper hydration was maintained with Lactate

Ringer's solution. Time of surgery was within 1 hour. Tracheal extubation was performed with reversal of neuromuscular blocking by Inj. Neostigmine (0.04mg/kg body weight) and Inj. Atropine (0.02mg/kg body weight).

STATISTICAL ANALYSIS:

The data were compiled and analyzed by using statistical software SPSS (ver. 12.0) significance test performed by ANOVA. Only p value <0.05 was considered statistically significant.

MATERIALS AND METHODS

This randomized prospective placebo control study, was carried out in the Department of Anaesthesiology & ICU, Dhaka Medical College Hospital, during the period of January, 2006-December, 2007. ASA class I and class II adult

RESULTS

No significant mean age, weight, BP, heart rate and Hb% differences were found among three groups. Female patients were predominant in the study groups and no significant differences were found among the three groups.

MEAN PULSE AND BP

The mean difference of pulse rate at different times were statistically significant (p<0.05) except just before induction, just after skin incision and Just after insufflations of CO₂ (p>0.05) (Table II).

The mean difference of systolic and diastolic blood pressure at different times were not statistically significant (p>0.05) (Table III). The mean difference of average mean BP at different times were not significant (p>0.05) (Table IV).

Table I
Demographic and baseline characteristics of the study subjects

Variables	Group I (n=25)		Group II (n=25)		Group III (n=25)		p value
Age (years)	38.0	±10.6	38.4	±15.3	40.5	±16.3	0.125
Weight (kg)	55.3	±3.1	56.7	±4.3	55.1	±2.9	0.970
Male/Female	7	/18	5	/20	6	/19	0.803
Systolic BP (mmHg)	110.9	±10.4	116.9	±7.5	119	±9.9	0.410
Diastolic BP (mmHg)	70.5	±8.5	75.6	±6.2	75.5	±12.1	0.285
Heart rate (/min)	80.5	±8.3	81.1	±7.2	79.0	±13.1	0.658
Hb%	56.1	±36.6	52.6	±34.4	54.6	±36.8	0.445

Values are expressed as mean±SD, Age and weight analysis done by ANOVA test and sex analysis done by Chi square test Value are regarded significant if p<0.05.

Group I: Oral clonidine 150 µgm

Group II: Oral atenolol 25 mg

Group III: Placebo

ns=not significant, n=number of subjects

Table II
Mean pulse at different times in group three groups

Pulse	Group I (n=25)		Group II (n=25)		Group III (n=25)		p value
Just before induction	91.3	±15.9	83.4	±12.8	90.5	±13.2	0.258
Just after intubations	91.8	±14.9	75.8	±9.4	92.6	±11.4	0.019
Just after skin incision	80.5	±09.3	71.1	±6.7	78.5	±11.1	0.056
Just after insufflations of CO ₂	81.0	±08.5	71.9	±8.2	80.2	±9.8	0.142
5 min. after insufflations of CO ₂	81.2	±11.4	64.4	±7.0	77.6	±13.4	0.003
10 min. after insufflations of CO ₂	82.0	±10.4	62.6	±5.1	73.9	±11.2	0.047
15 min. after insufflations of CO ₂	81.6	±10.0	60.8	±7.9	75.2	±8.5	0.022
20 min. after insufflations of CO ₂	81.0	±09.0	63.3	±3.9	75.6	±9.7	0.013

Table III
Mean systolic and diastolic blood pressure at different times in three groups

Systolic BP (mmHg)	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Just before induction	121.3 ±18.1	125.5 ±18.9	135.0 ±18.4	0.568
Just after intubations	123.8 ±28.0	126.4 ±9.2	133.5 ±22.1	0.595
Just after skin incision	120.0 ±20.0	117.3 ±18.5	131.0 ±19.1	0.516
Just after insufflations of CO ₂	121.3 ±17.2	128.2 ±12.5	135.0 ±19.1	0.819
5 min. after insufflations of CO ₂	121.3 ±14.7	131.8 ±11.3	129.0 ±17.3	0.344
10 min. after insufflations of CO ₂	122.1 ±12.3	131.4 ±18.7	132.0 ±25.3	0.915
15 min. after insufflations of CO ₂	125.0 ±11.2	124.5 ±23.8	127.2 ±14.8	0.972
20 min. after insufflations of CO ₂	127.5 ±18.4	117.8 ±12.6	126.9 ±17.1	0.464
Diastolic BP (mmHg)				
Just before induction	78.8 ±11.9	79.5 ±12.7	82.0 ±14.0	0.954
Just after intubations	81.3 ±18.0	83.6 ±08.3	94.0 ±13.5	0.438
Just after skin incision	85.6 ±22.4	70.0 ±10.5	86.0 ±22.2	0.84
Just after insufflations of CO ₂	87.5 ±08.5	90.5 ±08.9	97.5 ±09.8	0.292
5 min. after insufflations of CO ₂	85.6 ±11.4	89.1 ±06.2	93.0 ±11.6	0.338
10 min. after insufflations of CO ₂	82.9 ±10.1	90.5 ±12.5	91.0 ±08.4	0.608
15 min. after insufflations of CO ₂	85.0 ±07.6	85.5 ±17.3	88.9 ±07.0	0.692
20 min. after insufflations of CO ₂	87.5 ±05.2	83.8 ±09.6	87.5 ±08.0	0.397

Table IV
Mean blood pressure at different times in three groups

Mean BP (mmHg)	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Just before induction	92.9 ±13.7	94.8 ±14.3	99.8 ±13.6	0.794
Just after intubations	95.5 ±20.8	98.7 ±09.4	109.5 ±15.1	0.529
Just after skin incision	96.1 ±13.8	91.1 ±12.6	105.1 ±11.6	0.144
Just after insufflations of CO ₂	99.1 ±12.6	101.5 ±09.2	110.1 ±12.5	0.462
5 min. after insufflations of CO ₂	98.8 ±12.8	102.6 ±06.8	105.3 ±13.5	0.568
10 min. after insufflations of CO ₂	96.4 ±10.1	104.0 ±14.4	100.5 ±08.2	0.572
15 min. after insufflations of CO ₂	98.3 ±08.3	97.7 ±19.3	100.4 ±07.6	0.868
20 min. after insufflations of CO ₂	101.8 ±07.9	97.3 ±10.2	99.8 ±09.0	0.721

Table V
Mean SPO₂(%) at different times in three groups

SPO ₂ (%)	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Just before induction	99.2 ±0.6	98.4 ±0.7	98.2 ±1.3	0.061
Just after intubations	99.6 ±0.5	99.3 ±0.5	98.7 ±1.1	0.810
Just after skin incision	99.5 ±0.5	98.9 ±0.6	98.3 ±0.9	0.150
Just after insufflations of CO ₂	99.1 ±0.7	98.9 ±0.6	98.1 ±1.4	0.276
5 min. after insufflations of CO ₂	99.2 ±0.8	98.9 ±0.6	98.1 ±1.4	0.199
10 min. after insufflations of CO ₂	99.2 ±0.8	98.9 ±0.7	98.0 ±1.6	0.226
15 min. after insufflations of CO ₂	98.9 ±0.7	98.3 ±1.7	98.2 ±1.4	0.143
20 min. after insufflations of CO ₂	98.8 ±1.0	98.8 ±1.0	98.1 ±1.8	0.373

SPO₂ (%) AND ETCO₂

The mean difference of SPO₂ at different times were not statistically significant (p>0.05) except just after intubations and just after skin incision were statistically significant (p<0.05) (Table V).

The mean difference of ETCO₂ at different times were not statistically significant (p>0.05) except after 5 minutes insufflations was significant (p<0.05) (Table VI).

Table VI
Mean ETCO₂ at different times in three groups

	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Just before induction	35.3 ±0.8	35.4 ±0.9	34.8 ±1.0	0.647
Just after intubations	36.0 ±0.9	35.9 ±0.6	35.5 ±1.0	0.606
Just after skin incision	35.5 ±1.1	35.6 ±0.7	35.2 ±0.8	0.918
Just after insufflations of CO ₂	36.3 ±0.8	36.4 ±0.7	36.1 ±0.7	0.927
5 min. after insufflations of CO ₂	35.8 ±0.8	36.5 ±0.5	35.5 ±0.8	0.90
10 min. after insufflations of CO ₂	35.5 ±0.9	36.1 ±0.4	35.4 ±1.5	0.933
15 min. after insufflations of CO ₂	35.7 ±0.8	36.3 ±0.5	35.1 ±0.8	0.431
20 min. after insufflations of CO ₂	35.6 ±0.7	36.3 ±0.5	35.3 ±0.7	0.647

Table VII
Halothane and analgesic requirement of the patients

	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Halothane (%)	0.49 ±0.06	0.56 ±0.10	0.66 ±0.09	0.001 ^s
First demand of analgesic (min)	90.8 ±8.5	74.0 ±8.5	72.2 ±8.7	0.001 ^s

Table VIII
Post operative anaesthetic aldrete recovery score of the patients

Recovery status	Group I (n=25)	Group II (n=25)	Group III (n=25)	p value
Original criteria				
Color	1.8 ±0.1	1.3 ±0.6	1.2 ±0.2	0.462 ^{ns}
Respiratory	1.6 ±0.5	1.8 ±0.7	1.7 ±0.1	0.449 ^{ns}
Circulation	1.6 ±0.5	1.9 ±0.7	1.5 ±0.2	0.137 ^{ns}
Consciousness	1.2 ±0.5	1.5 ±0.5	1.4 ±0.5	0.327 ^{ns}
Activity	1.5 ±0.3	1.2 ±0.4	1.2 ±0.5	0.324 ^{ns}

Halothane and analgesic requirement

The mean difference of halothane requirement and duration of first analgesic demand were significant (p<0.05).

Post operative anaesthetic Aldrete recovery score

The Aldrete recovery status of original criteria was were almost similar in three groups (p>0.05).

DISCUSSION

This prospective placebo control study was carried out with an aim to evaluate the oral clonidine and atenolol in controlling tachycardia & hypertension associated in pneumoperitoneum with CO₂ during laparoscopic cholecystectomy under general anaesthesia and also to find the best premedicant in controlling haemodynamic instability in laparoscopic cholecystectomy.

Regarding sex incidence of laparoscopic cholecystectomy surgery in the present study it was higher in female. In this study mean age of patients in three groups were within 40 years ranging from 25 to 60 years and no significant difference was found among the three groups. Baseline characteristics, systolic BP, diastolic BP, heart rate, Hb% and platelet count were almost consistent among the three groups ($p > 0.05$).

The mean pulse rate was comparatively higher in group I than group II and group III since just before induction to 20 minutes after insufflations except just after intubations where group III was higher. However in group I was almost stable but group II significantly ($p < 0.05$) declined just after intubations, where the mean (\pm SD) pulse rate was 92.6 ± 11.4 /min in group III, 91.8 ± 14.9 /min group I and 75.8 ± 9.4 /min in group II. Just after skin incision pulse rate consequently decreased in all the three groups, where the mean pulse rate more decreased in group III followed by group I and group II. Just after skin incision the mean (\pm SD) pulse rate was 80.5 ± 9.3 /min in group I, 71.1 ± 6.7 /min in group II and 78.5 ± 11.1 /min in group III. However pulse rate became static just after skin incision to the end of the surgery, where the pulse rate was 80 - 82 /min in group I, whereas in group III the pulse rate varied from 74 to 80/min, but more variation was observed in group II, where the pulse rate varied from 60 to 71/min. The pulse rate difference were significant ($p < 0.05$) from just after skin incision to the end of the surgery. Yu et al. (2003)⁵ done a study to investigate the clinical efficiency of oral clonidine premedication in anaesthesia and analgesia. Anaesthesia and analgesia in patients undergoing laparoscopic cholecystectomy on 32 patients, out of which 16 patients received oral clonidine 150 μ g and rest 16 placebo control received oral antacid (alugel hydroxide 300 mg) before anaesthesia and they found oral clonidine preserved the heart rate control, which is consistent with the present study. Cevheroglu,

Ozcan and Bilgin (1999)⁶ observed that heart rate decrease in preoperative period, 2, 4 and 6 minutes after intubation and in postoperative period in the clonidine group, where 150 μ gm received oral clonidine in group I, 10mg oral diazepam in group II and oral placebo in group III were used for premedication. The results of the above authors are similar with the present study. Naris et al. (2004)⁷ followed a standard anesthetic protocol and observed a significant difference in overall mean heart rate between the placebo and beta-blocker groups. Zaugg et al. (2003)⁸ evaluated the effects of preoperative atenolol administration. The performance of routine anesthetic depth indicators were analyzed in 45 patients undergoing abdominal surgery: group I (n=12), isoflurane/fentanyl/ nitrous oxide in oxygen anesthesia; group II (n=16) isoflurane/fentanyl/ nitrous oxide in oxygen with 10mg atenolol intravenously prior to anesthesia; group III (n=17) isoflurane/fentanyl/ nitrous oxide in oxygen with a maximum end-tidal isoflurane concentration of 0.4 vol.% and incremental doses of atenolol (5mg intravenously stepwise) enously prior to anesthesia. In all groups, BP was maintained within $\pm 20.0\%$ of preoperatively defined baseline BP and heart rate between 50 to 80 beats/minute. The performance of haemodynamic variables was moderate even at critical intraoperative events but unaffected by atenolol, which are comparable with the present study.

The mean systolic blood pressure was comparatively higher in group III followed by group I and group II just before induction. But just after intubations the mean systolic blood pressure increased in all the three groups and also declined in all the three groups just after skin incision and the decline was higher in group III followed by group II and group I. Just after skin incision the mean (\pm SD) systolic BP was 120.0 ± 18.5 mmHg in group I, 117.3 ± 20.0 mmHg in group II and 131.0 ± 19.1 mmHg in group III. The mean systolic blood pressure became almost stable just after skin incision to the end of the surgery and the systolic blood pressure was 120 – 128 mmHg in group I, whereas in group III the systolic blood pressure varied from 127 to 135 mmHg, but more variation was observed in group II, where the systolic blood pressure varied from 118 to 132 mmHg. There was no significant (> 0.05) difference in systolic blood pressure just before induction to the end of the operation in the present study, whereas systolic blood

pressure was found moderately higher in group III than other two groups. Cevheroglu, Ozcan and Bilgin (1999)⁶ observed in their study that systolic blood pressure significantly decreases in the preoperative, after induction, during the operation and in postoperative period. Similarly, Yotsui (2001)⁹ has observed that systolic blood pressure was lower in the clonidine group than in the placebo control group immediately after endotracheal intubation and extubation, where the control and clonidine groups received placebo on clonidine 4 microg/kg orally 2 hours before the induction of anesthesia, which are almost similar with the present study.

In the present study diastolic blood pressure was almost similar just before induction. But just after intubations the mean diastolic blood pressure increased in all the three groups and also declined in group I and group II, however in group I increased. Just after skin incision the decline of diastolic blood pressure was higher in group II and than group III. The mean(\pm SD) diastolic blood pressure was 85.6 \pm 10.5mmHg in group I, 70.0 \pm 22.4 mmHg in group II and 86.0 \pm 22.2 mmHg in group III just after skin incision. The mean diastolic blood pressure became invariable just after skin incision to the end of the surgery and the diastolic blood pressure was 83 – 88 mmHg in group I, whereas in group III the diastolic blood pressure varied from 86 to 97 mmHg, but more variation was observed in group II, where the diastolic blood pressure varied from 70 to 91 mmHg. There was no significant ($p>0.05$) change in diastolic blood pressure just before induction to the end of the operation in the present study. The diastolic blood pressure was also found reasonably higher in group III than other two groups. Same authors Cevheroglu, Ozcan and Bilgin (1999)⁶ also observed that diastolic blood pressure decreased after intubation and 2, 4 and 6 minutes after intubation. Yotsui (2001)⁹ also observed that the diastolic blood pressure was in the clonidine group than in the placebo control group, which is also comparable with the present study. Zaugg et al. (2003)⁸ found blood pressure maintained $\pm 20.0\%$ preoperatively defined baseline blood pressure in their comparative study, which is similar to the present study.

Regarding the mean blood pressure of the current study it was found comparatively higher in group III followed by group I and group II just before induction. But just intubations the mean blood

pressure increased in all the three groups and also declined in group II and group III just after skin incision and the decline was higher in group II and group, however in group I slightly increased. Just after skin incision the mean(\pm SD) mean blood pressure was 96.1 \pm 13.8 mmHg in group I, 91.1 \pm 12.6 mmHg in group II and 105.1 \pm 11.6 mmHg in group III. The mean blood pressure became almost stable just after skin incision to 10 minutes after insufflations but during the end of the surgery there was a little increase and the average blood pressure was 96 – 102 mmHg in group I, whereas in group III the mean blood pressure varied from 100 to 110 mmHg, but more variation was observed in group II, where the systolic blood pressure varied from 91 to 104 mmHg. There was no significant ($p>0.05$) change in mean blood pressure just before induction to the end of the operation, whereas mean blood pressure was found higher in group III than others two groups. In another study Sung et al. (2000)¹⁰ investigated the clinical efficiency of oral clonidine premedication in anesthesia and analgesia in patients undergoing laproscopic cholecystectomy. One hundred and ten patients randomly allotted to the placebo group ($n=65$) were premedicated with oral antacid (alugel hydroxide 300 mg) and clonidine group ($n=45$) were premedicated with oral clonidine 150 micrograms prior to anesthesia and found in clonidine received patients displayed greater haemodynamic stability preoperatively and the isoflurane requirement also reduced (30.0% less) in comparison with the placebo group. As regard to the haemodynamic parameters, results obtained in the present study were comparable with the findings of the mentioned above authors. The value of mean heart rate and mean arterial pressure in the present study strengthened by similar observation made by Howie et al. (1996)¹¹.

Howie et al. (1996)¹¹ had done a double blind, placebo controlled study on 54 patients under-going elective coronary artery bypass graft (CABG) surgery. Patients received approximately 5 micrograms/kg of oral clonidine or a placebo together with 40 micrograms/kg lorazepam 90 minutes prior to titrated sufentanil induction of anesthesia. Thirty minutes prior to cardiopulmonary bypass, a second dose of either approximately 5 micrograms/kg of oral clonidine or placebo was given as a slurry via a nasogastric tube and observed heart rate and mean arterial pressure

within 15% of baseline without significant difference in other vasoactive drugs. Pawlik et al. (2005)¹² conducted a prospective study in 30 adult patients with obstructive sleep apnea, under-going elective ear-nose throat surgery. The patients were randomly assigned to receive placebo or clonidine (2 µg/kg oral) the night before & the next morning 2 hours before surgery & the investigators observed consistent heart rate and blood pressure in oral clonidine. Yamakage et al. (2004)¹³ investigated the effect of oral premedication with atenolol on volatile anesthetic induction with sevoflurane by monitoring the cardiac output (CO) and bispectral (BIS) index. Twenty four patients undergoing general anesthesia with endotracheal intubation were randomly divided into two groups: a control group (n=12) & a β blocker group (n=12). Each patient in the β blocker group was premedicated with oral atenolol 25mg 1 hour before the induction of anesthesia. Anesthesia was induced by repeated vital capacity technique with 5% sevoflurane and 66% nitrous oxide as well as the authors observed the haemodynamic changes caused by endotracheal intubations were inhibited in the β blocker group but not in the control group, on effect of oral atenolol on volatile anesthetic induction with sevoflurane in adults.

