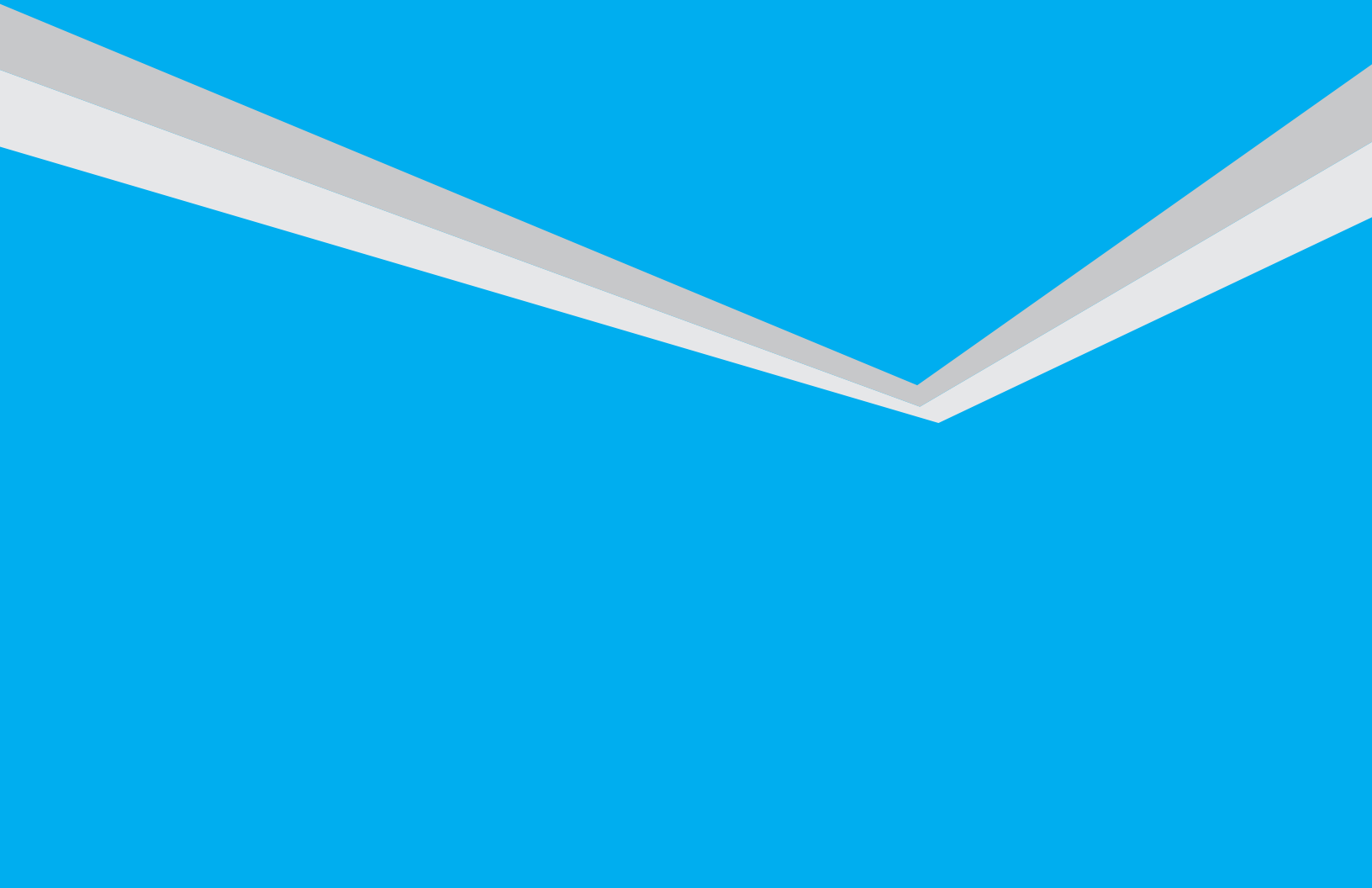


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An abstract geometric design at the bottom of the cover, consisting of several overlapping, angled lines in shades of blue and grey, creating a sense of depth and movement.

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Minimizing Stress Responses at Intubation

It is well known to the anesthesiologists of all levels that complications happen in perioperative period. It also happens in all levels of hospitals. Among the long list of complications adverse cardiovascular events occupy a significant position.¹ Around 200 million adults undergo major noncardiac surgery each year.² and more than 10 million adults worldwide have a major cardiac complication in the first 30 days after noncardiac surgery.³

Like overall Perioperative morbidity and mortality related to anesthesia, cardiovascular complications involve multiple factors. The most often cardiac complications found are systemic arterial hypertension, abnormalities of cardiac rhythm and perioperative myocardial ischemia. Factors independently associated with these complications include the type of surgical procedure, advanced age, duration of anaesthesia and surgery, preoperative abnormal electrocardiogram, abnormal preoperative chest radiography and diabetes. The Cardiac complications (systemic arterial hypertension, systemic arterial hypotension, abnormalities of cardiac conduction and cardiac rhythm, perioperative myocardial ischemia and acute myocardial infarction).⁴ Following anaesthesia and surgery, several triggers for cardiac complications like inflammation, hypercoagulability, hemodynamic compromise, bleeding, and hypothermia are established well. But sympathetic nervous system activation comes in first place commonly.

The cardiovascular derangements may result at any moment of the perioperative period but an anaesthesiologist encounters such changes at the start of an anaesthetic procedure specially at direct laryngoscopy and orotracheal intubation.⁵

The rise in blood pressure and heart rate occurs about 15second after the start of laryngoscopy and becomes maximal after 30-45s. Though transient, these haemodynamic changes may be detrimental in patients particularly associated with cardiovascular and cerebrovascular diseases. Both

the hypertension and tachycardia are associated with decrease in left ventricular ejection fraction and myocardial ischaemia.⁶ To minimize the catastrophe at laryngoscopy and intubation, premedication is practiced for last few decades. Various drugs are practiced starting from antihypertensive to the drugs used in treating neuropathic pain such as oral pregabalin and gabapentin. *Gabapentin* and *pregabalin* vary in terms of binding affinity and potency. Both the drugs are structurally related to inhibitory neurotransmitter gamma-aminobutyric acid (GABA). They act by decreasing the synthesis of glutamate to act in the central nervous system. By this mechanism they exert analgesic, anticonvulsant and anxiolytic activity and is proven effective in preventing neuropathic component of acute nociceptive pain.^{7,8}

In several studies it has been found that gabapentin and pregabalin effectively control haemodynamic derangements at intubation maintains intraoperative haemodynamic stability without post-operative side-effects. While comparing different doses it has been found 1000mg of gabapentine and 150 mg of pregabalin one hour before operation results in better control. So it appears that higher doses are needed to fulfill the purpose.

Another popular premedicant is oral clonidine. It is an imidazoline derivative which has selective agonistic action at alpha-2 adrenoceptors in the vasomotor center of medulla and presynaptically at the peripheral nerve terminals. Its oral application is popular as its bioavailability is 100%. The outcome is blocking of the release of norepinephrine from the nerve terminals leading to hypotension and bradycardia. The parasympathetic outflow is stimulated which results in the slowing of heart rate. In addition, clonidine increases the cardiac baroreceptor reflex sensitivity to an increase in the systolic BP (SBP), and hence stabilizes the BP.⁹

One Study shows that oral clonidine is better than pregabalin.¹⁰ while another shows that both the

drugs are equally effective along with gabapentine. The study reveals that blood pressure is fairly attenuated by pregabalin and gabapentine and heart rate is attenuated by clonidine significantly following laryngoscopy and intubation.¹¹

While the patient is on operating table attenuation is tried with many different techniques using inj. Propofol, short acting opioids, lignocaine, IV betablockers, deepening anaesthesia with volatiles. But newer drugs with improved pharmacokinetics and pharmacodynamics are of paramount interest now a days, dexmedetomidine is such a drug. It is a α -2 adrenergic agonist. It has anesthetic sparing, analgesic, sedative, anxiolytic and sympatholytic effects in a dose-dependent manner. It inhibits sympathetic outflow and has analgesic effects. Concerning the deleterious effects of intubation reflexes, attenuation of it has become of great interest. It is evident that large number of studies are being done and on progress. It is also found most studies are mainly done on American Society of Anesthesiologists (ASA) physical status I and II patients. Studies are needed on different patient groups and different types of surgeries for whom laryngoscopy and intubation are needed as the development of safe techniques can further improve the perioperative cardiac morbidity and mortality.

JBSA 2020; 33(2): 46-47

Dr. Manash Kumar Basu

Professor & Head

Department of Anaesthesiology

National Institute of Cancer Research & Hospital
Mohakhali, Dhaka.

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Effectiveness of Oral Clonidine & Oral Gabapentin in Attenuation of Haemodynamic Stress Response to Laparoscopic Cholecystectomy

Hasan Ali Talukder¹, Muhammad Mamun Ur Rashid¹, Md. Abdur Rahman², Shukha Ranjan Das¹, Mohammad Shaddam Hossain Mondol¹

¹Anaesthesiologist, Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine, Dhaka Medical College Hospital, Dhaka, ²Professor, Department of Anaesthesiology & ICU, Bangladesh Medical College Hospital, Dhaka

Corresponding Author: Dr. Hasan Ali Talukder, Anaesthesiologist, Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine, Dhaka Medical College Hospital, Dhaka.

Abstract:

Background: In laparoscopic surgery, Carbondioxide (CO₂) is routinely used to create pneumoperitoneum. Elevated intra-abdominal pressure, due to pneumoperitoneum, and Carbondioxide (CO₂) insufflation have adverse effects on the cardiovascular system. Plasma level of catecholamines and vasopressin are increased immediately after pneumoperitoneum. Increased catecholamine level activates the renin-angiotensin-aldosterone system, leading to characteristic hemodynamic alterations such as decreased cardiac output, elevated arterial pressure and increased systemic/pulmonary vascular resistance. Various drugs have been used to attenuate these hemodynamic responses.

Objectives: Purpose of this study was to evaluate the efficacy of oral Clonidine and oral Gabapentin premedication in attenuation of haemodynamic stress responses to laparoscopic cholecystectomy.

Setting & study design: This Placebo control study was conducted in Department of Anaesthesiology and ICU, Dhaka Medical College Hospital from 1st March 2015 to 31st August 2015. Total 60 patients with ASA grade I, II and planned for elective laparoscopic cholecystectomy were selected. Exclusion criteria were patients with history of hypersensitivity to Clonidine, Gabapentin, and patients with chronic pain, history of cardiovascular, psychiatric disease, use of psychotropic drugs, pregnancy other comorbid condition- CKD, COPD, IHD etc. Study subjects were allocated in to groups as placebo or control group (or Group P), gabapentin (300 mg) or Group G and clonidine (100 µg) or Group C. Tested drugs were given 75 to 90 minutes before surgery as oral premedication. All groups were compared for sedation, anxiety level along with changes of haemodynamic status.

Result: Majority of patients (40%) belongs to age 41 to 50 yrs. Out of 60 cases 55% were male and 45% were female. Male – female ratio was 1.22:1. A clear increase in sedation and a moderate decrease in anxiety were observed in both premedicated groups as compared with control groups. Preoperative anxiolysis and sedation was higher in oral clonidine group as compared with Gabapentin group. Compared with group P, gabapentin & clonidine group showed statistically significant decrease in heart rate before induction (98, 80, 74 beat/min respectively). The heart rate increased significantly immediately after intubation in control group P, whereas no such changes were observed in group G and in group C (132, 125, 112 beat/min respectively). After laparoscopy, the attenuation of mean arterial blood pressure in premedicated group was statistically significant as to control group (Group P) and remained stabilized during intraoperative period. Study showed that premedication (Group C and G) patients were comparatively well oriented and were able to obey commands than control (Group P) in the postoperative care unit. Postoperative analgesic need was much less with gabapentin (Group G) and clonidine group (Group C) as compared with control (Group P).

Conclusion: The gabapentin and clonidine are effective oral premedicant drugs with safe and multimodal drug profile as they cause sedation, anxiolysis, and analgesia, with successful attenuation of the hemodynamic response of laparoscopy. Efficacy of Clonidine is superior to other also proven.

Key words: Laparoscopic Cholecystectomy, Haemodynamic Stress Response, Oral Clonidine, Oral Gabapentin

Introduction:

Laparoscopic surgery has gained popularity over open conventional surgery as it offers benefits to both patients and health care practitioners. Advantages of laparoscopic cholecystectomy are shorter hospital stay, early ambulation, smaller scar, and less compromised postoperative respiratory and gastro-intestinal functions. However, the procedure is not risk free as it is associated with significant hemodynamic changes due to creation of pneumoperitoneum, potential for systemic absorption of carbon dioxide, and reverse Trendelenberg position. Pneumoperitoneum, Trendelenberg position in laparoscopic cholecystectomy predictably leads to tachycardia and hypertension, which are usually transient, variable, and unpredictable. Usually, these changes are well tolerated by healthy patients but may be fatal in patients with hypertension and coronary artery disease¹. Various pharmacological agents like nitroglycerine, β blocker, and opioids are used to provide hemodynamic stability during pneumoperitoneum, but they have their own disadvantages. Gabapentin (GBP) is a second generation anticonvulsant and Clonidine, a α_2 adrenergic receptor agonist commonly used for maintaining haemodynamic stability, has shown promising results for attenuation of hemodynamic response associated with laparoscopic surgery. However, there is a wide difference in the dose of such drug used by various authors and there is need for further studies to determine the minimum effective and safe dose in laparoscopic surgery.

Maintenance of intraoperative haemodynamic stability, any adverse events, postoperative nausea, vomiting (PONV), and pain continue to be a major challenge in the postoperative care. Many pharmacological techniques are being used to overcome haemodynamic alteration due to CO₂ pneumoperitoneum, such as deepening the anesthesia, pretreatment with vasodilators, adrenoreceptor blockers, calcium channel blocker, and opioids, with variable results¹, but there is still lack of ideal for this purpose. Clonidine and Gabapentin has been shown to have significant effects in maintenance of haemodynamic stability and PONV. Clonidine preserves heart rate control in pneumoperitoneum and recovery periods. Oral clonidine premedication also reduces the

requirement for postoperative analgesia². Gabapentin effectively suppresses nausea and vomiting and controls the neuro-endocrine factors by chemical agent in laparoscopic cholecystectomy and post-operative rescue analgesic requirement³. This study designed for evaluation of the effects of oral clonidine and gabapentin as premedication on haemodynamic stability.

The gabapentin and clonidine possesses several properties to make them valuable premedicants to attenuate the hemodynamic response of laryngoscopy and pneumoperitoneum. Gabapentin, an antiepileptic drug, is effective in controlling neuropathic component of acute nociceptive pain of surgery by inhibiting membrane voltage-gated calcium channels. It does not interact with GABA receptors. Its analgesic, anticonvulsant, and anxiolytic activities make it useful oral premedicant. It is well absorbed after oral administration, with peak plasma concentrations occurring within 60 minutes. another drug Clonidine activates the α_2 -adrenergic receptors in the brain and spinal cord to decrease sympathetic outflow, causing sedation, analgesia, hypotension, and bradycardia without significant respiratory depression. It is well absorbed after oral administration (3-5 $\mu\text{g.kg}^{-1}$) with peak plasma concentration in 75 to 90 minute and does not require transformation into another substance prior to its action. The preoperative use decreases the intraoperative stress response by reducing the nociceptive transmission and decrease norepinephrine concentration in serum, provided hemodynamic stability¹. Previous study reported that Oral pregabalin provided a moderate level of anxiolysis and minimal sedation as compared to placebo⁴. Anti-hyperalgesic drugs such as gabapentin may have a role in postoperative pain, and the combination with other antinociceptive drugs may produce synergistic analgesic effect. Study found that both gabapentin and clonidine reduce postoperative pain and total morphine consumption. Gabapentin has been also reported to be effective in the treatment of emesis in patients receiving cytotoxic drugs^{5, 6, 7}.

Anxiety, an unpleasant emotion, is another factor to adversely influence the anesthetic induction and patient recovery. These hemodynamic changes can be detrimental in elderly and hemodynamically compromised patients. More recently, Aronson and

Fontes⁸ found that among the various component of haemodynamic stability, blood pressure & pulse pressure control is independently and significantly associated with postoperative outcome. Prevention and treatment of postoperative pain and PONV continue to be a major challenge in postoperative care and plays an important role in the early mobilization and well-being of the surgical patient. Gabapentin is an anticonvulsant that has antinociceptive and anti-hyperalgesic properties. In pain models it has shown anti-hyperalgesic properties, possibly by reducing central sensitization⁹. Clonidine, a α_2 adrenergic agonist, has shown clinically useful drug profile due to its sympatholytic, hypnotic, sedative, anxiolytic, analgesic and anesthetic sparing effects without respiratory depression. In recent studies clonidine has shown attenuation of the pressor responses associated with laryngoscopy by reducing norepinephrine release¹⁰. Therefore present study was designed as prospective blind randomized controlled study to find out the efficacy of oral premedication with gabapentin or clonidine for changes in heart rate and mean arterial blood pressure during laryngoscopy and laparoscopy, along with perioperative hemodynamic stability.

Materials & Methods:

This study was conducted to evaluate the efficacy of oral clonidine and oral Gabapentin premedication in attenuation of haemodynamic stress responses to laparoscopic cholecystectomy. Total sixty (60) patients with ASA physical status I or II and planned for laparoscopic cholecystectomy were enrolled for study. Patients were allocated into three groups according to the premedication used. The patients randomly assigned to receive either 100 μ gm oral clonidine (C group, n=20), 300mg gabapentin (G group, n=20), Placebo (P group, n=20). Drug was given by an independent anesthetist in the ward therefore both the anesthesiologist and the patient was blinded to the group assignment. All patients were anesthetized with the same technique. Demographic data, vital signs were recorded. Perioperative any complication- likes bleeding, hypotension, hypertension, tachycardia, bradycardia, oxygen saturation, urinary output was recorded.

Study Procedure:

On arrival in the operation theatre all patients were cannulated with 18 gauge intravenous canula and patients pulse rate systolic blood pressure, diastolic blood pressure and peripheral oxygen saturation were noted down. Patient pre-oxygenated with 100% oxygen for 5 minutes, receiving Injection. Fentanyl (1.5 μ g /kg body weight, I.V. thiopental sodium (5 mg/kg body weight) was given. Endotracheal intubation was facilitated with Inj. Succinylcholine 1.5 mg/kg body weight. Anesthesia was maintained with 0.5% Halothane, 66% Nitrous Oxide in Oxygen. Controlled ventilation was maintained for all study patients. Muscle relaxation was achieved with Inj. vecuronium (0.1mg/kg body weight). Intraoperative hydration was maintained with Ringer's lactate solution. Pneumoperitoneum was created by insufflation of carbon dioxide and operation table was tilted about 15° reverse Trendelenberg position. Intra-abdominal pressure was not allowed to exceed 15mm Hg throughout the surgical procedure. Throughout the procedure any rise in mean arterial pressure more than 20% from baseline was treated with 50 μ g I.V. nitroglycerine. Monitoring including systolic, diastolic, mean arterial pressure, pulse rate, SpO₂ were recorded at the following points of time-prior to intubation, 2 minutes after endotracheal intubation, before pneumoperitoneum, ten minutes after pneumoperitoneum, twenty minutes after pneumoperitoneum, ten minutes after release of carbon dioxide, ten minutes after extubation. At the end of surgery residual neuromuscular blockade was reversed by appropriate dose of neostigmine and atropine intravenously. After extubation patients were transferred to recovery room. Finally, occurrence of adverse effects such as nausea, vomiting, dizziness, hallucination, and allergic reactions was recorded in the postoperative period. In case of vomiting, ondansetron 4 mg was given intravenously.

Statistical analysis:

Statistical analysis of the data was done using the Statistical Package for the Social Sciences for Windows (SPSS Inc., Chicago) software version 22. Qualitative data such as sex, ASA physical status,

adverse effects was compared using Chi-square test. Quantitative data such as age, numeric rating scales, time to first analgesic request and total analgesic requirement in 24 h will be compared using independent t-test. $P < 0.05$ will be taken as statistically significant. All collected questionnaire checked very carefully to identify the error in the data. Data processing work consist of registration schedules, editing computerization, preparation of dummy table, analyzing and matching of data.

Result & Observation:

Total of 60 patients fulfilling inclusion/exclusion criteria were studied. Results and observations are given below:

Table I Demographic characteristics of the patients (n=60)

Demographic variables	Group C (n=20)	Group G (n=20)	Group P (n=20)
Age (years)			
Mean $\pm$ SD	39.4 $\pm$ 4.98	41.1 $\pm$ 6.31	38.85 $\pm$ 3.96
Range	(25-60)	(20-50)	(30-60)
Sex			
Male	10(50%)	12(60%)	11(55%)
Female	10(50%)	8(40%)	9(45%)

While studying the distribution of cases by age it was found that mean age was found to 39.4 $\pm$ 4.98 years in Group C, 41.1 $\pm$ 6.31 years in group G & 38.85 $\pm$ 3.96 years in group P. Unpaired student's 't'-test was employed to analyze the data and data were expressed as mean $\pm$ SD. No significant differences were found between groups with respect to age (Table I).

Table II American Society of Anesthesiologist (ASA) physical status (n=60)

ASA status	Group C (n=20)	Group G (n=20)	Group P (n=20)
ASA I	12(60%)	15(75%)	11(55%)
ASA II	8(40%)	5(25%)	9(45%)

All patients were with ASA physical status I and II (Table II). Group C received clonidine (100 μ g), among them 12(60%) were ASA I and 8(40%) were ASA II. Group G received gabapentin (300 mg), among them 15(75%) were ASA I and 5(25%) were ASA II. Group P received placebo, among them 11(55%) were ASA I and 9(45%) were ASA II. Medication given with sips of water about 75 to 90 minutes before induction of general anesthesia. The differences was statistically not significant between two group, p-value was 0.096 ($p > 0.05$).

