Original Article

Esmolol Hydrochloride and Dexmedetomidine on Pressure Response during Laryngoscopy, Intubation and Pneumoperitoneum in Laparoscopic Surgery

A.K.M Fakhrul Alam[1], Md. Mahbub-Ur-Rahman[2], Md. Nazmul Ahsan[3], Kaneez Fatema[4], Md. Salim Matber[5]

ABSTRACT

Background: Laparoscopy procedures require pneumoperitoneum for adequate visualisation and operative manipulations which affects many homeostatic systems causing alterations in acid-base status, cardiovascular system, stress response and pulmonary physiology. This study was conducted **t**o compare the effect of esmolol and dexmedetomidine on pressure response during laryngoscopy, intubation and pneumoperitoneum in laparoscopic surgery.

Methods: This was a randomized open labelled, prospective control type of study was conducted at Anaesthesia, Analgesia & ICU Department, Sher-e-Bangla Medical College Hospital, Barishal, Bangladesh from July 2020 to December 2020. Eighty Four patients aged between 25-60 years, belonging to ASA I or II of either sex posted for elective laparoscopic surgery under general anaesthesia were selected for the study. Patients were allocated randomly in to three groups (28 patients in each group).Patients of group-A received dexmedetomidine (0.5 mcg/kg) IV as loading dose over 10min, followed by 0.4mcg/kg/hr till the end of pneumoperitoneum and patients of group-B received esmolol (0.5mg/kg) IV as loading dose over 5 min followed by 50mcg/kg/min till the end of pneumoperitoneum. Patients of group-C received same volume of normal saline. During laryngoscopy, intubation, pneumoperitoneum, at reversal and extubation HR, MAP, oxygen saturation were observed. Recovery in terms of time to respond to oral-commands, extubation and full orientation was noted along with any adverse effects.

Results: In control group, there was significant increase in HR and MAP during intubation, extubation and pneumoperitoneum. In dexmedetomidine group we observed better control of HR and MAP as compare to esmolol and control groups.

Conclusion: Both dexmedetomidine hydrochloride and esmolol hydrochloride were effective in attenuating pressure response to laryngoscopy, intubation and pneumoperitoneum in patients undergoing laparoscopic surgeries. Dexmedetomidine was more effective to control HR and MAP as compared to esmolol. With dexmedetomidine, the recovery from anaesthesia was prolonged than esmolol.

Key words: Laryngoscopy, Laparoscopic Surgery, Pneumoperitoneum, Hemodynamic Response, Dexmedetomidine, Esmolol.

INTRODUCTION

Laparoscopy procedures require pneumoperitoneum for adequate visualisation and operative manipulations which affects many homeostatic systems causing alterations in acid-base status, cardiovascular system, stress response and pulmonary physiology. Laparoscopic procedures include smaller incisions, lower risk of wound complications, reduced postoperative pain and pulmonary complications, shorter hospital stay, more

1. Dr. A.K.M Fakhrul Alam, Assistant Professor, Anaesthesia, Analgesia & ICU Department, Patuakhali Medical College, Patuakhali, Bangladesh
2. Dr. Md. Mahbub-Ur-Rahman, Assistant Professor, Anaesthesia, Analgesia & ICU Department, Sher-e-Bangla Medical College, Barishal, Bangladesh
3. Dr. Md. Nazmul Ahsan, Assistant Professor, Anaesthesia, Analgesia & ICU Department, Sher-e-Bangla Medical College, Barishal, Bangladesh
4. Dr. Kaneez Fatema, Assistant Professor, Anaesthesia, Analgesia & ICU Department, Sher-e-Bangla Medical College Barishal, Bangladesh
5. Md. Salim Matber, Assistant Professor, Department of Ortho-surgery, Patuakhali Medical College, Patuakhali, Bangladesh

Correspondence: Dr. A.K.M Fakhrul Alam, Assistant Professor, Anaesthesia, Analgesia & ICU Department, Patuakhali Medical College, Patuakhali, Bangladesh, Email: alamf5940@gmail.com