The mean SPO₂ was comparatively higher in group I followed by group II and group III just before induction. But just after intubations the mean SPO₂ increased in all the three groups and also declined in all the three groups just after skin incision and the decline was higher in group III and group II and lesser in group I. Just after skin incision the mean(\pm SD) SPO₂ was 99.5 \pm 0.6% in group I, 98.9 \pm 0.6% in group II and 98.3 \pm 0.9 % in group III. The mean SPO₂ of group I was comparatively higher from just before induction to the end of the operation and became stable just after insufflations to the end of the surgery. On the other hand the mean SPO₂ of group III was comparatively lesser from just before induction to the end of the operation and group II became stable just after skin incision to 10 minutes after insufflations and became unstable after 10 minutes after insufflations. The mean SPO₂ at different times were significant (p>0.05), however just after intubations and just after skin incision the mean SPO₂ was significant (p<0.05). The mean difference of ETCO₂ was 36.5 + 0.5 in group II and 35.5 \pm 0.8 mmHg in group III. The mean (\pm SD)

halothane intake of group I patients was significantly (p<0.05) higher in group III and lesser in group II where the mean (\pm SD) halothane intake of group I patients was 0.56 \pm 0.10 %, 0.49 \pm 0.06 % in group II and 0.66 \pm 0.09 years in group III. Regarding the mean (\pm SD) duration of first analgesic demand of group I patients significantly (p<0.05) delayed, which was 90.8 \pm 8.5 minutes, however in group II and group III were 74.0 \pm 8.5 minutes and 72.2 \pm 8.7 minutes respectively after the end of the operation. The aldrete recovery status of original criteria was almost similar in the three groups and no statistical significant (p>0.05) difference was found among the groups.

CONCLUSION

Under the condition of the present study, we can conclude that oral clonidine and atenolol to control heart rate and haemodynamic instability in laparoscopic cholecystectomy under general anaesthesia is better than placebo. On the other hand, when compared oral clonidine with atenolol as premedicant in laparoscopic cholecystectomy surgery, clonidine is superior in controlling heart rate.

REFERENCES

1. Edward Morgan G., Maged S. Mikhali Michael J. Murray: Case discussion: Laparoscopic Surgery, Clinical anaesthesiology 2002, third ed; 23:522-523.
2. Wikipedia, the free encyclopedia, 2006. Atenolol. (Hitting the headline article) [Online] (Update 17 Nov 2007) Available at:<http://www.chm.bris.ac.uk/motm/motm.htm> [accessed 28 Nov 2007].
3. Funsun F. Yao: 2003. Laparoscopic surgery: Yao and Artusio's: Anesthesiology: Problem oriented patients management. 5th edition 41; 858-88.
4. Wylie and Churchill Davidson's: Intra-abdominal laparoscopic surgery: Anaesthetic Implications: A practice of anaesthesia 2003, Seventh ed; 54: 893-901.
5. Yu HP, Hues SS, Yuen HW, Tang YH, Chan KH, Oral clonidine premedication preserves heart rate variability for patients under going laparoscopic cholecystectomy. Acta Anesthesiology Scand. 2003 Feb; 47(2): 185-90.

6. Cevheroglu D, Ozcan B and Bilgin Hutya. Comparison of the effects of clonidine and diazepam using during preoperative period on period on sedation, anxiety, amnesia and haemodynamics. Uludag Universities Tip Fakultesi Anesthesiology ve Reimasyon Anabilim Dali *VII. ESA Kongresinde poster olarak sunulmustur.29.Mayis- 1 Haziran 1999 Amsterdam.
7. Naris, Collins M, Hung P, Ree G, Close D, Wormald PJ. The effect of beta blocker premedication on the surgical field during endoscopic sinus surgery. *Laryngoscope*. 2004 Jun; 114(6):1042-6.
8. Zaugg M, Tagliente T, Silverstein JH, Lucchinetti E. Atenolol may not modify anesthetic depth indicators in elderly patients-a second look at the data. *Can J Anaesth*. 2003 Aug-Sep; 50 (7):627-30.
9. Yotsui T. Clonidine premedication prevents sympathetic hyperactivity but does not prevent hypothalamo-pituitary-adrenocortical responses in patients undergoing laparoscopic cholecystectomy. 2001;15(2):78-82.
10. Suug CS, Lin SH, Chan KH, Chang WK, Chow LH, Lee Ty Effect of oral clonidine premedication on perioperative haemo-dynamic response and post operative analgesic requirement for patients under-going laparoscopic cholecystectomy. *Acta Anesthesiology Sin*. 2000 Mar, 38(1): 23-9.
11. Howie MB, Campagni MA, White PF, McSweeney TD. Comparative effects of oral clonidine and Intravenous esmolol in attenuating the haemodynamic response to epinephrine injection. *J Clin Anesth*. 1999 May; 11(3): 208-15.
12. Pawlik MT, Hansen E, Waldhauser, Selig C and Kuehnel TS. Clonidine premedication in patients with sleep apnea syndrome: A randomized, double-blind, placebo-control study. *Anesth and Analgesia* 2005;101:1374-1380.
13. Yamakage M, Sasaki H, Mizuuchi M, Iwasaki S, Namiki A. Effects of oral atenolol on volatile anesthetic induction with sevoflurane in adults. *J Anesth*. 2004;18(3):185-9.

Original Article

EFFECT OF LOW CONCENTRATION ISOFLURANE WITH THIOPENTAL SODIUM FOR CRANIOTOMIES OF INTRACRANIAL SPACE OCCUPYING LESION

Md. Rafayet Ullah Siddique¹, Md. Mustafa Kamal¹, Nezamuddin Ahmed², Lutful Aziz³, KM Iqbal⁴

ABSTRACT

The primary objective of anaesthesia is to facilitate surgery at minimal risk to the patient and to ensure safe optimal recovery following the procedure. The minimal risk to the neurosurgical patient can be achieved with meticulous attention to the detail of intraoperative systemic and brain homeostasis. Safe early recovery from craniotomy necessitates an anaesthetic technique pharmacology adequate to permit early awakening. The present study was designed to observe the effect of different anaesthetic technique that permits early recovery and hemodynamic stability. A total number of thirty patients both male and female age range 18 to 60 yrs having ASA grade-I & II and were randomly selected. They were equally divided into two groups. Group A received TPS infusion and group B received isoflurane inhalation with low dose of TPS infusion. Other drugs remained same for both group. Group A Received induction dose of TPS 4 – 5 mg/kg, maintained by TPS (4 – 5 mg/kg/h infusion), fentanyl (3 mgm/kg bolus, 1 - 2 mgm/kg/h infusion), oxygen/N₂O mixture FiO₂ being 0.3. Group B- Received induction dose of TPS 4 – 5 mg/kg and maintained by isoflurane 0.5%, oxygen/N₂O mixture FiO₂ being 0.3, fentanyl (3 mgm/kg bolus, 1 - 2 mgm/kg/h infusion), and low dose TPS (1 - 2 mg/kg/h) infusion.

In all patients induction was done with TPS 4 - 5 mg/kg and vecuronium (0.1 mg/kg) was used for tracheal intubation, muscle relaxation was maintained by vecuronium 0.01 mg/kg intermittently. Both groups received midazolam

(0.1 mg/kg), lignocaine 1.5 mg/kg 2 minutes before induction. Both groups received frusemide 1 mg/kg just after induction and mannitol 1 gm/kg when scalp incision was given. Anaesthetic procedure was performed with monitoring of hemodynamic variable pulse, blood pressure, SPO₂, E_TCO₂, temperature, urine output. Hemodynamic variable pulse, blood pressure were measure before induction, at intubation, every 15 min. interval and before extubation. Data were analyzed by paired and unpaired student's t-test as appropriate using SPSS software. Hemodynamic response to intubation does not differ significantly between the two groups. But it was observed that at intubation in both groups the pulse and mean arterial blood pressure was raised in compare to baseline, which gradually came down as anaesthetic depth increased and then remained stable all through the procedure.

Recovery was evaluated using Aldrete score. Total score significantly differ between two groups up to 30 min after extubation. Group A showed delay recovery up to 30 min in compare to group B. But after 30 min there was no significant difference in scoring between two groups. Total cost of main anaesthetic agent used significantly lower in group A. This study showed that the total infusion of TPS technique was as equally effective as using low concentration of isoflurane with conjunction of low dose TPS regarding perioperative hemodynamic stability. But the cost was minimal in thiopental sodium infusion group with the expense of a little bit delayed recovery.

-
1. Assistant Professor, Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University
 2. Associate Professor, Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University
 3. Consultant and Head, Department of Anaesthesia, ICU and Pain Management, Apollo Hospitals, Dhaka
 4. Consultant, Department of Anaesthesia, ICU and Pain Management, Apollo Hospitals, Dhaka

INTRODUCTION

The primary objective of anaesthesia is to facilitate surgery at minimal risk to the patient and to ensure optimal recovery following the procedure. General anaesthesia can be regarded as a 'quadrate' of the hypnosis, analgesia, muscle relaxation and amnesia. To achieve these effects, a combination of therapeutic agents is administered in the practice known as balanced anaesthesia. The hypnosis, analgesia, muscle relaxation could now be produced by separate agents without the cardiovascular risk of providing all three with the same technique deep inhalation anaesthesia or extensive regional technique¹.

At present there are different surgical procedures that are being performed under different kind of anaesthesia. Different procedures have different anaesthetic goals and techniques. Researchers are continuously looking for better anaesthesia by improving the quality of drugs, instruments and different procedures to provide a safe landing from anaesthesia and good operative condition. Anaesthesia for neurosurgical procedures also needs some special technique and maneuver. Major goals in neurosurgical anaesthesia are to provide adequate tissue perfusion to the brain (and spinal cord) so that the regional metabolic demand is met and adequate surgical conditions (a "relaxed brain") is provided. If anaesthetic drugs or anaesthetic techniques are improperly used, they can worsen the existing intracranial pathologic condition and may produce new damage. Some anaesthetics or anaesthetic techniques may help protect the brain subjected to metabolic stress or even ameliorate damage from such an insult².

Neuroanaesthetic procedure for surgery of intracranial space occupying lesion (ICSOL) is a major component of neuroanaesthesia. About 60% of all brain tumors are primary and supratentorial, and the most common ones presented by adults are gliomas, astrocytomas, oligodendrogliomas ($\approx 35\%$), meningiomas ($\approx 15\%$), and pituitary adenomas ($\approx 8\%$)³. For patients the problems associated with intracranial tumors result from local and generalized pressure, whereas for surgeons the difficulties arise during surgical exposure, as the brain is particularly susceptible to retraction and mobilization damage. Anaesthesia for intracranial space occupying lesion (ICSOL) thus requires an

understanding of the pathophysiology of localized or generalized rising intracranial pressure (ICP); the regulation and maintenance of intracerebral perfusion; the effect of anaesthesia on ICP, perfusion, and metabolism; and the therapeutic options available for decreasing ICP, brain bulk, and tension perioperatively. Specific problems include massive intraoperative hemorrhage, seizures, and air embolism in the head-elevated or sitting position or if venous sinuses are traversed. Further questions are how to monitor the brain's function and environment and whether to aim for rapid anaesthetic emergence or for prolonged post operative sedation and ventilation. Finally, the concurrence of various intracranial or extracranial pathologic conditions should not be forgotten, such as presence of cardiovascular or pulmonary disease or in case of metastases the existence of paraneoplastic phenomena and the effects of chemotherapy or radiotherapy should also be considered.

At present, the major argument for the still extensive and successful use of volatile-based technique remains the controllability, predictability, and attainability of early awakening⁴. However, the increasing consensus is that, volatiles are otherwise far from ideal agents for neuroanaesthesia because of their ability to increase cerebral blood flow (CBF), ICP, and brain bulk⁵⁻⁷. Although intravenous technique offer good control for CBF, ICP, and brain bulk⁸⁻¹¹, prolonged or unpredictable awakening remains the main concern with intravenous technique, with possible resulting difficulties in the differential diagnosis of delayed awakening and the need for emergent CT scanning to rule out surgical complication.

Volatile anaesthetics such as halothane, sevoflurane, isoflurane are commonly used in neuroanaesthesia. Among these agents isoflurane seems to more neurofriendly as because it increase CBF, and ICP to a lesser extent than halothane or sevoflurane, while cerebro-metabolic rate of oxygen ($CMRO_2$) reduces significantly^{5-7,12}. But isoflurane is a very costly agent as compared to other volatile agents at present available here.

Among intravenous anaesthetics agents' thiopental sodium (TPS) and propofol, are used commonly. Both agents make a favorable condition of brain for ICSOL surgery as both reduces CBF, ICP, $CMRO_2$, and also gives some cerebral protection from focal

cerebral ischemia, but it seems that there are delayed awakening while using thiopental sodium, while it is early in case of propofol¹¹.

In Bangladesh, many neurosurgical procedures are being performed. Traditionally the volatile anaesthetic agent used is halothane, which does not provide a desirable neuroanaesthetic condition and thiopental sodium acts as intravenous anaesthetics counterpart. Recently isoflurane have become available here, though it is very expensive. The recommended concentration for maintaining general anaesthesia seems to be outweigh the otherwise claimed benefit. To improve the present anaesthetic status in intracranial surgery isoflurane looks quite attractive, but at the same time TIVA, one of the alternative technique has already got good grounds⁴. But this technique suffer from the problem associated with delayed awakening which makes difficulties in early neurological assessment to rule out any surgical complication. Literature survey does not reveal any work on below 1 MAC isoflurane with combination of infusion anaesthetic agent. This study was done with isoflurane in a low concentration to avoid the deleterious effect of increased ICP and to reduce cost. This may be helped by adding an intravenous infusion of low dose TPS to compensate using low conc. isoflurane with the aim to achieve a good operating condition for the surgical procedure, stable hemodynamic and quick recovery of the patient and compare it with total infusion of TPS.

MATERIAL AND METHOD

Study Population

Total 30 patients with different neurosurgical problem with intracranial space occupying lesion for craniotomy under general anaesthesia were selected for the study. Both male and female patient within age group 18 - 60 years were selected. They were recruited and grouped randomly by blind envelope method. 30 envelopes of which 15 for group-A and 15 for group-B were kept in a box. Patient was asked to pick up one envelope randomly from that thirty pre fixed envelope to be assigned in one group. The purpose of the study, methodology, complications, side effects of each method of anaesthesia were clearly explained to each of the subject and recruited only after they had given written consent. The approval of the University Departmental Ethics Committee was duly taken before carrying out the study.

Grouping of Patients

Group A – Received induction dose of TPS 4 – 5 mg/kg, maintained by Thiopental (4 - 5 mg/kg/h infusion), Fentanyl (3 mgm/kg bolus, 1 mgm/kg/h infusion), oxygen/N₂O mixture FiO₂ being 0.3. Group B – Received induction dose of TPS 4 – 5 mg/kg, maintained by isoflurane 0.5%, oxygen/N₂O mixture FiO₂ being 0.3, Fentanyl (3 mgm/kg bolus, 1 mgm/kg/h infusion), and low dose TPS (1-2 mg/kg/h) infusion.

PROCEDURES

Preoperative Management

After obtaining the permission and the informed consent of the patient this study was performed. Preanaesthetic assessment was done on the previous day of surgery. Preanaesthetic assessment attempted to establish the neurologic and general state of patient. Preanaesthetic history of headache, nausea, vomiting, blurred vision evaluated to establish the presence of intracranial pressure. History of seizure, decreased level of consciousness, somnolence, hemiparesis, and sensory deficits are noted. Medication history was noted because concurrent medicine also affects intracranial compliance, perfusion and reserve as well as recovery. Examination included general examination, cardiovascular, respiratory renal, hepatic, endocrine and nervous system. Examination included neurological assessment documenting mental status and existing sensory or motor deficit. Neurological status comprising ability follows commands, patient's degree of orientation, presence or absence of speech deficit and the Glasgow Coma Score.

Medication was reviewed with special reference to corticosteroid, diuretics and anticonvulsants. Laboratory investigation included complete blood counts, hematocrit, X ray chest, ECG, blood glucose, blood urea, serum creatinine, urine for R/E. Laboratory investigation evaluated to rule out corticosteroid induced hyperglycemia and electrolytes disturbances due to diuretics. Computerized tomography and magnetic resonance images reviewed for evidence of brain edema. Evidence of midline shift of the brain (greater than 0.5 cm) on computed tomography also suggests the presence of increased ICP.

Preoperative medication

Preoperative medication that produces sedation or ventilatory depression was avoided in the patient with intracranial tumor. In case of tumor with no clinical or other sign of increase ICP, a small dose benzodiazepines 5 mg midazolam orally was used to decrease the level of anxiety. Steroid continued on the morning of operation 4 mg/i.v dexamethasone. For longer-term steroid treatment with probable pituitary axis suppression, stress coverage was provided by 100 mg methyl prednisolone.

Intra-operative Management

Patient was identified and preanaesthetic assessment was reevaluated. Size and position of the tumor, the tissue diagnosis, the surgical approach, the structures in proximity and likelihood of their involvement by surgery, and whether the tumor is to be removed radically, age, physical status, predictable intraoperative blood loss, position during surgery was considered before induction of anaesthesia.

A large bore intravenous catheter was placed as were electrocardiogram leads, blood pressure cuff, pulse oximeter and capnometer. Bladder catheterization was done. Ventilatory control (avoidance of hypercapnia and hypoxemia, early establishment of mild hyperventilation), sympathetic and thus blood pressure control (adequate depth or an anaesthesia and antinociception to prevent CNS arousal), and prevention of cranial venous out flow obstruction (head positioning) were considered for induction of anaesthesia.

Before induction of anaesthesia patient breathed 100% oxygen for three minutes.

If patient seems to be light as indicated by heart rate >100 and sweating then TPS infusion was increased at the discretion of attending anaesthesiologist to bring heart rate <100.