Heart rate alteration shows in figure 1. Maximum increase in heart rate from baseline was observed after intubation. The heart rate increased significantly immediately after intubation in control group P, whereas no such changes were observed in group G and in group C (132, 125, 112 beat/min respectively). During pneumoperitoneum, it increased by 20-30 beats/min in control (P group), while decrease in gabapentin (G group) by 5-10 beat/min and clonidine (C group) by 15-20 beat/min was observed. There was statistically significant attenuation of heart rate in premedicated groups. (Figure 1)

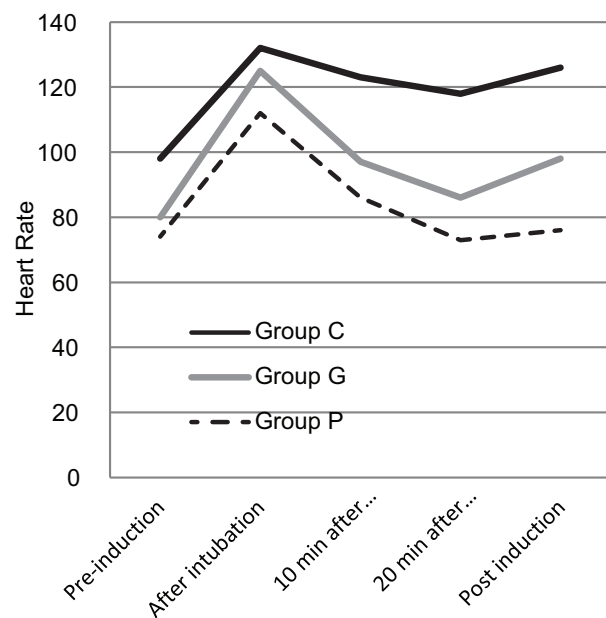


Figure 1 Heart rate alteration (n=60)

Table III
Changes of Mean arterial blood pressure (n=60)

	MBP (mmHg)		
	Group C (n=20)	Group G (n=20)	Group P (n=20)
Before induction	97.70±3.27	98.55±4.54	106.25±6.73
After intubation	98.45±3.28	99.20±4.47	109.10±12.47
10 min after pneumoperitoneum	85.05±6.39	91.85±6.03	103.00±6.10
20 min after pneumoperitoneum	90.35±5.95	92.8±6.55	105±6.70
Post-extubation	88.15±6.59	94±5.08	102.45±5.88

The statistically significant differences were observed in the MAP at different times ($p < 0.05$) pneumoperitoneum among groups (Table III).

Table IV *Evaluation of Post-operative pain and analgesic requirement (n=60)*

Variables	Group C	Group G	Group P
VAS Score			
0-3	19	16	0
4-6	1	4	2
7-10	0	0	18
Analgesic requirements			
NSAIDS	16	11	4
NSAIDS + Opids	3	5	9
Opids analgesic	1	4	7

VAS score >3 denotes moderate to severe pain. Patients in placebo and gabapentin groups experienced more pain than clonidine group during post-operative period. Postoperative analgesic need was much less with gabapentin (Group G) and clonidine group (Group C) as compared with control (Group P). Maximum number of Group C patients 16(80%) took NSAID for postoperative pain care (Table IV).

Discussion:

Total of 60 patients, 20 in each group, were evaluated. All groups were comparable with respect to the demographic and operational factors. No significant differences were found between groups with respect to age, gender, weight, time between oral premedication to anesthetic induction, duration of anesthesia, and surgical procedure time.

In our study, we have used oral premedication with gabapentin 300 mg or clonidine 100 µg and found

them to be effective for perioperative hemodynamic stability. The hemodynamic results of our study were in agreement with recent results with clonidine and gabapentin. Both drugs possess several properties to make them valuable premedicants to attenuate the hemodynamic response of laparoscopy. Reid and Brace¹¹ first described the hemodynamic response to laryngoscopy and intubation, probably due to intense sympathetic discharges caused by stimulation of epipharynx and laryngopharynx. Shribman et al¹² reported that laryngoscopy and tracheal intubation increases arterial blood pressure, heart rate, and catecholamine levels, whereas Hassan et al.¹³ reported high incidences of cardiac arrhythmias, myocardial ischemia, acute left ventricular failure, and cerebrovascular accidents following intubation in hypertensive patients. Hypertension may affect perioperative morbidity through the extent of end organ damage.

In this study heart rate increased significantly immediately after intubation in control group P, whereas no such changes were observed in group G and in group C (132, 125, 112 beat/min respectively). During pneumoperitoneum, it increased by 20-30 beats/min in control (P group), while decrease in gabapentin (G group) by 5-10 beat/min and clonidine (C group) by 15-20 beat/min was observed. There was statistically significant attenuation of heart rate in premedicated groups. The heart rate decreased (125, 98, 76 beat/min respectively). In clonidine group, heart rate remained stabilized in comparison with group G and P.

Hayashi and Maze¹⁴ and Sung et al.¹⁵ reported that clonidine increases perioperative circulatory stability in patients undergoing laparoscopic cholecystectomy and potentiates parasympathetic nervous system. Laisalmi et al¹⁶ concluded that premedication with clonidine blunts the stress response to surgical stimuli and reduces the requirement of narcotic and anesthetic doses.

Khan A et al reported that compared with control and pregabalin groups, clonidine group showed statistically significant decrease in heart rate before induction. Throughout anaesthesia there was statistically significant attenuation in the HR values when clonidine was compared with placebo and pregabalin. Similarly after laryngoscopy and intubation, there was statistically significant attenuation in the MAP values when clonidine was compared with placebo and pregabalin⁴. In this study no significant difference was observed in the MAP before premedication in groups. The attenuation of mean arterial blood pressure in premedicated group was statistically significant as to control group (Group P) and remained stabilized during intraoperative period.

Conclusions:

Present study concluded that oral premedication with gabapentin or clonidine provides better haemodynamic stability and analgesia in laparoscopic cholecystectomy, without prolongation of recovery time and side effects. Clonidines impersonate as superior to gabapentin for attenuation of the hemodynamic responses to laparoscopy. However, it may increase the incidence of intra- and postoperative bradycardia, but not significant. Near stable hemodynamic

variables and absence of any sympatho-somatic response with oral premedication in the present study was an indication of adequate analgesia and sedation. therefore Clonidine or gabapentine can be used routinely.

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Original Article

Comparison of Intravenous Ketamine and Midazolam Premedication on Emergence Agitation (EA) in Children following Tonsillectomy with or without Adenoidectomy under General Anaesthesia

Abdullah Al Maruf¹, Md. Mozaffer Hossain², Reza Ershad³, Sayeda Nazrina⁴,
Md. Mustafa Kamal⁵

¹Classified Specialist in Anaesthesiology, Border Guard Hospital, Dhaka, ²Head of the Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine, DMCH, ³Classified Specialist in Anaesthesiology, Border Guard Hospital, Dhaka, ⁴Associate Professor, Department of Pharmacology, Armed Forces Medical College, Dhaka Cantonment, ⁵Associate Professor, Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka.

Corresponding Author: Dr. Abdullah Al Maruf, Classified Specialist in Anaesthesiology, Border Guard Hospital, Dhaka

Abstract

Background: Management of emergence agitation (EA) following tonsillectomy with or without adenoidectomy under general anaesthesia in children has been a major challenge for anaesthesiologists. Several medications have been investigated in an attempt to reduce the occurrence and severity of EA.

Objectives: The purpose of this study is to determine the effect of premedication with intravenous midazolam and ketamine on EA following tonsillectomy with or without adenoidectomy under general anaesthesia in children.

Study design: Randomised clinical study.

Methods: Sixty children of both sex, American Society of Anaesthesiologists (ASA) physical status I & II age 5 to 12 years scheduled to undergo elective tonsillectomy with or without adenoidectomy were randomly assigned into two groups. Patients in group K (n=30) received premedication of intravenous ketamine 0.25 mg/kg body weight in 5 ml total volume and in group M (n=30) received premedication 0.1 mg/kg body weight intravenous midazolam in 5 ml total volume. After completion of surgery patients were transferred to recovery. Incidences and severity of EA (Paediatric Anaesthesia Emergence Delirium Scale), pain score (Wong-Baker FACES Pain scale) and postoperative nausea and vomiting (PONV) were assessed at admission in the recovery (T0) and in the post anaesthesia care unit (PACU) at 5 min (T5), at 15 min (T15) and at 30 min (T30).

Results: Incidences of EA in Group K remained significantly lower than Group M at admission to the recovery and in the PACU at 5 min and 15 min ($P<0.05$). Severity of EA was significantly lower patients in Group K than Group M at admission in recovery and in PACU at 5 minute and 15 minute ($P<0.05$). There were no significant differences in pain scores between two groups. Regarding PONV there was no significant difference between two groups.

Conclusion: Premedication with ketamine was more effective than midazolam in the prevention of EA following tonsillectomy with or without adenoidectomy in pediatric patients under general anaesthesia.

Key words: Emergence agitation (EA), ketamine, midazolam, children, tonsillectomy, adenoidectomy, general anaesthesia.

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Introduction

Postoperative agitation, also referred to as emergence agitation (EA) in international literature, is a well-documented clinical phenomenon, particularly in children. EA has been described as “a mental disturbance during the recovery from general anesthesia consisting of

hallucinations, delusions and confusion manifested by moaning, restlessness, involuntary physical activity, and thrashing about in bed.”¹ It is during the first 30 minutes after emergence that the greatest incidence of agitation is observed, and duration is generally limited and recovery spontaneous. However, prolonged episodes of

agitation lasting for up to 2 days have been described.²

The prevalence of EA in children generally ranges from 25% to 80%, depending on the definition of EA used to measure this phenomenon,³ but may be as high as 80%.^{3,4} The incidence of EA largely depends on age, anaesthetic technique, surgical procedure, and application of adjunct medication.⁵ Surgical procedures that involve the tonsils, thyroid, middle ear, and eye have been reported to have higher incidences of postoperative agitation and restlessness.^{5,6} Eckenhoff et al.⁷ speculated that a "sense of suffocation" during emergence from anesthesia may contribute to EA in patients undergoing head and neck surgery.

Treatment strategies evolve largely around drug administration, manipulation, or administration of preventative drugs. Standard pharmacological interventions such as propofol, ketamine, midazolam and fentanyl have been shown to have prophylactic effects in preventing EA in children.⁸ Ketamine has been one of the studied pharmacological agents in the management of EA. ketamine was effective in the prevention of EA without delay in awakening and both subhypnotic doses of ketamine 0.25 and 0.5 mg/kg were effective.⁹ Midazolam is a commonly used sedative in children that has beneficial effects in reducing paediatric EA. Preoperative oral midazolam decreases both preoperative separation anxiety and the degree of EA observed with sevoflurane anaesthesia.¹⁰

The aim of the present study was to compare the effects of preoperative premedication with intravenous midazolam and ketamine on EA following tonsillectomy with or without adenoidectomy in pediatric patients under general anaesthesia.

Patients and Methods

It was a randomized clinical study of sixty patients (thirty patients in each group) of both sexes age between 5-12 years, ASA physical status I and II scheduled to undergo elective tonsillectomy with or without adenoidectomy under general anaesthesia in Border Guard Hospital, Dhaka in one calendar year from January 2016 to December 2016. Patients with clinically significant neurological, respiratory, cardiovascular,

psychiatric diseases, hypersensitivity to ketamine or midazolam and children with developmental or cognitive disorder were excluded from the study. The study was conducted after approval from the Institutional review board. Pre-anaesthetic check up was done 24 hours prior to surgery and the procedure was explained to the parents and written consent was obtained from parents. All eligible patients were randomized in to two groups. Patients in group K (n=30) receive intravenous premedication of ketamine 0.25 mg/kg body weight in 5 ml total volume and in group M (n=30) receive intravenous premedication of midazolam 0.1 mg/kg body weight in 5 ml total volume. Operation was done under general anaesthesia with controlled ventilation. Fentanyl 1 mcg/kg body weight was given intravenously before induction of general anesthesia. Induction was done with Propofol 2 mg/kg body weight and atropine 0.01 mg/kg body weight intravenously. After oral intubation with vecuronium 0.1 mg/kg body weight, anaesthesia was maintained with 70% nitrous oxide in oxygen, halothane 0.5-1% and muscle relaxation was maintained with incremental doses of vecuronium. Patient's heart rate, blood pressure, ECG, respiratory rate, and SpO₂ were monitored and recorded in every 5 minutes interval. At the completion of operation the patients were extubated after reversal of muscle relaxant with neostigmine and atropine and then admitted to the post anaesthesia care unit (PACU). Postoperative analgesia was maintained with inj ketorolac 0.5mg/kg body weight intravenously.

Postoperatively, the EA was assessed in both the groups using Paediatric Anaesthesia Emergence Delirium (PAED) scale¹¹ (Table: IV) for initial 30 minutes. The incidence and severity of emergence delirium were measured upon admission to the recovery (T0) and in the PACU at 5 min (T5), at 15 min (T15) and at 30 min (T30). A PAED scale 10 or more was considered as positive cases of EA. Children were considered severely agitated if they had a PAED scale of 15 or higher. Pain score (Wong-Baker FACES Pain scale) were assessed at admission in the recovery (T0) and in the post anaesthesia care unit (PACU) at 5 min (T5), at 15 min (T15) and at 30 min (T30). The Wong-Baker FACES Pain scale¹² (Figure: 1) is often useful for assessing pain in patients who do not have ability

to use language to describe pain. This scale uses faces:

- Face 0 : is very happy because he doesn't hurt at all.
 Face 2 : hurts just a little bit.
 Face 4 : hurts a little more.
 Face 6 : hurts even more.
 Face 8 : hurts a whole lot.
 Face 10 : hurts as much as you can imagine.

Postoperative nausea and vomiting (PONV) were recorded every one hour during these six hours. Vomiting was defined as the forceful expulsion of gastric contents from the mouth and was brought about by the powerful sustained contraction of the abdominal muscle; nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit.

All statistical analysis was carried out using SPSS (Statistical Package for social sciences) 22.0 for windows. All results are expressed as mean $\pm$ standard deviation (SD) or in frequencies as applicable. Results are considered statistically significant if $p < 0.05$.

Results

The Patients criteria and anaesthetic data were shown in table I. Two groups were similar and fairly comparable with respect to age, body weight, sex, ASA physical status and differences were statistically not significant. Duration of surgery and duration of anaesthesia were almost similar and differences were statistically not significant. Incidences and severity of emergence delirium were shown in table II. Incidences of EA in Group K remained significantly lower than Group M at admission to the recovery and in the PACU at 5 min and 15 min ($P < 0.05$). Severity of EA (PAED scale) in Group K remained significantly lower than Group B at admission to the recovery and in the PACU at 5 min and 15 min ($P < 0.05$). Pain scores (Wong-Baker FACES Pain scale) and incidences of PONV were shown in table III. There were no significant differences in pain scores (Wong-Baker FACES Pain scale) between two groups at admission to the recovery and in the PACU at 5 min, 15 min and 30 min. Regarding the incidence of PONV, there was no statistically significant difference among the studied groups. These were no incidences of hemodynamic instability, or postoperative hallucinations or nightmares.



Figure 1: The Wong-Baker FACES Pain Scale

Table I Patients criteria and anaesthetic details

Variables	Group K (n=30)	Group M (n=30)	P Value	Result
Age in years	7.36 $\pm$ 1.46	6.93 $\pm$ 1.69	0.83	NS(Student 't' test unpaired)
Body weight in kg	18.47 $\pm$ 4.63	19.76 $\pm$ 4.91	0.86	NS(Student 't' test unpaired)
Sex				
Male	19(63.33%)	17(56.67%)	0.76	NS(Chi Square test)
Female	11(36.67%)	13(43.33%)	0.65	NS(Chi Square test)
Duration of surgery in minutes	39.79 $\pm$ 9.76	42.17 $\pm$ 10.07	0.57	NS(Student 't' test unpaired)
Duration of anaesthesia in minutes	45.53 $\pm$ 12.27	47.29 $\pm$ 11.83	0.52	NS(Student 't' test unpaired)
ASA physical status				
I	27(90%)	26(86.67%)	0.72	NS(Chi Square test)
II	3(10%)	4(13.33%)	0.68	NS(Chi Square test)

Values are expressed in mean $\pm$ SD or percentage as applicable NS – Not Significant

Table II Incidence of EA and severity of EA (PAED scale).

Variables	Group K (n=30)	Group M (n=30)	P value	Result
Incidences of EA				
T0	1(3.33%)	3(10%)	0.021	Sig(chi square test)
T5	2(6.66%)	7(23.33%)	0.015	Sig(chi square test)
T15	2(6.66%)	5(16.66%)	0.025	Sig(chi square test)
T30	1	1	-	NS(Chi Square test)
Severity of EA (PAED scale)				
T0	9.78±3.22	12.6±2.89	0.034	Sig (Student 't' test unpaired)
T5	5.26±2.67	8.63±2.79	0.039	Sig (Student 't' test unpaired)
T15	4.34±2.71	7.61±2.37	0.043	Sig (Student 't' test unpaired)
T30	3.52±2.25	4.14±2.64	0.615	NS(Student 't' test unpaired)

Values are expressed in mean±SD or percentage as applicable

Sig – Significant NS – Not Significant

Table III Pain score (Wong-Baker FACES Pain scale) in recovery at different time and incidence of PONV

Variables	Group K (n=30)	Group K (n=30)	P Value	Result
Pain score				
T0	4.13±1.71	4.71±1.58	0.716	NS(Student 't' test unpaired)
T5	3.03±1.63	3.43±1.69	0.806	NS(Student 't' test unpaired)
T15	2.13±1.67	2.48±1.52	0.821	NS(Student 't' test unpaired)
T30	1.53±1.51	1.83±1.43	0.871	NS(Student 't' test unpaired)
Incidences of PONV	5(16.66%)	4(13.33%)	0.832	NS(Chi Square test)

Values are expressed in mean±SD or percentage as applicable

Sig – Significant NS – Not Significant

Table IV Paediatric Anaesthesia Emergence Delirium Scale (PAED) Scale. Score is sum of all values.

Behavior	Not at all	Just a little	Quite a bit	Very much	Extremely
Make eye contact with caregiver	4	3	2	1	0
Actions are purposeful	4	3	2	1	0
Aware of surroundings	4	3	2	1	0
Restless	0	1	2	3	4
Inconsolable	0	1	2	3	4

Discussion

Tonsillectomy with or without adenoidectomy is a long practiced and one of the most frequently performed surgical procedures in paediatric age. These operations appear to exhibit an increased

incidence of EA.⁵ It is speculated that the sensation of suffocation in otorhinolaryngological procedures may be responsible for these events. Post anesthetic EA is a self-limiting phenomenon and etiology of EA in children is not fully understood

but possible risk factors are intrinsic characteristics of an anaesthetic, rapid emergence from anaesthesia, postoperative pain, preschool age, otolaryngologic surgical procedures, preoperative anxiety, and child temperament.² This complication can be severe and prolonged, exposing the patient to physical harm, pain or bleeding, and prolong the recovery period.⁷

In this study, the incidence and severity of EA were significantly lower with premedication of intravenous low dose ketamine (0.25 mg/kg body weight). Yoon Sook Lee et al.¹³ found that ketamine was effective in the prevention of EA without delay in awakening and both subhypnotic doses of ketamine 0.25 and 0.5 mg/kg body weight were effective. Kawaraguch et al.¹⁴ reported that the administration of ketamine 1 mg/kg after the induction of anaesthesia and the instillation of ketamine 1 mg/kg body weight/hr during surgery in pediatric strabismus surgery succeeded in decreasing EA. Abu-Shahwan et al.¹⁵ showed that an intravenous injection of ketamine 0.25 mg/kg body weight, 10 min before the end of surgery in a dental operation for young children under general anesthesia with sevoflurane decreased the incidence of EA without a delay in recovery. Dalens et al.¹⁶ reported that the intravenous administration of ketamine 0.25 mg/kg body weight or nalbuphine 0.1 mg/kg body weight in general anesthesia with sevoflurane for young children undergoing magnetic resonance imaging was effective in preventing the incidence of EA without delaying awakening or recovery. Regarding the mechanism of ketamine in reducing the incidence of emergence delirium, Lerman et al.¹⁷ suggested that ketamine inhibits the central nervous system effect in ether-linked inhalation anaesthetics.

Studies have demonstrated lower incidences of EA when midazolam are administered in the perioperative stage.^{18,19} Eun Jung Cho et al.²⁰ reported intravenous administration of 0.03 mg/kg of midazolam just before the end of surgery reduces emergence agitation without delaying the emergence time in children having strabismus surgery with sevoflurane anesthesia. Chen J et al.²¹ also reported intravenous administration of a subhypnotic dose of midazolam (0.05 mg/kg body weight), in addition to fentanyl before discontinuation of sevoflurane, was also found to

be effective in decreasing EA. In contrast, others found that intravenous midazolam did not reduce the incidence of EA,^{22,23} which is similar to our findings. A meta-analysis of pharmacological prevention of EA in children indicated that midazolam was ineffective in the prevention of EA in this context.²⁴

Regarding postoperative pain score the present study using Wong-Baker FACES Pain scale, pain score was almost similar with ketamine or midazolam. Abu-Shahwan et al.²⁵ showed that ketamine 0.25 mg/kg body weight at induction time did not decrease postoperative pain in pediatric patients undergoing tonsillectomy. Batra et al.²⁶ in another study found that postoperative pain score after tonsillectomy in pediatric patients was not decreased by small dose ketamine. De Conceicao et al.²⁷ reported that a single dose of ketamine (0.5mg/kg body weight) in the pediatric patients undergoing tonsillectomy could reduce postoperative pain and use of rescue analgesia. This study suggested that small dose of ketamine or midazolam had no effective role in reducing postoperative pain in pediatric population.

The incidence of PONV after adenotonsillectomy is more than 70% and may cause serious complications such as pulmonary aspiration, hypoxemia, and increase chance of bleeding.²⁸ Studies that used low dose ketamine to decrease postoperative pain showed that low dose ketamine did not increase the incidence of PONV.^{29,30} Splinter WM et al.³¹ reported intraoperative administration of intravenous midazolam reduced vomiting in children after tonsillectomy. The current study showed that the incidence of PONV did not increase significantly with ketamine than midazolam. This study did not encounter a case of hemodynamic instability, or postoperative hallucinations or nightmares.