Received: 06 May 2023 Revised: 26 May 2023 Accepted: 15 June 2023

rapid return to normal activity which in turn reduces cost to the patient. These hemodynamic responses are mainly due to increased release of catecholamines, vasopressin, or both. Esmolol, an ultrashort-acting cardioselective β_1 adrenoceptor antagonist, has been used to control tachycardia and hypertension. They cause increase in systemic vascular resistance which increases mean arterial pressure, decreases cardiac output and compromise tissue perfusion. Various pharmacological agents like nitroglycerine[1], opioids[2], gabapentin[3], pregabalin[4], magnesium sulfate[5], clonidine[6], dexmedetomidine[7] and beta blocker[8] has been used to maintain hemodynamic during pneumoperitoneum. Dexmedetomidine by its agonist effect on α_2- adrenergic receptor thereby inhibiting the release of catecholamine and vasopressin released during laparoscopic surgery[9] controls hemodynamic response of pneumoperitoneum. Esmolol, an ultra-short acting cardio-selective β1- receptor antagonist, blunts hemodynamic responses to perioperative noxious stimuli during laryngoscopy, intubation and pneumoperitoneum.[8] Dexmedetomidine, an α_2 adrenergic receptor agonist, possesses hypnotic, sedative, anxiolytic, sympatholytic, and analgesic properties without producing significant respiratory depression.[10] Its sympatholytic effect decreases mean arterial pressure (MAP) and heart rate (HR) by reducing norepinephrine release.[11] Bhattacharjee *et al* [12] have shown that dexmedetomidine is effective in attenuating the adverse hemodynamic response to CO_2 pneumoperitoneum. Anaesthetic manoeuvres like direct laryngoscopy, tracheal intubation, extubation, pneumoperitoneum and CO2 insufflations necessary in laparoscopic surgeries causes increase in plasma stress hormone which leads to increase in heart rate (HR), mean arterial blood pressure (MAP), systemic and pulmonary vascular resistance and decrease cardiac output. In this randomized open labeled observer blinded study, we compared effect of esmolol and dexmedetomidine to attenuate pressure response to laryngoscopy, intubation and pneumoperitoneum during laparoscopic surgery. Our aim of study was to compare the effectof esmolol and dexmedetomidine on pressure response during laryngoscopy, intubation and pneumoperitoneum in laparoscopic surgery.

METHODS

This was a randomized open labelled, prospective control type of study conducted at Anaesthesia, Analgesia & ICU Department, Sher-e-Bangla Medical College Hospital, Barishal, Bangladesh from July to December 2020. Eighty Four patients aged between 25-60 years, belonging to ASA I or II of either sex posted for elective laparoscopic surgery under general anaesthesia were selected for the study. Patients who refuses or with history of hypertension, diabetes mellitus, morbid obesity, allergy to study drugs, renal and hepatic insufficiency, cardiopulmonary or respiratory disease, patients on beta blocker drugs, anticipated difficult intubation, pregnant or breast feeding female were excluded from the study. Patients were allocated randomly in to three groups (28 patients in each group).

Group-A: Inj. Dexmedetomidine hydrochloride.

Group-B: Inj. Esmolol hydrochloride.

Group-C: Inj. 0.9% normal saline was administered to the control group.

Pre-anaesthesia check-up was conducted and a detailed history and complete physical examination was done. Routine

investigations like complete blood count, random blood sugar, renal function test, liver function test, chest x-ray and electrocardiogram were done. Monitors for pulse oximetry, NIBP and multipara monitor. Baseline values of heart rate (HR), non-invasive blood pressure (NIBP) were recorded. Intravenous access was secured. All the patients were premedicated with intravenous Inj. glycopyrrolate 0.004 mg/kg, Inj. ondansetron 0.01 mg/kg, Inj. Omeprazole and antibiotic. Group-A: Inj. Dexmedetomidine hydrochloride intravenously (IV) bolus of 0.5 µg/kg was given over 10 minutes by infusion pump starting 5 minutes before induction following which infusion rate was set at 0.4 mcg/kg/hr till the end of pneumoperitoneum. Group-B: Inj. Esmolol hydrochloride IV bolus of 0.5 mg/kg was given over 5 minutes by infusion pump starting 2 minutes before induction, followed by infusion was set at 50 mcg/kg/min till the end of pneumoperitoneum. Group-C: 0.9% normal saline was given as bolus 3 ml/min starting 5 min before induction by infusion pump following which infusion was continued till the end of pneumoperitoneum.