In all patients induction was done with TPS 4 - 5 mg/kg and vecuronium (0.1 mg/kg) was used for tracheal intubation, muscle relaxation was maintained by vecuronium 0.01 mg/kg intermittently. **Group A** patients were maintained by TPS (4 - 5 mg/kg/h infusion), fentanyl (3mgm/kg bolus, 1-2 mgm/kg/h infusion), 30% N₂O in O₂. **Group B** were maintained by isoflurane 0.5%, 30%

N₂O in O₂, fentanyl (3mgm/kg bolus, 1-2 mgm/kg/h infusion), and low dose TPS (1-2 mg/kg/h infusion). Both groups received midazolam (0.1 mg/kg), lignocaine 1.5 mg/kg 2 minutes before induction. Both groups received frusemide 1 mg/kg just after induction and mannitol 1 mg/kg when scalp incision was given. Ventilation was adjusted to maintain E_TCO₂ at 28 - 30 mmHg in both groups. Intraoperative hypertension (B.P >20% of baseline) was managed by Glyceryl trinitrate (GTN) (0.5 - 1 mgm/kg/min) infusion. In both groups at the end of procedure when dural stich was finished then TPS and fentanyl infusions were stopped. Isoflurane was stopped about 20 min before the end of the procedure. Patients were reversed with neostigmine (0.05 mg/kg) and atropine (0.015 mg/kg) and extubated when adequate spontaneous ventilation was established.

Preoperative intravascular deficit was estimated with duration of fast. The deficit was estimated by multiplying the normal maintenance rate by the length of fast. Normal maintenance fluid requirement was estimated as follows. For the first 10 kg, 4 ml/kg/h, for next 10 - 20 kg, 2 ml/kg/h for each kg, above 20 kg- 1 ml/kg/h. Abnormal fluid losses due to vomiting, diuresis, diarrhoea, blood loss and fever was considered. Intravascular fluid volume depletion due to blood loss was corrected with the whole blood. Intraoperative maintenance fluid considered was normal saline solution. Recovery from anaesthesia was assessed by Aldrete Score.

Dural condition and tension were measured by subjective assessment of the surgeon. Tension of dura would be used as a guide. When the dura was opened then the surgeon was asked to provide an assessment of the condition of the brain. This was done using a four- point scale developed by Todd *et al.*¹³,

1= excellent, no swelling; 2= minimal swelling but acceptable; 3= serious swelling but no specific change in management required; 4= sever brain swelling requiring some intervention, such as a change in position, a further reduction in PaCO₂, additional mannitol, or furosemide. After reversal patients were assessed with Aldrete post-anaesthetic recovery score (Annexe-A), every 10 minutes interval for one hour.

All information was collected in a spreadsheet format, and data were analyzed by student's "t" test (paired and un-paired as appropriate) using 'SPSS' software.

P < 0.05 was considered as significant.

OBSERVATION AND RESULTS

Demographic characteristics of patients

No differences were found between groups with regard to demographics.

The age, sex and weight are presented in Table-I. The median age (range) in year 38 (18 - 55) in group A and 40 (18 - 60) in group B. The weight (mean \pm SEM) in kg were 57.00 ± 2.11 in group A and 52.00 ± 1.87 in group B.

Age and weight are almost similar in two groups.

Table I

Age, sex and weight distribution of the study subjects

	Group A	Group B
No of patients (n)	15	15
Sex (Male/Female)	11/4	9/6
Age, Median (range) in year	38 (18 - 55)	40 (18 - 60)
Weight, (mean \pm SEM) in Kg	57.00 ± 2.11	52.00 ± 1.87

Hemodynamic Values

The study showed there was no significant difference between two techniques regarding hemodynamic stability. In both groups the pulse and mean arterial blood pressure was increased from base line value during induction and intubation. But as the anaesthetic depth increased these value gradually came down and then remained stable throughout the intraoperative period. Pulse before operation, at intubation, during maintenance of anaesthesia and before extubation was shown in Figure 1. Mean arterial pressure preoperatively, at intubation, during maintenance of anaesthesia and before extubation was shown in Figure 2.

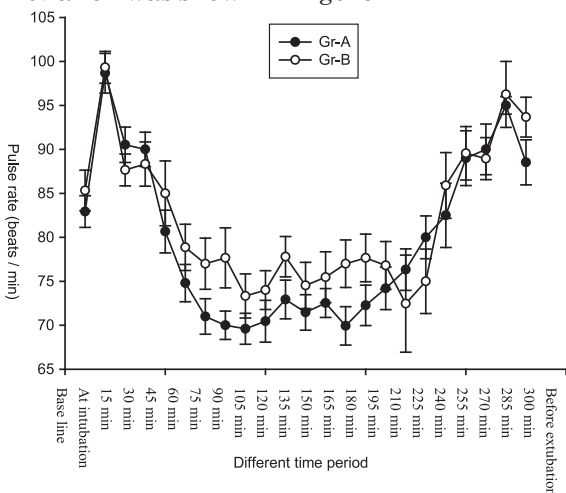


Fig.-1: Changes of pulse rate in two groups at different time period

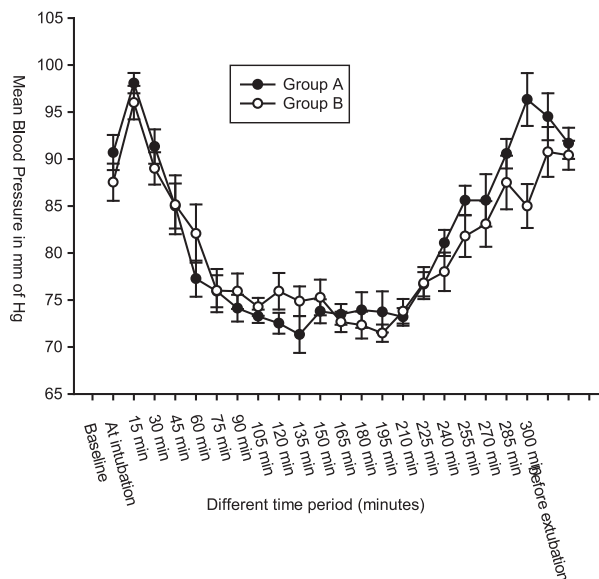


Fig.-2: Changes of mean arterial blood pressure in two studied groups at different time period Dural condition

The surgeon at the opening of the bone flap assessed dural condition. There was no significant difference of the dural tension and condition between the two groups.

Table II

	Group A	Group B	P value
Score of Dura	1.33 ± 0.12	1.26 ± 0.11	0.702

Data are presented as mean \pm SEM. Between groups, unpaired t test was performed.

RECOVERY

After extubation neurologic status was assessed repeatedly and recorded. Assessment consisted with Aldrete post anaesthesia score. Patients were evaluated every 10 min until a normal score 9 - 10 obtained when the patients were regarded awake and alert, oriented, responding to commands, and normal motor function. In terms of neurological assessment patients with score below 9 shows some signs of drowsiness, partially co-operative and partially awake.

Recovery score from anaesthesia using Aldrete recovery score every 10 min interval for 60 min from extubation were shown in Table - III

Table-III

Aldrete recovery score every 10 min interval for 60 min from extubation

Time in min.	Group A	Group B	P value
10 min.	7.13 ± 0.236	8.73 ± 0.238	0.001
20 min.	8.60 ± 2.890	9.90 ± 0.066	0.001
30 min.	9.53 ± 0.165	10.00 ± 0.000	0.009
40 min.	9.93 ± 0.066	10.00 ± 0.000	0.326
50 min.	10.00 ± 0.000	10.00 ± 0.000	-
60 min.	10.00 ± 0.000	10.00 ± 0.000	-

Data are presented as mean ± SEM. Between groups, unpaired t test was performed.

The mean Aldrete score significantly differ among group A and group B upto 30 min from extubation.

The Aldrete score at every 10 min interval were, at 10 min 7.13 ± 0.236 vs 8.73 ± 0.238, at 20 min. 8.60 ± 2.89 vs 9.90 ± 0.066, at 30 min. 9.53 ± 0.165 vs 10 ± 0.000. These values showed significant difference between the two groups.

Total TPS used

Total TPS used in group A naturally significantly higher then group B. But it was observed that very low dose TPS used in conjunction with isoflurane in group B with stable hemodynamic status during maintenance of anaesthesia.

Total cost of used TPS and isoflurane (in Taka)

Table-IV

Total cost of used main anaesthetics agents (TPS and isoflurane)

	Group A	Group B
Isoflurane	—	2000
TPS	195	65
Total	195	2065

Total cost of used main anaesthetic agents (TPS and isoflurane) significantly differs between two groups because of higher cost of isoflurane.

DISCUSSION

Anaesthesia, the gateway to surgery, its successful exit ends with safe recovery. Recovery from

anaesthesia has respiratory, cardiovascular, metabolic, endocrine and neurologic consequence¹⁴. Ideally patient recovery from neurosurgery should emerge rapidly from anaesthesia to permit immediate assessment of the result of surgery and to provide base line for continuing postoperative neurologic follow-up¹⁵. Different anaesthetic agents have different effects on cerebrovascular physiology. However- the importance of these differences in neuroanaesthetic practice is unclear. In general volatile anaesthetic are far from ideal agents for neuroanaesthesia because of their ability to increase CBF, ICP and brain bulk⁵⁻⁷. Adams⁶, showed the effect of Isoflurane on cerebral fluid pressure (CSFP) in patients undergoing craniotomy for intracranial supratentorial neoplasm or hepatoma. He used 1% isoflurane in two groups of patients. One group maintained hypocapnia and other group maintained normocapnia. He found that CSFP did not increase in hypocapnic group but in the normocapnic patients CSFP consistently increased. Although intravenous technique offer good control for CBF, ICP, and brain bulk⁸⁻¹⁰. Van¹⁰, found in one study that propofol 2.5 mg/kg in bolus injection does not increase ICP but can produce a significant decrease of the cerebral perfusion pressure due to a marked decrease in mean arterial pressure in patients with a brain tumor. Prolonged or unpredictable awakening remains the main concern with intravenous technique, with possible resulting difficulties in the differential diagnosis of delayed awakening and the need for emergent CT scanning to rule out surgical complication.

Present study compared total TPS infusion based anaesthesia technique with low concentration isoflurane supplemented by low dose infusion of TPS anaesthesia in resection of supratentorial intracranial mass in relation to hemodynamic stability and recovery, which are desirable in intracranial surgery.

The study showed there was no significant difference between two techniques regarding hemodynamic stability. In both groups the pulse and mean arterial blood pressure was increased from base line value during induction and intubation. But as the anaesthetic depth increased these value gradually came down and then remained stable throughout the intraoperative period. These findings are similar to many previous studies^{2,13,16}. Van *et al*¹¹, studied

two anaesthetic technique, where in one group anaesthesia induced with thiopental sodium, fentanyl and maintained with fentanyl, dehydrobenzperidol, isoflurane, nitrous oxide, and a thiopental sodium infusion. Other group anaesthetized with propofol loading infusion followed by a maintenance infusion at a fixed rate. They found significant increase in mean arterial blood pressure and pulse during intubation with thiopental group but did not change in propofol group.

But it was observed in the present study that pulse rate in isoflurane group were a little bit higher than TPS group throughout the intraoperative period, although not significantly different between two groups, which is similar to the study done by Todd *et al.*¹³, when he used propofol/fentanyl, isoflurane/nitrous oxide, fentanyl/nitrous oxide. He observed increased pulse rate in the intraoperative period in isoflurane group, though it was not significantly different to other groups. Many previous studies^{13,16} also showed that there were no significant differences regarding hemodynamic stability when using different anaesthetic techniques. Towards the end of anaesthesia in both groups pulse and mean arterial pressure were gradually increased though there was no significant difference between two groups. This increased pulse and mean arterial blood pressure may be due to lack of anaesthetic agents and patient become lighter as the anaesthetics were discontinued when the dura was closed. From dural closer to head dressing approximate elapsed time about 30 min to 45 min. This finding was also seen in one study¹⁶ where propofol infusion, isoflurane inhalation, and combined propofol and isoflurane were used. But in another study¹⁷ where propofol, isoflurane used showed propofol group had a more stable pulse and blood pressure then isoflurane group. These variations may be due the differences in dose and type of the anaesthetics agents used.

Present study also observed dural tension when the bone flap was removed. It was found that dura was relaxed enough to perform surgery comfortably in both groups. There was no significant difference between two groups regarding dural tension. It was similar finding as found in one study¹³ where anaesthetics used- propofol/fentanyl, isoflurane/N₂O, fentanyl/N₂O. But in another study¹⁸⁻¹⁹ found that the dural tension was significantly lower

in propofol group then isoflurane group but not sevoflurane group. The difference between the groups was presumed to be caused by differences in the degree of vasoconstriction elicited by the anaesthetics.

Recovery is one of the key factor of standard neuroanaesthetic procedure. Present study evaluated recovery from anaesthesia using Aldrete recovery score every 10 min interval for 60 min from extubation of patient. It showed significant difference in recovery score between the two groups. Group A showed delayed recovery score (score <9) up to 20 min then group B but after 30 min there was no significant difference in recovery score. In group B recovery score <9 for about 10 minute, this differences was may be due to using low concentration of isoflurane with a background of very low dose infusion of TPS. So that the residual effect of anaesthetics wearied off very quickly and recovery was faster which is desirable.

Although many previous studies showed no significant difference in recovery using different types of anaesthetics^{2,13,16}.

Though the present study was not a health economic investigation. Using current cost of one bottle (100 ml) isoflurane taka 3000/- and one vial TPS (500 mg) taka 65/-. It was estimated that a patient with average weight and average duration of surgery anaesthesia cost in group A of TPS 3 vial taka 195/- and in group B of isoflurane 2000/-(1 bottle contain 100 ml liquid isoflurane, costing TK.3000/- and at a concentration of 0.5%, the average total isoflurane used was estimated as 60 ml at 15 ml/h) + 1 vial TPS 65/-. Anaesthesia with isoflurane was costly then TPS. Time to discharge from recovery room was earlier with isoflurane. This provides advantage of short duration stay in recovery room with isoflurane. ICU management and ventilator support with delay was minimized with the use of low concentration isoflurane supplemented by low dose TPS infusion, which may impact in reducing total cost by isoflurane.

CONCLUSION

Low concentration of isoflurane with low dose TPS infusion has been found quite effective and showed better recovery compared to total TPS infusion technique. But in terms of cost benefit, use of TPS technique has come out lot cheaper.

Although there are modest differences between the two tested anaesthetics, short-term outcome was not affected. These results indicate that, despite their respective cerebrovascular effects, all of the anaesthetic regimens used were acceptable in these patients undergoing elective intracranial surgery.

Low concentration isoflurane technique can be recommended for further studies for surgery with large intracranial mass where fear of neuronal damage exists by manipulating brain tissue preoperatively and early recovery needed to evaluate neurological status early postoperatively.

REFERENCES

1. Healy TEJ, Cohen PJ. Muscle relaxants and clinical monitoring. Wylie and Churchill Davidson's A practice of Anesthesia. 6th ed. London: Edward Arnold 1995; p 149.
2. Grundy BL, Pashayan AG, Mahla ME, et al. Three balanced anesthetic techniques for neuroanesthesia: infusion of thiopental sodium with sufentanil or fentanyl compared with inhalation of isoflurane. *J Clin Anesth* 1992; 4: 372-377.
3. Ojemann RG. Meningiomas: clinical features and surgical management. In: Wilkins RH, Rengachary SS, eds. Neurosurgery, vol 1, New York: McGraw-Hill, 1985: pp 635-654.
4. Ravussin P, de Tribolet N, Wilder-Smith OH. Total intravenous anesthesia is best for neurological surgery. *J Neurosurg Anesthesiol* 1994; 6: 285-289.
5. Adams RW, Gronert GA, Sundt TM, et al. Halothane, hypocapnia, and cerebrospinal fluid pressure in neurosurgery. *Anesthesiology* 1972; 37: 510-517.
6. Adams RW, Cucchiara RF, Gronert GA, et al. Isoflurane and cerebrospinal fluid pressure in neurosurgical patients. *Anesthesiology* 1981; 54: 97-99.
7. Grosslight K, Foster R, Colohan AR, et al. Isoflurane for neuroanesthesia: Risk factors for increases in intracranial pressure. *Anesthesiology* 1985; 63: 533-536.
8. Hunter AR. Thiopentone supplemented anesthesia for neurosurgery. *Br J Anaesth* 1972; 44: 506-515.
9. Vandesteene A, Trempont V, Engelman E, et al. Effect of propofol on cerebral blood flow and metabolism in man. *Anaesthesia* 1988; 43: 42-45.
10. Van Hemelrijck J, Van Aken H, Plets C, et al. The effects of propofol on intracranial pressure and cerebral perfusion pressure in patients with brain tumors. *Acta Anaesthesiol Belg* 1989; 40: 95-100.
11. Van Hemelrijck J, Van Aken H, Merckx L, et al. Anesthesia for craniotomy: total intravenous anesthesia with propofol and alfentanil compared to anesthesia with thiopental sodium, isoflurane, fentanyl, and nitrous oxide. *J Clin Anesth* 1991; 3: 131-136.
12. Madsen JB, Cold GE, Hansen ES, et al. The effect of isoflurane on cerebral blood flow and metabolism in humans during craniotomy for small supratentorial cerebral tumors. *Anesthesiology* 1987; 66: 332-336.
13. Todd MM, Warner DS, Sokol MD, et al. A comparative trial of three anaesthetics for craniotomy: propofol/fentanyl, isoflurane/nitrous oxide, and fentanyl/nitrous oxide. *Anesthesiology* 1993; 78: 1005-1020.
14. Muzzi DA, Black S, Losasso TJ, et al. Labetalol and esmolol in the control of hypertension after intracranial surgery. *Anesth Analg* 1990; 68: 70.
15. Bracco D, Ravussin P, Stondeur JM. Early awakening or long term sedation after neuro anesthesia. *Eur J Anesthesiology* 1998; 28S: 15.
16. Talke P, Caldwell JE, Brown R, et al. A comparison of three anesthetic techniques in patients undergoing craniotomy for supratentorial intracranial surgery. *Anesth Analg* 2002; 95: 430-435.
17. Ittichailkulthol W, Pausawasdi S, Srichintai P, et al. Propofol vs isoflurane for neurosurgical anesthesia in Thai patients. *J Med Assoc Thai* 1997; 80: 454-460.
18. Petersen KD, Landsfeldt U, Cold GE, et al. ICP is lower during propofol anaesthesia compared to isoflurane and sevoflurane. *Acta Neurochir Suppl* 2002; 81: 89-91.
19. Petersen KD, Landsfeldt U, Cold GE, et al. Intracranial pressure and cerebral hemodynamic in patients with cerebral tumors: a randomized prospective study of patients subjected to craniotomy in propofol-fentanyl, isoflurane-fentanyl, or sevoflurane-fentanyl anaesthesia. *Anaesthesiology* 2003; 98: 329-336.

Original Article

PROPHYLACTIC USE OF KETAMINE HYDROCHLORIDE FOR PREVENTION OF POST OPERATIVE SHIVERING

Rabeya Begum¹, Rezaul Islam², Paresh Chandra Sarker³, Kamal Krishna Karmakar¹, ABM Muksudul Alam⁴

SUMMARY:

Postoperative shivering is one of the recognized complications following general, regional anaesthesia and also effect of some surgical procedure specially in the recovery room¹. Shivering increases the muscular activity, O₂ consumption, CO₂ production and may result in hypoxaemia, hypercarbia and lactic acidosis². It is not only uncomfortable but also cold sensation which is even worse feeling than pain sensation. As a result preventing the symptoms is clearly desirable and beneficial for the patient. Different methods are suggested for prevention of postoperative shivering including biogenic monoamines, cholinomimetics, cations, endogenous peptides, opioids, GA agents, NMDA antagonists³.