Conclusion

Premedication with intravenous ketamine 0.25 mg/kg body weight was more effective than intravenous midazolam 0.1 mg/kg body weight in the prevention of early postoperative in reducing EA following tonsillectomy with or without adenoidectomy in pediatric patients under general anaesthesia. Both have no significant effect at this dose in decreasing postoperative pain and PONV in these patients.

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Haemodynamic Changes & Complications between Unilateral and Bilateral Spinal Anesthesia in Elderly Type-2 Diabetic Patient Undergoing Hemiarthroplasty – A Comparative Study

Ferdous Ali¹, Ibrahim Khalilullah², A Jabbar³, M Hasan⁴, M Rahman⁵

¹Registrar & Specialist, Department of Anaesthesiology & SICU, BIRDEM, Dhaka, ²Assistant Professor & Associate Consultant, Department of Anaesthesiology, Ibrahim Cardiac Hospital & Research Institute, Shahbag, Dhaka, ³Medical Officer, Department of Anaesthesiology & SICU, BIRDEM, Dhaka, ⁴Professor, Department of Anaesthesiology & SICU, BIRDEM, Dhaka, ⁵Associate Professor, Department of Anaesthesiology & SICU, BIRDEM, Dhaka.

Corresponding Author: Dr. Ferdous Ali, Registrar & Specialist, Department of Anaesthesiology & SICU, BIRDEM, Dhaka

Abstract

Background: During spinal anesthesia, extend of sympathetic blockade causes hemodynamic instability, such as hypotension and bradycardia. It can lead to develop cardiac arrest in some cases. Elderly patient do not compensate these haemodynamic change easily because of aging process leads some physiological changes in all system especially on cardio vascular system e.g; decreased elasticity of vessels, decreased vascular and myocardial compliance and also decreased autonomic responsiveness. It is hypothesized that unilateral spinal anesthesia restrict the spread of hyperbaric bupivacaine to one side only (dependent side) thus sparing the opposite sympathetic chain and hence would cause less haemodynamic changes.

Materials & Methods: This cross sectional study, took place in the department of Anaesthesiology and SICU, BIRDEM General Hospital, Shahbag, Dhaka. A total 60 elderly (age-60 to 80 years), ASA grade II and III, type-2 Diabetic patients scheduled for hemiarthroplasty were enrolled in this study. Patients were divided into two groups U & A, 30 patients in each. Subarachnoid (spinal) anaesthesia was performed in all patients with 0.5% hyperbaric bupivacaine intrathecally, at L3 - L4 interspinous spaces, with 25G Quinke's spinal needle. Patients of group U were kept in lateral decubitus position which was maintained for 15 minutes after injecting bupivacaine and patients of group B were kept in supine position. Changes of BP, pulse and development of any complication was recorded in 5 minute interval after spinal anesthesia. All the informations were recorded in preformed data collection sheet.

Result: Compared with group U, group B showed statistically significant increase in heart rate at 10 min after spinal anesthesia ($p < 0.05$). Systolic BP was significantly lower in group B compared to group U in all recorded time interval except at 60 minute. Diastolic blood pressure was significantly lower in group B compared to group U at 15, 30 and 45 minute reading. Regarding mean arterial pressure we found it was reduced significantly in group B compared to group U in all the recorded time except at 60 minute ($p < 0.05$). Present study showed none of the patients in the unilateral group experienced vomiting; only two patients noticed nausea. In the bilateral group, seven patients had nausea and three of them experienced episodes of vomiting ($p = 0.02$). In group U, no case found hypotensive, only single developed bradycardia. In Group B 7 patients experienced hypotensions and 4 patients had bradycardia.

Conclusion: This study showed that the unilateral spinal anesthesia reduces the incidence and severity of hypotension, bradycardia and other complication in elderly type-2 diabetic patients. So unilateral spinal anaesthesia is more beneficial for elderly type-2 diabetic patient in hemiarthroplasty.

Key words: Haemodynamic changes, complications, Unilateral SAB, Bilateral SAB, Type-2 DM, Hemiarthroplasty

Introduction

The most common and serious side-effects of spinal anaesthesia are hypotension and bradycardia. In addition, many representative case reports through literature have discussed cardiac arrest fatalities during spinal anaesthesia. A high ASA physical status and advanced age of patients could contribute to such cardiac arrest fatalities. Hemiarthroplasty is a major portion of orthopaedic surgery. Most of the patients are elderly. Anaesthesia of elderly patients is always challenging for the anesthesiologist. Spinal anaesthesia induced hypotension is more common and hazardous in elderly, as they have decreased physiological reserve and compromised blood supply to various vital organs¹. An important effect of sympathetic inhibition during spinal or epidural anaesthesia is a significant decrease in venous return due to dilatation of resistance and capacitance vessels. Unilateral spinal anaesthesia is very effective in restricting the sympathetic block as all high risk patients showed minimal haemodynamic changes following the technique². Several factors are required for successful unilateral spinal anaesthesia, including: the type of needle and its bevel direction, the speed of injection³, volume, baricity, the concentration of local anaesthesia as well as the position of the patient on the operating table⁴. Unilateral spinal anaesthesia with a low dose (7.5 mg), limited volume (1.5 ml) and low-flow injection (1 ml/30 s) technique induces sufficient sensory and motor block with an appropriate level of analgesia. The technique is therefore suitable for lower limb surgery. This technique achieves stable haemodynamics, particularly in elderly and ASA class III/IV patients. It also results in rapid recovery and greater satisfaction among outpatients, in addition to preventing unnecessary nerve block in the contra lateral limb⁵. To comprehensively investigate the benefits of unilateral

as compared with bilateral spinal anaesthesia, we evaluated the effects on sufficient sensory and motor block, optimum analgesia, hemodynamic changes, nausea, vomiting and headache.

Materials & Methods

It was a cross sectional study took place in the department of Anaesthesiology and SICU, BIRDEM General Hospital, Shahbag, Dhaka from 1st July

2016 to 31st December 2016. This study was carried out to assess the haemodynamic changes & complications between unilateral and bilateral spinal anaesthesia in elderly type-2 diabetic patient undergoing Hemiarthroplasty. Ethical clearance was taken from the concerned authority. Informed written consent was taken from all individual participants.

Participants were elderly type-2 Diabetic patient scheduled for hemiarthroplasty. Total 60 patients were enrolled in this study, divided into two groups, U & A, 30 in each. Inclusion criteria's were patients undergoing hemiarthroplasty, age 60 to 80 years, ASA physical status II & III, Type-II diabetic patients (well control with insulin). Exclusion criteria's were patient refusal, infection at the site of injection, uncontrolled hypertension, coagulopathy, patients with neurological disorder, patients with sinus tachycardia or bradycardia, patients with hypo or hyperthyroidism, patient with renal impairment, low EF.

Sample was selected by random sampling in two group distributed as- group B (bilateral block), group U (Unilateral Block). Sixty patients, classified by American Society of Anesthesiologists (ASA- II, III, listed for operative procedure under spinal anaesthesia were randomized by card method in two groups of 30 patients each. After arrival to preoperative room, all patients were inserted an 18 gauge venous cannula in the largest apparent vein on the dorsum of hand. Then all patients started lukewarm fluids of Lactated Ringer's solution, infused at 10ml/kg/h over 30 min before spinal anaesthesia. The infusion rate was then reduced to 6 ml/kg/h. The ambient temperature was maintained at 22-24 °C. Base line parameters like BP, Pulse, oxygen saturation, ECG and axillary temperature were recorded before anaesthesia. Subarachnoid (spinal) anaesthesia was performed in all patients with 7.5mg (1.5ml) of 0.5% hyperbaric bupivacaine intrathecally, at L₃ - L₄ interspinous spaces, with 25G Quinke's spinal needle. U group patient's were kept in lateral decubitus position which was maintained for 15 minutes after anaesthesia and B group patient was at sitting position then remain in supine position. Motor block assessed by bromage scale. Sensory block was assessed by icepack, pin prick sensation and dermatome levels tested every 2 min until

the highest level had stabilized by consecutive tests. On achieving T10 sensory blockade level, surgery was allowed. Main outcome variables were heart rate, blood pressure, intraoperative complications (e.g. nausea, vomiting, hypotension, cardiac arrest).

Changes of BP, pulse and development of any complication was recorded in 5 min interval after unilateral and bilateral spinal anesthesia. Appearance of hypotension, bradycardia or any complication recorded and managed accordingly. If blood pressure decreased by more than 30% of baseline and heart rate dropped to less than 50 beats/min, the patient was considered to suffer from hypotension and bradycardia respectively. The hypotension was managed by rapid IV infusion of 250 mL of lactated Ringer's solution. Bradycardia was managed using 0.5-1 mg of intravenously administered atropine. If the hypotensive patient did not respond to treatment, ephedrine 5 mg was injected. All the informations were recorded in preformed data collection sheet. All collected questionnaire checked very carefully to identify the error in the data. Data processing work consist of registration schedules, editing computerization, preparation of dummy table, analyzing and matching of data.

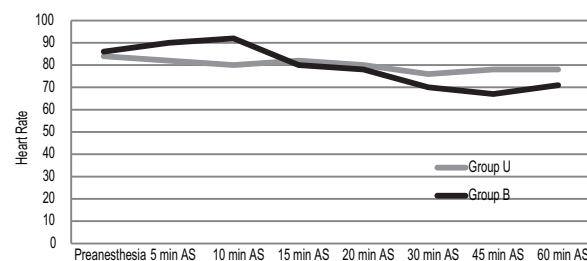
Statistical analysis

Data were collected in questionnaire. Data processing work consist of registration schedules, editing computerization, preparation of dummy table, analyzing and matching of data. After collection of all information, these data were checked, verified for consistency and edited for finalized result. After editing and coding, the coded data directly entered into the computer by using SPSS version 6. Data cleaning validation and analysis was performed using the SPSS/PC software and graph and chart by MS excel.

Results and observations

Regarding age it was found that majority of the patients i.e. 81.6% (n=49) were between 60-70 years, 18.3% (n=11) were between 71-80 years. Mean age was found 66.3 ± 11.5 years. In the Group U, 19(63.3%) were ASA II and 11(36.6%) were ASA III. In Group B, 18(60%) were ASA II and 12(40%) were ASA III.

After introducing bupivacaine to the sub arachnoid space, The average time to anesthetic onset in the unilateral group was 6.18 ± 1.3 min. In the bilateral group, this value was 4.12 ± 0.41 min. The difference between groups was statistically significant ($p= 0.0001$). The rate of block progression of the unilateral side was higher than other groups (group B); at the same time the level of block was higher and the duration of block was longer. At the time of 10th min after injection, in case of Group-U highest level of sensory block was T9 in all patients 30(100%) achieved sensory block. But in case of Group B at that same time highest sensory level blockade found T₁₁ 28(93%) to T₁₂ 2(7%) of patients.



AS= after spinal anaesthesia.

Figure 1 Trends of heart rate (HR) in the studied group (n=60)

Regarding heart rate, no significant difference was detected between groups at preanesthesia and 5 min afterwards. Compared with group U, group B showed statistically significant increase in heart rate at 10 min after spinal anesthesia ($p<0.05$). Following that heart rate decreased in both the groups but the difference was not significant statistically.

Table 1 Trends of systolic blood pressure (SBP) between groups with respect to time

Systolic BP (mmHg)	Group U (n=30) Mean±SD	Group B (n=30) Mean±SD	p value
Preanesthesia	120.6±6.3	121.3±5.0	0.261
After 5 min	115.5±6.8	104.4±9.2	0.001
After 10 min	95.3±7.1	85.5±5.1	0.001
After 15 min	95.6±11.2	84.3±4.8	0.001
After 20 min	95.9±4.7	82.3±5.0	0.001
After 30 min	97.6±15.6	87.8±5.0	0.002
After 45 min	98.6±11.6	86.3±8.2	0.001
After 60 min	100.6±6.0	102.2±9.4	0.467

Regarding systolic blood pressure no significant difference was there before anaesthesia (sub arachnoid block). But there were significant difference found from the 5 minutes to 45 minutes after anaesthesia ($p < 0.05$). At 60 minute the difference was not significant statistically.

Table II Trends of diastolic blood pressure (DBP) between groups with respect to time

Diastolic BP (mmHg)	Group U (n=30)	Group B (n=30)	<i>p</i> value
	Mean±SD	Mean±SD	
Preanesthesia	80.6±6.0	81.2±9.4	0.348
After 5 min	73.9±5.2	71.2±9.6	0.213
After 10 min	65.4±5.6	62.5±9.5	0.186
After 15 min	60.6±7.4	54.5±9.7	0.013
After 20 min	60.5±7.1	54.9±9.7	0.096
After 30 min	66.0±6.8	61.2±9.4	0.039
After 45 min	67.2±5.6	63.5±9.5	0.001
After 60 min	68.5±5.0	69.2±7.4	0.432

When we compared diastolic blood pressure between groups, we found at 15, 30 and 45 minute difference was statistically significant ($p < 0.05$). But other follow up were not statistically significant ($p > 0.05$) between groups.

Table III Trends of mean arterial pressure (MAP) between groups with respect to time

Time point after spinal anaesthesia	Mean arterial pressure -MAP(mmHg)		<i>p</i> value
	Group U (n=30)	Group B (n=30)	
Preanaesthesia	93.60±11.6	94.93±9.1	0.883
After 5 min	84.45±8.2	78.90±9.5	0.0001
After 10 min	75.40±7.9	70.25±10.2	0.0001
After 15 min	76.92±8.1	69.18±9.5	0.0001
After 20 min	76.31±8.6	68.73±9.1	0.0001
After 30 min	77.57±10.2	71.18±7.5	0.0001
After 45 min	78.05±9.3	79.46±11.4	0.035
After 60 min	81.55±6.8	82.52±7.1	0.486

Regarding meanarterial pressure no significant difference was there before anaesthesia (sub arachnoid block). But there were significant

difference found from the 5 minutes to 30 minutes after anaesthesia ($p < 0.05$). At 45 minutes onwards the difference was not statistically significant.

Table IV Occurrence of complication

Complications	Frequency of occurrence	
	Group U(n=30)	Group B(n=30)
Nausea	2	7
Vomiting	0	3
Headache	3	10
Hypotension	0	7
Bradycardia	1	4

When we assessed complications, none of the patients in the unilateral group experienced vomiting, only two patients noticed nausea. In the bilateral group, seven patients had nausea and three of them experienced episodes of vomiting ($p = 0.02$). Three patients in the unilateral group and ten patients in the bilateral group had headaches ($p = 0.03$).

Discussion

In this study, it was found that unilateral spinal anaesthesia is associated with stable cardiovascular profile and therefore is a valuable technique in high risk patients. From 5th minute to recovery room readings, significant difference was found at various time intervals between groups with systolic blood pressure, mean blood pressure and diastolic blood pressure. The unilateral group found more stable in this study.

Diabetes mellitus (DM) is a strong risk factor for cardiovascular (CV) disease⁶. Compared with those who do not have DM, people with DM have a 2- to 4-fold increased risk of subsequent CV disease⁷⁻⁹. Several risk factors like microvascular and macrovascular complication are associated with DM patients. A study by Sen and Aydin concluded that elderly patients with low ejection fractions were more likely to predispose to higher sensorial block level. Hypotension was more common during spinal anaesthesia with supine position compared to lateral decubitus position¹⁰. The choice of anesthetic has important implications, not only for the intra-operative course, but also for the post-operative outcome. The most common serious side-effects from spinal anaesthesia are hypotension and bradycardia. Unilateral spinal

anaesthesia is effective in restricting the sympathetic block in high risk patients like elderly with existence of co-morbid condition e.g. DM.

The patient's position during and immediately after spinal anesthesia influences the spinal distribution of drugs. If an anesthetic drug solution is hypo- or hyperbaric with respect to the cerebrospinal fluid, it is possible to create a unilateral block. Moreover, the distance between the left and right nerve roots in the lumbar and thoracic regions is about 10-15 cm, which makes it possible to achieve unilateral spinal anesthesia¹¹.

Kuusniemi et al. reported that hyperbaric bupivacaine is more effective in achieving unilateral spinal anesthesia than plain bupivacaine¹². However, determining the optimal time for lateral positioning is difficult when a high dose of hyperbaric bupivacaine (12-20 mg) is used¹³⁻¹⁴. The anesthetic drug may migrate even when the patient is placed in the lateral position for 30-60 min. Conversely, if a low dose (5-8 mg) of anesthetic solution is used, putting the patient in the lateral position for 10-15 min may prevent migration of the anesthetic drug. In this study, we injected hyperbaric bupivacaine 0.5% at a dose 7.5mg to achieve spinal anesthesia. The patients were kept in the lateral position for 10-15 min, which led to unilateral spinal anesthesia in 94.45% of cases. In a study performed by Esmaglu et al. the patient was in the lateral position for 10 min. This approach yielded an 85.7% success rate. This discrepancy in terms of the success rate seems to be dependent on the duration of time spent in the lateral position¹⁵.

In another study by Imbelloni et al. all patients received unilateral spinal anaesthesia with 5 mg of 0.5% hyperbaric bupivacaine at the rate of 1 ml/minute had observed no hypotension. These patients were kept in lateral decubitus position for 20 minutes resulted in block on dependent site with minimal haemodynamic changes¹⁶. Similar results were observed in another study done by Park et al. in which the patients positioned immediately supine showed a greater decrease in arterial blood pressure and heart rate than the patients who were kept in the lateral decubitus position for 20 minutes after the induction of spinal anaesthesia.¹⁷

The observations recorded in this study support the view that unilateral spinal anaesthesia is

associated with a more stable cardiovascular profile than the conventional spinal anaesthesia². A similar study conducted by Khan and colleagues found haemodynamic stability slightly more in unilateral spinal group but results were statistically insignificant.¹⁸ Rao concluded that unilateral block could be a more useful concept in older age group and autonomically compromised patients. As in younger age group, patients haemodynamic changes were negligible most probably due to active sympathetic system at the unblocked area.¹⁹ Unilateral sensory and motor block, a faster recovery profile, and a stable haemodynamic state can be achieved with doses of 5 mg and 7.5 mg of hyperbaric bupivacaine 0.5% injected slowly through pencil-point directional needles in patients who are maintained in the lateral decubitus position for 20 minutes.²⁰ Unilateral spinal anaesthesia ensures higher intraoperative haemodynamic stability.²¹

Valanne used 4 or 6 mg of bupivacaine to induce unilateral spinal anesthesia in 106 patients scheduled to undergo knee arthroscopy. While both doses were sufficient for sensory and motor block, 4 mg of bupivacaine achieves a more rapid regression of motor function²². Headache after spinal anesthesia was reported in two and eight patients in the unilateral and bilateral groups, respectively. In contrast, Smaoglu used 1.5 cm³ and 3 cm³ of hyperbaric bupivacaine 0.5% for unilateral and bilateral anesthesia, respectively: six and nine patients, respectively, experienced headache. This discrepancy may be related to the type of needle used (Quincke) or the relatively young age of the patient population¹³. Notably, spinal anesthesia can disturb bladder function by disabling the micturition reflex. Kamphuis and colleagues reported that voiding disturbance continues until the nerve block has regressed to the third sacral root²³. In our study, there was no bradycardia in the unilateral group, but in the bilateral group, 5 patients had bradycardia ($p = 0.04$). On average, the time to the onset of anesthesia and immobility was faster in the bilateral as compared to the unilateral spinal anesthesia group ($p = 0.00$). The sensory and motor block lasted for less time in the unilateral as compared to the bilateral group. Unilateral spinal anesthesia is therefore suitable for lower limb surgery.

Conclusions

In this study, it was found that unilateral spinal anaesthesia is associated with stable cardiovascular profile and less associated with nausea and vomiting. This valuable technique is a good alternative of conventional spinal anaesthesia for elderly diabetic high risk patients. But there is found some extends of contralateral block which is minimum.

Limitations of the study

This study was not without limitation. The limitations of the studies were as follows:

- Small sample size of the study population.
- It was a single centre study. Only patients admitted in BIRDEM general hospital were taken for the study. So this will not reflect the overall picture of the country. A large scale study needs to be conducted to reach to a definitive conclusion
- Others limitation were short duration of study and limited investigation facility.

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Original Article

Different doses of Dexmedetomidine in attenuating the pressor response to laryngoscopy in controlled hypertensive patient under general anesthesia

Rumana Afroz¹, Rabeya Begum², Mahin Muntakim³, Taneem Mohammad⁴, Subrata Kumar Mondal⁵, Mohammad Jahid Iqbal⁶, Md. Ali Haider⁷, Md. Humayun Kabir⁸

¹Registrar, Department of Neuroanaesthesia and Neurocritical Care, Evercare Hospitals Dhaka, ²Professor and Head of the Department of Anaesthesia, Greenlife Medical College, Dhaka, ³Medical Officer, DGHS, ⁴Assistant Professor, Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine, Dhaka Medical College, Dhaka, ⁵Associate Professor, Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine, Dhaka Medical College, Dhaka, ⁶Junior consultant, Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine, Dhaka Medical College, Dhaka, ⁷Specialist Cardiac Anesthesia and CT ICU, Square Hospital Limited, Dhaka, ⁸Registrar specialist, Ibrahim Cardiac Hospital and Research Institute, Dhaka

Corresponding author: E-mail: preith007@yahoo.com

Abstract

Background: Laryngoscopic manipulation and endotracheal intubation are always a matter of concern which capable of producing tachycardia, arrhythmias and hypertension which is generally well tolerated in healthy patient. In Hypertensive patient cardiovascular response to laryngoscopy and intubation is exaggerated.

Aims: To assess the effectiveness in attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with different doses of intravenous dexmedetomidine in controlled hypertensive patients with no adverse effects.

Methods: This prospective Randomized controlled trial was carried out with 60 patients belonging to American Society of Anesthesiologists (ASA) Physical Status II posted for elective general anaesthesia. Patients were randomly divided into three groups with fixed card sampling, where, patients who received IV dexmedetomidine 0.5 µg/kg diluted to 50 ml with normal saline as infusion over 10 min was considered as group A, patients who received IV dexmedetomidine 0.75 µg/kg diluted to 50 ml with normal saline was considered as group B and patients who received IV dexmedetomidine 1 µg/kg diluted to 50 ml with normal saline was considered as group C. The primary outcome measures were haemodynamic response at 1, 3 and 5 min after intubation. The secondary outcome measures were to note down any adverse effects associated with drugs.