The patients were pre oxygenated with 100% oxygen by face mask for 3 min. Anaesthesia was induced with intravenous Inj. fentanyl 2 mcg/kg, Inj. thiopentone 6mg/kg and Inj. Vecuronium 0.1mg/kg to facilitate intubation. Oro-tracheal intubation with Macintosh laryngoscope was done with an appropriate sized portex cuffed endotracheal tube. Intubation was done by experienced anaesthesiologist. Patients were maintained with oxygen, nitrous oxide (O2:N2O, 40:60), Halothen* 7 MAC and intermittent boluses of Inj. vecuronium (0.01 mg/kg). Patients were ventilated manually with tidal volume 500-550 ml/kg and respiratory rate 12–14 breaths/min. Intraabdominal pressure was maintained to 12-14 mm of Hg. CO2 insufflation flow was maintained at the rate of 6 L/min. HR, oxygen saturation (SpO2), urine output and blood loss was monitored. As soon as the pneumoperitoneum was released, study drug infusion was stopped. At the end of procedure, residual neuromuscular blockade was reversed with IV glycopyrrolate (.004mg/kg) and neostigmine (0.05 mg/kg). HR, MAP and SpO2 were recorded at baseline, after study drug administration, after induction, immediately after intubation, at the time of gas insufflation, at every 5 minute interval after pneumoperitoneum, at the end of pneumoperitoneum, at the time of reversal and at the time of extubation. Hypertension (MAP >110 mmHg) was treated with intermittent bolus of Inj. Propofol. Bradycardia (HR<50/min) was treated with inj. atropine 0.6mg IV. Any case of failure to intubate within 15 second, massive blood loss, laparoscopic surgery converted to open laparotomy and surgical time extended more than 3 hr was excluded from the study.

Statistical Analysis: Statistical analysis was carried out using the Graph pad prism 8.0 statistical software. Results of continuous measurements were presented as Mean±SD and results of categorical measurements are presented in number and percentage (%). Patient characteristic data were analysed with one-way analysis of variance (ANOVA) for continuous variables and Chi-square test for categorical variables. Inter group comparison of HR; MAP was done with ANOVA, followed by an unpaired t-test. A p-value of <0.05 was considered statistically significant.

RESULTS

Our study included 84 adult patients of ASA grade I and II posted for laparoscopic surgery. They were randomly assigned into three groups of 28 patients in each. None of the patient was excluded from the study. As shown in Table 1 there was no significant difference in age, sex, weight, duration and type of surgery (P value >0.05) in all groups. Table-2 shows, there was no significant difference in baseline HR between the groups. After administration of the study drugs and induction agent, there was a significant decrease in HR in group-B and group-C as compared to group-A ($p<0.05$).

Table 1: Demographic Data (N=84)

Variables	Group A Mean+ SD	Group B Mean+ SD	Group C Mean+ SD	P-value
Age (year)	52.2+9.06	49.26±10.34	48.8+10.43	0.30
Sex (Male/Female)	13/15	14/14	13/15	
Weight (kg)	54.66±7.89	52.86±9.58	53.71±8.83	0.67
Duration of surgery(min)	147.33±36.69	144±41.11	150.4+31.73	0.79

Table-2: Comparison of heart rate at various time intervals (N=84)

	Group A	Group B	Group C	P value
Baseline	88.4±8.6	89.32±6.8	87.22±6.4	0.69
After intubation	100.4±10.6	102.4±11.2	103.32+12.6	0.70
Before pneumo-peritoneum (PP)	97.6±10.8	98.6±11.24	96.8±9.4	0.83
5 min after PP	95.4±8.4*	96.2±8.6*	106.42±10.6	0.0005
15 min after PP	96.6±11.6*	94.4±10.6*	108±12.6	0.0005
30 min after PP	94.6±10.6*	93.6±9.6*	106.4±11.6	0.0003
60 min after PP	95.6±9.6*	94.6±11.4*	108.24±12.6	0.0003
After release of PP	90.4±9.2**	89.32+8.4*	101.8±11.4	0.0003
After extubation	94.8±10.36*	92.8±9.4**	104.6±10.6	0.0008