The present study was designed to compare the efficacy of ketamine on the patients undergoing elective surgery for prevention of postoperative shivering. The study was also done to deffect incidence of shivering, haemodynamic status, untoward effects of drug used (hallucination, unpurposeful movement, restlessness).

A total number of 60 patients of ASA I and II grade of both sex, age range 30-60 yrs, weight 50-70 kg, undergoing elective gynaecological surgery was randomly selected into two groups Gr K and Gr P and received ketamine 5mg. kg⁻¹ and placebo (normal saline) respectively at 20 minutes before the end of the operation. In the postoperative period, incidences of shivering were 80% & 50% in group "K" and "P" which are highly significant between the groups P<001. Cardiovascular parameters SAP, DAP, MAP and SpO₂ between the groups were not significant P>.05. The study showed that patients of group 'K' were less shivering with good recovery.

Key words: Postoperative shivering, ketamine.

INTRODUCTION:

Post anaesthetic shivering is remarkably uncomfortable, some patients find cold sensation worse than surgical pain. Shivering aggravates post-operative pain by stretching surgical incision⁵. Shivering interferes with monitoring technique, increases intracranial and intraocular pressure, can double or triple O₂ consumption and CO₂ production. The incidence of post-operative shivering is 6-65% in GA and 30% in regional anaesthesia. Etiology of Post operative shivering in multifactorial. Different methods are available for prevention of Post operative shivering. Multimodal approaches like warming, O₂ therapy, correction of metabolic abnormalities, drugs opioids, benzodiazepine, clonidine, corticosteroids, ketamine, nefopam, doxapram, are used to prevent and for management of postoperative shivering⁶. Among which drugs are more popular mode. Intravenous ketamine .5mg/kg 20 min before completion of surgery will abolish shivery in most subjects⁷. NMDA receptor agonists increase the firing rate of neuron in the preoptic anterior hypothalamus, modulate noradrenergic and serotonergic neuron in brain. NMDA receptor antagonists modulate shivering by interfering central thermoregulatory control mechanism⁸, Ketamine is cheaper and easily available in our country. The objective of current study was to evaluate effectiveness of ketamine in prevention of postoperative shivering in low dose without major side effects.

Material & Methods

In the preoperative period patients were fasted at least 6 hrs. and on arrival at OT I/V line was inserted; pulse, BP respiratory rate and SpO₂ were recorded. After 3 minutes preoxygenation induction was facilitated by suxamethonium 1.5 mg. kg⁻¹,

1. Consultant, Department of Anaesthesiology, SSMC
2. Associate Professor, Department of Anaesthesiology, SSMC
3. Asst. Professor, Department of Anaesthesiology, SSMC
4. Professor, Department of Anaesthesiology, SSMC

General anaesthesia was maintained by halothane. 5%, N₂O 70 % in O₂. Muscle relaxation was maintained by intermittent vecuronium. Hartmann's solution was used for proper hydration and patients were covered with sheets as usual. Neostigmine 40 ug. kg⁻¹, atropine 20 ug. kg⁻¹ were given for reversal from muscle relaxant. (At the end of operation 'K' & P Gr. were given .5mg kg⁻¹ ketamine and IO cc normal saline respectively.)

The severity of postanaesthetic shivering was assessed according to a 4 point scale by Wrench et al⁴

0 = no shivering

- 1= piloerection, peripheral vasoconstriction, peripheral cyanosis without other cause but without visible muscular activity.
- 2- Visible muscular activity confined to one muscle group.
- 3- Visible muscular activity in more than one muscle group
- 4- gross muscular activity involving the entire body.

The evaluation of shivering was carried out by independent anaesthesiologist who is unaware of grouping. If a score >2, 25mg ketamine was given intravenously as rescue medication. BP, Pulse rate, SpO₂ were measured during induction and 10, 20, 30 & 60 min after extubation. All patients received diclofenac suppository rectally at the end of operation. Post anaesthetic recovery score was graded by using Aldrete score and Patients were carefully observed for adverse effects like hallucinations, restlessness, drowsiness and dream.

Results:

Demographic data concerning the patient age, weight as well as duration of anaesthesia and type of surgery were comparable in two groups (Table I & II) which are fairly matched. In preoperative situation in group P mean pulse rate was 78 ± 2.30, in Gr-k 81 ± 1.04, mean arterial pressure 91.71 ± 1.04 (Gr P), 93.01 ± 1.12 (Gr K), SpO₂ 98 ± .55 Gr P, 97 ± 0.25 (Gr K) which showed no significant difference between the groups (Table III). There were no clinically relevant differences in measured results as regards to blood pressure and heart rate between the study group (group K) through out the study period (table IV & table V). Except 20 minutes before

the end of surgery when ketamine was administered the heart rate in group 'P' was 96.7 ± 1.85 and in group 'K' was 101.0 ± 1.22 MAP (mean arterial pressure) in group 'P' was 105.80 ± 1.32 and in group 'K' was 110.97 ± 1.20. But after 30 minutes and onwards of ketamine given, the blood pressure and the heart rate both came down to normal range and even to lower level than the initial pre-anesthetic states though it was not significant only two are significant. Before induction in group 'P' arterial oxygen saturation was 98.28 ± 0.72, and in group 'K' was 99.35 ± 0.78. But 20 minutes after the end of surgery SpO₂ in group 'P' 98.94 ± 0.48 and in group 'K' 98.82 ± 0.08, P > 0.05, so pulse oximetry showed no such significant difference between the two groups (table VI). The incidence of post operative shivering was 80% in group-P, 50% in group-K. Analysis was done by "Z" test; p < 0.001. The difference between the two groups was highly significant (table VII)

Shivering score 60 minutes after the end of surgery varies at the post operative period for both the groups. Severity of shivering is expressed by using four-point scale. In patients treated with placebo 0.5 mg.kg⁻¹, 06 of 30 (20%) have no symptoms of shivering (shivering score grade 0) but twelve patients (40%) showed signs of piloerection, peripheral vasoconstriction or peripheral cyanosis (shivering score grade 1). In grade (2-4) patients from four-point scale revealed shivering of 20%, 16.66 %, 3.33% respectively. They also showed visible gross muscular activity. In patients treated with ketamine 0.5 mg.kg⁻¹, 15 of 30 (50%) have no symptoms of shivering but eleven patients (33.33%A) showed signs of piloerection, peripheral vasoconstriction or peripheral cyanosis (shivering score grade 1). In grade (2-4), patients from four –point scale revealed shivering of 6.66 %, 3.33%, 32.33% respectively. Analysis done by "Z" test: p < 0.001-highly significant, p > 0.05-not significant. Analyzing the shivering score we found a significant higher grading in the placebo group compared to ketamine group (table VIII). Table IX: — In placebo group there was no untoward effects such as (hallucinations, unpurposeful movements, restlessness, drowsiness) but in ketamine group 2 of 30 patients (6.66%), 3 of 30 (10 %), 1 of 30 (3.33%) p < 0.001 highly significant.

Table-I
Demographic Data of the Patients.

Parameter	Group – P N = 30	Group – P N = 30
Age in years	36.3(30-60)	37.4(30-60)
Sex, M : F	14 : 16	15 : 15
Body weight in Kg	52.3(50 – 70)	54 (50-70)
Duration of Surgery in minutes	85 min(60 – 120)	80 min(50 – 115)

Values are expressed in mean (Range)

Results : fairly matched

Table II
Types of operation :

Operation	Group – P N = 30	Group – P N = 30
Gynaecological Laparotomy, Hysterectomy.	120309	110308
Surgical Cholecystectomy	120804	130805
Urological.Nephrolithotmy.NephrectomyPyeloplasty	06030201	06030201
Total	30	30

Table III
Comparison of the control states of the study population :

Parameter	Group – P N = 30	Group K N=30	P – Value (unpaired student's t-test)
Pulse/minute	78 ± 2.3	81 ± 2.3	> 0.05
MAP (mm of Hg)	91.71 ± 1.04	93.01 ± 1.12	> 0.05
SpO ₂	98 ± 0.55	97 ± 0.25	> 0.05

Values are expressed in mean ± SEM

unpaired students t-test, P-> 0.05 not significant

MAP = mean arterial of pressure, SpO₂ = Arterial oxygen saturation.

Table IV. (a)
Pulse and mean arterial pressure at different point of observation of two groups:

60 minutes Parameters	20 minutes before the end of surgery	At recovery 10 minute	20 minutes	30 minutes	40 minutes	50 minutes
Heart rate /minute	80.77 ± .20	91.0 ± .82	90.71 ± 1.01	82.28 ± 0.92	81 .25 ± .72	81 .05 ± .70
MAP	97.72 ± 0.95	96.25 ± .72	94.15 ± 0.70	88.60 ± 0.96	87 .85 ± 0.80	87.85 ± 0.80
						87.22 ± .73

Values are expressed in mean ± SEM

Table IV. (b)

60 minutes Parameters	20 minutes before the end of surgery	At recovery 10 minute	20 minutes	30 minutes	40 minutes	50 minutes	
Heart rate/ minute	92.03 ± 0.98	93.02 ± .80	92.0 ± 0.05	88.01 ± 1.02	84 .32 ± 0.98	81.90 ± 1.00	79.91 ± 0.90
MAP	100.62 ± 1.01	110.82 ± 1.61	100.51 ± 0.97	91 .34 ± .92	88.14 ± 0.92	87.34 ± 0.78	87.01 ± 1.10

Values are expressed in mean ± SEM.

Table V

Comparison of changes produced in the mean values of the two groups

Observation Time	Parameters	Group-P	Group-K	P - Value
Before Induction	Pulse	84.56 ± 1.23	86.32 ± 1.20	> 0.05
	MAP	91.71 ± 1.04	94.68 ± 1.24	> 0.05
Start of drugs 20 minutes before the end of surgery	Pulse	96.71 ± 1.85	101.0 ± 1.22	<0.01
	MAP	105.80 ± 1.32	110.97 ± 1.20	<0.01
At recovery = 10 minutes	Pulse	91.00 ± 0.82	92 .03 ± 0.98	> 0.05
	MAP	97.22 ± 0.95	100.82 ± 1.61	< 0.01
20 minutes	Pulse	87.88 ± 0.93	90.01 ± 1.02	> 0.05
	MAP	90.71 ± 1.01	94.34 ± 0.92	''
30 minutes	Pulse	84.71 ± 1.06	88.32 ± 0.98	''
	MAP	88.60 ± 0.96	88.14 ± 0.97	''
40 minutes	Pulse	82.28 ± 0.92	81.90 ± 1.00	''
	MAP	87.85 ± 0.80	87.34 ± 0.78	''
50 minutes	Pulse	80.77 ± 0.20	84.90 ± 0.90	''
	MAP	87.22 ± 0.73	89.03 ± 1.25	''
60 minutes	Pulse	84.26 ± 1.22	86.02 ± 0.98	''
	MAP	92.65 ± 1.01	94.28 ± 1.21	''

Values are expressed in mean SEM

Unpaired student's " t-test'

MAP = mean arterial pressure

P-Value > 0.05 not significant

P – Value < 0.01 significant

Table VI
Incidence of shivering in two groups

Observation time	Group-P	Group-K	P-Value
Before Induction	98.28 ± 0.72	99.35 ± 0.78	> 0.05
20 minutes before the end of surgery	98.97 ± 0.45	96.08 ± 0.78	„
At recovery + 10 minutes	97.97 ± 0.52	97.29 ± 0.67	„
20 minutes	98.94 ± 0.48	98.82 ± 0.08	„
30 minutes	98.71 ± 0.57	97.05 ± 0.70	„
40 minutes	98.80 ± 0.63	97.00 ± 0.63	„
50 minutes	98.65 ± 0.63	98.01 ± 0.08	„
60 minutes	98.70 ± 0.97	97.40 ± 0.83	„

Analysis done by Unpaired student's "t-test" Values are expressed in mean ± SEM
P-Value > 0.05 not significant

Table VII
Shivering score in post operative period in two groups

Incidence of post operative shivering	Group – P	Group –K	P-Value Z-test
	24	15	<0.001 (z>3)
	80%	50%	„

Values are expressed in mean ± SEM Analysis done by "Z-test"
(P<0.001) highly significant

Table-VIII
Shivering score in post operative period in two groups

Shivering score	Group-P		Group-K		P-Value (z test)
0	06	20%	15	50%	0.001 (z value 3.3)
1	12	40%	11	33.33%	>0.05
2	06	20%	02	6.66%	<0.001
3.	05	16.66%	01	3.33%	< 0.001
4.	01	3.33%	01	3.33%	>0.05

4
Analysis done by "Z-test"
(P-<0.001) – highly significant
(P->0.05) – Not significant

Table IX
Untoward effects

Variable	Group-P	Group-K	P-Value(Z-test)
Hallucination	0	2 6.66%	<0.001
Unpurposeful	0	3 10%	<0.001
Movement of Face	0	1 3.33%	<0.001
Restlessness	0	6 20%	<0.001

DISCUSSION:

Postanaesthetic shivering is a frequent complication following surgery and anaesthesia and incidence about 5- 65% following GA and 33% under SAB. The frequency and severity has been reduced by identifying precipitating factors, improving surgical techniques, newer anaesthetic agents and technique and also by newer drugs. Despite these changes there is still an unacceptable frequency which need to be reduced for betterment of future surgery and anaesthesia.

The aetiology of post-operative shivering is multifactorial. Factors associated with an increased risk of post-operative shivering include age, sex, obesity, anxiety, pain, hypoxia, type of anesthetic, hypotension, type & duration of the surgical procedure. Patient undergoing gynecological surgery are at high risk for post-operative shivering. Because most of them are female & most of the surgery done in winter season.

D.Dal *et al* studied the efficiency of pethidine, ketamine with placebo⁸. S.N. Piper *et al* also have studied the effectiveness of three doses of Nefopam with clonidine & placebo in the prevention of post-operative shivering¹¹. There was significantly greater number of asymptomatic patients in the ketamine, pethidine, clonidine and nefopam group 60 minutes after operation at PACU as compared to placebo (p<0.01). The average duration of anesthesia was 60 minutes. There was no significant difference between the groups respect to heart rate, MAP and SpO₂.

In our study, incidence of post operative shivering in group-P (those received placebo) were 80% and in group-k (those received ketamine) were 50% that means the data shows the incidence (p<0.01) of shivering is highly significant in placebo group. Heart rate differences between the groups at control

states (p>0.05) and post operative period (p>0.05) were not significant. Mean arterial pressure and arterial oxygen saturation between the two groups were not (p>0.05) significant. The difference in the results of asymptomatic patients in our study 19% compared with those S. N. piper *et al* 15 % may be explained by a small number of population and the meant duration of anesthesia was greater in our study.

Shivering score after one hour post-operatively varies from 0-4 (four-point scale) in both groups. In placebo-treated patients, it was 0 for 20%, 1 for 40%, 2 for 20%, 3 for 3.33% and 4 for 3.33% respectively and statistically significant (p<0.001). It may be explained that patients of group-k were less shivering with good recovery Aldrete score.

CONCLUSION:

On the basis of present, controlled, prospective clinical study it can be concluded that the post operative shivering are the most common complaints. The aetiology of postoperative shivering is multifactorial including anesthetic, patients and surgical factors. All surgical patients should be kept normothermic unless hypothermia is specifically indicated for putative protection against cerebral ischaemia. Antishivering prophylaxis may be justified in patients who are at great risk of developing post-operative shivering after general anaesthesia.

The incidence of major side effects is not significant in ketamine group and contributes to some extent to post operative analgesia with acceptable recovery score (Aldrete).

We can conclude that prophylactic use of ketamine hychloride is effective in small doses without major side effects and some analgesic effects in preventing post operative shivering under general anaesthesia.

REFERENCES

1. Crossley AWA. Peri-operative shivering. *Anaesthesia* 1992; 47: 193-5
2. Ciofolo MJ, Clergue F, Devilliers C, Ammar MB, Viars P. Changes in ventilation, oxygen uptake and carbon dioxide output during recovery from isoflurane anaesthesia. *Anaesthesia* 1989; 70:73-74.
3. White, Daniel I. Perioperative shivering; Physiology & Pharmacology. *Anaesthesiology* 2002; 96(2): 467-484
4. Wrench Ij, Cavill G, Ward JEH, Crossley AWA. Comparison between alfentanil, pethidine and placebo in the treatment of postanesthetic shivering *BJA* 1997; 79:541-2.
5. De Courcy JG, Elderred C: Artefactual “hypotension” from shivering. *Anesthesia* 1989; 44; 787-8
6. Parveen K. Michael C, Hypothermia in Clinical Medicine 5th edition P-992-3
7. Kurz A, Ikeda T, Sessler DI, Larson M, Bjorksten AR, Dechert M, Christensen R: Meperidine decreases the shivering threshold twice as much as the vasoconstriction threshold. *Anesthesiology* 1997; 86; 1046-54
8. Dal D, Korse A, Honca M et all. Effects of Ketamine in post operative shivering. *BJA* 2005; 95 (2): 189-192
9. Alan R. David J. R. Graham. S. Postoperative Shivering In Textbook of Anesthesia 4th edition Churchill Livingstone P-307.
10. Crossley AWA. Postoperative shivering: influence of body temperature *BMJ* 1995, 311: 764-765.
11. Piper SN, Suttner SW et al. A comparison *Anesthesia* 2004; 59, P-559- 564.

Original Article

A COMPARATIVE STUDY ON HAEMODYNAMIC AND RECOVERY STATUS IN DAY-CASE ANAESTHESIA BETWEEN INFUSION OF PROPOFOL, MIDAZOLAM, NALBUPHINE AND KETAMINE, DIAZEPAM, TRAMADOL

M Masudul Haque¹, Md Rabiul Alam², Md Al Mamun³, Md. Mozaffer Hossain,⁴ Md Zahurul Islam⁵

ABSTRACT:

A prospective comparative study was carried out to evaluate haemodynamic and recovery status using infusion of propofol-midazolam-nalbuphine and ketamine-diazepam-tramadol in surgical day-cases. Fifty patients of either sex aged within 18-60 years ASA grade I or II requiring routine surgery as day-case basis under GA were selected in Dept of Anaesthesia, CMH, Dhaka during February-May 2006. Cases were randomly divided equally into two groups of 25 each. Group-A received propofol-midazolam-nalbuphine infusion and infusion of ketamine-diazepam-tramadol was used in Group-B for anaesthesia. Haemodynamic parameters, recovery status and home readiness time were monitored and recorded at 10 min intervals. The variations in heart rate, systolic and diastolic BP of both groups were found statistically insignificant (p-values: 0.0524, 0.0513 and 0.0575 respectively). Recovery scores were high in Group-A (p-0.0443) and time for home-readiness were found 242±35 (mean±SD) minutes in Group-A and 367±83 minutes in Group-B (p-0.0329). Drugs used in Group-B were found highly cost effective. It is concluded that by using ketamine, diazepam and tramadol combination (group-B), we can reduce the cost of anaesthesia, which is necessity for majority of patients in our country. On the other hand, propofol, midazolam and nalbuphine combination (group-A), a costlier regime appears suitable for the patients from affluent population. Both the regimes can be practiced with safety.