Result: The groups were well matched for their demographic data. Male to female ratio was 1:1 in all three group. The mean height, weight and BMI were almost similar among three groups. In this study baseline readings of SBP, DBP, MAP and HR were almost similar in all three groups and statistically not significant. Maximum intubation response was seen at 1 min post intubation in all the three groups. The mean SBP of group A varied from 144.8±8.4 mmHg to 118.5±4.4 mmHg that of group B varied from 134.8±4.1 to 122.0±4.2 mmHg and then group C varied from 126.5±15.5 mmHg to 103.8±8.4 mmHg during different evaluation period (p<0.05). The mean DBP of group A varied from 91.8±7.6 mmHg to 72.4±5.8 mmHg that of group B varied from 81.3±5.2 to 70.3±2.5 mmHg and then group C varied from 80.9±6.7 mmHg to 63.4±2.4 mmHg during different evaluation period (p<0.05). The mean MAP of group A varied from 109.0±5.6 mmHg to 87.5±4.4 mmHg that of group B varied from 98.7±2.5 to 86.3±3.4 mmHg and then group C varied from 95.5±9.2 mmHg to 76.5±3.4 mmHg during different evaluation period (p<0.05). The mean heart rate of group A varied from 94.5±12.7 bpm to 75.2±10.5 bpm that of group B varied from 87.3±8.3 to 75.0±6.6 bpm and then group C varied from 81.1±7.2 bpm to 66.2±8.1 bpm during different evaluation period (p<0.05).

Conclusion: Dexmedetomidine in doses of 0.75 µg/kg was more effective compared to 0.05 µg/kg and 1µg/kg in attenuating haemodynamic response to laryngoscopy and endotracheal intubation without producing adverse effects in control hypertensive patients.

Keywords: Efficacy; different doses; dexmedetomidine; haemodynamic response; laryngoscopy; controlled hypertensive patient; randomized control trial.

Introduction

The anaesthesiologist is mainly responsible for providing a secure airway for a proper ventilation of the patient during anaesthesia and surgery. No medication and anaesthetic method is reassuring, unless a secure airway is maintained with great efforts. Laryngoscopy and endotracheal intubation is a commonly used measure for the maintenance of a secure airway during general anesthesia and it has specific indications¹⁵.

However both laryngoscopy and intubation are noxious stimuli and are associated with stress responses and haemodynamic responses in the form of laryngo-sympathetic stimulation which is manifested as hypertension, tachycardia and arrhythmias¹⁵. These haemodynamic responses are well tolerated in otherwise healthy individuals, but in patients with hypertension, coronary heart these transient changes can result in potentially deleterious effects like left ventricular failure, pulmonary edema, myocardial ischemia, ventricular dysrhythmias and cerebral hemorrhage⁸.

Dexmedetomidine is effective during intubation and maintained intraoperative cardiovascular stability. These drugs decrease tachycardia, hypertension, and sympathetic activity, which are beneficial for the cases with a presence of myocardial ischemia².

Various researchers of different countries have suggested that dexmedetomidine is significantly reduced the haemodynamic responses during laryngoscopy and endotracheal intubation among the hypertensive patients³. Choudhury et al⁴ and Sulaiman et al³ have both performed two separate studies by using dexmedetomidine with a dose of 0.05 µg/kg for reduction of blood pressure responses during laryngoscopy and endotracheal intubation. The pretreatment with dexmedetomidine 0.05 µg/kg attenuate the stress responses, but did not totally abolish the cardiovascular and catecholamine surge responses to tracheal intubation. Smitha et al⁵ have used dexmedetomidine with the dose of 0.5 and 1 µg/kg and have found that the dose of 1 µg/kg is more effective for the reduction of stress response to laryngoscopy and endotracheal intubation. However, this is a promising results; furthermore

the dose of 1 µg/kg is associated with some incidence of cardiovascular system. Sebastian et al⁶ have used dexmedetomidine (0.75 µg/kg) for reduction of stress response to laryngoscopy and endotracheal intubation. In 0.75 µg/kg group, intubation responses is completely obtunded when compared to 0.5 µg/kg without any adverse effects.

Appropriate premedication can prevent the associated risks of haemodynamic pressure response to laryngoscopy and intubation in controlled hypertension patients; which is essential to prevent negative outcomes such as tachycardia, hypertension, myocardial ischemia, ventricular arrhythmias. Dexmedetomidine is highly specific and selective potent alpha-2 agonist which potentially offer a superior effect in attenuating stress-induced sympathoadrenal responses during laryngoscopy. Therefore, the search of effective dose of dexmedetomidine premedication for controlled hypertensive patients uncovering the possibilities for better management of those patient with less side effects in perioperative period and reduce mortality and morbidity.

Methodology

Study Population and Settings: This single blind, parallel randomized controlled trial was conducted in Department of Anaesthesia, Analgesia, Palliative and intensive Care Medicine, Dhaka Medical College Hospital, Dhaka from August 2016 to July 2018 for a period of two (02) years. Data was gathered after approval of protocol by ethical review committee. Patients who were categorized as American society of Anesthesiology (ASA) class II, patients who had a history of essential hypertension for which they were being treated and controlled as well as posted for elective surgeries under general anesthesia were selected as study population. Any anticipated difficult intubation or patients who had a history of bronchial asthma, drug or alcohol abuse, patients who had a history of cerebrovascular, neurologic, respiratory or ischemic heart disease and renal or hepatic dysfunction, patients who were physically dependent on narcotics, known drug allergy to dexmedetomidine, patients on antidepressants, anxiolytics, anticonvulsant or antipsychotics, pregnant or nursing woman, participation in another drug study during the preceding 1 month period were excluded from this study.

Randomization and Blinding: A total number of sixty (60) patients belonging to ASA Physical Status II posted for elective general anaesthesia was finally selected. All the information were recorded in a prefixed data sheet. Patients were randomly divided into three groups and each group had twenty patients. Randomization allocated by fixed card sampling. One assigned anesthesiologist performed the grouping. Data were collected by the volunteer anaesthesiologist who was expert enough take data and was fully unaware of the study.

Intervention: Group A consisted of twenty (20) patients who were received IV dexmedetomidine 0.5 µg/kg diluted to 50 ml with normal saline as infusion over 10 min. Group B consisted of twenty (20) patients who were received IV dexmedetomidine 0.75 µg/kg diluted to 50 ml with normal saline as infusion over 10 min. Group C consisted of twenty (20) patients who were received IV dexmedetomidine 1 µg/kg diluted to 50 ml with normal saline as infusion over 10 min. All infusions were started 10 minutes prior induction of general anesthesia. All patients were evaluated a day before surgery. The patients were kept fasting overnight after 10:00 pm and was received tablet Ranitidine 150 mg orally and tablet midazolam 7.5 mg orally as premedication at night before surgery. All patients monitored with non-invasive blood pressure monitor (philips sure signs VS3). An IV line was secured, and the patients were administered 500ml of IV fluid Ringer's lactate. Baseline systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and heart rate (HR) were measured by one volunteer anaesthesiologists by non-invasive blood pressure monitor and pulse oximetry(philips sure signs VS3). Then study drug infusion was given over 10 min by principal investigator. All the patients were pre-oxygenated for 3 minutes. Then, patients was induced with IV Thiopental Sodium 5 mg/kg body weight, IV fentanyl 1 µg/kg, endotracheal intubation was facilitated by IV succinylcholine 1.5 mg/kg body weight. Laryngoscopy and intubation was done by principal investigator.

Follow up and Outcome Measures: Following laryngoscopy and endotracheal intubation, the parameters recorded was SBP, DBP, MAP and HR

at 1, 3 and 5 min after intubation by non-invasive blood pressure monitor. After adequate recovery, patients were shifted to post-anaesthesia care unit and monitored for 2 hours. The principle investigator was assessing the patients directly postoperatively in the recovery room and was also personally follow-up the patients in the ward for monitoring purposes. If any unforeseen complication occurs in the ward, the principle investigator was available to come and examine the patient, address and manage any problems.

Statistical analysis: All the parameters were expressed as mean and standard deviation (mean $\pm$ SD) and percentage. ANOVA for repeated measures followed by post hoc analysis with Least Significance Difference (LSD) was performed for comparing continuous variables within the groups at different time points. For intragroup comparison at the same time point, between the groups, Students 't' test was applied. p value <0.05 was accepted as level of significance. Statistical analyses were performed by using a computer based statistical program SPSS (Statistical Package for Social Sciences) Version 22 with the help of a biostatistician.

Result

This present study was carried out with an aim to find out the specific dose of Dexmedetomidine in attenuation of haemodynamic responses to laryngoscopy and tracheal intubation in controlled hypertensive patients without adverse effects. The groups were well matched for their demographic data. Male to female ratio was 1:1 in all three group. The basal readings of SBP, DBP, MAP and HR were similar in all the three groups. Maximum intubation response was seen at 1 min post-intubation in all the three groups. Regarding the side effects it was observed that Hypotension was found in 6(30.0%) and bradycardia was found in 4(20.0%) cases in group C and hypertension was found in 4(20.0%) cases of group A. The difference was statistically significant ($p<0.05$) among three groups. The mean age were 45.2 ± 3.1 years in group A, 50.3 ± 7.4 years in group B and 47.5 ± 7.9 years in group C. Male was found 10(50.0%) in group A, 10(50.0%) in group B and 10(50.0%) in group C. The difference was statistically not significant ($p>0.05$) among three groups (Table 1).

Table I Age and Gender Distribution of the Study Participant (n=60)

Variables	Group A (n=20)	Group B (n=20)	Group C (n=20)	P value
Mean Age (Years)	45.2±3.1	50.3±7.4	47.5±7.9	^a 0.053 ^{ns}
Range(min-max)	33 to 43	40 to 60	35 to 60	
Gender				
• Male	10(50.0%)	10(50.0%)	10(50.0%)	^b 1.000 ^{ns}
• Female	10(50.0%)	10(50.0%)	10(50.0%)	

ns= not significant; ^ap value reached from ANOVA test; ^bp value reached from Chi- square test; Data are expressed as Mean±SD

Baseline mean Systolic blood pressure was found 130.2±6.5 (mmHg) in group A, 135.6±4.3 (mmHg) in group B and 134.9±11.9 (mmHg) in group C. The Baseline difference was statistically not significant (p>0.05) among three groups. The mean SBP of group A varied from 144.8±8.4 mmHg to 118.5±4.4 mmHg that of group B varied from 134.8±4.1 to 122.0±4.2 mmHg and then group C varied from 126.5±15.5 mmHg to 103.8±8.4 mmHg during different evaluation period. The difference was statistically significant (p<0.05) among three groups (Table II).

Baseline mean diastolic blood pressure baseline (DBP) was found 79.8±2.2 (mmHg) in group A, 80.6±3.7 (mmHg) in group B and 82.2±4.5 (mmHg) in group C. The Baseline difference was statistically not significant (p>0.05) among three groups. The mean DBP of group A varied from 91.8±7.6 mmHg to 72.4±5.8 mmHg that of group B varied from 81.3±5.2 to 70.3±2.5 mmHg and then group C varied from 80.9±6.7 mmHg to 63.4±2.4 mmHg during different evaluation period. The difference was statistically significant (p<0.05) among three groups (Table III).

Table II Distribution of the Study Participant by Systolic Blood Pressure (n=60)

Systolic blood pressure (mmHg)	Group A (n=20)	Group B (n=20)	Group C (n=20)	P value
Baseline	130.2±6.5	135.6±4.3	134.9±11.9	0.086 ^{ns}
Range(min-max)	120 to 140	130 to 142	127 to 158	
After drug administration	118.5±4.4	129.0±5.5	124.5±10.9	0.001 ^s
Range(min-max)	110 to 122	120 to 137	110 to 143	
1 min	144.8±8.4	134.8±4.1	126.5±15.5	0.001 ^s
Range(min-max)	130 to 155	130 to 140	105 to 145	
3 min	128.6±5.8	126.3±5.7	112.2±8.9	0.001 ^s
Range(min-max)	118 to 135	120 to 135	100 to 124	
5 min	119.1±8.0	122.0±4.2	103.8±8.4	0.001 ^s
Range(min-max)	105 to 128	118 to 130	90 to 120	

s=significant; ns=not significant; p value reached from ANOVA test; Data are expressed as Mean±SD

Table III Distribution of the study participant by diastolic blood pressure (n=60)

Diastolic BP (mmHg)	Group A (n=20)	Group B (n=20)	Group C (n=20)	P value
Baseline	79.8±2.2	80.6±3.7	82.2±4.5	0.108 ^{ns}
Range(min-max)	75-82	75-87	80-92	
After drug administration	72.4±5.8	73.7±4.2	78.1±5.7	0.003 ^s
Range(min-max)	60-80	70-82	70-86	
1 min	91.8±7.6	81.3±5.2	80.9±6.7	0.001 ^s
Range(min-max)	79-100	78-85	71-90	
3 min	86.3±6.5	75.7±2.9	73.1±6.7	0.001 ^s
Range(min-max)	75-95	70-80	68-90	
5 min	77.8±3.9	70.3±2.5	63.4±2.4	0.001 ^s
Range(min-max)	70-82	65-75	60-68	

s=significant; p value reached from ANOVA test; Data are expressed as Mean±SD

Baseline mean MAP was found 96.8 ± 4.1 (mmHg) in group A, 98.3 ± 3.8 (mmHg) in group B and 100.3 ± 7.1 (mmHg) in Group C. The Baseline difference was statistically not significant ($p > 0.05$) among three groups. The mean MAP of group A varied from 109.0 ± 5.6 mmHg to 87.5 ± 4.4 mmHg that of group B varied from 98.7 ± 2.5 to 86.3 ± 3.4 mmHg and then group C varied from 95.5 ± 9.2 mmHg to 76.5 ± 3.4 mmHg during different evaluation period. The difference was statistically significant ($p < 0.05$) among three groups (Table IV).

Baseline mean heart rate was found 83.4 ± 9.6 bpm in Group A, 90.2 ± 13.4 bpm in Group B and 84.9 ± 3.9 bpm in Group C. The baseline difference was statistically not significant ($p > 0.05$) among three groups. The mean heart rate of group A varied from 94.5 ± 12.7 bpm to 75.2 ± 10.5 bpm that of group B varied from 87.3 ± 8.3 to 75.0 ± 6.6 bpm and then group C varied from 81.1 ± 7.2 bpm to 66.2 ± 8.1 bpm during different evaluation period. The difference was statistically significant ($p < 0.05$) among three groups.

Table IV Distribution of the study participant by MAP ($n=60$)

MAP (mmHg)	Group A ($n=20$)	Group B ($n=20$)	Group C ($n=20$)	P value
Baseline	96.8 ± 4.1	98.3 ± 3.8	100.3 ± 7.1	0.113 ^{ns}
Range(min-max)	91 to 106	93 to 105	95 to 114	
After drug administration	87.5 ± 4.4	91.9 ± 3.7	92.6 ± 7.7	0.007 ^s
Range(min-max)	80 to 94	88 to 99	83 to 104	
1 min	109.0 ± 5.6	98.7 ± 2.5	95.5 ± 9.2	0.001 ^s
Range(min-max)	101 to 117	96 to 103	84 to 108	
3 min	99.9 ± 4.3	91.8 ± 4.2	85.9 ± 5.4	0.001 ^s
Range(min-max)	94 to 106	85 to 97	80 to 96	
5 min	91.4 ± 3.4	86.3 ± 3.4	76.5 ± 3.4	0.001 ^s
Range(min-max)	84 to 96	80 to 93	70 to 82	

s=significant; p value reached from ANOVA test; Data are expressed as Mean $\pm$ SD.

Table V Distribution of the Study Participant by Heart Rate ($n=60$)

Heart Rate (bpm)	Group A ($n=20$)	Group B ($n=20$)	Group C ($n=20$)	P value
Baseline	83.4 ± 9.6	90.2 ± 13.4	84.9 ± 3.9	0.078 ^{ns}
Range(min-max)	60 to 94	80 to 120	76 to 90	
After drug administration	75.2 ± 10.5	83.6 ± 12.5	73.6 ± 6.7	0.006 ^s
Range(min-max)	54 to 90	67 to 110	65 to 86	
1 min	94.5 ± 12.7	87.3 ± 8.3	81.1 ± 7.2	0.006 ^s
Range(min-max)	78 to 120	75 to 98	70 to 90	
3 min	87.4 ± 11.7	79.4 ± 5.8	75.0 ± 7.8	0.002 ^s
Range(min-max)	70 to 112	70 to 90	60 to 85	
5 min	78.7 ± 6.9	75.0 ± 6.6	66.2 ± 8.1	0.001 ^s
Range(min-max)	66 to 90	65 to 87	52 to 74	

s=significant; p value reached from ANOVA test; Data are expressed as Mean $\pm$ SD

Note: ADA= after drug administration

Table VI Distribution of the study participant by side effects (n=60)

Side effects	Group A (n=20)		Group B (n=20)		Group C (n=20)		P value
	n	%	n	%	N	%	
Hypotension	0/20	0.0	0/20	0.0	6/20	30.0	0.001 ^s
Hypertension	4/16	20.0	0/20	0.0	0/20	0.0	0.014 ^s
Bradycardia	0/20	0.0	0/20	0.0	4/16	20.0	0.013 ^s

s= significant, p value reached from chi square test

Table VI shows side effects of the study patients, it was observed that bradycardia had 4(20.0%) in group C. The difference was statistically significant ($p < 0.05$) among three groups.

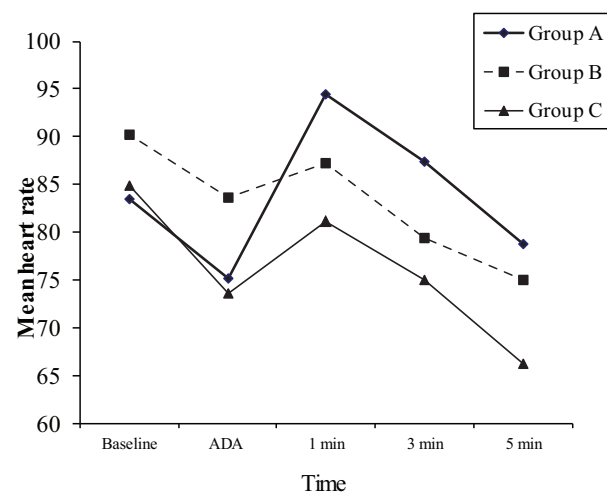


Figure 1: Line graph showing heart rate of the study populations

Discussion

In this present study, the mean age was 45.2 ± 3.1 years in group A, 50.3 ± 7.4 years in group B and 47.5 ± 7.9 years in group C. The difference was statistically not significant ($p > 0.05$) among three groups. Samala et al⁸, Pramanick et al⁹ and Smitha et al⁵ found almost similar mean age and age ranged in their respective studies. On the other hand Sebastian et al⁶ found the mean age was 32.50 ± 9.12 years in Group A, 36.96 ± 10.33 years in Group B, 31.20 ± 9.30 years in Group C, which is smaller with the present study. The lower mean age and age range maybe due to geographical variations, racial, ethnic differences, and genetic causes.

In this study, dexmedetomidine is effective significantly in blunting the increase in mean SBP

and DBP due to laryngoscopy and intubation. However, the baseline difference of mean SBP and DBP is not statistically significant ($p > 0.05$) among the group A, B and C. Though mean SBP and DBP have been increased at 1 minute after intubation in all three groups. The haemodynamic variables fell below the base line in group B and C all the time. The findings indicates that there is a disparity of SBP and DBP in group A and group C but in group B it was almost unswerving from baseline to 5 minutes follow-up. Inter group comparison revealed statically significant among three groups ($p < 0.05$). Smitha et al⁵ compared the effect of 0.5 and 1 $\mu\text{g/kg}$ of dexmedetomidine with normal saline in attenuating stress response. They found out that dexmedetomidine 1 $\mu\text{g/kg}$ was more effective than dexmedetomidine 0.5 $\mu\text{g/kg}$ in controlling haemodynamic responses to tracheal intubation. The intergroup comparison revealed a statistically significant ($p < 0.05$). Similar observations regarding the SBP and DBP were also Samala et al⁸, Pramanick et al⁹ and Sebastian et al⁶.

At baseline, the MAP ($P = 0.113$) is almost same among the group A, B and C. However, it has been also found that group B and group C have a significantly lower MAP ($p = 0.001$) to 5 min follow up. Dexmedetomidine attenuates sympatho-adrenal response by activation of presynaptic α_2 receptors in sympathetic nerve endings resulting in decreased release of noradrenaline. Moreover, stimulation of postsynaptic α_2 receptors of locus coeruleus causes inhibition of norepinephrine release¹⁰. Patel et al¹¹ have administered dexmedetomidine intravenously as loading dose of 1 $\mu\text{g/kg}$ over 10 min prior to induction in group B and observed, dexmedetomidine significantly attenuated stress response to intubation with lesser increase in systolic (6% vs. 23%) and diastolic (7% vs. 20%) blood pressure as compared to the control group ($P < 0.05$).

In this current study, the baseline mean MAP is 96.8 ± 4.1 (mmHg) in group A; however, in group B and group C the MAP are slightly higher than group A which are 98.3 ± 3.8 (mmHg) and 100.3 ± 7.1 (mmHg) respectively. The baseline difference of mean arterial pressure among these three groups is not statistically significant ($p > 0.05$). Maximum intubation response is found at 1 min post-intubation among the three groups. In group B, they approached near the baseline by 3 minutes. Interestingly, the variables fell below the baseline by 3 min in group C. In group A statistically higher values of SBP, MAP at all-time intervals are found in post-intubation when compared to group B and group C. Therefore, it can be inferred that the haemodynamic response is better observed in group B and group C, when it is compared with group A. However, the parameters fell below the baseline value at 1 min after intubation in group C. This clearly indicates that the dexmedetomidine in a dose of $0.75 \mu\text{g/kg}$ and $1 \mu\text{g/kg}$ is superior to dexmedetomidine in a dose of $0.5 \mu\text{g/kg}$.