Gas insufflation caused an increase in HR from baseline values in group-C, however this increase was not seen in group-B and group-A ($P<0.001$). In group-C, HR was maintained near baseline values and below baseline value in group-B. However HR was statistically lower in group-A ($p<0.05$). In group-A there was significant rise from baseline value in the HR immediately after intubation and remained higher till the end of pneumoperitoneum. In group-B, after loading dose HR was decrease from baseline value and remained decreased at all-time intervals till the end of surgery. In group-C, there was minimal increase in HR from baseline value immediately after intubation which came to baseline values within 3 min after intubation and remained near baseline values till the end of pneumoperitoneum.

Table-3: Comparison of mean arterial blood pressure at various time intervals (N=84)

	Group A	Group B	Group C	P value
Baseline	80.2+6.3	81.2+4.2	81.34±4.6	0.77
After intubation	97.6±10.44	98.2+9.6	100.2±1 1.6	0.78
Before pneumo-peritoneum (PP)	86.6±9.4	87.2±8.6	88.4±8.8	0.92
5 min after PP	78.2±8.8*	80.4±6.8*	93.4±1 1.4	0.0001
15 min after PP	80.4±10.4*	79.2±8.2*	94.8±1 1.6	0.0001
30 min after PP	81.6±9.4*	79.6±7.2**	96.8±10.4	0.0001
60 min after PP	81.4±9.4*	79.6±7.2*	96.8±10.4	0.0013
After release of PP	79.4±9.6*	81.4±8.6*	90.2±10.4	0.0001
After extubation	85.2±10.4*	84.4±9.6*	98.84±1 1.6	0.69

Table-3 shows, there was no statistically significant difference in baseline MAP between the groups but after administration of the study drugs and induction agent, significant decrease was seen in MAP in group-A, while no significant difference between group-A and group-B (P>0.05) was found. The rise in MAP immediately after intubation was 25% in group-A and 15% in group-B. Gas insufflation caused an increase in MAP from baseline values in group-A, it was not seen in group-A and group-C (P<0.001). There was significant difference in MAP values between all the groups during pneumoperitoneum (p<0.001). During pneumoperitoneum MAP was higher in group-A at all-time intervals as compared to baseline values. Where as in group-A, MAP was maintained near baseline values, while it was below baseline value in group-C. There was no significant difference in MAP values between group-A and group-C at the end of gas insufflation, at the time of reversal and at the time of extubation (P>0.05), however MAP was statistically lower in group-A (P<0.05). While comparing group-A and group-C, there was significant difference between the groups in MAP at all-time interval during pneumoperitoneum (P<0.001). In group-A and group-B, statistically significant increase in MAP after intubation and during pneumoperitoneum was observed. Decrease in MAP was found in group-A after administration of dexmedetomidine, which was persisted till the end of surgery and extubation.

Table-4: Post-operative complications

Post-operative complication	Group A	Group B	Group C
Nausea	1	2	3
Vomiting	1	3	4
Respiratory Depression	1	-	-
Bradycardia	5	3	-
Hypotension	4	1	-

Table-4 shows bradycardia was found in 5 patients of group-A and 3 patients in group-B which responded to inj. atropine (0.6mg) IV stat. Hypotension was found in 4 patients of group-A and 1 patient of group-B. Respiratory depression was found in 1 patient of group-A.

As shown in table-5, time to respond to oral commands was longer in dexmedetomidine (8.5±1.3 min) as compared to esmolol group (5.8±0.99 min) and control group (5.7±0.97 min) which is statistically Significant (P<0.001).

Table-5: Recovery profile.