INTRODUCTION:

One of the most dramatic transformations in health care delivery in the recent past is shift from inpatient to outpatient surgery & associated day-case anaesthesia. The primary impetus for this change is the economic savings afforded by not admitting patients the night before surgery or keeping them in hospital the night after surgery. Other advantages of outpatient surgery include earlier ambulation, patient convenience, and a lessened risk of nosocomial infection¹. Many operations are performed at one-fifth cost of inpatient surgery if carried out on a day-case basis². Such type of day-case anaesthesia is only economical if it can be carried out safely. Optimum prerequisite for agents of day-case anaesthesia is early discharge & cost effectiveness. Problem is that none of the currently available anaesthetic agents have duration of action short enough to leave the patient with no residual effects within a few hours of surgery³.

Comparison of anaesthetic technique to determine which is least likely to impair the patient's postoperative mental and physical well-being requires the measurement of residual effects. Even when this is established, it is important to realise that each patient is an individual who will have a variable response to anaesthetic drugs. Thus, for each individual patient, it is necessary to assess the degree and quality of recovery from a particular anaesthetic technique³. Recovery from intravenous anaesthetic agents is produced usually by the rapid redistribution of the drug from the brain into the other well-perfused tissues, viscera and particularly

-
1. Graded Specialist in Anaesthesiology, Combined Military Hospital, Momenshahi Cantonment
 2. Lt Col Combined Military Hospital, Chittagong Cantonment
 3. Lt Col Combined Military Hospital, Savar Cantonment
 4. Consultant, Dhaka Medical College Hospital.
 5. Ex. Col Combined Military Hospital, Jessore Cantonment.

muscles. Metabolisms of the drug, which mainly occur in the liver, also contribute to some extent to the recovery. A small proportion of the drug may be excreted unchanged through the kidneys^{4,5}. Aims of this study were to assess and compare haemodynamic and recovery status after infusion of propofol-midazolam-nalbuphine and ketamine-diazepam-tramadol in day-case anaesthesia, to evaluate and compare the speed of home readiness of the groups and to find out the cost effectiveness of two regimes.

MATERIALS AND METHODS:

With approval from the departmental ethical committee and after taking informed consent from patients, this prospective, comparative study was carried out in the Dept of Anaesthesia, CMH Dhaka. In this randomized study 50 patients of either sex of 18-60 years of age and ASA grade I or II were scheduled for routine surgery as day case basis under general anaesthesia. Exclusion criteria were: Obese and epileptic patients, Patients of psychological instability and on CNS depressants, anti-coagulants and steroids. Total 50 patients were divided randomly into 2 (two) equal groups (25 patients in each group): **Group-A** Patients received infusion of propofol, midazolam and nalbuphine and **Group-B** Patients received infusion of ketamine, diazepam and tramadol.

In the operating room, after establishment of i.v. line and recording of HR & BP (baseline parameters), patients were pre-oxygenated for 05 minutes before

induction. In group-A patient Intubation was done by using propofol 2 mg/kg, vecuronium 0.1 mg/kg and was maintained by propofol 10 mg/kg/hr for 1st 10 minutes, 08 mg/kg/hr for next 10 mins and 06 mg/kg/hr thereafter⁶⁻⁷, midazolam 0.2 mg/kg/hr^{8,9,10}, nalbuphine 15mg i.v. stat than 0.25-0.5 mg/kg at 30 minute interval¹¹⁻¹². In group-B patient intubation was done by using ketamine 2 mg/kg, vecuronium 0.1 mg/kg and was maintained by ketamine 50µg/kg/min¹³⁻¹⁴, diazepam 0.2 mg/kg i.v. stat^{8,15,16}, tramadol 100 mg i.v. stat than 20 mg/min up to cumulative dose of 01 mg/kg and thereafter 0.05 mg/kg/min¹⁷⁻¹⁸. All patients ventilated with a mixture of 30% O₂ in air with Bain circuit.

Patients' Heart rate and blood pressure (as recorded by non invasive monitoring) were noted during induction, one minute after intubation and at 10 minutes interval up to the reversal. After reversal recovery score were recorded adapting PADS scoring system (Post Anaesthesia Discharge Scoring system for determining home readiness)¹⁹ at 10 minutes interval until the patients responded to vocal command. After complete recovery, fitness to go home was assessed by adapting the following home readiness (Time in minutes) parameters at 10 minutes interval. The maximum score of home readiness is 10. Patients scoring e" 9 were considered fit for discharge. The time taken for home readiness was recorded. Data were analyzed by Students 't' test and Chi-square test as appropriate. P value < 0.05 (CL-95%) was regarded as significant.

PADS system for determining home readiness parameters were¹⁹:

Vital signs

Patient's vital signs being stable and consistent with age and preoperative baseline

- BP and pulse : Within 20% of preoperative baseline - 2
- BP and pulse : 20-40% of preoperative baseline - 1
- BP and pulse : >40% of preoperative baseline - 0

Activity level

Patient's ability to ambulate at pre operative level

- Steady gait, no dizziness or meets pre operative level - 2
- Requires assistance - 1
- Unable to ambulate - 0

Nausea and vomiting

The patient had minimal nausea and vomiting prior to discharge

- Minimal : Successfully treated with post operative medication - 2
- Moderate : Successfully treated with IM medication - 1
- Severe : Continue after repeated treatment - 0

Pain

The patient had minimal or no pain prior to discharge. The level of pain was acceptable to the patient.

- Acceptability : Yes - 2
- : No - 1

Surgical bleeding

Post operative bleeding was consistent with expected blood loss for procedure

- Minimal : Does not require dressing change - 2
- Moderate : Up to two dressing changes required - 1
- Severe : More than three dressing changes required - 0

Results:

Patient's characteristics were comparable among the groups (Table-I). No significant difference was found in demographic characteristic except Height. Recovery score at different timing were comparable among the groups (Table-II). Significant recovery score was found among the groups. Time taken for fitness to go home was comparable among the groups (Table-V). Significant difference in Time taken for fitness to go home was found among two groups. Cost status of the agents used in different groups was comparable (Figure-2). Significant $P < 0.05$ (among two groups) difference were found for cost of induction agents. Just after induction in group-B there were significant (considering 20% change from base line) increase in heart rate (Figer-1). Arterial pressure was statistically non significant among the groups. The ASA grade ^{2,22} was 88% (n=22) : 12% (n=3) in group A and 92% (n=23) : 8% (n=2) in group B. The male female ratio was 76% (n=19):24% (n=6) in group A and 80% (n=20):20% (n=5) in group B.



Fig.-1: Per-operative heart rate variation among the two groups

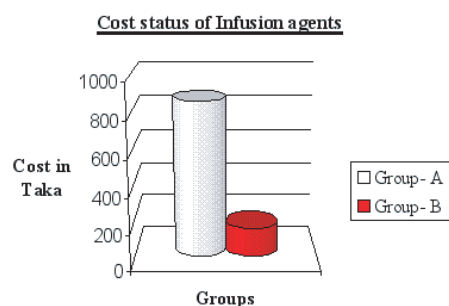


Fig.-2: Costing of the agents used for the study among the two groups

Table-I
Demographic data

Characteristics	Group A	Group B	p- value
Age (years)	27.20±3.14	25.95±3.80	0.064 ^{ns}
Body wt (kg)	63.80±4.37	61.50±3.46	0.052 ^{ns}
Height (cm)	156.25±3.49	152.65±4.04	0.013 ^s

Values are expressed as mean±SD.ns- not significant; s- significant $p < 0.05$, Analysis were done by 't' test.

Table-II
Recovery score in various timing (adapting SOCA scoring system)

Group	At reversal	Just after reversal	After 5 min	After 10 min	After 20 min	After 30 min	After 40 min	<i>p</i> -value
Group- A	5.98±2.01	6.00±3.43	7.02±9.72	7.28±6.23	8.86±8.54	9.5±2.89	9.99±4.93	0.0443 ^s
Group- B	5.26±4.33	5.66±5.11	6.11±4.06	6.46±7.01	6.86±3.59	8.01±9.01	9.00±6.81	

Values are expressed as mean±SD s: significant $p < 0.05$ Analysis were done by ANOVA.

Table-III
Per-operative systolic blood pressure variations

Group	Pre-op (baseline)	At induction	At intubation	After 5 min	After 10 min	After 20 min	After 30 min	After 40 min	After 50 min	After 60 min	<i>p</i> -value
Group-A	112±10	102±8	121±12	115±9	116±15	114±8	117±20	115±10	116±14	116±4	0.0513 ^{ns}
Group-B	118±8	122±9	134±9	131±7	128±10	123±13	127±11	132±12	126±5	129±15	

Values are expressed as mean±SD ns: not significant $p > 0.05$, Analysis were done by ANOVA test.

Table-IV
Per-operative diastolic blood pressure variations

Group	Pre-op (baseline)	At induction	At intubation	After 5 min	After 10 min	After 20 min	After 30 min	After 40 min	After 50 min	After 60 min	<i>p</i> -value
Group-A	74±11	72±3	82±10	78±8	75±2	70±3	75±5	77±11	71±10	74±3	0.0575 ^{ns}
Group-B	73±4	91±7	93±9	88±5	89±12	82±10	87±7	90±4	88±5	86±11	

Values are expressed as mean±SD.ns: significant $p > 0.05$, Analysis were done by ANOVA test.

Table-V
Time required for Home readiness

Group	Time required for home readiness (min±SD)	<i>p</i> -value
Group- A(n=25)	242±35	0.0329 ^s
Group- B(n=25)	367±83	

S: significant denotes $p < 0.05$ Analysis were done by using Student's 't' test.

DISCUSSION:

The results from the present study show that haemodynamical stability and recovery status (both per- and post-operatively) from group-A population (propofol, midazolam and nalbuphine infusion) were

always satisfactory than that from group-B population (ketamine, diazepam and tramadol infusion). However, there was no clinically significant difference in arterial pressure among the groups

Day-care treatment has come to stay and economic and social pressures dictate that it will expand in the future. Although the importance of patient selection cannot be overemphasized, anaesthetists and their pharmaceutical colleagues must adapt their skills to meet the challenges of providing safe, smooth anaesthesia followed by a rapid, pain free recovery.

At the inception of day-care procedures, a case was considered suitable if it took less than 90 min. Procedures that are commonly selected today are those taking less than 60 min and which do not

cause severe haemorrhage or produce excessive postoperative pain⁵.

Many operations are performed at one-fifth cost of inpatient surgery if carried out on a day-case basis². Such type of day-case anaesthesia is only economical if it can be carried out safely. Problem is that none of the currently available anaesthetic agents have duration of action short enough to leave the patient with no residual effects within a few hours of surgery³. Propofol is having distribution and elimination half-lives of 1-2 minutes and 1-5 hours respectively and providing rapid recovery with minimal residual effects which is suitable for day-case anaesthesia²⁰. But high price of propofol is a hindrance to its use in day-case anaesthesia in our socioeconomic condition. On the other hand, though ketamine is much cheaper than propofol, but its elimination depends on the mixed-function oxidase system associated with the smooth endoplasmic reticulum. Its main metabolite, nor-ketamine has some hypnotic activity with a potency of around 30% of that of the parent drug and a longer elimination half-life. Both ketamine and nor-ketamine may be metabolised further to hydroxylated derivatives. These are subsequently conjugated and eliminated in the urine as glucuronides. Hence the efficacy of ketamine may be enhanced in patients with renal impairment¹³⁻¹⁴.

Nalbuphine is a potent semi-synthetic analgesic. It is equipotent with morphine and three to four times as potent as pentazocine. The opioid antagonist activity of nalbuphine is one-fourth as potent as nalorphine and 10 times that of pentazocine. It is an agonist at μ -receptors, an antagonist at m -receptors and has no effects on α -receptors¹². Analgesic tolerance is uncommon and nalbuphine has low abuse potential. Devoid or much less respiratory depression property makes the drug as one of the popular choice for maintaining analgesia in the day-case surgery. On the other hand, good results have been published for cancer pain management with tramadol in several studies. Tramadol can be recommended as a safe and efficient drug for step II according to the World Health Organisation guidelines²¹.

Optimum prerequisite for agents of day-case anaesthesia is early discharge & cost effectiveness. Extrapolation of our data suggests that there is significant difference ($p < 0.05$) between the two study

groups of observation (propofol-midazolam-nalbuphine and ketamine-diazepam-tramadol) in day-case anaesthesia.

Postoperative complications like airway obstruction, hypoxia, and hypoventilation are quite common in the recovery period². Many of the death occur in the postoperative ward due to inadequate recovery from anaesthesia². To reduce mortality and morbidity due to inadequate recovery, various recovery scoring systems are used namely SOCA, modified Steward Coma scale, ABC score, clinical scoring system etc^{23,24,25,19}. Many workers have compared various recovery scoring system. In this study, it is tried to compare the haemodynamic and recovery status in day-case anaesthesia between infusion of propofol, midazolam, nalbuphine and ketamine, diazepam, tramadol. Recovery time and quality varies with the techniques used and the recovery time was recorded as per SOCA²³ recovery scoring system and home readiness time was recorded as per clinical scoring system¹⁹.

The characteristic of the population among the two groups of this study was same. Immediately after reversal, the recovery time is significant ($p < 0.05$) between the two groups of observation (group-A and group-B). In group-A (propofol, midazolam and nalbuphine) patients, the cardiovascular parameters remained stable and there was no respiratory and cardiovascular depression. Blood pressure and heart rate were not changed remarkably during induction, intubation, maintenance and after recovery on all reading points, i.e. immediately after reversal. The recovery is slightly prolonged in group-B (ketamine, diazepam and tramadol) than group-A and the difference is significant ($p < 0.05$).

The difference between preoperative and after reversal mean value of SBP, DBP, HR is significant ($p < 0.05$) in group-A and group-B patients. But the differences between in group-A and group-B patients of same values and at the same point are significant in initial 5-6 reading points. Those were not significant in later half of the study.

Recovery from group-A population is slightly better than that of group-B in terms of cardiovascular stability, its recovery time as expected with clear-headed recovery. The time for home readiness is less in case of group-A (mean time 242 ± 35 minutes) than that with group-B (mean time 367 ± 83 minutes). But if the cost is considered, then the

agents of the later group (group-B) are much more economic than the agents of group-A. The extended time that is required for home readiness in group-B is not that much lengthier.

In the LDC countries like Bangladesh with low economic status, cost of drugs is a matter of consideration during operative procedures. Though, group-A agents are proved to be good for day case anaesthesia regarding its recovery criteria/profile, its cost is very much higher (almost 05 times) than that of group-B agents. In our study, it was found that the price of the agents used for per person in group-A was taka 868.00 and the price of the agents used in group-B was taka 168.00 for each patient i.e. 18.894% of group-A.

CONCLUSION:

In conclusion, it would appear that there could be substantial clinical and financial benefits in developing a day case surgery unit. From this study it may be concluded that haemodynamical stability and recovery status (both per- and post-operatively) from group-A population (propofol, midazolam and nalbuphine infusion) were always satisfactory than that from group-B population (ketamine, diazepam and tramadol infusion). Group-A drug regime ensures clear-headed recovery at a higher cost while recovery score with group-B drug regime is not too far at a much lower cost. Regarding the discharge criteria, it is almost same in two groups. By using ketamine, diazepam and tramadol combination (group-B), we can reduce the cost of anaesthesia, which is necessity for majority of patients in our country. On the other hand, propofol, midazolam and nalbuphine combination (group-A), a costlier regime appears suitable for the patients from affluent population. Both the regimes can be practiced with safety.

REFERENCES:

1. Stuart Ackerman MD. Outpatient Anaesthesia. Clinical Anaesthesiology, 3rd Edition. Lange Medical Books 2002; 882-888.
2. Miller RD (ed). Anaesthesia, 4th Edition. New York: Churchill-Livingstone 1994.
3. Cooper G. Recovery from Anaesthesia, Recovery Rounds. England: Imperial chemical industries PLC 1986; 19:3-7.

4. Monteiro JN. Ambulatory anaesthesia offers low cost and low infection rate. Express Healthcare Management 2005 (From internet).
5. Hitchcoch M, Ogg TW. Anaesthesia for day-case surgery. British Journal of Hospital Medicine 1995; 54: 2002-2006.
6. Hartmannsgruber MWB, Schulte-Steinberg H, Conzen P, Doenicke A. New intravenous induction agents. In: Frink EJ, Brown BR, eds. *Bailliere's Clin Anaesthesiol* 1995; 9: 51-66.
7. Myles PS, Hendrata M, B Ennett AM, Langly M, Buckland MR. Postoperative nausea and vomiting. Propofol or thiopentone: Does choice of induction agent affect outcome? *Anaesth Intensive Care* 1996; 24: 355-9.
8. Vicker M.D, Morgan M, Spencer P.S.J. Central nervous system depressants. In: Drugs in Anaesthetic and intensive care practice. Butter worth-Heinemann. 1999; 70-119.
9. Ahmed N and Khan F.A. Evaluation of oral midazolam as premedication in day care surgery in adult Pakistani patients. *JPMA* 1995; 45(9): 239-241.
10. Devis PJ, Tome JA, McGowan FX. Preanaesthetic medication with intranasal midazolam for brief paediatric surgical procedures. *Anaesthesiology* 1995; 82(1): 2-5.
11. Prescription drug information for consumers & professionals. Data last updated 15 August 2005 (from internet).
12. Acorus therapeutics limited. Document last updated 03 October 2005 (from internet).
13. Oye I, Ketamine analgesia. NMDA receptors and the gates of perception. *Acta Anaesthesiol Scand* 1998; 42: 747-9.
14. Articles in: White PF, ed. Kinetics of Anaesthetic drugs in clinical Anaesthesiology. In: *Bailliere's Clin Anaesthesiol* 1991; 5.
15. Reynolds JEF, Martindale. The Extra Pharmacopoeia 1993. London: The Pharmaceutical Press; 586.
16. Hori M, Satoh S, Maibach HI, Guy RH. Enhancement of propranolol hydrochloride and diazepam skin absorption in vitro: effect of enhancer lipophilicity. *J Pharm Sci* 1991; 80(1):32-35.