Similarly Sebastian et al⁶ showed the mean of Mean Arterial Blood Pressure (MAP) in first minute 114.57 ± 5.14 mmHg in Group A, 98.87 ± 5.86 mmHg in Group B and 96.33 ± 5.40 mmHg in Group C ($p < 0.001$). In third minute 108.47 ± 4.97 mmHg in Group A, 94.83 ± 5.13 mmHg in Group B and 90.27 ± 5.49 mmHg in Group C ($p < 0.001$). In fifth minute 103.37 ± 4.51 mmHg in Group A, 91.80 ± 5.48 mmHg in Group B and 85.47 ± 5.08 mmHg in Group C ($p < 0.001$). Similar observations regarding the MAP pressure was also reported by Smitha et al⁵.

At baseline, the HR ($P = 0.078$) was almost same among three groups. However, it was found that, group B and group C had a significantly lower HR just after intubation ($P = 0.006$) to 5 min follow up. The heart rate showed that there is discrimination in group A and group C but in group B it was almost consistent from baseline to 5 minutes follow-up. Dexmedetomidine attenuates sympathoadrenal response by activation of presynaptic α_2 receptors in sympathetic nerve endings resulting in decreased release of noradrenaline. Moreover, stimulation of postsynaptic α_2 receptors of locus coeruleus causes inhibition of norepinephrine release³. Patel et al¹¹, administered dexmedetomidine intravenously as loading dose of $1 \mu\text{g/kg}$ over 10 min prior to induction in group B and

observed, dexmedetomidine significantly attenuated stress response to intubation with lesser increase in heart rate (10% vs. 17%).

The group A had statistically higher values of HR at all-time intervals post-intubation when compared to Group B and Group C. Hence, it can be inferred that the haemodynamic response was better obtained in Group B and Group C, when compared with Group A. In Group C, the parameters fell below the baseline value at 1 min after intubation. This indicates that dexmedetomidine in a dose of $0.75 \mu\text{g/kg}$ and $1 \mu\text{g/kg}$ was superior to dexmedetomidine in a dose of $0.5 \mu\text{g/kg}$.

In this present study, hypotension was found in 6(30.0%) and bradycardia was found 4(20.0%) in group C. In group A hypertension has found in 4(20.0%) cases. The differences among the three groups is statistically significant ($p < 0.05$). Smitha et al⁵ have reported that different doses of dexmedetomidine has shown irregular breathing with varied episodes of apnoea. Furthermore, dexmedetomidine ($1 \mu\text{g/kg}$) has been associated with the increased incidence of adverse effects like bradycardia and hypotension observed by Kartik et al¹² and Menda et al¹³. It has been established that the activation of post-synaptic α_2 receptors in CNS brings the decreased sympathetic activity which can lead to bradycardia as well as hypotension¹⁴. Furthermore dexmedetomidine ($1 \mu\text{g/kg}$) is associated with increased incidence of adverse effects¹³.

Yallapragada et al¹⁵ have been reported that the dexmedetomidine ($1 \mu\text{g/Kg}$) is effective on the blood pressure responses during laryngoscopy and intubation showed that BP increased by 4.0% initially but later declined by 11.0% following a 5 minute infusion of dexmedetomidine. After intubation the SBP rose only slightly above baseline. In four patients in dexmedetomidine Group hypotension (SBP < 90 mmHg) was observed following induction of anaesthesia. In this study also six patients had developed hypotension in group C.

Patients have been shifted to the post anaesthesia care unit after complete clinical recovery and they have been observed for 2 hours for nausea, vomiting, bradycardia, hypotension and sedation.

In present study results suggested that to control blood pressure during laryngoscopy and tracheal intubation, Dexmedetomidine is a better drug and 0.75 µg/kg dose is more effective than Dexmedetomidine with the dose of 0.5 µg/kg and 1 µg/kg which causes no significant side effects in controlled hypertensive patients. In this study no significant respiratory depression, apnea, muscle rigidity or decrease in SpO₂ was seen in any patient in post-operative period.

Conclusion

Under the condition of present study it can be concluded that Dexmedetomidine dose of 0.75 µg/kg is safe and effective in obtunding the blood pressure response to laryngoscopy and endotracheal intubation without producing side effects compared to doses of 0.5 µg/kg and 1 µg/kg

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Laparoscopic Cholecystectomy in High Risk Cardiac Patient with DM

Md. Mushfiquir Rahman¹, Shafiul Alam Shaheen², Md. Mahbubul Hasan Munir¹, Kawsar Sardar³, Md. Abdus Salam Khan⁴, AKM Nurnobi Chowdhury⁴, M Khalilur Rahman⁵, Shamiron Kumar Mondal⁶, Taposh Kumar Mitra⁷

¹Associate Professor, Department of Anaesthesia, Analgesia & Surgical-ICU, BIRDEM General Hospital, Shahbagh, Dhaka, ²Assistant Professor, Department of Anaesthesia, Analgesia & Surgical-ICU, BIRDEM General Hospital, Shahbagh, Dhaka, ³Professor & Head, Department of Anaesthesia, Analgesia & Surgical-ICU, BIRDEM General Hospital, Shahbagh, Dhaka, ⁴Professor, Department of Anaesthesia, Analgesia & Surgical-ICU, BIRDEM General Hospital, Shahbagh, Dhaka, ⁵Senior Consultant (Hon), Department of Anaesthesia, Analgesia & Surgical-ICU, BIRDEM General Hospital, Shahbagh, Dhaka, ⁶Professor, Department of Surgery, BIRDEM General Hospital, Shahbagh, Dhaka, ⁷Professor & Head, Department of Surgery, BIRDEM General Hospital, Shahbagh, Dhaka.

Corresponding Author: Dr. Md. Mushfiquir Rahman, E-mail: rahmaanmushfique@gmail.com

Abstract

Introduction: Laparoscopic cholecystectomy remains the standard treatment for cholelithiasis. Ever increasing number of patients with myriad of medical illness is being treated by this technique. However, significant concern prevails among the surgical community regarding its safety in patients with cardiac co-morbidity. Patients with diabetes, significant cardiac dysfunction and multiple co-morbidities were prospectively evaluated. Patients were assessed by cardiologists and anesthesiologists and laparoscopic cholecystectomy was performed.

Results: Patient demographics, details of peri-operative management and post-operative complications were studied. Between July 2014 and January 2018, 32 patients (M:F=24:08) with mean age of 55 years (range 36–78) and having significant cardiac dysfunction had undergone laparoscopic cholecystectomy. Of these, 24 patients were in NYHA class-II, while 8 belonged to class-III. Left ventricular ejection fraction, as recorded by transthoracic echocardiography, was 20–30% in 08 (25%) patients and 30–40% in the rest 24 (75%). In addition, 21 (71%) patients had regional wall motion abnormalities, 11 (34%) patients had cardiomyopathy while 09 (39%) patients had prior cardiac interventions. Following laparoscopic cholecystectomy, hypertension (21), tachyarrhythmia (4) and bradycardia (2) were the commonest events encountered. Two patients required dopamine in the immediate postoperative period but all other patients made an uneventful recovery.

Conclusion: With appropriate cardiological support, laparoscopic cholecystectomy may be safely performed in patients with significant cardiac dysfunction.

Keywords: Laparoscopy, Cholecystectomy, High Risk Cardiac Patient.

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Introduction

Laparoscopic surgery has become very popular as its advantages include minimally invasive nature, less postoperative pain, early return to activities, less postoperative ileus, less wound infections and superior cosmesis¹. Since the introduction of laparoscopic cholecystectomy by Philip Mouret in 1987, the technique was rapidly accepted by the surgical community². The appeal of diminished pain and fatigue, early return to

normal activities and superior cosmesis has made it a popular surgery³. Previous abdominal surgery, acute cholecystitis⁴, morbid obesity⁵, old age⁶ and pregnancy⁷ were traditional contraindications for laparoscopic cholecystectomy.

However, in the recent years, development of surgical skills and better understanding of the pathophysiology of pneumoperitoneum have made it possible to offer laparoscopic cholecystectomy to patients suffering from myriad of medical illness.

Nonetheless, concerns remain about the safety of this technique in patients with cardiac comorbidity.

Diabetes mellitus is the most common endocrine abnormality encountered in surgical patients and is associated with increased perioperative morbidity and mortality mainly due to the complications of the disease.

Diabetic patients frequently have cardiovascular disorders such as hypertension, ischaemic heart disease and left ventricular dysfunction and very often associated with autonomic neuropathy which may aggravate during pneumoperitoneum. Therefore effective measures are to be sought to reduce these responses and minimize intra-operative hazards.

During laparoscopy, positive pressure pneumoperitoneum using carbon dioxide could have deleterious effects on the cardiovascular system [8]. Therefore, standard text books often cite patients with cardiac dysfunction a relative contraindication to laparoscopic cholecystectomy [4]. Similar anxiety also prevails amongst the surgical and anaesthetist community and laparoscopic cholecystectomy is often discouraged in patients with significant cardiac diseases.

On the contrary, the physiological stress following minimally invasive surgery is lesser as compared to patients undergoing open cholecystectomy [9–11]. This begs the question whether the purported risk of pneumoperitoneum could be offset by the diminished stress following minimally invasive surgery, thereby bringing the patients with cardiac co-morbidity within the ambit of laparoscopic cholecystectomy. This prospective study was undertaken in a tertiary care hospital to evaluate the safety of laparoscopic cholecystectomy in patients with ischemic heart disease and significant cardiac dysfunction.

Materials and Methods

This observational study was started in July 2016. Since inception, patient demographics, operative data and post-operative course of all patients were prospectively recorded in a computerised database. Pre-operative Assessment Patients with significant ischemic heart disease were evaluated by resting ECG and transthoracic echocardiography. They were subsequently evaluated by cardiologists and anaesthetist in pre anesthetic check up.

The patients were grouped according to the New York Heart Association (NYHA) functional classification system¹². For this study, patients belonging to NYHA II and III were included.

Diabetic was controlled by short acting insulin and other associated systemic diseases (like HTN, Br. Asthma) if present were optimized by taking consultation from respective consultant. Patients on antiplatelet drugs were asked to stop these medicines 5 days before surgery. Beta-blockers were started preoperatively in those who were not receiving such drugs previously. Patients on anti-coagulants were switched over to some form of heparin according to standard dosage schedule and were taken up for surgery when international normalized ratio (INR) fell below 1.5.

All patients were premedicated with Midazolam (7.5 mg), Ondansetron (4 mg) and Omeprazole (20 mg) in the night before surgery and cardiac medications, except angiotensin converting enzyme inhibitors, were continued till the morning of surgery.

Operative management laparoscopic cholecystectomy was performed early in the morning after a minimum of 4 hours of fasting. Venous access was obtained with an 18 G peripheral venous cannula. Monitoring was started with the patient awake, pulse oximeter, temperature, noninvasive blood pressure (BP), and five lead electrocardiogram (ECG).

In patients who have had permanent pacemaker implanted, the mode was changed to fixed mode prior to surgery. Arrangement of temporary pacing, defibrillator and syringes with preloaded life saving drugs were kept ready. After preoxygenation with 100% oxygen, anaesthesia was induced with Fentanyl (2–3 mcg/kg), midazolam 0.03 mg/kg and Propofol (1–2 mg/kg) IV slowly. Atracurium (0.5 mg/kg) was used for intubation/ Laryngeal mask insertion while anaesthesia was maintained with Oxygen, continuous propofol pump, intermittent Atracurium and Fentanyl. Heart rate, blood pressure, oxygen saturation, ECG and end-tidal CO₂ (ETCO₂) were monitored continuously (Philips®, MP20, Germany). Intravenous crystalloid solution administered cautiously. All patients were mechanically ventilated and ETCO₂ was maintained between 30–35 mmHg. Standard 4-port laparoscopic cholecystectomy was performed. The initial intra-umbilical camera port was introduced using the open technique¹². Carbon dioxide insufflation was initiated and maintained at 5 litres/min and other ports were introduced under vision. The higher limit of intra-abdominal pressure was kept at 8 mmHg and surgery was performed in 15°–20° reverse Trendelenburg position with right tilt.

The following parameters were measured heart rate (HR), BP, SpO₂, peak airway pressures (PAPs), and lung compliance.

Upon completion of surgery, peritoneal carbondioxide was released very slowly. Post-operative Management after the procedure, patients were closely monitored in the post-anaesthetic care unit for 4 to 5 hrs. Majority of the patients were shifted to the ward, while those with troubled intra-operative course were shifted to SICU for overnight observation. Adequate post-operative analgesia was ensured by continuous intravenous morphine (1 mg/hour) in the immediate post-operative period with oral paracetamol (10 mg/kg/dose) was administered subsequently.

Intravenous fluid was continued till the evening while oral intake was commenced after 4–5 hours. Anticoagulants and insulin were started according to well described guidelines.

Results

Between July 2016 and December 2018, a total of 3287 diabetic patients underwent laparoscopic cholecystectomy. Of these, 665 patients gave history of ischaemic heart disease, 11 patients had dilated cardiomyopathy, well maintained on cardiac medicines, 38 had undergone coronary artery bypass grafting while 58 patients had angioplasty and stenting in the past.

Amongst this heterogeneous group, 32 patients belonging to NYHA grade II (24 patients) and grade III (8 patients) were included in this study (Table 1). The mean age was 55 years (range 38–76) with a striking male preponderance. Ten (31%) patients had some kind of cardiac intervention prior to surgical referral while the rest were under medical management. Two patients had bifascicular block but did not require temporary pacemaker during the perioperative period (Table 2). Transthoracic echocardiography showed a left ventricular ejection fraction of 20–30% in 08 patients, while it was between 30–40% in the rest 24 patients. In addition, echocardiography also picked up regional wall motion abnormalities in 21 (65%), cardiomyopathy in 11 (34%).

Laparoscopic cholecystectomy was performed in all patients (Table 3). The commonest intra-operative problem was episodes of hypertension (21 patients), which always started during peritoneal insufflation, and was controlled by GTN infusion.

On the other hand, 5 patients developed hypotension necessitating immediate desufflation and intravenous infusion of vasopressor agents (noradrenaline and adrenaline). One patient developed tachyarrhythmia during surgery, requiring Amiodarone infusion.

These Intraoperative situations did not require conversion to laparotomy and all the patients were extubated/removed LMA in the operating room. In the post-operative period, 3 patients developed tachyarrhythmia, which required defibrillation in 1 patient.

In the rest 2 patients, there was no haemodynamic compromise. These patients were monitored and the tachycardia subsided spontaneously.

Table-I : Patient Profile

Parameter	Number of Patient	Percentage
Mean age	55 years (38-76)	
Male:Female ratio	24:08	
Presence of Medical - Comorbidity	30 patients	
Hypertension	28	87.50
Hypothyroidism	01	3.2
Asthma/ COPD	05	15.62
CRF	21	65.62
Previous history of cardiac intervention	10	31.25
CABG	03	9.37
PTCA	07	21.87
Pacemaker	01	3.125
NYHA		
Class-II	24	75.00
Class-III	08	25.00

COPD: chronic obstructive pulmonary disease, CRF: chronic renal failure, CABG: coronary artery bypass grafting, PTCA: percutaneous transcatheter coronary angioplasty, NYHA: New York Heart Association

Table -II: Pre-operative cardiac status of 32 patients as per Echocardiography findings

Parameters	No. of patients	Percentage
1. LVEF between 20-30%	08	25
LVEF between 30-40%	24	75
Regional wall motion abnormality	21	65.62
Dilated cardiomyopathy	11	34.37
Bifascicular block	2	6.25
Valvular disease	2	6.25

LVEF: left ventricular ejection fraction

Table -III: Results of laparoscopic cholecystectomy in 32 patients with cardiac co-morbidities

Intra-operative course and complications	Number	percentage	Treatment
Intra-operative complications			
• Persistent HTN	21	65.62	GTN, Desufflation
• Hypotension and	05	15.62	IV pressor support
• Bradycardia	01	3.12	Inj. Atropine
• Tachyarrhythmia	01	3.12	Inj. Esmalol
Post-operative complication			
• Tachyarrhythmia	03	9.37	Beta-blocker

HTN: Hypertension, GTN:Glycerin tri-nitrate

Discussion

This multispecialty hospital is the largest diabetic hospital in Bangladesh. More than 40,000 diabetic patients admitted in this hospital per year for their treatment. Amongst these a large number of patients are admitted for laparoscopic cholecystectomy. Most of these patients suffer from diabetic with cardiac illness or have had some kind of cardiac intervention.

Haemodynamic and cardiovascular changes of positive pressure CO₂ pneumoperitoneum on an anaesthetized patient lying in a reverse Trendelenburg position are often interrelated and their individual contribution is difficult to disentangle.

As a generalisation, pneumoperitoneum orchestrates a neurohormonal stress response which increases systemic vascular resistance, mean arterial blood pressure and heart rate¹⁴⁻¹⁶. These factors increase the afterload and myocardial oxygen consumption which are poorly tolerated by patients with cardiac dysfunction¹⁷. Elevated intra-abdominal pressure and reverse Trendelenburg position reduce venous return and preload and decrease cardiac output^{18,19}. This combination of decreased preload and increased afterload increase cardiac work load and could precipitate cardiac ischemia or infarction.

Patients with ischemic heart disease are prone to develop atrial fibrillation, a condition which could be precipitated by CO₂ pneumoperitoneum²⁰. Most of the studies addressing cardiovascular effects of CO₂ pneumoperitoneum have been performed in healthy subjects, whose seem to tolerate pneumoperitoneum without untoward problem [15, 16, 21].

Similar issues have not been studied under the setting of randomized trial in patients with cardiac co-morbidities²². May be hence, there is considerable reticence among surgeons in performing laparoscopy in patients with compromised heart.

However, laparoscopic cholecystectomy has been successfully performed in small series of 10-14 patients^{23,24,25} with ASA III/IV cardiac dysfunction. To avoid the complications of pneumoperitoneum, gasless laparoscopic cholecystectomy (abdominal wall lifting) has been used as an alternative to laparoscopy in high risk patients²⁶. Although abdominal wall lifting is associated with less circulatory changes and improved post-operative cognitive function, there is increased risk of surgical error²⁷.

Meticulous history taking and subjective assessment of patients undergoing laparoscopic cholecystectomy is an important aspect of managing such patients. Scoring systems like ASA physical status, Goldman cardiac Index, Canadian Cardiac Scoring system, NYHA functional classification have been devised to assess the risk of intra- and postoperative cardiac complications.

Of these, the NYHA is the most commonly used grading system of cardiac dysfunction^{12,28}. It is interesting to note that although the left ventricular ejection (LVEF) on resting transthoracic echocardiography is very commonly used to assess cardiac function. LVEF is not apart of any of these scoring systems.

Hence there is little reason to discourage laparoscopic cholecystectomy on the basis of single

LVEF value. Moreover, assessment of LVEF is operator dependant²⁹.

Despite these shortcomings, some textbooks continue to lay importance on LVEF, where a 40% cutoff value is considered safe for surgery^{30,31}. As a matter of policy it has been our practice to refer such patients for rigorous preoperative assessment by cardiologist and anesthesiologist. Premedication with midazolam helps reduce anxiety and stress and the heart rate³². Preoperative hydration or volume loading is thought to preserve cardiac output during laparoscopic surgery³³. But, in this study intravenous volume overloading was not practiced; instead fasting more than 4 hours was avoided and patients were operated early in the morning. Due to cardiac dysfunction, intravenous fluid was administered judiciously while oral fluid was commenced as early as 4-5 hours after surgery.

To diminish the stress on the heart during induction and maintenance of anaesthesia, midazolam, propofol, fentanyl and low dose halothane were used. These agents cause very little cardiac and circulatory changes. Tachycardia should be prevented and in 6 (21%) patients, intravenous esmolol, a cardio-specific betablocker, was used to control intraoperative tachycardia. Adequate depth of anaesthesia and pain control also helps prevent tachycardia. The pressure effects of pneumoperitoneum could be partially offset by using a low insufflation pressure. Some study define 'normal' insufflation pressure as 12–15 mmHg and a 'low' pressure as 5–7 mmHg²² while a recent review arbitrarily considered anything less than 12 mmHg as low pressure³⁴. Studies in healthy individuals have shown less pronounced decrease in cardiac index using low pressure peritoneal insufflation, while the pulmonary parameters have remained more or less similar in both the groups^{14,35,36}. By and large, the low pressure group have also reported less post-operative pain and diminished analgesic requirement, but such was always not the case³⁴.

In patients with cardiac dysfunction, four nonrandomized studies have shown less haemodynamic alterations under low insufflation pressure^{6, 37-39}.

In the present study, a peritoneal pressure of 8 mmHg was used and this figure was arbitrarily chosen. On occasions this low intra-peritoneal

pressure prevented adequate exposure of the Calot's triangle. In such situations either the peritoneal pressure was temporarily increased to 12 mmHg till the triangle was safely dissected and cystic duct/artery were clipped and then the pressure was decreased to 8 mmHg. Rapid insufflation with CO₂ stretches the peritoneum and could precipitate cardiac arrhythmia [40]. Therefore, a low rate of insufflation of 5 liters/min was routinely used in this study.

Conclusion

The present study showed that laparoscopic cholecystectomy may be safely performed in patients with significant cardiac dysfunction. Such patients need proper evaluation in pre anaesthetic check up and by the cardiologists.

A single transthoracic echocardiographic estimation of left ventricular ejection fraction should not be given undue importance. If considered safe to undergo general anaesthesia, such patients should not be denied the benefits of laparoscopic cholecystectomy.

Optimization of cardiac status, administration of balanced anaesthesia and low-pressure pneumoperitoneum are essential steps to ensure patient safety. The chances of life threatening complications are rare, and in the eventuality, can be easily managed in a hospital with adequate cardiologic support.

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Original Article

Clinico-demographic profile and outcome of critically ill poisoning patient admitted in the ICU of the largest tertiary care government hospital in Dhaka, Bangladesh

Subroto Kumar Sarker¹, Mohammad Salim¹, Alisa Ahmed², Mousume Mahjaben²,
Benozir Sofi Tumpa²

¹Assistant Professor, Critical Care Medicine, Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine, Dhaka Medical College, Dhaka, Bangladesh, ²Resident, Critical Care Medicine, Department of Anaesthesia, Analgesia, Palliative and Intensive Care Medicine, Dhaka Medical College, Dhaka, Bangladesh

Address of Correspondence: Dr. Subroto Kumar Sarker, E-mail: subrotormc@gmail.com

Abstract

Background: Acute poisoning is a common chief complaint leading to emergency department visits and hospital admissions in developing countries such as Bangladesh.