Recovery Profile	Group A	Group B	Group C
Time to respond to oral-commands (min)	11	12	14
Time to extubation (min)	9	8	8
Time to full orientation (min)	8	8	6

There was no significant difference in time to respond to oral commands between esmolol group and control group (P>0.05). The time to extubation was longer in dexmedetomidine group (11±1.86 min) as compared to esmolol group (8.7±1.4 min.) and control group (8±1.03 min) which is statistically significant (P<0.01). There was no significant difference in time to extubation between esmolol group and control group in our study. Time to full orientation was longer in dexmedetomidine (14.03±2.78min) as compared to esmolol group (10.43±1.45min) and control group (10.2±1.32min) which is statistically significant (P<0.001). There was no significant difference in time to full orientation between esmolol group and control group (P>0.05). In group-A decrease in respiratory rate (RR) 10/min and tidal volume (300 ml) was found in one patient. Patient was observed in operation theatre, RR was improved to 14/min and tidal volume to 500 ml within 30 min.

DISCUSSION

For laparoscopic procedures, CO2 is used to create pneumoperitoneum because of which intra-abdominal pressure increases, which causes stretching and stimulation of peritoneum by CO2 which leads to activation of sympathetic nervous system which in turn increases plasma catecholamine and vasopressin level, which further activates renin angiotensin aldosterone system leading to abrupt increase in HR, MAP, cardiac output and systemic vascular resistance.[13] Administration of general anaesthesia, laryngoscopy, tracheal intubation and extubation are one of the critical events which lead to transient yet marked sympathoadrenal response leading to hypertension and tachycardia.[14] This can leads to complications like myocardial ischemia, infarction, etc. Bon Sebastian et al[15] conducted study for an optimal bolus dose of dexmedetomidine by comparing two doses 0.5mcg/kg and 0.75 mcg/kg with placebo to attenuate stress response during laryngoscopy and endotracheal intubation and found that both the doses were effective in attenuating the pressure response. If dexmedetomidine given as rapid infusion, it leads to a biphasic response on blood pressure which is initial hypertension followed by fall in blood pressure due to stimulation of α2 receptors in vascular smooth muscles.[16] In our study, we choose lower dose 0.5 µg/kg and administered slowly as an infusion over 10 min as bolus and found it effective to control pressure response during laryngoscopy and intubation as compared to control group. Siddareddigari Reddy et al.[17] compared dexmedetomidine (1mcg/kg) and esmolol (2mg/kg) for attenuating hemodynamic response and found esmolol effectively control HR after intubation but no effect on

systolic blood pressure whereas, dexmedetomidine suppressed both HR as well as MAP to laryngoscopy and tracheal intubation. In our study, we found that both the drugs blunted HR response to laryngoscopy and intubation significantly (P<0.001). We used low dose dexmedetomidine infusion (0.4mcg/kg/hr) and found it effective to control the hemodynamic changes due to pneumoperitoneum during laparoscopic surgeries. Similar to our study, Gourishankar Reddy et al.[18] studied dexmedetomidine (0.4mcg/kg/hr) infusion for hemodynamic stability and found it effective in attenuating hemodynamic stability. Decrease in MAP was significant only at higher dose. In our study, bolus dose of 0.5mg/kg esmolol significantly blunted rise in HR but did not blunted blood pressure response. The rise in HR during intubation was 4% inesmolol group whereas; the rise in blood pressure during intubation was 14% in esmolol group. Similar to this, A. M. Koivusalo et al.[8] studied effects of esmolol (1mg/kg bolus followed by 200 mcg/kg/min infusion) on hemodynamic response to CO2 pneumoperitoneum for laparoscopic surgery. They concluded that esmolol effectively prevent the pressure response to induction and maintenance of CO2 pneumoperitoneum. In our study, we found effective control of HR and MAP throughout the pneumoperitoneum with esmolol 0.5mg/kg bolus followed by 50mcg/kg/min infusion as compared to control group without intra-operative complication. Effect on HR was faster while control of MAP was delayed, which may be related to the gradual decline in the plasma renin activity occurring with a half- life of 11.9 minutes. Ahmed nabil ibrahim et al.[19] compared the efficacy of clonidine (2mcg/kg bolus) versus esmolol (1.5mg/kg bolus followed by 10 mcg/kg/min infusion) on the hemodynamic response during laparoscopic cholecystectomy and concluded that esmolol and clonidine both provided hemodynamic stability in laparoscopic cholecystectomy but clonidine was associated with postoperative sedation. We compared esmolol with dexmedetomidine and found more sedation in dexmedetomidine group with better control of hemodynamic response to laryngoscopy, intubation and pneumoperitoneum. In accordance to our study, Nirav kotak et al.[20] also compared dexmedetomidine and esmolol in similar dose for attenuation of pressure response during pneumoperitoneum in patients undergoing laparoscopic cholecystectomy. However, MAP was not significantly controlled during intubation but values were lower compared to control group. Study done by Vinit K. Srivastava et al.[21] with dexmedetomidine (bolus dose of 1mcg/kg followed by 0.5mcg/kg/h infusion) and esmolol (bolus dose of 1mg/kg followed by 0.5mg/kg/h infusion) during laparoscopic cholecystectomy also showed dexmedetomidine is better than esmolol for attenuation of hemodynamic response to pneumoperitoneum. Kol et al.[22] studied desflurane with esmolol or dexmedetomidine for controlled hypotension during tympanoplasty. They found significantly shorter extubation and recovery times and significantly less postoperative sedation in esmolol group as compare to dexmedetomidine. In accordance to our study Ibraheim et al.[23] compared esmolol and dexmedetomidine in similar dose and found dexmedetomidine was associated with prolonged recovery as compared to control group. In consistent to above studies we also found prolong recovery time with dexmedetomidine as compared to control and esmolol group. The