17. Stankov G, Schmieder G, Lechner FJ, et al. Observer-blind multicentre study with metamizole versus tramadol in postoperative pain. *Eur J Pain* 1995; 16:56-63.
18. Chrubasik J, Buzina M, Schulte-Mönting J, et al. Intravenous tramadol for post-operative pain - comparison of intermittent dose regimens with and without maintenance infusion. *Eur J Anaesth* 1992; 9:23-28.
19. Marshall S, Chung F. Assessment of 'home readiness': discharge criteria and post discharge complications. *Current Opinion in Anaesthesiology* 1997; 445 – 450.
20. Yentis SM, Hirsch NP, Smith GB. Day-case surgery. *Anaesthesia and Intensive Care A-Z, An Encyclopaedia of Principles and Practice*. London: Butterworth Heinemann; 2004: 152 – 153.
21. Hennies HH, Friderichs E, Schneider J. Receptor binding, analgesic and antitussive potency of tramadol and other selected opioids. *Drug Res* 1988; 38:877-880.
22. Amrcin R, Hatzel W. Pharmacology of drugs frequently in ICU midazolam and flumazenil. *Intensive care medicine* 1991; 17: S1-S10.
23. Alon F, Baitfella L, Hossli G. Double blind study of the prevalence of midazolam supplemented general anaesthesia with RO 15-1788. *Br J Anaesthesia* 1987; 59: 455.
24. Salem M. Post Anaesthetic Recovery. *Br J Anaesthesia* 1988; 61: 241 (Letter).
25. Robertson CS, MacGregor DM, Jones CJ. Evaluation of doxapram for arousal from general anaesthesia in out patient. *Br J Anaesthesia* 1986; 49: 133.

Original Article

COMPARISON OF ONDANSETRON AND ONDANSETRON PLUS ALPRAZOLUM FOR PREVENTION OF NAUSEA AND VOMITING FOLLOWING ELECTIVE CAESAREAN SECTION

Md. Rafiqul Hasan Khan¹, S.N. Samad Choudhury²

SUMMARY

Pregnancy & operation both causes anxiety. Excessive anxiety & noncompliance with fasting can increase gastric volume & predispose patients to postoperative nausea & vomiting. Prevention rather than treatment of postoperative nausea and vomiting should be the anesthetist's aim.

It was a prospective double blind comparative study of 60 parturient scheduled for elective caesarean section under subarachnoid block to see the effect of anxiolytic drug on per & PONV in LUCS. We have carried out comparative study with alprazolam as anxiolytic agent & compared the action of Ondansetron with Ondansetron +alprazolam. Parturient at term or elective caesarean section included in the study were ASA grade I & II.

A total of 60 cards, 30 in each group were prepared by another person who was blind for the study. Every parturient was allowed to draw one card and grouped accordingly. Group A: Inj. Ondansetron (8mg), Group B: Oral alprazolam (0.25mg) +inj. ondansetron (8mg). After 20 minutes of pre-hydration under all aseptic precaution lumbar puncture was performed with 25 gauge Quincke's needle in the L3-L4 or L4-L5 space in sitting position and 0.5% Hyperbaric Bupivacaine 2.5 ml (12.5 mg.) was injected within 10-12 sec. Immediately after administration of spinal anaesthesia fetal heart rate was noted for any changes in pulse rate, blood pressure, rate of respiration, discomfort and occurrence of side effects: shivering, nausea, vomiting was recorded every 2 minute for first 10 minutes, then at 10 minutes interval for remainder of the operation.

Per operative monitoring such as ECG, continuous SpO₂, non invasive arterial blood pressure was recorded each two minutes interval from time of intrathecal injection up to 10 minutes and then at 10 minutes interval until the end of operation. In the recovery room postoperative analgesia was provided with injection ketorolac tromethamine 30 mg IM on complaining pain and repeated in all patients if necessary. Presence of nausea and vomiting patients were interviewed at one hourly over the first 3 hours then at 3 hourly up to 24 hours postoperative period. Rescue antiemetic of prochlorparazine 10 mg I/M was given if vomiting occurs once, nausea for 10 minutes or at the patient request. Rest other parameters as for example; heart rate, BP, respiration and SpO₂ were also recorded at same interval. Patients were carefully observed for any adverse effects like headache, flushing, drowsiness or any other symptoms.

In the present study incidence of nausea and vomiting in group-A was one and in group-B was zero. Regarding hemodynamic changes (Pulse, Blood pressure) SpO₂, respiratory changes, during operation and 24 hours post operative period in some occasions significant changes were observed (P<0.05) but in other occasions no significant changes occur. No other adverse effect like headache, constipation and flushing during operation and 24 hours postoperative period were observed in this study.

In this study we have found that Ondansetron reduces peroperative and postoperative nausea and vomiting. But addition of Alprazolam (an anxiolytic) to Ondansetron, the chance of nausea and vomiting was less.

1. Assistant Professor, Department of Anaesthesia, Bangladesh Medical College, Dhanmondi, Dhaka
2. Professor & Head, Department of Anaesthesia, Dhaka National Medical College & Hospital

INTRODUCTION

Nausea is the subjective, unpleasant sensation of the desire to vomit but without any attempt at expulsive movement, frequently accompanied by salivation, sweating, tachycardia, and change in rate and depth of respiration.¹ It may be brief or prolonged, often occurring in waves and preceding vomiting or occurs in isolation.

Vomiting is a reflex mechanism integrated in the brain stem, by means of which the gastrointestinal tract rids itself of its contents in an attempt to rid the body of toxic harmful material when almost any part of the gastrointestinal tract becomes excessively irritated, over distended or even stimulated-by surgery, pregnancy, radiation, anesthesia, etc.²

Vomiting should not be confused with regurgitation or gastro oesophageal reflux neither of which is an active process like vomiting and retching. Emesis is a natural response that may be regarded as body's defense system against ingested toxins, But in spite of advancement in prevention and treatment, nausea and vomiting still occur in unacceptable frequency in association with surgery and anaesthesia and the description of it as "big little problem"³ capsule much of the general perception.

Unrelieved pain is a common cause of postoperative nausea and vomiting and opioids, widely used in pain relief are also cause of postoperative nausea and vomiting. Postoperative nausea and vomiting is multifactorial. Several other causes are age, sex (female are 2-4 times more prone to postoperative nausea and vomiting), mental status, obesity, gastro paresis, previous anaesthesia with postoperative nausea and vomiting, hypoxia, hypotension, site, duration and type of operation. The current incidence of postoperative nausea and vomiting varies from 10 to 60% depending on the patient, type of surgery, and anaesthetics. However, the incidence is as high as 85% has been observed after ophthalmic surgery in children and 75% after gynaecological surgery⁴.

Although emesis is a common symptom of disease, side effect of many therapies, and result of natural stimuli (pregnancy, motion), the physiology of emetic mechanism has not been an area of particularly intense research since the classical studies of Wang and Borison in late 1940s and 1950s.⁵

The common cause of peroperative and PONV in LUCS under SAB is hypotension and vagal

irritation. By using vasopressor and anticholinergic drugs we can control peroperative and PONV. Sedatives and anxiolytic often have an anti-emetic effect by reducing psychological component of the nausea⁶. Sedatives & hypnotics are often used to control anticipatory nausea & vomiting⁷.

Though there is no such study available in LUCS under SAB but clinically we found that there are some possible factors such as physiological changes during pregnancy (distention of abdomen, compression of stomach, relaxation of lower oesophageal sphincter) which may contribute to PONV in LUCS under SAB. Though actual mechanism is not known but there may be some correlation between serotonin receptor (5HT₃) with PONV in LUCS under SAB. Ondansetron is approved for use in the prevention of nausea and vomiting associated with surgery⁸.

Pregnancy & operation both causes anxiety. Excessive anxiety & noncompliance with fasting can increase gastric volume & predispose patients to postoperative nausea & vomiting⁹.

Prevention rather than treatment of postoperative nausea and vomiting should be the anesthetist's aim. However, there is less agreed protocol as to which patients should receive preventive antiemetic therapy, but the relative indication for prophylaxis increases as the number of risk factors increase. Anti-emetics are occasionally used prophylactically to prevent postoperative nausea and vomiting, more often given postoperatively as treatment for postoperative nausea and vomiting. For prophylaxis to be acceptable, the drug must be effective, sufficiently long acting to last throughout the operative period, and especially without appreciable side effects⁷.

The introduction of an effective well-tolerated antiemetic would allow the prevention of postoperative nausea and vomiting and its related consequences, particularly for high-risk patient. The efficacy of antiemetic therapy for the prevention or treatment of postoperative nausea and vomiting may be enhanced by combination therapy. It makes pharmacological sense to administer drugs, which act at different receptors. Presently, there is considerable interest in this and most studies have found combinations to be significantly more efficacious than a single drug⁸. No study is available on anxiolytic drug to prevent peroperative & PONV.

Aim and objectives:

We had become interested to see the effect of anxiolytic drug on per & PONV in LUCS. We have carried out comparative study with alprazolam as anxiolytic agent & compared the action of Ondansetron with Ondansetron +alprazolam.

MATERIAL AND METHOD

Subject:

It was a prospective double blind comparative study of 60 parturient scheduled for elective caesarean section under subarachnoid block in the department of Anaesthesiology, DNMH and Dhaka.

Parturient at term of elective caesarean section willing to be included in the study are ASA grade I & II.

Patient who are unwilling to be included in the study, Bleeding diathesis, Eclampsia, COPD, Patient having H/O motion sickness, hormonal imbalance, disturb mental state, Operation continued more than one hour are excluded from the study.

Grouping:

A total of 60 cards, 30 in each group were prepared by another person who is blinded for the study. Every parturient was allowed to draw one card and grouped accordingly.

Group A: Inj. Ondansetron (8mg)

Group B: Oral alprazolam (0.25mg) +inj. ondansetron (8mg)

Method:

After taking informed consent from each parturient during preoperative visit she was instructed for overnight fasting. After lottery, patients in group A received orally Vitamin B₁ and Inj. Ondansetron and group B received orally alprazolam and Inj. Ondansetron. All drugs were given 30 minutes before operation. In the operation room an intravenous cannula (18G) was inserted and the patient was received IV pre-hydration with 15ml/kg body weight- Ringers lactate solution within 20 minutes. Pulse rate, blood pressure, rate of respiration was recorded before spinal anaesthesia and catheterization was done.

After 20 minutes of pre-hydration under all aseptic precaution lumbar puncture was performed with

25 gauge Quincke's needle in the L3-L4 or L4-L5 space in sitting position and 0.5% Hyperbaric Bupivacaine 2.5 ml (12.5 mg.) was injected within 10-12 sec. After noting the time of injection, patient was immediately placed in supine position. A wedge was placed under the right hip. All patient were received supplemental O₂ (4 liter per minute) via mask or nasal cannula. Immediately after administration of spinal anaesthesia fetal heart rate was noted for any changes in pulse rate, blood pressure, rate of respiration, discomfort and occurrence of side effects: shivering, nausea, vomiting was recorded every 2 minute for first 10 minutes, then at 10 minutes interval for remainder of the operation.

Per operative monitoring such as ECG, continuous SpO₂, non invasive arterial blood pressure was recorded each two minutes interval from time of intrathecal injection up to 10 minutes and then at 10 minutes interval until the end of operation. Hypotension defined as a decrease in systolic BP to less than 90mm Hg or a decrease of 20% from the baseline. APGAR score was observed but at 1 and 5 minutes after delivery of baby.

In the recovery room postoperative analgesia was provided with injection ketorolac tromethamine 30 mg IM on complaining pain and repeated in all patients if necessary. Presence of nausea and vomiting patients were interviewed at one hourly over the first 3 hours then at 3 hourly up to 24 hours postoperative period. Rescue antiemetic of prochlorparazine 10 mg I/M was given if vomiting occurs once, nausea for 10 minutes or at the patient request. Rest other parameters as for example; heart rate, BP, respiration and SpO₂ were also recorded at same interval. Patients were carefully observed for any adverse effects like headache, flushing, drowsiness or any other symptoms.

STATISTICAL ANALYSIS:

The data was collected in a pre designed 'Data collection form'. All data was compiled and analyzed using 't' test with the help of SPSS. The result was regarded as significant if P<0.05 or á Value of .05 with confidence interval 95%.

OBSERVATION & RESULTS:

All the observations were presented in a tabulated form. Observed parameters were expressed as mean±SEM.

The mean ages of Group-A and Group-B were 23.87 (± 0.96 SEM), 24.14 (± 0.67 SEM). The mean weight of Group-A, and Group-B were 62.63 (± 0.96 SEM) and 72.60 (± 0.93 SEM). The mean duration of surgery of Group-A and Group-B were 52.20 (± 0.96 SEM) and 44.50 (± 0.61 SEM). All this data were subjected to 't' test. The difference in two groups regarding age was not significant ($P > 0.05$), but it was significant ($P < 0.05$) regarding weight and duration of surgery.

Mean values of pulse rate at different occasions during surgery and 24 hours postoperative period were compared in two groups. The mean changes of heart rate per minute varied in group-A from 74.07 \pm 0.40 SEM to 105.13 \pm 0.93 SEM, In group-B from 83.87 \pm 1.42 SEM to 92.67 \pm 1.31 SEM. Significant changes were observed at 2 min, 8 min, 10 min, 20 min, 30 min, 40 min, 50 min, 12 hour, 15 hours, 18 hours, 21 hours, 24 hours, ($P < 0.05$). In other occasions no significant changes were observed ($P > 0.05$).

Mean values of SBP at different occasions during surgery and 24 hours post operative period compared in two groups. The mean changes of SBP varied in group A from 94.10 \pm 0.82 SEM to 119.00 \pm 0.56 SEM, In group – B from 103.17 \pm 1.93 SEM to 126.00 \pm 1.89 SEM. Significant changes were observed at 4 min, 10 min, 20 min, 30 min, 40 min, 50 min, at 1st hour, 2nd hour, 3rd hour ($p < 0.05$). In other occasions no significant changes were observed ($P > 0.05$).

Mean values of DBP at different occasions during surgery and 24 hours post operative period were compared in three groups. The mean changes of DBP per minute varied in group-A 60.00 \pm 0.00 SEM to 76.00 \pm 0.91 SEM. In group-B from 67.67 \pm 1.57 SEM to 82.83 \pm 1.72 SEM. Significant changes were observed at 10 min, 20 min, 30 min, 40 min, 50 min, 2nd hr, 24th hr ($p < 0.05$). In other occasions no significant changes were observed ($P > 0.05$) were compared in three groups. the mean changes of DBP per minute varied in group-Ave ($P > 0.05$).

Mean values of MBP at different occasions during surgery and 24 hours postoperative period were compared in two groups. The mean changes of MBP per minute varied in group-A from 71.53 \pm 0.31 SEM to 90.60 \pm 0.53 SEM, In group-B from 79.50 \pm 1.57 SEM to 97.22 \pm 1.61 SEM. Significant changes were observed at 10 min, 20 min, 30 min, 40 min, 50 min, 1st hr, 2nd hr, 3rd hr ($P < 0.05$). In other occasions no significant change were observed ($P > 0.05$)

Mean values of SpO₂ at different occasions during surgery and 24 hours postoperative period were

compared in two groups. The mean changes of SpO₂ per minute varied in group-A from 96.63 \pm 0.13 SEM to 99.03 \pm 0.08 SEM, In group – B from 97.30 \pm 0.12 SEM to 97.40 \pm 0.10 SEM. Significant changes were observed at 2 min, 4 min, 6 min, 30 min, 40 min, 50 min, at 9th hr, 15th hr, 18th hr, 21st hr, 24th hr ($P < 0.05$). In other occasions no significant changes were observed ($P > 0.05$).

Mean values of respiratory changes at different occasions during surgery and 24 hours post operative period were compared in two groups. The mean changes of respiratory rate per minute varied in group-A from 14.00 \pm 0.14 SEM to 15.57 \pm 0.10 SEM, In group B from 13.30 \pm 0.20 SEM to 14.00 \pm 0.26 SEM. Significant changes were observed at 2nd min, 4th min, 6th min, 8th min, 10th min, 20th min, at 6th hr, 12th hr, 15th hr, 18th hr, 21st hr, 24th hr ($P < 0.05$). In other occasions no significant changes were observed ($P > 0.05$).

In the present study incidence of nausea and vomiting in group-A is one and in group-B is zero.

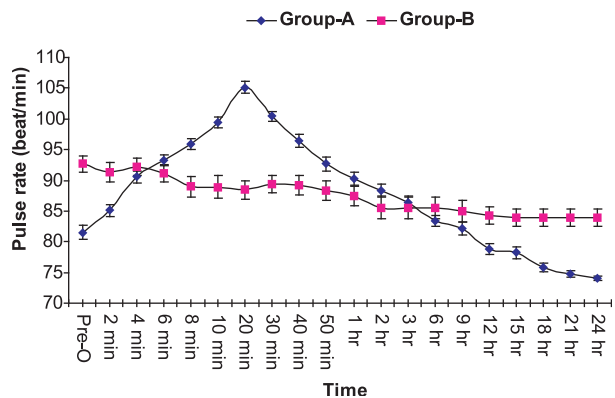


Fig.-1: Intra operative and post operative pulse rate changes of different groups

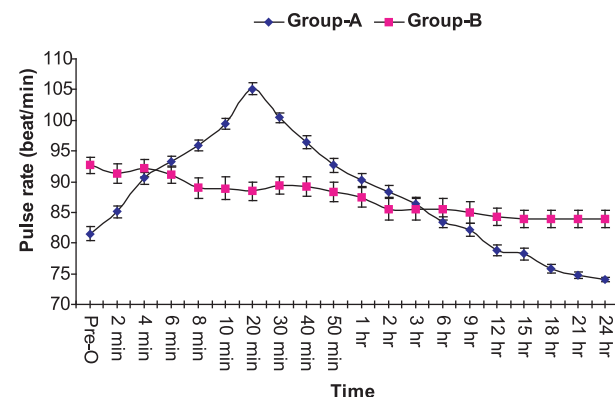


Fig.-2: Intra operative and post operative mean blood pressure changes of different groups

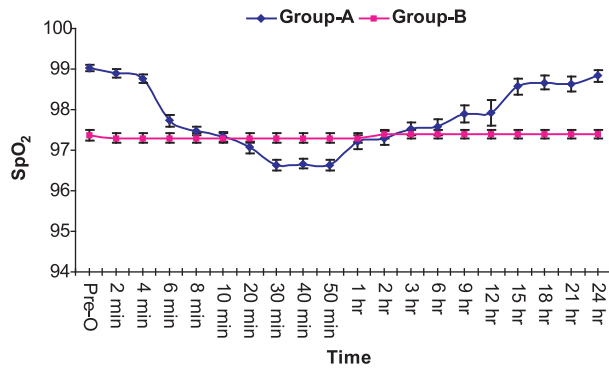


Fig.-3: Intra operative and post operative SpO₂ changes of different groups

DISCUSSION

Nausea and vomiting are common and sometimes dangerous side effects following surgery. Most of the incidence of nausea and vomiting occur during the first two hours of recovery from anaesthesia. The etiology of postoperative nausea and vomiting is multi-factorial. Many factor associated with anaesthesia and surgery may contribute to nausea and vomiting. In the present study concern factors are type of anesthesia, female patient and gynecological surgery. Incidence of nausea and vomiting is two to three times more in female due to changing endocrine environment which sensitize the brain stem emetic mechanism. During LUCS the regional anaesthesia as well as some traction of vagal innervated gut may play role in triggering emesis. The reported overall incidence of nausea and vomiting after gynecological surgery is 75%¹². In lower uterine caesarean section the incidence of nausea and vomiting is relatively more then other gynaecological procedure^{13, 14, 15}. The antiemetics are now mainstay of therapy to prevent PONV.