Aim: To study the demographic and clinical profiles of patients admitted to the ICU with acute poisoning and to study the factors that predict their mortality.

Methodology: This observational study recruited all eligible 74 poisoning patients admitted in the intensive care unit from 1st July 2019 to 30th June 2020. This study is conducted in the Intensive Care Unit of Dhaka Medical College Hospital, Dhaka, Bangladesh.

Result: Total 74 poisoning patients were admitted in the intensive care unit, of them female (55.54%) was more than male (44.59%). Among the patients 67 (90.54%) patient were Muslims and 43 (58.10%) were married. The highest incidence of poisoning 28 (37.83%) were observed in the age group 11 to 20 year and the mean age was 23.74 years. The majority of poisoning cases was suicidal intention (87.83%), accidental was 6.75% and homicidal or street poisoning was 5.40%. The most common type of poisoning was organophosphorus compound (52.70%) followed by Drug overdose (16.21%), Paraquat poisoning (9.45%), rat killer (5.4%), Insecticide poisoning (4.05%), Corrosive poisoning (2.74%). The most common route of poisoning was ingestion. Mechanical ventilation required 52.70% patients, majority of patients required shorter period (1 to 5 days) of mechanical ventilation and mean duration of mechanical ventilation is 6.33 days. 83% patient were shifted / discharged from the ICU within 1 to 5 days. Mean duration was 8.13 day in case of mechanical ventilated patients, but in non-ventilated patients, ICU stay was much less than ventilated patients. In this study, the mortality rate was 31%.

Conclusion: Early ICU admission and appropriate management of patients after ingestion of poisonous agent results in reduced morbidity and mortality.

Key words: Poisoning, Organophosphorous, Intensive care unit (ICU), Mechanical Ventilation, Mortality.

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Introduction

A poison administered by any route is capable to produce ill health, disease, or death¹. Acute poisoning is a major public health problem worldwide with significant morbidity and mortality in all age and sex groups. (is is more common in

the low- and middle-income countries due to socioeconomic factors, cultural diversity, development of agricultural activities, and the promotion of agrochemicals². Generally, children are more vulnerable to accidental poisoning, whereas the young adults are more committed to

suicidal poisoning attempts³. Pesticide self-poisoning is a major global health burden which is particularly prevalent in South East Asia. (there is a regional variation in the rate of suicides by pesticide self-poisoning from 0.9% in low- and middle-income countries in the European region to 48.3% in low- and middle-income countries in the Western Pacific region⁴. About 4.8 million healthy lives per annum are deceased by unintentional poisoning where pesticides play a significant role⁵. Bangladesh is one of the densely populated developing agriculture-based countries in South East Asia. There is increasing incidence of acute poisoning related to death and hospital admission in our country due to rapid development of agrochemicals and their easy availability in the community. Study has reported that pesticides are the commonest chemical agents used for acute poisoning in our country, whereas additive drugs are next to the insecticides⁶. Moreover, the commonly used substances for acute poisoning in our country are pesticides, insecticides, sedative drugs, copper sulphate, kerosene, rat killer, toilet cleaner, and nail polish. In self-poisoning, psychiatric illness plays a crucial role which always remains hidden during history documentation and management of poisoning cases. Patient's education and treatment of the underlying psychiatric illness may be a strategy which is scarcely discussed in acute poisoning where the psychiatrist may play a vital role to prevent further deliberating self-harm^{5,6}. The incidence of mortality and morbidity of acute poisoning depends on the several factors, but the early detection and prompt management of the critically ill poisoned patients are the key components. With the view of this concept, we have designed this observational study to assess the pattern, demographic characteristics, psychological aspect, and treatment outcome of different acute poisoning patient admitted in the intensive Care Unit, Dhaka Medical College Hospital, Dhaka, Bangladesh.

Methodology

Study Design and Duration: This observational study recruited all eligible 74 poisoning patients admitted in the intensive care unit from 1st July 2019 to 30th June 2020. This study is conducted in the Intensive Care Unit of Dhaka Medical College Hospital, Dhaka, Bangladesh.

Patient Selection Criteria: Patients with snake bite, electrocution, drowning, food poisoning, and allergic reaction due to drugs were excluded from the study. Patient's attendants who were unwilling to give informed written consent to use their data were also excluded from the study. Detailed history and relevant clinical examination data were collected from all the participated cases. The poisoning cases demonstrating on the basis of patient's statement, statement of the witness, smell of poisonous agents, and characteristics signs and symptoms of poisoning were recorded in the data sheet form.

Data Collection and Storage: A structured questionnaire was developed to collect the data from hospital admitted patients. The preformed data sheet included the following: (A) Demographic characteristics: age, sex, religion, marital status, residence, educational status, occupational status, and monthly income in BDT (B) Poison related: type of poisoning and intensity of poisoning (C) Data related to suicidal attempts: causes of suicidal attempts, previous history of suicidal attempts, and previous history of documented psychiatric illness (D) Data related to management: treatment received prior to hospital admission (E) Patient require intubation and mechanical ventilation, duration of mechanical ventilation and duration of ICU stay (F) Outcome of treatment after admission in the Intensive Care Unit.

Management: After taking proper history and completion of physical examination, all the patients were treated with standard protocol. In some cases, relevant investigations such as complete blood count (CBC), random blood sugar (RBS), liver function test (LFT), renal function test (RFT), toxicology screening prothrombin time, international normalized ratio (INR), serum electrolytes, arterial blood gas analysis and chest X-ray were done to see the complications and prognosis of the patients.

Ethical Clearance: Prior to the commencement of this study, institutional approval was taken from the Ethical Review Committee of the Dhaka Medical College, Dhaka, Bangladesh. Informed consent was taken from each case before analysis. Personal information of patient's privacy was not disclosed to any third party. Informed written consent was taken from every case before analysis.

Statistical Analysis: Analysis was carried out using SPSS version 23. Categorical data were grouped as percentages and mean with standard deviation (SD) measured from continuous data.

Results

Total number patients: 74

Table I Sex

Sex	No. of patient	Percentage(%)
Male	33	44.59
Female	41	55.40

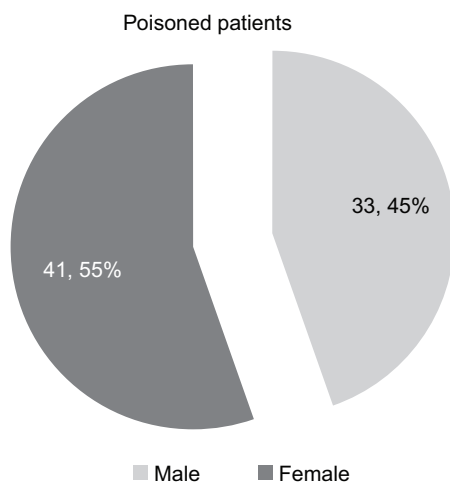


Table II Religion

Religion	No of patient	Percentage(%)
Muslim	67	90.54
Hindu	7	9.45

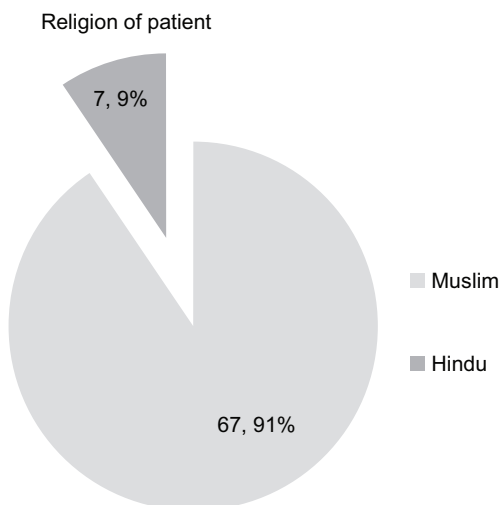


Table III Age distribution

Age	No of patient	Mean age	Percentage
0 to 10 year	5		6.75
11 to 20 year	28		37.83
21 to 30 year	25		33.78
31 to 40 year	8	23.74	10.81
41 to 50 year	7		9.45
51 to 60 year	1		1.35

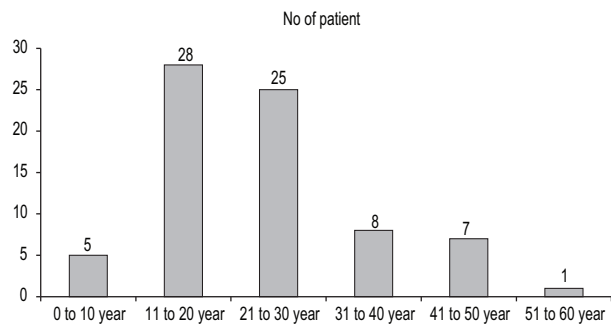


Table IV Marrital Status

	No patient	Percentage(%)
Single	31	41.83
Married	43	58.10

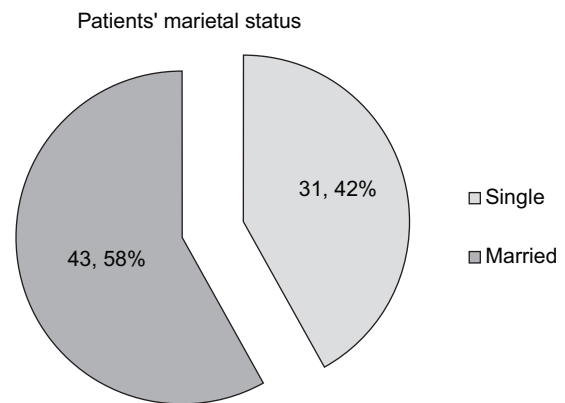
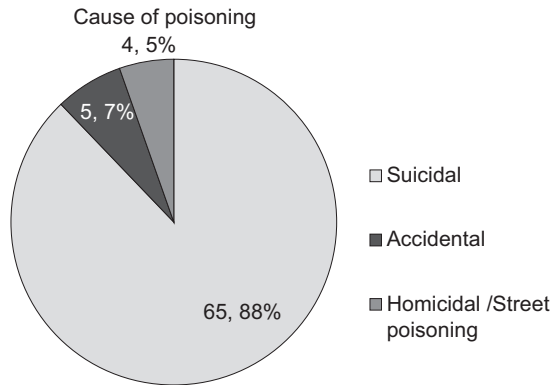


Table V Causes of poisoning

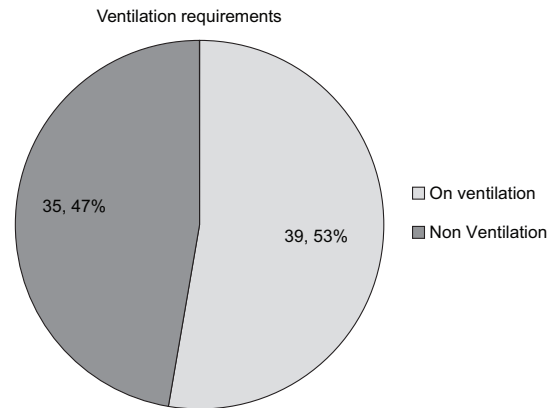
Cause	No. of patient	Percentage(%)
Suicidal	65	87.83
Accidental	5	6.75
Homicidal /	4	5.40
Street poisoning		

**Table VI** *Types of poisons*

Type	Sub-type	No of patients	Percentage (%)
Poisons	OPC	39	52.70
	Organochlorine	2	2.70
	Rat killer	4	5.40
	Coachroch killer	3	4.04
	Paraquate	7	9.45
	Insecticide	3	4.05
	Street poisoning	2	2.7
	Methanol	1	1.35
Drugs	<i>Amitriptyline</i>	5	16.21
	<i>Barbiturate</i>	2	
	<i>Benzodiazepine</i>	2	
	<i>Paracetamol</i>	2	
	<i>Minoxidril</i>	1	
Corossive	<i>Savlon</i>	1	2.74
	<i>Herpic</i>	1	

Table VII *Mechanical Ventilation Requirement*

	No of patient	Percentage(%)
On ventilation	39	52.70
Non Ventilation	35	47.29

**Table VIII** *Duration of Mechanical ventilation*

Duration (Days)	Number of patients (39)	Mean duration (days)	Percentage (%)
1-5	24		61.53
6-10	9		23.07
11-15	2	6.33	5.12
16-20	3		7.69
21-25	1		2.56

Table IX *Duration ICU Stay*

Duration (Days)	Number of Ventilated patients(39)	Mean duration in ICU (days)	Percentage (%)	Number of non-ventilated patiensts (35)	Percentage (%)
1 - 5	20		51.28	29	74.35
6 - 10	9		23.07	5	12.82
11 - 15	4	8.13	10.25	1	2.56
16 - 20	3		7.69		
21 - 25	1		2.56		
26 - 30	2		5.55		

Table X *Outcome*

	No. of patient	Percentage(%)
Survive	5168	
Death	23	31

Total 74 poisoning patients were admitted in the intensive care unit, of them 41(55.54%) were female and 33(44.59%) were male. Among the patients 67(90.54 %) patient were Muslim and 43(58.10%) were married. The highest incidence of poisoning

28 (37.83%) were observed in the age group 11 to 20 year, next incidence group 25(33.78%) were in the age group 21 to 30 years, the mean age was 23.74 years. The majority of poisoning cases 65 (87.83%) was suicidal intension, accidental was 6.75% and homicidal or street poisoning was 5.40%.The most common type of poisoning was organophosphorus compound (52.70%) followed by Drug overdose (16.21%), Paraquat poisoning (9.45%), rat killer(5.4%),Insecticide poisoning (4.05%),Corrosive poisoning (2.74%).The most common route of poisoning was ingetion. Table 9 Describes 39 (52.70%) patients required mechanical ventilation, majority of patients required shorter period (1 to 5 days) of mechanical ventilation and mean duration of mechanical ventilation is 6.33 days. Table IX illustrate the duration of ICU stay . Majority of the patient in the study had shorter stay in the ICU (83%) patient were shifted /dischared from the ICU within 1 to 5 days. Mean duration was 8.13 day in case of mechanical ventilated patients. But in non ventilated patients, ICU stay was much less than ventilated patients. Table 10 illustrates that 51 (68%) were survived and 23(31%) were died in the ICU.

Discussion

Acute poisoning is one of the most common causes of emergency hospital admission, whereas the patients with minor symptoms and asymptomatic cases may not seek the health care service from the hospital and they might be missed in the statistics. In Bangladesh, all the poisoning patients are remarked as a police case during their admission in the government hospital. So, the poisoning patients from the affluent family may seek their necessary treatment from the private health care settings. Therefore, the exact incidence of acute poisoning may not be found. The last census of Bangladesh was conducted in 2011, so we have calculated our incidence according to the census 2011 in Bangladesh. This result could not be compared to other studies from Bangladesh due to lack of regarding data, but the incidence rate of acute poisoning is very high in Srilanka⁷ and (Thailand⁸. We have conducted the study among all age groups with the mean age of our participants being 23.74 year. In our study, most of the acute poisoning cases (331, 68%) come from

the second and third decade age groups and the result is very similar to the other studies^{7, 9, 10,21,22,27,28}. The female gender has been more victimized from acute poisoning than that of the male group, and the younger women are affected more in this study.The possible reasons behind this are due to emotional liability, cultural belief, and social circumstances. Some studies have reported female preponderance of deliberated self-poisoning in Srilanka and Zimbabwe similar to our finding^{7,11,21,22,26,27}. Generally, many studies have shown the male domination of acute poisoning in their analysis, which is similar to this observation^{9,10,12,13}. Acute poisoning cases have got themselves admitted in the ICU through the 24 hours emergency department and medicine department of Dhaka Medical College Hospital during our time frame recruited in the present study.. The most common type of poisoning was organophosphorus compound (52.70%) followed by Drug overdose (16.21%), Paraquat poisoning (9.45%), rat killer (5.4%),Insecticide poisoning (4.05%),Corrosive poisoning (2.74%). The most common route of poisoning was ingetion. There are many studies that have reported that organophosphorus compounds occupy the leading cause of acute poisoning^{4,5,7,9,14,21,22,26,27}. This is due to easy availability of OPC in our society of agriculture-based country; even WHO has reported previously that use of pesticides is the most popular way of deliberating selfpoisoning worldwide, and it is estimated about one-third of the global suicides is resulting from the pesticides selfpoisoning¹⁵. The majority of poisoning cases 65 (87.83%) was suicidal intension, accidental was 6.75% and homicidal or street poisoning was 5.40%. (the common motive of acute poisoning in our study is due to suicidal intention which constituted 87.83%, whereas the accidental and stupefying /homicidal intention fills the rest of the intention.The same result of suicidal intention in the acute poisoning has been reported by others study conducted in Kathmandu, Nepal¹⁶ and Bangladesh^{21,22,27}.

In our study, suicidal intention is more among the females than that of the males. This result is supported by the other analysis conducted in India and Ilam Province of West Iran^{17,18}. In our study 52.70% patients required mechanical ventilation, majority of patients required shorter period (1 to 5 days) of mechanical ventilation and mean

duration of mechanical ventilation is 6.33 days . Table 9 illustrate the duration of ICU stay. Majority of the patient in the study had shorter stay in the ICU (83%) patient were shifted /discharged from the ICU within 1 to 5 days. Mean duration was 8.13 day in case of mechanical ventilated patients. But in non ventilated patients, ICU stay was much less than ventilated patients.

In this study the survival rate is 68% and the mortality rate is 31%. Hemani Ahuja et al study showed, out of 67 patients, 43 had required mechanical ventilation for an average of 3.81 days In their study, the mean duration of mechanical ventilation was $3.81 \pm \text{SD } 4.36$ days and the mean ICU stay was 3.9 ± 0.544 days. The overall ICU mortality was 18%²³. Easnem et al also showed Ventilator support was given in 48.80% cases and 51.2% cases were managed with oxygen support. Mean duration of ventilatory support was 2–14 days and mortality rate was 2.8%²⁶ Mehrpour et al ,showed their study (41.2%) were intubated, and the mean duration of 8.53 ± 8.99 days, 17.6% died and 23.6% survived²⁷. Aravind *et al.* also showed their study that 78% of the patients admitted to the ICU recovered and were discharged²⁸.

Limitation

This prospective observational study was conducted in a single centre government tertiary hospital in the centre of the capital of Bangladesh hence, the results cannot be generalized. It is a short duration of study, only 12 month study.

Conclusion

Acute poisoning is a medical emergency which require quick diagnosis and fast treatment. Early identification of type of poisoning, close observation, and standard management can reduce the complication and mortality rate. In present study a high proportion of male and young adults was found. In the majority of patients, OPC was ingested deliberately for committing suicide. we recommend limiting its use with caution. Timely initiation of medical management in the Intensive Care Unit can save the life in acute poisoning cases and reduces the mortality and morbidity rate.

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Dexmedetomidine for Sedation during Total Abdominal Hysterectomy under Spinal Anesthesia

Rajat Shuvra Das¹, Mohammad Shaddam Hoshain Mondol², Arman Ali ²,
Shahajad Hossain Md. Al Momen³, AKM Faizul Hoque⁴

¹Specialist, Department of Anaesthesia, BRB Hospitals Ltd. Panthapath, Dhaka. ²Anaesthesiologist, Department of Anaesthesia, Analgesia, Palliative & Intensive Care Medicine, Dhaka Medical College Hospital, Dhaka. ³Assistant Professor, Department of Anaesthesiology and Intensive Care Medicine, Kurmitola General Hospital, Dhaka, ⁴Associate Professor, Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka.

Corresponding Author: Dr. Rajat Shuvra Das, Specialist, Department of Anaesthesia, BRB Hospitals Ltd. Panthapath, Dhaka

Abstract

Intravenous Dexmedetomidine is associated with stable cardiovascular profile and less associated with fear, anxiety and agitation. Spinal anesthesia (SA) offers many advantages over general anesthesia, like providing analgesia and muscle relaxation in a conscious and compliant patient and an uneventful postoperative recovery. But retained consciousness during surgery or patient awake causes fear, anxiety in perioperative period. The fear of surgery, the unfamiliar environment of operation room, the sight and sounds of sophisticated instruments, and the masked faces makes the patient panic. The intense sensory and motor block, continuous supine position and the inability to move the body also brings a feeling of discomfort and phobia in many patients. Thus, adequate sedation and control of stress, pain, fear and patient satisfaction are essential components during anesthesia. Sedation has been shown to increase patient satisfaction during regional anesthesia. I conclude that, during spinal anesthesia, IV supplementation of dexmedetomidine is more effective than midazolam infusion, as it provides longer duration of sensory and motor blockade and postoperative analgesia with minimal and similar side effects. It provides satisfactory arousable sedation without respiratory depression. Haemodynamic changes observed in our patients were very small and could be ignored. Patient remained stable haemodynamically throughout the intra-operative period. So dexmedetomidine seems to be a good choice for sedation in spinal anesthesia (SA).

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Introduction

Hysterectomy is the most common major gynecological operation. Popular and common anaesthetic technique used for abdominal hysterectomy is spinal anaesthesia which is best to control intraoperative pain, excellent muscle relaxation with uneventful postoperative recovery. But intra-operatively the patients remain awake and anxious, ultimately hemodynamic stability could be changed momentarily. Thus, adequate sedation and control of stress, pain, fear are required for pleasant and smooth surgery. Many drugs are used like Benzodiazepines, Propofol and Narcotics to promote the sedation for their sedative and analgesic properties. But they are associated with cardiorespiratory depression. Intravenous

midazolam, which is used most often in this situation, has sedative action, but doesn't have analgesic effect. Dexmedetomidine (DMT), a highly selective α_2 -agonist, provides stable haemodynamic conditions, good quality of intra-operative analgesia, sedation and prolonged post-operative analgesia with minimal side effects. this study was to evaluate the effectiveness of Dexmedetomidine for sedation during total abdominal hysterectomy under spinal anesthesia.