study by Islam M. Massad et al.[24] and Necla Dereli et al.[25] demonstrated less postoperative nausea and vomiting with dexmedetomidine and esmolol infusion during laparoscopic surgery respectively. Similarly we also found less incidence of nausea and vomiting with both dexmedetomidine and esmolol group as compared to control group.

CONCLUSION

In concluded, both dexmedetomidine hydrochloride and esmolol hydrochloride were effective in attenuating pressure response to laryngoscopy, intubation and pneumoperitoneum in patients undergoing laparoscopic surgeries. Dexmedetomidine was more effective to control HR and MAP as compared to esmolol. With dexmedetomidine, the recovery from anaesthesia was prolonged than esmolol.

Conflict of Interest: None.
Source of Fund: Nil.

REFERENCES

1. Moon HS, Lee SK, Choi YS, In CB, Choi EJ. The effect of nitroglycerin on hemodynamic changes during laparoscopic low anterior resection. Korean journal of anesthesiology. 2011 Nov;61(5):388.

2. Damen SL, Nieuwenhuijs VB, Joosten W, Houweling PL, Clevers GJ. The effects of remifentanil and sufentanil on the quality of recovery after day case laparoscopic cholecystectomy: a randomized blinded trial. Journal of Laparoendoscopic & Advanced Surgical Techniques. 2004 Apr 1;14(2):87-92.

3. Pandey CK, Priye S, Ambesh SP, Singh S, Singh U, Singh PK. Prophylactic gabapentin for prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled study. Journal of postgraduate medicine. 2006 Apr 1;52(2):97-100.

4. Peng PW, Li C, Farcas E, Haley A, Wong W, Bender J, Chung F. Use of low-dose pregabalin in patients undergoing laparoscopic cholecystectomy. British journal of anaesthesia. 2010 Aug 1;105(2):155-61.

5. Paul S, Biswas P, Bhattacharjee DP, Sengupta J. Effects of magnesium sulfate on hemodynamic response to carbon dioxide pneumoperitoneum in patients undergoing laparoscopic cholecystectomy. Anesthesia Essays and Researches. 2013 May 1;7(2):228-31.

6. Singh M, Choudhury A, Kaur M, Liddle D, Verghese M, Balakrishnan I. The comparative evaluation of intravenous with intramuscular clonidine for suppression of hemodynamic changes in laparoscopic cholecystectomy. Saudi journal of anaesthesia. 2013 Apr 1;7(2):181-6.

7. Khanduja S, Ohri A, Panwar M. Dexmedetomidine decreases requirement of thiopentone sodium and pentazocine followed with improved recovery in patients undergoing laparoscopic cholecystectomy. Journal of Anaesthesiology Clinical Pharmacology. 2014 Apr 1;30(2):208-12.