In the present study incidence of nausea and vomiting in group-A is one and in group-B is zero. In one study M Naguib¹⁶ with his co-worker shows that prophylactic antiemetic treatment with ondansetron resulted in a lower incidence of PONV than with metochlopramide and placebo in a randomized double blind comparative study on laparoscopic cholecystectomy.

In our study the incidence of PONV occurred within first two hours after surgery in group-A but in rest of the period no nausea and vomiting occur which is similar with the study of Dr. Bridges¹⁷. It has some dissimilarity with the study of Dr. Naguib¹⁸

and Dr. Dipasri Bhattacharya¹⁹. Most of the operations in previous study done under general anaesthesia. The aggravating factor for PONV in general anaesthesia are anaesthetics agents, distention by gas, per and postoperative use of narcotics. But in our study the possible aggravating factor are female patient hormonal changes, regional block, and vagal irritation. Excessive anxiety & noncompliance with fasting can increase gastric volume & predispose patients to postoperative nausea & vomiting²⁰. Sedatives& hypnotics are often used to control anticipatory nausea & vomiting²¹. Pregnancy & operation both causes anxiety. Excessive anxiety & noncompliance with fasting can increase gastric volume & predispose patients to postoperative nausea & vomiting²².

Prevention rather than treatment of postoperative nausea and vomiting should be the anaesthetist's aim. However, there is less agreed protocol as to which patients should receive preventive antiemetic therapy, but the relative indication for prophylaxis increases as the number of risk factors increase. Anti-emetics are occasionally used prophylactically to prevent postoperative nausea and vomiting, more often given postoperatively as treatment for postoperative nausea and vomiting. For prophylaxis to be acceptable, the drug must be effective, sufficiently long acting to last throughout the operative period, and especially without appreciable side effects²³.

The introduction of an effective well-tolerated antiemetic would allow the prevention of postoperative nausea and vomiting and its related consequences, particularly for high-risk patient. The efficacy of antiemetic therapy for the prevention or treatment of postoperative nausea and vomiting may be enhanced by combination therapy. It makes pharmacological sense to administer drugs, which act at different receptors. Presently, there is considerable interest in this and most studies have found combinations to be significantly more efficacious than a single drug²⁴.

No study is available on anxiolytic drug to prevent peroperative & PONV.

Regarding hemodynamic changes (Pulse, Blood pressure) SpO₂, respiratory changes, during operation and 24 hours post operative period in some occasions significant changes were observed (P<0.05) but in other occasions no significant changes occur.

No other adverse effect like headache, constipation and flushing during operation and 24 hours postoperative period were observed in this study.

Pain as well as commonly used analgesic pethidine may cause nausea and vomiting. For this reason postoperative control of pain we used ketorolac tromethamine as required instead of pethidine. We chose a single oral dose because it is easier to give one dose before operation. Involution of the uterus may not be affected by single dose of ketorolac. The study confirmed the previous study regarding the safety of the patient as side effects were mild.

Considering the above discussions, we have observed that Ondansetron reduces peroperative and postoperative nausea and vomiting. But addition of Alprazolam (an anxiolytic) to Ondansetron, the chance of nausea and vomiting is less.

However further work is required to compare between ondansetron and ondansetron plus alprazolam about their efficacy for prevention of PONV in LUCS under SAB.

CONCLUSION

As emesis is not caused by a single mechanism at a special site, remedies with various combinations of antiemetic and different mechanism of action may be promising.

In this study we have found that Ondansetron reduces peroperative and postoperative nausea and vomiting. But addition of Alprazolam (an anxiolytic) to Ondansetron, the chance of nausea and vomiting is less.

There was no evidence of any adverse side effects and whole of the operative period was smooth.

However, further work is required to compare the efficacy between ondansetron and ondansetron plus alprazolam for prevention of PONV in large scale.

REFERENCES

1. Gregory JC, Anaesthesia and gastrointestinal tract, Wylie and Churchill- Davidson eds, A practice of anaesthesia 5th ed. Singapore, publishing pte ltd. 1985; 939-853
2. Naylor R.J The role of 5HT₃ receptors in the pathophysiology of emesis, abstract book page 11, Netherlands congress, 16 June, 1992.
3. Kapur PA. The Big 'little problem': The Anesthesia and analgesia, 1991;73: 243-245.-916
4. Kraus GB, Giebner M, Palackal R. The Prevention of postoperative nausea and vomiting following strabismus surgery in children. *Anaesthetist*- 1991;40:92:95
5. Donald G. Carino, M.D. laparoscopy in anaesthesia secrets, 2nd edition; 397.
6. Colin Pinonock, Ted Lin, Tim Smith, fundamentals OF anaesthesia;672.
7. Bertram G. Katzung, Basic & Clinical Pharmacology; 1070.
8. Bertram G. Katzung, Basic & Clinical Pharmacology; 282.
9. Fun-Sun F. Yao, M.D. Yao&Artusio's, Anesthesiology, Problem-Oriented Patient Management, 5th editio; 1152.
10. Rowbotham, DJ, Nausea, vomiting and their treatment, Aitkenhead AR Graham Smith, Textbook of Anaestheis 4th Edition p-244-245. Churchill livingstone, 2001; 244.
11. Alan R. Aitkenhead, David J. Rowbotham, Graham Smith, testbook of Anaestheisa 4th edition; 249.
12. Kraus GB, Giebner M, Palackal R. The Prevention of postoperative nausea and vomiting following strabismus surgery in children. *Anaesthetist*- 1991;40:92:95
13. Wang J.J, Ho TS, Liu SH and Ho MC. Prophylactic antiemetic effect of dexamethasone in women undergoing ambulatory laparoscopic surgery. *Br J Anaesth* 2000, 48(4): 459-62
14. Jimenez- Jimenez FJ, Garcia Ruiz PJ, Molinaja. Drug induced movement disorder. *Drug safety* 1997; 180-204.
15. Watcha MF, White PF. Post operative nausea and vomiting. Its etiology, treatment and prevention. *Anesthesiology* 1992; 77:162-184.
16. M Naguib, AK el Bakry, MH Khoshim, AB Channa, M el Gammal, K el Gammal, YS Elhattab, M Attia, R Jaroudi and A Saddique, Prophylactic antiemetic therapy with ondansetron, tropisetron, granisetron and metoclopramide in patients undergoing laparoscopic cholecystectomy: a randomized, double-blind comparison with placebo. Department of Anaesthesia, Surgery, Faculty

- of Medicine, King Khalid University Hospital, Riyadh, Saudi Arabia.
17. John D. Bridge, BS (Pharm), Cindy B. Nettle, PharmD, Vijaya J. Dugirrala MD, Katie J. Suda, PharmD, Kevin W. Garey, PharmD, Low-dose Granisetron for the Prevention of Postoperative Nausea and Vomiting, *The Journal of Applied Research*, Vol. 6, No. 3, 2006.
 18. M Naguib, AK el Bakry, MH Khoshim, AB Channa, M el Gammal, K el Gammal, YS Elhattab, M Attia, R Jaroudi and A Saddique, Prophylactic antiemetic therapy with ondansetron, tropisetron, granisetron and metoclopramide in patients undergoing laparoscopic cholecystectomy: a randomized, double-blind comparison with placebo. Department of Anaesthesia, Surgery, Faculty of Medicine, King Khalid University Hospital, Riyadh, Saudi Arabia.
 19. Dr. Dipasri Bhattacharya, Dr. Arnab Banerjee, Comparison of Ondansetron and Granisetron for prevention of Nausea and Vomiting Following day care Gynaecological Laparoscopy. *Indian J. Anaesth.* 2003; 47 (4): 279-282
 20. Colin Pinonock, Ted Lin, Tim Smith, *FUNDAMENTALS OF ANAESTHESIA*;672.
 21. Bertram G. Katzung, *Basic & Clinical Pharmacology*; 1070.
 22. Fun-Sun F. Yao, M.D. Yao & Artusio's, *Anesthesiology, Problem-Oriented Patient Management*, 5th editio; 1152.
 23. Rowbotham, DJ, Nausea, vomiting and their treatment, Aitkenhead AR, Graham Smith, *Textbook of Anaestheis* 4th Edition p-244-245. Churchill livingstone, 2001; 244.
 24. Alan R. Aitkenhead, David J. Rowbotham, Graham Smith, *testbook of Anaestheisa* 4th edition; 249.

Article of Special Interest

ANAESTHETIC MANAGEMENT FOR HAND ASSISTED LAPAROSCOPIC ENUCLEATION OF PANCREATIC INSULINOMA

AKM Akhtaruzzaman¹, Satyajit Dhar², AKM Asaduzzaman³, Md Abdus Samad⁴,
Manzoorul Haq Laskar⁵, Mustafa Kamal⁶, Md A Hye⁷

Key words: Insulinoma; laparoscopic surgery; hypoglycemia; anaesthetic management

INTRODUCTION:

Insulinoma is a rare tumour of the islet cells of the pancreas and was first described by Harris¹ in 1924. The incidence is 1–4 per million and male to female ratio is 2:3. The average age of presentation of the disease is fifth decade². They are typically sporadic, solitary and less than 2cm in diameter. About 90% of Insulinoma are benign and approximately 10% are malignant. These tumors produce large amounts of insulin which lowers blood glucose level opposite the diabetes mellitus.

Patients with Insulinoma usually develop neuroglycopenia and sympathoadrenal symptoms; these include hypoglycemia, recurrent headache, lethargy, Diplopia and blurred vision particularly with exercise or fasting. Severe hypoglycemia may result in seizures, coma and permanent neurological damage. Weight gain occurs in 20 - 40% of patients. Insulinoma are characterized clinically by the Whipple triad of episodic hypoglycemia, CNS dysfunction temporally related to hypoglycemia and dramatic reversal of CNS abnormalities by glucose administration.

Medications such as diazoxide and somatostatin can be used to block the release of insulin for patients

who are not surgical candidates or who otherwise have inoperable tumour. The definitive treatment is surgical removal of the adenoma or either subtotal or total pancreatectomy. Most patients with benign Insulinoma can be cured with surgery³. Laparoscopic approach has been applied in the management of patients with pancreatic disease. In this patient pancreatic insulinoma was successfully enucleated by laparoscope. Persistent or recurrent hypoglycemia after surgery tends to occur in patients with multiple tumors. About 2% of patients develop diabetes mellitus after surgery.

In this report, we describe the anaesthetic management of a patient with pancreatic Insulinoma enucleated laparoscopically.

CASE REPORT:

A 32-year old male weighing 71kg was admitted to the Hepatobiliary and Pancreatic Surgery unit, Department of Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh on January 13, 2008 with the history of repeated attack of headache, vomiting, restlessness, convulsion and unconsciousness several times in three and half years. The frequency of above episodes was typically occurs in the morning. Over the last six to eight

-
1. Associate Professor, Department of Anaesthesia, Intensive Care and Pain Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh.
 2. Resident, Department of Anaesthesia, Intensive Care and Pain Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh
 3. Consultant, Department of Anaesthesia, Intensive Care and Pain Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh
 4. Lt. Col, Department of Anaesthesiology, BNS Patanga, Chittagang
 5. Consultant, Department of Anaesthesia, Intensive Care and Pain Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh
 6. Assistant Professor, Department of Anaesthesia, Intensive Care and Pain Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh.
 7. Associate Professor, Department of Anaesthesia, Intensive Care and Pain Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh.

months the episodes were increasing in frequency and occurred in throughout the day. The patient was admitted to the Department of Neurology for further evaluation. His haemodynamic status was normal, ECG, EEG finding were also normal. His plasma fasting insulin level was 48.2 μ U/ml (reference value- 2-25 μ U/ml) and plasma fasting glucose 0.7mmol/L. With the help of biochemical test, USG, CT scan and MRI it was diagnosed as a case of Insulinoma in the region of head of the pancreas measuring of 2 \times 1.5 cm.

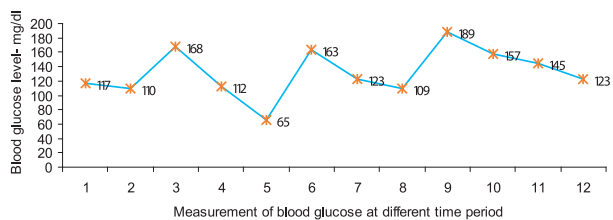
ANAESTHETIC MANAGEMENT

After pre-anaesthetic evaluation and optimization of patient was scheduled for elective surgery for hand assisted laparoscopic enucleation of Insulinoma on 2nd February 2008. The patient was allowed to take dinner at 10.00 pm day before operation. Intravenous infusion of 10% Dextrose in aqua started @ 30 drops per minute from 12:00 midnight. Patient arrived at operation theatre at 8.00 am. Fasting blood sugar was done and 10% Dextrose in aqua continued @ 30 drops per minute up to thirty minutes of removal of the tumour. Rapid infusion of 150ml of 10% Dextrose in Aqua during the handling of the tumour and thereafter it was stopped. Another IV channel established with 18G cannula and Hartman's solution started @ 10 drops per minute. Premedication was done with 5mg diazepam at night and 5mg diazepam in the morning. After pre-oxygenation for three minutes, induction of anaesthesia was done with Inj. Propofol and tracheal intubation with succinylcholine. Maintenance of anaesthesia was done with O₂, N₂O, Halothane, Inj. Fentanyl and Inj Vecuronium. Monitoring was done with pulse, NIBP, SpO₂, ECG, urine output and capillary blood glucose every 30 minute keeping short acting insulin ready for emergency use.

At the end of the surgery, the residual effect of vecuronium was reversed with Inj. neostigmine bromide 2.5mg and Inj. atropine sulphate 1.2mg. Patient was extubated smoothly after fulfilling the extubation criteria. Post-operative analgesia was ensured with IM pethidine hydrochloride 100 mg stat and per rectal diclofenac 50mg twice daily. With stable vital signs and SpO₂ patient was transferred to High Dependency Unit. Propped up position with 4 L O₂ by face mask was instituted for first 3 hour of postoperative period. Postoperative fluid was 1000 ml of 5% dextrose in aqua, 1000ml of 5% dextrose

in normal saline and 1000ml of Hartmann solution @ 30 drops per minute in the first postoperative day. At the HDU monitoring of heart rate, noninvasive blood pressure, SpO₂, urine output and capillary blood glucose every 2 hourly continued. Patient was shifted to surgical ward after 24 hours of surgery and advised to continue measuring of blood glucose level two hourly for another 48 hours and then three time daily for whole postoperative period.

Total duration of anaesthesia was 270 minutes and total duration of operation was 210 minutes. Histological examination of the dissected specimen disclosed as pancreatic endocrine neoplasm. The patient was discharged from the hospital after 10 days of operation.



- | | |
|------------------------|-----------------------------|
| 1. Pre-operative night | 7. Before Reversal |
| 2. In the morning | 8. After extubation |
| 3. Before induction | 9. 2 hrs after extubation |
| 4. Before Enucleation | 10. First postoperative day |
| 5. During Enucleation | 11. 2nd postoperative day |
| 6. After Enucleation | 12. 3rd postoperative day |

Fig 1: Blood glucose level at different time interval

DISCUSSION:

The maintenance of peri-operative adequate blood glucose level is the primary importance in the anaesthetic management of a patient of Insulinoma. The patient can go into hypoglycaemic attacks during perioperative period if glucose is withheld over a long period of time or the patients are kept fasting for a long period. Hargadon and Ormston reviewed the effect of glucose deprivation on blood glucose level in their study and confirmed the above statement⁴. Now a day's perioperative maintenance of near normal glucose level is possible by frequent measurement of capillary blood glucose level in the operating theatre. Adezati has been suggested perioperative steroid therapy during Insulinoma surgery in the view of adrenocortical suppression⁵. But its value is doubtful and sometimes it may be

harmful. Corticosteroid therapy may lead to hyperglycemia in the postoperative period and there is an increased chance of infection. Pramila Chari et al. advocated use of bolus corticosteroid in their case report⁶. In our case, we avoid use of steroid in the view of promoting infection and could produce unnecessary hyperglycemia. On the other hand it took 10-12 days for the blood glucose level to come within normal limits. During the course insulin requires rarely.

References:

1. Harris S. Hyperinsulinoma and dysinsulinoma. *Journal of the American Medical Association*. 1924. 83: 729.
2. Pandey D, Sharma B, Kumar S, Chauhan V, Gupta D, Sharma A. Insulinoma presenting with psychiatric symptoms. *Journal of Indian Academy of Clinical Medicine*. 2004. 5 (1): 72-74.
3. Fraser RA. Hyperinsulinism under anaesthesia in a case of islet cell tumour of the pancreas. *Anaesthesia*. 1963:18:3.
4. Hargadon JJ, Ormston TOG. Anaesthesia for excision of islet cell tumour of the pancreas-case report. *Anaesthesia*. 1963:36: 807.
5. Adezati L. Adrenal steroid and adipose tissue. In: *Hormonal steroids: biochemistry, pharmacology and therapeutics: proceeding of the first International Congress on Hormonal Steroid*, Milan. Ed. By L Martini & A Pecile: Vol-1, p-317. Academic Press, London.
6. Pramila Chari, SK Pandit, RN Kataria, Hariwir Singh, DK Baheti, Jyotsna Wig. Anaesthetic management of insulinoma. *Anaesthesia*, 1977:32:261-264.

Case Report

NEUROPATHIES IN SEPSIS: A DIFFICULT SITUATION TO WEAN FROM VENTILATOR.

Md. Mozaffer Hossain¹, SMA Alim², Muslema Begum³, Nasiruddin Ahmed⁴, UH Shahera Khatun⁵

ABSTRACT:

Neuromuscular weakness in critically ill patients is diagnostic challenge. Septic Polyneuropathy is an important cause of failure to wean from artificial ventilation. We studied patient of septic polyneuropathy to highlight the importance of regular neurological examination in the early diagnosis of this conditions. Availability of facilities for bed side electrophysiological study & histopathology of muscle are important to diagnose these entity. A 56 years old lady was admitted in gastro-enterology unit with complains of abdominal pain & fever, subsequently she was diagnosed as a case of burst appendix with septicemia in Surgery Unit. Appendicectomy and surgical toileting was done under general anaesthesia. In the early post-operative period the patient developed respiratory failure and was transferred to ICU. She was on ventilator for a long time with all other investigation electrophysiological study of nerve conduction showed septic polyneuropathy. On 21st POD the patient could be withdrawn from ventilator and after T-piece trial extubation was done on the next day. Neuropathies in sepsis, an important cause of failure to wean from ventilator, a high index of suspicion and regular bed side neurological & electrophysiological examination is required to make an early diagnosis.