Methods and methods

Sample was selected by random sampling in two groups distributed as- group D (dexmedetomidine), group M (midazolam). Sequence of study were pretesting of questionnaire, finalization of

questionnaire, sampling, consent taking, data collection with detailed history, physical examination etc. Sixty patients, classified by American Society of Anesthesiologists (ASA- I, II, listed for operative procedure under spinal anaesthesia were randomized by card method in two groups of 30 patients each. Subarachnoid (spinal) anaesthesia was performed in all patients with 0.5% hyperbaric bupivacaine intrathecally, at

L3 - L4 interspinous spaces, with 25G Quinke's spinal needle. The patients in the first group (group D) was administrated with an intravenous loading dose of $0.5 \mu\text{g} \cdot \text{kg}^{-1}$ dexmedetomidine and the second group (group M) administrated $0.04 \mu\text{g} \cdot \text{kg}^{-1}$ midazolam via a syringe infusion. Changes of BP, pulse and any complication was recorded. All the information recorded in data collection sheet. All collected questionnaire checked very carefully to identify the error in the data.

Result

Table 3.1 Age distribution of the patients (n=60)

Age (years)	Number of patients		Total & Percentage	P value
	Group D n(%)	Group M n(%)		
<50	7(23.3%)	4(13.3%)	11(18.3%)	0.471 ^{ns}
50-60	19(63.3%)	21(70.0%)	40(66.6%)	
61-70	4(13.3%)	5(16.6%)	9(15.0%)	
Mean $\pm$ S.D.	53.3 $\pm$ 11.5			

ns= not significant

P value reached from chi square test.

Table- 3.3: Distribution of the study patients according to types of heart rate (n=60)

Heart rate (beat/min)	Group D (n=30) Mean $\pm$ SD	Group M (n=30) Mean $\pm$ SD	P value
Baseline	93.1 $\pm$ 8.2	90.2 $\pm$ 7.3	0.184 ^{ns}
Range (min-max)	80-110	80-100	
5 minute after	93.7 $\pm$ 9.4	92.9 $\pm$ 7.1	0.231 ^{ns}
Range (min-max)	80-110	81-105	
10 minute after	94.2 $\pm$ 7.8	96.9 $\pm$ 7.4	0.206 ^{ns}
Range (min-max)	80-110	86-110	
15 minute after	102.2 $\pm$ 6.3	105.5 $\pm$ 6.0	0.182 ^{ns}
Range (min-max)	90-100	95-110	
30 minute after	93.5 $\pm$ 9.1	100.4 $\pm$ 9.1	0.008 ^s
Range (min-max)	80-115	89-120	
45 Minute after	87.7 $\pm$ 17.7	103.0 $\pm$ 8.9	0.001 ^s
Range (min-max)	45-110	90-120	
60 minute after	92.7 $\pm$ 8.2	104.5 $\pm$ 7.7	0.001 ^s
Range (min-max)	80-110	92-120	

s= significant, ns= not significant

P value reached from unpaired t-test.

At baseline, mean heart rate was found 90.2 ± 7.3 beat/min in group M and 93.1 ± 8.2 beat/min in group D. At 5 minute after, mean heart rate was 92.9 ± 7.1 beat/min and 93.7 ± 9.4 beat/min in group M and group D respectively. At 10 minute after, mean heart rate was found 96.9 ± 7.4 beat/min in group M and 94.2 ± 7.8 beat/min in group D. At 15 minute after, mean heart rate was found 105.5 ± 6.0 beat/min in group M and 102.2 ± 6.3 beat/min in group D. At 30 minute after mean heart rate was 100.4 ± 9.1 beat/min and 93.5 ± 9.1 beat/min in group M and group D respectively. At 45 minute, mean heart rate was 103.0 ± 8.9 beat/min in group M and 87.7 ± 17.7 beat/min in group D. At 60 minutes, mean heart rate was 104.5 ± 7.7 beat/min and 92.7 ± 8.2 beat/min in group M and group D respectively. At after 30 minute, 45 minute and 60 minute difference was statistically significant ($p < 0.05$) between two groups

Table shows systolic blood pressure during follow up it was observed that at baseline, mean

systolic BP was found 89.6 ± 6.3 mmHg in group M and 84.3 ± 5.0 mmHg in group D. At 5 minute after, mean systolic blood pressure was 92.5 ± 6.8 mmHg and 81.4 ± 9.2 mmHg in group M and group D respectively. At 10 minute after, mean systolic blood pressure was 95.3 ± 7.1 mmHg in group M and 85.5 ± 5.1 mmHg in group D. At 15 minute after, mean systolic blood pressure was 95.6 ± 11.2 mmHg and 84.3 ± 4.8 mmHg in group M and group D respectively. At 30 minute after, mean systolic BP was 97.9 ± 4.7 mmHg in group M and 84.3 ± 5.0 mmHg in group D. At 45 minute after, mean systolic blood pressure was 94.6 ± 15.6 mmHg and 84.3 ± 5.0 mmHg in group M and group D respectively. At 60 minutes after, mean systolic blood pressure was 59.6 ± 6.0 mmHg in group M and 61.2 ± 9.4 mmHg in group D. At 10, 15, 30 and 45 minute after difference was statistically significant ($p < 0.05$) between two groups.

Table 3.4 *Distribution of the study patients according to types of systolic blood pressure (SBP) (n=60)*

Systolic BP (mmHg)	Group D (n=30) Mean $\pm$ SD	Group M (n=30) Mean $\pm$ SD	P value
Baseline	84.3 ± 5.0	89.6 ± 6.3	0.271 ^{ns}
Range (min-max)	80-95	80-100	
5 minute after	81.4 ± 9.2	92.5 ± 6.8	0.083 ^{ns}
Range (min-max)	62-95	80-105	
10 minute after	85.5 ± 5.1	95.3 ± 7.1	0.001 ^s
Range (min-max)	80-110	86-110	
15 minute after	84.3 ± 4.8	95.6 ± 11.2	0.001 ^s
Range (min-max)	80-95	85-110	
30 minute after	84.3 ± 5.0	97.9 ± 4.7	0.001 ^s
Range (min-max)	80-95	45-105	
45 Minute after	84.3 ± 5.0	94.6 ± 15.6	0.002 ^s
Range (min-max)	80-95	90-105	
60 minute after	61.2 ± 9.4	59.6 ± 6.0	0.467 ^{ns}
Range (min-max)	80-95	45-110	

Discussion

This prospective randomized double blind study was conducted in Department of Anaesthesia, Analgesia, Palliative & Intensive Care Medicine, Dhaka Medical College Hospital, Dhaka from 8th June 2017 to 7th December 2017. Total of 60 patients fulfilling inclusion/exclusion criteria were studied to determine the effectiveness between Dexmedetomidine and Midazolam in attenuation of haemodynamic stability and sedation during total abdominal hysterectomy under spinal Anesthesia. While studying the distribution of cases by age it was found that majority of the patients i.e. 66.6% (n=40) were between 50-60 years, mean age was found to 53.3±11.5 years. The difference was not statistically significant (p>0.05) between two groups.

Central neuraxial blockade is a widely used anesthetic procedure. However, may promote some type of discomfort caused by the procedure itself or by a prolonged perioperative period, requiring the simultaneous administration of hypnotic, sedative and amnesic drugs. Benzodiazepines, propofol and opioids have these properties and provide some comfort to patients. However, these agents may cause respiratory depression, with consequent hypercarbia and hypoxemia. A promising alternative to these drugs is the α_2 -adrenergic agonists, which have excellent sedative and analgesic properties without respiratory depression.

Dexmedetomidine (D) is a α_2 agonist, has anesthetic and analgesic-sparing property. I.V. dexmedetomidine significantly prolongs the duration of sensory and motor block of bupivacaine in spinal anesthesia. Dexmedetomidine provides an excellent sedation during surgery¹⁰. Various studies have demonstrated that intravenous infusion of dexmedetomidine prolongs the sensory and motor blockade with intrathecal bupivacaine. Its effects are readily reversible with atipamezole, an α_2 -adrenoceptor antagonist. Potential desirable effects include decreased requirements of anesthetics and analgesics, a diminished sympathetic response to stress, and the potential for cardioprotective effects against myocardial ischemia with minimal effects on respiration⁶.

In this study at baseline, mean heart rate was found 90.2±7.3 beat/min in group M and 93.1±8.2

beat/min in group D. At 5 minute after, mean heart rate was 92.9±7.1 beat/min and 93.7±9.4 beat/min in group M and group D respectively. At 30 minute after mean heart rate was 100.4±9.1 beat/min and 93.5±9.1 beat/min in group M and group D respectively. At 45 minute, mean heart rate was 103.0±8.9 beat/min in group M and 87.7±17.7 beat/min in group D. At 60 minutes, mean heart rate was 104.5±7.7 beat/min and 92.7±8.2 beat/min in group M and group D respectively. At after 30 minute, 45 minute and 60 minute difference was statistically significant (p<0.05) between two groups.

On evaluation of systolic blood pressure during follow up it was observed that at baseline, mean systolic BP was found 89.6±6.3 mmHg in group M and 84.3±5.0 mmHg in group D. At 10 minute after, mean systolic blood pressure was 95.3±7.1 mmHg in group M and 85.5±5.1 mmHg in group D. At 45 minute after, mean systolic blood pressure was 94.6±15.6 mmHg and 84.3±5.0 mmHg in group M and group D respectively. At 10, 15, 30 and 45 minute after difference was statistically significant (p<0.05) between two groups. Regarding diastolic blood pressure during follow up, after 15 minute, mean diastolic blood pressure was found 67.6±7.4 mmHg in group M and 61.5±9.7 mmHg in group D. After 45 minute, mean diastolic blood pressure was 66.0±6.8 mmHg in group M and 61.2±9.4 mmHg in group D. Which statistically significant (p<0.05) between two groups but other follow up were not significant (p>0.05) between two groups.

Conclusion

In this study, it was found that intravenous Dexmedetomidine is associated with stable cardiovascular profile and less associated with fear, anxiety and agitation. I conclude that, during spinal anesthesia, IV supplementation of dexmedetomidine is more effective than midazolam infusion, as it provides longer duration of sensory and motor blockade and postoperative analgesia with minimal and similar side effects. It provides satisfactory arousable sedation without respiratory depression. Haemodynamic changes observed in our patients were very small and could be ignored. Patient remained stable haemodynamically throughout the intra-operative period. So dexmedetomidine seems to be a good choice for sedation in spinal anesthesia (SA).

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Efficacy of pregabalin in attenuation of laryngoscopy and intubation reflex-A comparison with gabapentin

Muhammad Mamun Ur Rashid¹, Hasan Ali Talukder¹, Moinul Hossain Chowdhury¹, Shukha Ranjan Das¹, Md. Mozaffer Hossain², Taneem Mohammad³, Nuzhat Ara⁴

¹Anesthesiologist, Department of Anaesthesia, Analgesia, Palliative & Intensive Care Medicine, DMCH, Dhaka. ²Professor and Head, Department of Anaesthesia, Analgesia, Palliative & Intensive Care Medicine, DMCH, Dhaka. ³Junior Consultant, Department of Anaesthesia, Analgesia, Palliative & Intensive Care Medicine, DMCH, Dhaka. ⁴Assistant Professor, Department of Anaesthesia, Analgesia, Palliative & Intensive Care Medicine, DMCH, Dhaka.

Corresponding author: Dr. Muhammad Mamun Ur Rashid, E-mail: rashidmamunur91@gmail.com

Abstract

Backgrounds: Direct laryngoscopy and tracheal intubation are noxious stimuli that can provoke undesirable responses in the cardiovascular, respiratory and other physiologic system. These physiological changes are well tolerated by healthy individuals. However, these changes may be detrimental or even fatal in patients with coronary artery disease, hypertension, cerebrovascular disease, intracranial aneurysm, valvular heart disease.

Many pharmacological techniques were introduced and evaluated either in the premedication or during induction to attenuate the hemodynamic pressor response to laryngoscopy and tracheal intubation, but results were controversial. A drug that has analgesic properties, opioid sparing effects, possibly reduces opioid tolerance, relieves anxiety and is not associated with adverse effect would be an attractive adjuvant. Gabamimetic drug like gabapentin have been successfully used as oral premedication to attenuate pressor response during airway instrumentation, to decrease the preoperative anxiety and to reduce perioperative fentanyl consumption. In contrast, newer generation Gabamimetic drug pregabalin is effective in preventing neuropathic component of acute nociceptive pain of surgery and is several times more potent than gabapentin. Pregabalin is being used as oral premedicant in some studies but very few comparative studies with gabapentin is present at time. So, there is a need to study the effectiveness of oral pregabalin in attenuating the hemodynamic response to laryngoscopy and intubation. If pregabalin is established as oral premedicant then it will bring a great benefit to peri-operative period with minimal cost.

Objectives: To compare the efficacy of pregabalin and gabapentin in attenuation of laryngoscopy and intubation reflex (HTN & Tachycardia).

Methods: This is hospital based randomized double-blind control study. Eighty patients, classified by (ASA) physical status category I-II, were randomized by card method in two groups of 40 patients each. The patients were randomly allocated to receive oral Pregabalin 150mg (Group A) and Gabapentin 600mg tablet (Group B) 1 hour prior to surgery. Before administration of the oral premedication, each patient's baseline heart rate, systolic and diastolic blood pressure, mean arterial pressure and oxygen saturation were recorded by an anesthesiologist who was not enrolled into the study about the occurrence. In addition, to measure anxiety and sedation Ramsay Sedation Score was completed for each patient. All measurements were repeated before induction. Grade 2 patient was selected. Systolic, diastolic and mean arterial blood pressure (SAP, DAP, MAP) and heart rate (HR), oxygen saturation (Spo₂) was recorded after administration of IV anesthetics, immediately after intubation and cuff inflation, and 1, 3, 5 and 10 minutes after intubation. After tracheal extubation the patients were monitored for 24 about the occurrence of any side effects, such as nausea, vomiting, dizziness, blurred vision, respiratory insufficiency, confusion and recorded if they were present.

Result: Patients characteristics in respect of age, residence, other socio-demographic characteristics, ASA status and type of surgery were similar between the groups. Oral tablet Pregabalin 150mg is more effective than tablet Gabapentin 600mg, in attenuation of intubation reflex. A single, oral dose of 150 mg of pregabalin premedication seems to be effective in attenuating the hemodynamic response to endotracheal intubation after the first attempt.

Conclusion: Pregabalin 150 mg is a better alternative to Gabapentin 600 mg in attenuation of intubation reflex without major side effect.

Keywords: Heart rate (HR), Systolic, diastolic and mean arterial blood pressure (SAP, DAP, MAP).

Introduction:

Direct laryngoscopy and tracheal intubation are noxious stimuli that can provoke undesirable responses in the cardiovascular, respiratory and other physiologic system³. These physiological changes are well tolerated by healthy individuals. However, these changes may be detrimental or even fatal in patients with coronary artery disease, hypertension, cerebrovascular disease, intracranial aneurysm, valvular heart disease. The sympathetic response is associated with Acute Left Ventricular Failure, ischemic ECG changes and ruptured cerebral aneurysm⁴. As today more and more patients with cardiovascular disorders are presenting themselves for surgery, anaesthesiologists are in search of safest and the most efficient drug which can prevent cardiovascular response to the laryngoscopy and tracheal intubation. Many pharmacological methods were evaluated either in premedication or during induction to attenuate the adverse hemodynamic response to laryngoscopy and intubation, such as deepening the anesthesia, pretreatment with vasodilators, adreno-receptor blocker and opioids⁵. Intranasal nitroglycerin diminished the hypertensive response but tachycardia was noted¹¹. The most commonly reported adverse effects of benzodiazepines are variability of patient response and respiratory complication¹². Opioid analgesia contributes to postoperative nausea, vomiting, bradycardia, delayed recovery of bowel function & respiratory depression¹³. Intravenous lidocaine prevented the increase in mean arterial pressure with no effect on heart rate¹⁴. Recently, an increasing emphasis has been made on the use of non-opioid analgesic as a part of multimodal regimen for preventing pain in the operative period, decrease anxiety and the intubation response. A drug that has analgesic properties, opioid sparing effects, possibly reduces opioid tolerance, relieves anxiety and is not associated with adverse effect would be an attractive adjuvant.

Pregabalin, a gabapentinoid compound, is described structurally as (S)-3 aminomethyl-5-methylhexanoic acid. Pregabalin is structurally related to the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), but is not functionally related to it. It acts by decreasing the synthesis of neurotransmitter glutamate to act on the central

nervous system. It is non-narcotic, with clinically important reduction in pain and adverse haemodynamic response⁶. Gabapentin is structurally related to the neurotransmitter GABA but does not modify GABA-A or GABA-B radioligand binding, it is not converted metabolically GABA-A or GABA-B agonist and it is not inhibitor of GABA uptake or degradation⁷. Gabapentin has an alternative mechanism of action in CNS, it acts by decreasing the synthesis of neurotransmitter glutamate thus producing analgesia, anxiolysis, and hemodynamic stability⁸.

Pregabalin and gabapentin share a similar mechanism of action, inhibiting calcium influx and subsequent release of excitatory neurotransmitters; however, the compounds differ in their pharmacokinetic and pharmacodynamic characteristics. Gabapentin is absorbed slowly after oral administration, with maximum plasma concentrations attained within 3-4 hours. Orally administered gabapentin exhibits saturable absorption—a Nonlinear (zero-order) process—making its pharmacokinetics less predictable. Plasma concentrations of gabapentin do not increase proportionally with increasing dose. In contrast, orally administered Pregabalin is absorbed more rapidly, with maximum plasma concentrations attained within 1 hour. Absorption is linear (first order), with plasma concentrations increasing proportionately with increasing dose. The absolute bioavailability of gabapentin drops from 60% to 33% as the dosage increases from 900 to 3600 mg/day, while the absolute bioavailability of pregabalin remains at > or = 90% irrespective of the dosage. Neither drug binds to plasma proteins. Neither drug is metabolized by liver nor inhibits hepatic enzymes that are responsible for the metabolism of other drugs. Both drugs are excreted renally, with elimination half-lives of approximately 6 hours. For neuropathic pain, a pregabalin dosage of 450 mg/day appears to reduce pain comparably to the predicted maximum effect of gabapentin⁹. Therefore, its pharmacologic, analgesic and anxiolytic properties make it a useful drug for premedication, oxygen saturation (SpO₂), pre-operative anxiety and sedation.

Materials and methods:

This study was conducted at Department of Anesthesia, Analgesia, Palliative & Intensive Care

Medicine, Dhaka Medical College Hospital, Dhaka from 1st January 2016 to 30th June 2016. After taking proper approval from Ethical Review Committee, Dhaka Medical College Hospital and taking informed written consent from the participant he/she was asked to draw any one of the cards previously marked for each group. Group A were received oral Pregabalin 150mg and Group B were received Gabapentin 600mg tablet 1 hour prior to surgery. ASA status I and II underwent surgical procedure under general anaesthesia.

Before administration of the oral premedication, each patient's baseline heart rate, systolic and diastolic blood pressure, mean arterial pressure and oxygen saturation was recorded. In addition, to measure anxiety and sedation, Ramsay Sedation Score was completed for each patient. All measurements were repeated before induction. Grade 2 patients were selected. Intravenous line was secured and all patients were started on intravenous fluids. After 3 mins of pre-oxygenation with 100% oxygen, 2 µg/kg IV Fentanyl was given for supplemental analgesia. Patient was induced with IV thiopentone 5mg/kg followed by IV suxamethonium 2mg/kg for intubation. After 60 second intubation was performed by investigator using Macintosh 3 laryngoscope blade and 7.0-8.0 mm endotracheal tube on the first attempt. The duration of laryngoscopy and intubation was limited to minimum possible time and being similar to all patients. Anesthesia was maintained with Nitrous Oxide 70%, Oxygen 30% and halothane 0.6% MAC. Muscle relaxation was achieved with IV Vecuronium 0.1mg/kg for loading dose and 0.02mg/kg for maintenance dose. Mechanical ventilation was adjusted to maintain normocarbida. Systolic, diastolic and mean arterial blood pressure (SAP, DAP, MAP) and heart rate (HR), oxygen saturation (Spo2) was recorded after administration of IV anesthetics, immediately after intubation and cuff inflation, and 1, 3, 5 and 10 minutes after intubation.

All collected data checked very carefully to identify the error in the data. Data processing work consist of registration schedules, editing, computerization, preparation of dummy table, analyzing and matching of data. After collection of all information, these data were checked, verified for consistency and edited for finalized result. After editing data directly entered into the computer by using SPSS version 16. Data cleaning validation and analysis was performed using the SPSS software and graph and chart by MS excel. The hemodynamic variables

represented by mean value $\pm$ SD. The statistical significance in mean difference was performed using analysis of variance (ANOVA) and Chi Square test as appropriate. p value of < 0.05 was considered significant and < 0.001 as highly significant. The failure rate of drug was defined by operational definition.

Results:

Table 3.1 Demographic characteristics of the patients (n=80)

Demographic variables	Group A (n=40)	Group B (n=40)	P value
Age (years)			
Mean $\pm$ SD	26.4 $\pm$ 8.2	25.3 $\pm$ 9.3	0.892NS
Sex (male: female)	26 : 14	24:16	0.234NS
Weight (kg)	65 $\pm$ 13.23	67 $\pm$ 11.23	0.423NS

A total of 80 patients, 40 in each group, were evaluated. All groups were comparable with respect to the demographic and operational factors. No significant differences were found between groups.

Table 3.2 American Society of Anesthesiologist (ASA) physical status (n=80)

Status	Number of Patient		P value
	Group A	Group B	
ASA I	26(65%)	29(72.5%)	
ASA II	14(35%)	11(27.5%)	0.950NS

Patient distribution as regard to ASA status, there were no significant difference between the groups (p=0.950). Comparison was done by Chi-Square (χ^2) test.

Table 3.3: Types of surgery in different groups

Types	Number of patients		Total	P value
	Group A	Group B		
Laparoscopic				
cholecystectomy	26(65%)	24(60%)	50	0.726NS
Mastoidectomy	8(20%)	9(22.5%)	17	
Tympanoplasty	6(15%)	7(17.5%)	13	

No significant differences were found among groups with respect to type of surgery. The difference was statistically not significant ($P>0.05$).