INTRODUCTION:

A number of disorders producing generalized neuromuscular weakness specifically associated with critical illness, these include neuropathies, myopathies & combinations of both¹.

Sepsis, neuromuscular blocking drugs (NMBA), disuse atrophy, asthma, corticosteroids, & the multiorgan failure have all been implicated. Two major subgroups are outlined. One is critical illness

polyneuropathy (CIP) which is acute, diffuse mainly motor neuropathy is the commonest of these disorders, another is critical illness myopathy which is linked with asthma and with the use of corticosteroids,

NMBA and less convincingly, aminoglycosides and beta-adrenergic agonists.

In spite of existing knowledge of the condition, it is rarely diagnosed. Availability of facilities for bedside electrophysiological studies & histopathology of muscle are important to diagnose this entity².

We discuss the presentation, diagnosis and outcome of a patient with Septic Polyneuropathy with an aim to highlight the importance of regular neurological examination in the early diagnosis of this condition, as it might have a bearing on the management and prognosis of critically ill patients.

Case Report:

A 56 years old lady named Mrs. Tahera Malek, C/O Mr. G M Faruk, Mohammadpur, Dhaka was brought to Dhaka Medical College Hospital under gastroenterology unit on 10.04.08 with the complains of abdominal pain for 10 days and fever for seven days. In gastroenterology unit the patient was diagnosed as acute pancreatitis with hypokalemia with pseudocyst and treated accordingly. She was a known case of DM and hypertension. Aspirate from abdominal cavity examined for cytology & bacteriology. Gm(+ve), gm(-ve), bacteria and pus cell (+++) were present. No malignant cell was found. Injectable antibiotics were given with all other management.

But pain did not subside and then consulted with gynae & obs. unit and also with surgical unit. Patient was referred to surgical unit where she

1. Consultant, Dept of Anaesthesiology & ICU DMCH, Dhaka
2. Anaesthesiologist, Dept of Anaesthesiology & ICU DMCH, Dhaka
3. Anaesthesiologist, Dept of Anaesthesiology & ICU DMCH, Dhaka
4. Anaesthesiologist, Dept of Anaesthesiology & ICU DMCH, Dhaka
5. Professor, Dept. of Anaesthesiology & ICU, DMCH, Dhaka

diagnosed as intrabdominal abscess and decided for laparotomy. Patient was critically ill and was in septic condition. Just before operation patient was semiconscious, BP-160/90mmHg, pulse-132/min, R/R -20/min, RBS-9.5mmol/L, SPO₂-83%, ASA-4E. Then O₂ given by face mask @ 6 L/min and found SPO₂ 98%, pulse 120/min BP-140/90mmHg. On 20.04.08. Induction of anaesthesia was done with inj. Propofol, Fentanyl & vecuronium & was maintained with 50% N₂O with O₂, vecuronium & halothene.

During laparotomy it was found that there was collection of pus in the ilio-cecal region, appendix was burst and gangrenous condition. Appendisectomy and surgical toileting was done and intrabdominal drainage was given. During operative procedure haemodynamic condition was stable.

Unfortunately patient developed respiratory failure in the early post operative period. Patient was transferred to ICU with following condition: Pulse 123/min, BP- 200/90mmHg, heart-NAD, lungs-clear, SPO₂ 95% with 100% O₂ with Bain circuit & controlled ventilation with muscle relaxant.

At ICU patient was managed as continuous Controlled ventilation with inj. PCB then gradually weaning by assessing the capability of the patients to maintain SPO₂ with less external support. On 1st POD patient was unconscious on assist controlled ventilation, pulse-70/min, BP- 170/90mmHg, Temp-98° F. On 2nd POD patient come conscious, gain respiratory effort, ventilator set with SIMV mode with FiO₂ .7, SPO₂ 95%, pulse-100/min, BP- 120/70mmHg. But on 3rd POD patient develop respiratory distress, suction given, 100% O₂ given through Bain circuit & nebulization done. Respiratory distress dose not subside so put on ventilator with A/C mode again. Investigation CBC, serum creatinine, serum Urea, serum Electrolytes, ABG, RBS, Blood for MP (thick & thin film), ICT for p. falciparum, ECG, EMG, USG of whole abdomen, CXR done. All investigation was within normal limit except hypokalaemia which was corrected & electrophysiological study of nerve condition shows septic polyneuropathy. On 10th POD temp suddenly raised to 104° F. All investigation done repeatedly on every alternate day which was within normal limit. Temp become normal on next day (11th POD) but ventilatory support can not be withdrawn for many days. On 15th POD ventilatory

support was withdrawn, O₂ was given through T-piece with spontaneous respiration. Respiratory distress in spont. resp. through T-piece so patient again put on ventilator with SIMV.

Ventilatory support off on 21st POD & patient was kept spontaneous respiration through T-piece with O₂ 5 L/min and extubation done on 22nd POD (10.05.08), O₂ given by face mask.

Next 3 days followed up at ICU on 24th POD patient was transferred to surgical ward with following parameters:

Patient was conscious

Respirate spontaneously,

R/R-14/min

SPO₂ 97%

BP- 100/70 mmHg

DISCUSSION:

Neuropathies in sepsis, an important cause of failure to wean from assisted ventilation are often missed due to lack of suspicion and initiative to undertake regular bedside neurological and electrophysiological examinations in critically ill patients. A high index of suspicion is required to make an early diagnosis⁽²⁾. Sepsis neuromuscular blocking agents (NMBA), disuse atrophy, asthma, corticosteroids and the multiorgan dysfunctions syndrome (MODS) have all been implicated. In CIP there is flaccid paralysis of all the four limbs and absent deep tendon jerk⁽³⁾.

The frequency of CIP is approximately 70% in patient with sepsis. Prospective studies have explored the causality and clinical outcome of CIP. Clinical outcome of patients and CIP includes difficulty weaning from mechanical ventilation, increased length of stay, prolonged recovery and an overall mortality rate of 26-71%.

Hyperglycemia, sepsis and decreased serum albumin concentration are associated with decrease in peripheral nerve function. Cytokines secreted in sepsis increases microvascular permeability leading to endoneurial oedema which causes hypoxia leading to axonal degeneration.

In 1984, Botton *et al* reported five cases who were critically ill and had difficulty in weaning from mechanical ventilation. These patients had sensory motor weakness and electrophysiological studies revealed primary axonal neuropathy.

Neurological evaluation of such patient is often difficult because of ventilatory support and other equipment attached to the patient. The present case had difficulty in weaning from mechanical ventilation and developed hypercarbia when put on a T-piece trial in spite of fulfilling all other criteria for weaning.

From India two case reports of CIP found. One in a patient with asthma and the other in a patient with renal failure. Primary axonal degeneration has been reported in 70% of critical ill patients and sepsis & multiorgan failure of which 30% had weakness of clinical examination.

Electrophysiological studies were consistent with predominantly motor axonal polyneuropathy and were very helpful in confidently making the diagnosis of CIP. In one study of survivors of at least 28 days of ICU treatment, nearly all patients displayed electrophysiological evidence of chronic partial denervation 05 (five) years after ICU discharge.

Another prospective evaluation confirmed the association between multiorgan failure, sepsis and CIP. According to clinical and electrophysiologic testing Ninety four percent of septic patients diagnosed with CIP.

No specific therapies are available but most patients improve after a period of supportive care. The condition is reversible, hence intensive physiotherapy and extended rehabilitation should be continued until the neuropathy improves adequately

REFERENCES:

1. G Skowronski Neuromuscular diseases in intensive care. Oh's Intensive Care Manual, 5th edition ;47;537-47.
2. G.C. Khilnani ,Ravi Bansal ,O.P. Malhotra How often do we Diagnose It? Indian J.Chest Dis Allied Sei 2003; 45:209-213.
3. Nates JL,Cooper DJ Day B, Tuxen DV 1997. Acute weakness syndromes in critically ill Patients – a reappraisal. Anaesth Intens Care. 25:502-13.
4. Sliwa JA 2000. Acute weakness syndromes in the critically ill patient. Arch Phys Med Rehabil. 81: 545-52.
5. Will NJ, Zochodne DW, Bolton CF *et al* 1991. Peripheral nerve function in sepsis and multiple organ failure, Chest: 99; 176-84.
6. Bolton CF, Gilbert JJ, Halin AF, Sibbald WJ 1984. Polyneuropathy in critically ill patients. J, Neurol Neurosurg Psychiat. 47: 1223-31.
7. DR. John Griffiths. Critical illness poly-neuropathy and myopathy. Critical care UK Editor.
8. Bolton CF, Brown JD, Sibbald WJ 1983. The electrophysiologic investigation of respiratory paralysis in critically ill patients. Neurology; 33;2: 186.
9. Sandra L. Kane, Pharm D, Joseph F, Dastan MS 2002. Clinical Outcomes of critical illness Polyneuropathy. Pharmacotherapy, 22; 373-9.
10. Visser LH 2006. Critical illness polyneuropathy and myopathy: clinical feature risk factors and prognosis. Eur J Neurology, 13(11): 1203-12.

Case Report

SUPRAVENTRICULAR TACHYCARDIA DURING REGIONAL ANAESTHESIA (SPINAL ANAESTHESIA)

Tahmina Banu¹, Wahiuddin Mahmood²

SUMMARY:

Supraventricular tachycardia, though not very common may develop in any patient under spinal anaesthesia. A 50 years old lady admitted at square hospital through the emergency unit with left loin pain and fever with chill. She was already diagnosed as a case of left ureteric stone and was scheduled for Uretereoscopic Intracorporeal Pneumatic Lithotripsy (URS-ICPL) under spinal anaesthesia. During anaesthesia, she developed supraventricular tachycardia of unknown origin. Ultrashort-acting (3-blocker was given slowly. As there was no improvement, intravenous propranolol was given slowly, which resulted in a conversion to sinus rhythm. This paper discussed methods of cardio version for patients with supraventricular tachycardia in such clinical settings.

Key words: Spinal anaesthesia, SVT.

INTRODUCTION:

Supraventricular tachycardia (SVT) is a rapid rhythm of the heart in which the origin of the electrical signal is higher, the atrial or the AV nodal. This is in contrast to the deadlier ventricular tachycardia, in which rapid rhythms that originate from the ventricle of the heart i.e. below the atria and AV node. SVT can develop suddenly and may go away without treatment. It lasts for a few minutes to 1-2 days. Heart rate varies between 140-250/min. Diagnosis of SVT is confirmed by ECG. i) Absence of P wave (hidden by QRS) ii) Narrow QRS complex (less than 0.6 sec), iii) Short regular PR interval. Abnormally short PR interval can be seen with either low atrial rhythm or pre-excitation phenomenon. Pre-excitation usually refers to early depolarization of the ventricles by an abnormal conduction pathway from the atria to ventricles. The most common form of pre-excitation

is due to the presence of an accessory pathway (bundle of Kent) that connects one atria with one of the ventricles. The Wolff-Parkinson-White (WPW) syndrome is often applied to ventricular pre-excitation associated with tachyarrhythmia. Pre-excitation occurs approximately in 0.3% of the general population⁵. Supraventricular tachycardia is one of the commonest tachyarrhythmias during anaesthesia particularly during spinal anaesthesia. Thus all patients with history of SVT should be evaluated preoperatively by a cardiologist for possible electrophysiological studies, for curative radio frequency ablation of the bypass tract or the need for perioperative drug therapy. However, patient with only occasional asymptomatic tachyarrhythmia generally do not require investigations or prophylactic drug therapy. Those with frequent episodes of tachyarrhythmia associated with significant symptoms require drug therapy and close evaluations.

CASE REPORT:

Sakina Begum, a female aged fifty years was admitted to square hospital on September 16, 2008 through the emergency department with the complaints of

- High grade fever with chill
- Left loin pain
- Burning sensation during micturation for few days

The patient was a known case of left ureteric stone. She was planned for URS and ICPL on September 18, 2008. Her co-morbidity was diabetes mellitus, controlled with diet. Other parameters were normal except ECG, which showed sinus tachycardia (Heart-rate 105/min). Spinal anaesthesia was given at L3-L4 space with 0.5% bupivacaine (2.5 ml)

with fentanyl 20 µg. Continuous monitoring of oxygen saturation, blood pressure at 5 minutes

1. Associate Consultant, Department of Anaesthesia, Square Hospital Limited.
2. Consultant, Department of Anaesthesia, Square Hospital Limited.

interval and ECG tracing was going on. The procedure was uneventful throughout the operation except pulse-rate of the patient varied from 120 to 130 per minute. Blood pressure was normal, no vasopressor was needed at all.

As the stone was high up in the left ureter, it was pushed to the left kidney instead of removal. Thick pass was drained out of the left kidney on normal saline wash. A D-J stent with bichannel foley's catheter was kept in for free drainage. The whole procedure took about one hour. During the process of transfer from the OT table, the patient suddenly developed severe shivering. 25 mg pethidine was given intravenously. Oxygen saturation fell down and oxygen was started with nasal prong immediately. But oxygen saturation was not improving, then 100% oxygen was given through bain circuit. As shivering continued, 25 mg pethidine IV was repeated after 10 minutes. Her heart-rate was increasing and went up to 166/min. As the patient developed supraventricular tachycardia, carotid massage was started. As there was no improvement, patient was treated with Dormicum 2 mg I-V. Ultrashort-acting (3 blocker esmolol 30 mg I-V was given slowly. It caused little improvement, 1.0 mg propranolol was given slowly I-V. As the cause of shivering could not be diagnosed and assuming allergic reaction 100 mg hydrocortisone IV was also given. Arterial blood gas analysis as done, base excess was -10 meq/litre. Sodi-bi-carb was given slowly. 500 mg meropenem was given I-V slowly to prevent septicaemia. After improvement of oxygen saturation and decrease of heart-rate (about 140/min), the patient was transferred to post-operative ward. No additional treatment was needed except continuation of oxygen support. The patient's condition was uneventful in the post-operative ward, and she was transferred to cabin in the next morning.

DISCUSSION:

The incidence of WPW syndrome in asymptomatic individuals has been reported to be between 0.1 and 2.5 per 1000². Regional anaesthesia may result in increased arrhythmogenicity by causing a sudden decrease in atrial filling pressure due to sympathetic blockade³. Historically pharmacological interventions includes digoxin, a-agonist, example: methoxamine and phenylephrine, b antagonist example propranolol, esmolol, calcium channel

blocker example: verapamil and finally the rapid acting vasodilator adenosine^{4,5,6}.

Under anaesthesia where a 12 lead ECG is not available, diagnosis of exact cause of arrhythmia is difficult, particularly, when there was no previous diagnosis such as in this case. Certain SVT's such as atrial flutter and other atrial tachyarrhythmia may be difficult to manage pharmacologically. Calcium channel blocker may not only be ineffective, but also may precipitate prolonged hypotension in this setting^{8,9}. In recent years, adenosine has become the agent of choice for pharmacological conversion of SVT. It has very rapid onset of action of less than 1 minute with very short duration. In our case, as esmolol was readily available we treated the patient with esmolol first.

An a-agonist such as phenylephrine has in isolated cases been shown to be helpful for slowing the heart rate of patient with SVT under spinal and general anaesthesia^{3,10}. Esmolol may be effective as propranolol in converting the SVT and is without the vasodilatory effects of the adenosine and verapamil.

Propranolol nonselectively block (31 and (32 receptors. It slows atrioventricular conduction and stabilizes myocardial membranes. It is very effective in slowing the ventricular response to SVT². So in this case when esmolol failed to convert sinus rhythm, then we switched on to another option i.e. long acting b blocker, propranolol. Slow intravenous injection of 1 mg propranolol converted the SVT to sinus rhythm. The patient was completely recovered from SVT with any additional drug therapy and was transferred to postoperative ward with oxygen support only.

DC cardioversion may be another choice^{13,14,15} although extreme caution and airway protection would be required in the administration of additional sedation.

Anaesthetic vigilance and prompt intervention even with esmolol and propranolol saved a life, which is a lesson for all in day to day anaesthetic practice.

REFERENCES:

1. Morgan GE, Mikhail MS, Murray MJ: Clinical Anesthesiology, 4th ed. McGraw-Hill, 2006;
2. Averill KH, Fosmoe RJ, Lamb LE. Electrocardiographic findings in 67,375

- asymptomatic patients, IV. Wolff-Parkinson-White syndrome. *Am J Cardiol* 1960; 6: 108-129.
3. Van Zijl DHS, Dyer RA, Scott Miller RN James MFM. Supraventricular tachycardia during spinal anaesthesia for caesarian section. *Int J Obstet Anesth* 2001; 10: 202-205.
 4. Sprague DH, Mandel SD. Paroxysmal supraventricular tachycardia during anesthesia. *Anesthesiology* 1977; 46: 75-77.
 5. Mason BA, Ricci-Goodman J, Koos BJ. Adenosine in the treatment of maternal paroxysmal supraventricular tachycardia. *Obstet Gynecol* 1992; 80: 478-480.
 6. Afridi I, Moise KJ, Rokey R. Termination of supraventricular tachycardia with adenosine in a pregnant women with Wolff-Parkinson-White syndrome. *Obstet Gynecol* 1992; 80: 481-483.
 7. Chow T, Galvin J, McGovern C. Antiarrhythmic drug therapy in pregnancy and lactation. *Am J Cardiol* 1998; 82: 581-621.
 8. Ferguson JE, Siukola LV, Albright GA. Use of verapamil for Paroxysmal supraventricular tachycardia during epidural anesthesia for caesarian section. *Am J Perinatol* 1988; 5: 128-130.
 9. Treakle K, Kostic B, Hulkower S. Supraventricular tachycardia resistant to treatment in a pregnant woman. *The J Fam Pract* 1992; 35: 581-584.
 10. Lawrenson JB, Okreglicki AM, Scott Miller RN. Cardiovascular collapse due to intravenous verapamil in two patients with persistent atrial tachycardia. *S Afr Med J* 1995; 85: 1236-1238.
 11. Gajraj NM, Wallac DH, Pace NA. Supraventricular tachycardia in a parturient under spinal anesthesia. *Reg Anesth* 1993; 18: 261-263.
 12. Jacobson I, Tumquist K, Masley S. Wolff-Parkinson-White syndrome: Termination of supraventricular tachycardia with phenylephrine. *Anaesthesia* 1985; 40: 657-660.
 13. Stickles BJ. Idiosyncratic supraventricular tachycardia after epidural anesthesia. *J Nurse Midwifery* 1993; 38: 42-44.
 14. Klepper I. Cardioversion in late pregnancy. The anesthetic management of a case of Wolff Parkinson-White syndrome. *Anesthesia* 1981: 36. 611- 616.
 15. Joglar J A, Page R L. Treatment of cardiac arrhythmias during pregnancy: safty considerations. *Drug Saf* 1999; 20: 85-94.