Table 3.4 Mallampati grading in different groups:

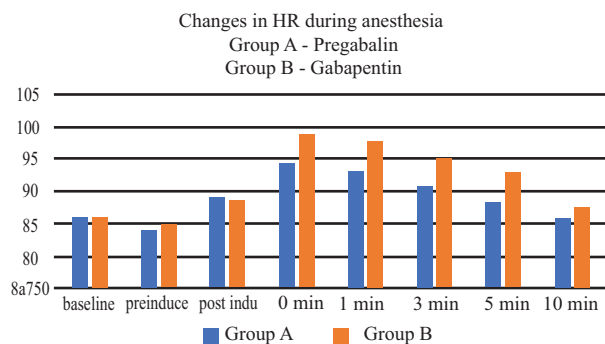
Mallampati	Number of patients		Total	P value
	Group A	Group B		
Grade 1	27(67.5%)	28(70%)	55	0.921 ^{NS}
Grade 2	13(32.5%)	12(30%)	25	

No significant differences were found among groups with respect to Mallampati grading. The difference was statistically not significant ($P>0.05$).

Table 3.5 Changes in HR during anesthesia

Parameters	Group A	Group B	P value
Baseline	86.05 ± 5.20	86.00 ± 7.50	0.634NS
After Preme-dication	84.26 ± 5.19	85.16 ± 9.29	0.543NS
After induction	89.20 ± 3.90	88.72 ± 10.21	0.587NS
During laryngoscopy (0 min)	94.39 ± 3.70	98.96 ± 7.23	<0.001S
1 min	93.15 ± 2.23	97.88 ± 5.33	<0.001S
3 min	90.98 ± 2.45	95.31 ± 5.34	<0.001S
5 min	88.44 ± 4.79	93.1 ± 4.32	<0.001S
10 min	85.93 ± 4.12	86.78 ± 4.68	0.872NS

There was no significant difference in the pre-anesthesia and prior of medication heart rate values between group A and group B. During laryngoscopy, at 1, 3- and 5-mins heart rate was significantly increased in group B than group A. Results showed statistically significant p value. (<0.001)



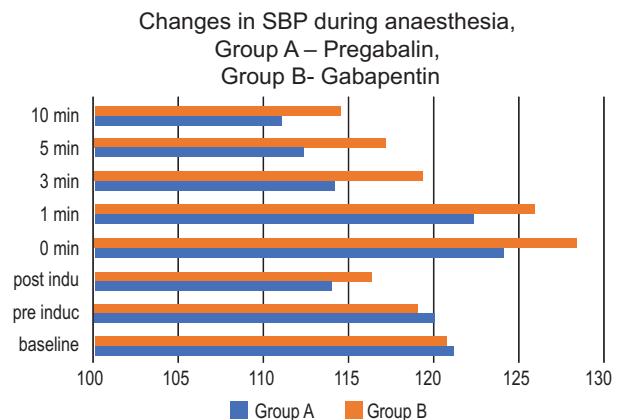
Graph 1 Graphical presentation of changes in HR during.

Table 3.6 Changes in SBP during anesthesia

Parameters	Group A	Group B	P value
Baseline	121.324±4.247	120.893±3.87	0.451NS
After Premedication	120.214±3.834	119.234±3.12	0.495 ^{NS}
After induction	115.121±5.664	116.45±6.125	0.231NS
During laryngoscopy (0 min)	124.324±2.34	128.634±6.43	<0.001S
1 min	122.532±3.72	126.12±5.42	<0.001S
3 min	114.231±2.67	119.521±4.21	<0.001S
5 min	112.421±3.512	117.342±5.76	<0.001S
10 min	111.122±6.167	114.64±6.32	<0.001S

There was no significant difference in the pre-anesthesia and prior of medication Systolic blood pressure values between group A and group B. During laryngoscopy, at 1,3,5, 10 mins systolic blood pressure was significantly increased in group B than group A. where p value was less than 0.001.

Changes in SBP during anaesthesia, Group A – Pregabalin, Group B- Gabapentin

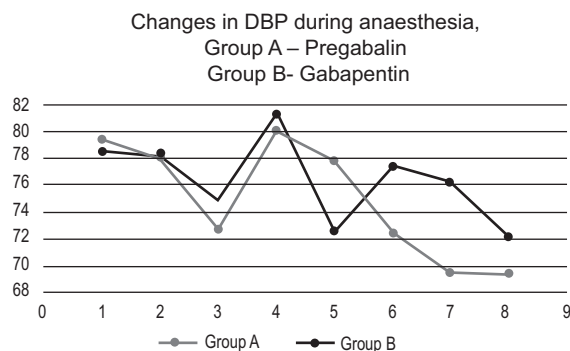


Graph 2 Graphical presentation of changes in SBP during anaesthesia.

Table 3.7 Changes in DBP during anesthesia

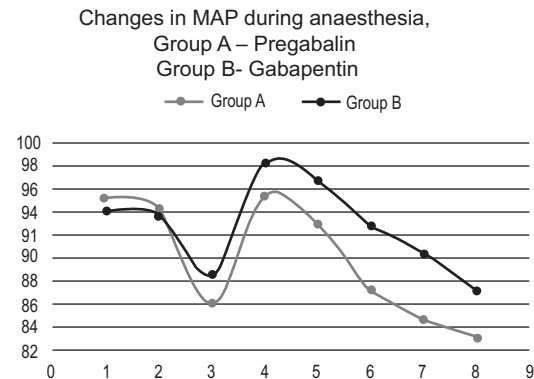
Parameters	Group A	Group B	P value
Baseline	79.231 ± 2.43	78.421 ± 3.97	0.623S
After Premedication			
After	72.451 ± 3.421	74.76 ± 6.38	0.027S
induction			
During	79.91 ± 2.26	82.18 ± 7.45	<0.001S
laryngoscopy (0 min)			
1 min	76.64 ± 3.89	79.35 ± 5.75	<0.001S
3 min	72.226 ± 2.43	77.275 ± 6.36	<0.001S
5 min	69.241 ± 3.49	76.134 ± 5.81	<0.001S
10 min	70.189 ± 3.61	72.02 ± 7.43	0.003NS

There was no significant difference in the pre-anesthesia and prior of medication diastolic blood pressure values between group A and group B. During laryngoscopy, at 1, 3- and 5-mins diastolic blood pressure significantly increased in group B than group A.

**Graph 3** Graphical presentation of changes in DBP during anesthesia**Table 3.8** Changes in MAP during anesthesia

Parameters	Group A	Group B	P value
Baseline	95.3 ± 5.8	94.12 ± 6.7	0.812NS
After Premedication			
After	94.2 ± 2.9	93.7 ± 7.85	0.672NS
induction			
During	95.33 ± 2.87	98.2 ± 10.5	0.012NS
laryngoscopy (0 min)			
1 min	92.96 ± 2.9	96.7 ± 11.43	<0.001s
3 min	87.22 ± 2.5	92.8 ± 9.4	<0.001s
5 min	84.68 ± 2.12	90.43 ± 8.3	<0.001s
10 min	83.1 ± 3.4	87.2 ± 7.12	<0.001s

There was no significant difference in the pre-anesthesia and prior of medication mean blood pressure values between group A and group B. After laryngoscopy, at 1, 3, 5 and 10 mins mean blood pressure significantly increased in group B than group A. where p value was statistically significant ($p < 0.001$).

**Graph 3** Graphical presentation of changes in MAP during anesthesia**Table 3.9** Per-operative Ramsay sedation score

	Group A (40)	Group B (40)
Before Induction	Grade 2 – (28)	Grade 2 – (06)
	Grade 1 – (12)	Grade 1 – (34)
1 hours after extubation	Grade 2 – (37)	Grade 3 – (16)
	Grade 1 – (03)	Grade 2 – (18)
		Grade 1 – (06)

Group A patients were adequately tranquil before induction and recovery was not delayed and patients were not agitated or sleepy. Opposite situation was occurred in group B, where patients were not tranquil before induction and recovery was delayed and patient was too deep for more than hour. This was for several hours in case of patient's age from 45 yrs to 55 yrs.

Table 4.0 Per-operative complication

Complication	Group A (40)	Group B (40)
Hypotension	0	0
Bradycardia	0	0
Vomiting	0	0
Blurred vision	0	0
Respiratory depression	0	0

Though group B patients were too deep during recovery time, both groups showed no complications during per-operative period such as hypotension, bradycardia, vomiting, blurred vision and respiratory insufficiency. So, with pregabalin premedication near normal physiology of patients was maintained per-operatively.

Discussion:

Pregabalin administered as a premedication significantly attenuated the pressor response to tracheal intubation in adults. The elevation of the pulse rate and blood pressure may be transient, variable. Usually these changes are well tolerated by healthy individuals. Although many studies proved the efficacy of gabapentin to attenuate intubation response, but a few studies showed the efficacy of pregabalin to suppress intubation response.

In this study all 80 enrolled patients were randomized to one of the two medication treatment groups of 40 patients each. All patients were with ASA physiological status I and II. In pregabalin group 26(65%) were ASA I and 14(35%) were ASA II. In gabapentin 29(72.5%) were ASA I and 11(27.5%) were ASA II. Group A and group B patients had no significant changes in heart rate, after premedication, after induction and 10 minutes after laryngoscopy and intubation. Heart rate increased during laryngoscopy in pregabalin & gabapentin group. During laryngoscopy results were statistically significant where p value was less than 0.001. After 5 mins of laryngoscopy, pregabalin group showed stable heart rate which was near baseline but in gabapentin group heart rate was still away from baseline, where p value was statistically significant.

In a study published in Saudi Journal of Anesthesia, kumkum gupta, Deepak Sharma et al¹¹, presented similar result by using oral pregabalin 150mg, where heart rate was decreased slightly before induction but stable after intubation.

In journal of Anesth Essays Res, Chandrakant Waikar, Jaideep Singh Et al²¹ found similar result with use of pregabalin 150 mg, showing HR was increased after intubation which was near this study result.

So, group A patient's heart rate was significantly stable during laryngoscopy, after 1 min, 3 minutes

and 5 minutes than group B patients which had similarity with others study published in journal. Group A and group B patient have no significant changes in Systolic blood pressure at baseline, after premedication and after induction. Systolic blood pressure in both groups increase during laryngoscopy but higher in gabapentin group. During laryngoscopy results was statistically significant where p value was less than 0.001. So, group A patient's Systolic blood pressure was significantly stable during laryngoscopy, after 1 min, which was significantly decrease after 3 minutes, 5 minutes and 10 mins than group B patients. So, in group A patient's systolic blood pressure was near normal during and after laryngoscopy

In Journal of Clinical and Diagnostic research, Shirin Parveen, Devendra Singh Negi, Rajesh Kumar and Mohd Chand Bagwan²⁰, presented in their study, 150mg was effective in blunting hemodynamic stress response to laryngoscopy and tracheal intubation. Systolic blood pressure was not increase after intubation; systolic blood pressure was found near normal. This finding was near same as investigator found in this study.

Group A and group B patient have no significant changes in Diastolic blood pressure at baseline, after premedication, after induction and 10 minutes after laryngoscopy. Diastolic blood pressure in each group increases during laryngoscopy which was higher in gabapentin group. During laryngoscopy results was statistically significant where p value was less than 0.001. After 5 mins of laryngoscopy pregabalin group showed diastolic blood pressure near to baseline which was less than gabapentin group, where p value was statistically significant.

In Journal of Clinical and Diagnostic research Shirin Parveen, Devendra Singh Negi, Rajesh Kumar and Mohd Chand Bagwan²⁰, presented in their study, 150mg was effective in blunting hemodynamic stress response to laryngoscopy and tracheal intubation. Preoperative baseline diastolic blood pressure was not increase after intubation, diastolic blood pressure was same as before laryngoscopy and intubation. This result was slightly higher than my result.

So, both groups showed stable diastolic blood pressure after laryngoscopy but in group A

patient's diastolic blood pressure was significantly less during after 1 min, 3 minutes and 5 minutes than group B patients. Group A and group B patient had no significant changes in Mean blood pressure at baseline, after premedication and after induction. Mean blood pressure was increased during laryngoscopy especially in gabapentin group. During laryngoscopy results was statistically significant. In 10 mins after laryngoscopy both groups showed stable mean blood pressure.

Another study published in Indian journal of Anesthesia, Bhawna Rastogi, Kumkum Gupta, Himanshu Chauhan¹² showed in their study no significant difference was observed in the mean arterial pressure before and after premedication with pregabalin 150 mg but after laryngoscopy and intubation, the attenuation of mean arterial blood pressure in pregabalin group was statistically significant as compared with the control group. After intubation MAP value was near to this study.

In Journal of Anaesthesia Essays and Researches, Chandrakant Waikar, Jaideep Singh Et al²¹ showed in their study oral premedication with oral pregabalin 150 mg attenuate laryngoscopy and intubation reflex successfully. Mean blood pressure after intubation raised slightly higher which was near baseline.

So, group A patients mean blood pressure was significantly stable during laryngoscopy, after 1 min, 3 minutes and 5 minutes than group B patients which had similarity with others study published in journal. Investigator result correlated well with the report of Eren et al¹⁷. They determined the effect of a single dose of pregabalin 150 mg, administered 1 h prior to surgery on reducing the cardiovascular response and stated that 150 mg of pregabalin had significantly decreased the mean arterial pressure and heart rate response to tracheal intubation of the patients undergoing lumbar discal hernia repair under general anesthesia.

According to Ramsay sedation score, in group A maximum patients were in grade 2 sedation level before induction of anesthesia and recovery was adequate without prolonging and postoperatively patients were in grade 2 sedation level. In group B maximum patients were in grade 1 sedation level and they were anxious. After extubation many patients were too deep for more than hours,

sedation score was grade 3 for maximum patients and grade 4 for some patients which were not desirable. So, pregabalin group patients were adequately sedated without prolonging recovery time, which is beneficial for many patients.

Though group B patients were too deep during recovery time, both groups showed no complications during per-operative period such as hypotension, bradycardia, vomiting, blurred vision and respiratory insufficiency. So, with pregabalin premedication near normal physiology of patients was maintained per-operatively.

Conclusions:

The results of this study indicate that oral tablet Pregabalin 150mg is more effective than tablet Gabapentin 600mg, in attenuation of intubation reflex. The Heart rate and Mean blood pressure is well control in the A group (pregabalin), with less side effects. The Heart rate and Mean blood pressure increase in the group B (gabapentin), with more side effects.

Pregabalin is emerging as an effective and safe drug as it leads to sedation, analgesia and hemodynamic stability. A single, oral dose of 150 mg of pregabalin premedication seems to be effective in attenuating the hemodynamic response to endotracheal intubation after the first attempt, an effect which may be useful in patients suffering from coronary insufficiency and might enable laparoscopic cholecystectomy in obese, hypertensive, and cardiac compromised patients. As there was no postoperative respiratory depression, it may be used in asthmatic and airway compromised patients.

Study patients age was between 15 – 60 years, but elderly patients more often take drugs such as antidepressants, hypnotics and anti-hypertensives with increased sensitivity to anesthetic medications and the safety and effectiveness of pregabalin in children and adolescent has not been established.

So, further study should be encouraged to established oral pregabalin for attenuation of laryngoscopy and intubation reflex in all age group with co-existing disease.

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Case Report

Successful Anaesthetic Management of a Patient with Post Burn Contracture and Difficult Airway: A Case Report

Mushfiqur Rahman¹, Md. Khalilur Rahman²

¹Associate Professor, Department of Anaesthesia and Surgical-ICU, BIRDEM General Hospital, Shahbagh, Dhaka ²Senior Consultant (Hons), Department of Anaesthesia and Surgical-ICU, BIRDEM General Hospital, Shahbagh, Dhaka

Corresponding Author: E-mail: rahmaanmushfique@gmail.com

Abstract

The Anaesthetic management of patients with post burn contracture release poses many problems to anaesthesiologist. Airway management in such cases is still challenging to anaesthesiologist as the contracture and deformity due to fibrous tissue resulting in non-alignment of oral, pharyngeal and laryngeal planes, makes laryngoscopy and endotracheal intubation very difficult or impossible and this can result in many life threatening and serious complications. We report the successful airway management of a patient with restricted neck extension and fixed flexion deformity by Laryngeal mask airway (LMA) followed by endotracheal intubation.

Keywords: Post burn Contracture, LMA, Difficult Airway

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Introduction

Management of airway in patients with orofacial and neck burn contracture is often a challenge to the anaesthesiologist. It is so because of the restricted mouth opening, decreased oropharyngeal space, limited extension at the atlanto-occipital joint, reduced compliance of the submandibular space and presence of fibrosed tissue over the neck¹. The reported incidence of difficult intubation is 5.85%, cannot intubate situation is 0.35% and cannot intubate-cannot ventilate situation is 0.02% and these can be major causes of anaesthesia related morbidity and mortality².

We report the successful anaesthetic management of a patient with severely limited neck movements associated with limited mouth opening by Laryngeal mask airway then followed by direct laryngoscope and endotracheal intubation.

Case Report

A 40 year old male patient weighing 65 kgs ASA grade-I had presented with severe burns over chin (lower jaw), neck and trunk area (35%), of six months duration with fibrosed scar tissue that

was extending from neck involving lower jaw, anterolateral aspect of neck, upper anterior chest wall and upper abdomen. His medical history was not significant. On examination fibrosed scar was present over the lower jaw, anterior neck with a slightly fixed flexion deformity with Mouth Opening < 3 Fingers Mallampati Grading was Grade III³.

Thyromental distance could not be assessed because of distorted neck anatomy. Trachea was not palpable and no extension and lateral Rotation of neck were possible. She was planned for release of contracture and free tissue transfer from forearm to neck. We planned introduced of laryngeal mask airway and release of contracture of neck, then direct laryngoscopic aided endotracheal intubation.

Difficult airway was predicted hence preoperative preparation with necessary masks, airways, endotracheal tubes, laryngeal mask airway (LMA's) [4], stylets, bougie and straight blade laryngoscope were kept ready. ENT Surgeon was available for emergency tracheostomy, if necessary.

Anaesthetic Management

Patient was reassured and was explained about the procedures that were to be carried out and Written Informed Consent taken including for the surgical release of contracture and tracheostomy if required.

Connections were made to the monitors and patient's IV access was secured. An intravenous infusion of Ringer lactate was started. Inj. Ranitidine 50 mg+ Inj. Ondansetron 4 mg+ Inj. Atropine 0.6 mg was given as premedication monitoring included standard 5 lead electrocardiogram, noninvasive blood pressure, oxygen saturation and capnography.



Figure 1: Preoperative photo of the patient



Figure 2: After LMA insetion



Figure 3: ETT intubation after release of neck scar



Figure 4: At the end of surgery

Pre-oxygenation for 5 min with oxygen at 8 l/min by face mask kept closely over mouth opening and testing the beg mask ventilation. After testing of beg musk ventilation Induction with 120 mg of propofol and fentanyl 100mcg was done.

After induction, ventilation became difficult as there was no visible thrust of chest wall movement. However by maintaining sustained pressure with 100% oxygen we could maintain oxygenation of the patient. Saturation was found to be 98% throughout mask ventilation. After one minute, 3 size lryngeal musk airway LMA was introduced by index finger. The cuff was inflated and the LMA was connected to Boyle's machine

via Bain's circuit. The proper position of LMA was confirmed by bilateral auscultation of chest.

Patient was ventilated with a breathing mixture of 4 litres of nitrous oxide, 2 litres of oxygen and 1% Halothane. Surgeon was allowed to proceed and we continued with intermittent positive pressure ventilation. After adequate release of neck scar full range of neck extension was achieved. Later patient was induced with inj. Vecuronium 0.1mg/kg total 60 mg. When adequate relaxation was achieved, removed the laryngeal mask airway and endotracheal intubation was proceeded by ID 7.5mm endotracheal tube.

Anaesthesia maintained with 0.5% Halothane + Inj. Vecuronium on Intermittent Positive Pressure Ventilation. Surgery was completed in 5 hour 30 minutes. Vitals were stable.

At the end of surgery the process of extubation was not expedited and ventilation was continued. We let the patient completely recover. Reversal was done by Neostigmine + Atropine.

After noticing eye opening and obeying commands, suction of the oral cavity was carried out and the patient was extubated. She was observed for another 15 minutes in the operation theatre. Supplementary oxygen was given during this period. Patient was then shifted to post operative ward. Observation was made by monitoring vitals and oxygen saturation. From here on she made uneventful recovery.

Discussion

Post burn neck contracture following burns is a known complication and airway management in such patients offers a challenge. The fixed flexion deformity of head causes difficult Endotracheal intubation as there will be limited oro-pharyngeal space, decreased pharyngeal space, decreased atlanto-occipital extension and submandibular compliance.

Many options are available for intubation in such cases like: awake fiberoptic intubation, Laryngeal Mask Airway, Intubation Laryngeal Mask Airway, Blind nasal intubation, Retrograde intubation, tracheostomy, Release of contracture using tumescent mixture of local anaesthetic but the use of fibre optic intubation is the gold standard when compared to other techniques^{5,6}.

Tracheostomy was not suitable as there was fibrosed tissue over the neck making anatomy distorted. However in patient with extreme deformity the functional and anatomical distortion may be such that all attempts at intubation may fail⁷. Hence the primary plan for airway management of our patient was testing of bag mask ventilation then induced inj. Propofol 120 mg and inj. Fentanyl 100 microgm and airway secured by Laryngeal Mask Airway for contracture release followed by direct laryngoscope and endotracheal intubation. Fiberoptic bronchoscope guide considered as safest and most effective method in known or suspected cases of difficult intubation. The primary advantage of fiberoptic bronchoscope guided intubation is that it permits direct visual control of the intubation procedures.⁷ There are studies indicating the success rate of Fiberoptic Bronchoscope guided intubation of 88-100% in difficult airway patients^{8,9,10,11,12}. Fiberoptic bronchoscopy provides excellent visualization of glottis and the endotracheal tube insertion can be continuously viewed until intubation is accomplished.

Conclusion

Vigilance and pre-anaesthetic meticulous preparation for difficult airway management is the key to successful management of difficult airways. The anaesthesiologist should have multi layered contingency plan to handle the airway. Proper preoperative preparation and intraoperative planning and a team work are always necessary for a successful outcome. Fiberoptic endoscopy was another frequently used technique, but is not available everywhere.

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