8. Koivusalo AM, Scheinin M, Tikkanen I, Yli-Suomu T, Ristkari S, Laakso J, Lindgren L. Effects of esmolol on haemodynamic response to CO2 pneumoperitoneum for laparoscopic surgery. Acta anaesthesiologica scandinavica. 1998 May;42(5):510-7.

9. Ghodki PS, Thombre SK, Sardesai SP, Harnagle KD. Dexmedetomidine as an anesthetic adjuvant in laparoscopic surgery: An observational study using entropy monitoring. Journal of Anaesthesiology Clinical Pharmacology. 2012 Jul 1;28(3):334-8.

10. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic

properties of small-dose dexmedetomidine infusions. Anesthesia & Analgesia. 2000 Mar 1;90(3):699-705.
11. Guler GÜ, Akin AY, Tosun ZE, Eskitascoglu E, Mizrak A, Boyaci A. Single-dose dexmedetomidine attenuates airway and circulatory reflexes during extubation. Acta anaesthesiologica scandinavica. 2005 Sep;49(8):1088-91.
12. Bhattacharjee DP, Nayek SK, Dawn S, Bandopadhyay G, Gupta K. Effects of dexmedetomidine on haemodynamics in patients undergoing laparoscopic cholecystectomy-A comparative study. Journal of Anaesthesiology Clinical Pharmacology. 2010 Jan 1;26(1):45-8.
13. Mann C, Boccara G, Pouzeratte Y, Eliet J, Serradeil-Le Gal C, Vergnes C, Bichet DG, Guillon G, Fabre JM, Colson P. The relationship among carbon dioxide pneumoperitoneum, vasopressin release, and hemodynamic changes. Anesthesia & Analgesia. 1999 Aug 1;89(2):278-83.
14. Kayhan Z, Aldemir D, Mutlu H, Öğüş E. Which is responsible for the haemodynamic response due to laryngoscopy and endotracheal intubation? Catecholamines, vasopressin or angiotensin?. European journal of anaesthesiology. 2005 Oct;22(10):780-5.
15. Sebastian B, Talikoti AT, Krishnamurthy D. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine: A comparison between two doses. Indian journal of anaesthesia. 2017 Jan 1;61(1):48-54.
16. Gurudatt CL. Dexmedetomidine-the wonder drug, for the present and the future. RGUHS J Med Sciences. 2013 Jun;3(3):170-6.
17. Reddy SV, Balaji D, Ahmed SN. Dexmedetomidine versus esmolol to attenuate the hemodynamic response to laryngoscopy and tracheal intubation: A randomized double-blind clinical study. International Journal of Applied and Basic Medical Research. 2014 Jul 1;4(2):95-100.
18. Manne GR, Upadhyay MR, Swadia VN. Effects of low dose dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. Indian journal of anaesthesia. 2014 Nov 1;58(6):726-31.
19. Ibrahim AN, Kamal MM, Lotfy A. Comparative study of clonidine versus esmolol on hemodynamic responses during laparoscopic cholecystectomy. Egyptian Journal of Anaesthesia. 2016 Jan 1;32(1):37-44.
20. Kotak N, Patil N, Rathod Y. Attenuation of Intra-Operative Pressure Response to Pneumoperitoneum in Patients Undergoing Laparoscopic Cholecystectomy–A Comparative Study between Dexmedetomidine and Esmolol. J Dent Med Sci. 2016;15(2):85-95.
21. Srivastava VK, Nagle V, Agrawal S, Kumar D, Verma A, Kedia S. Comparative evaluation of dexmedetomidine and esmolol on hemodynamic responses during laparoscopic cholecystectomy. Journal of clinical and diagnostic research: JCDR. 2015 Mar;9(3):UC01.
22. Kol IO, Kaygusuz K, Yildirim A, Dogan M, Gursoy S, Yucel E, Mimaroglu C. Controlled hypotension with desflurane combined with esmolol or dexmedetomidine during tympanoplasty in adults: A double-blind, randomized, controlled trial. Current therapeutic research. 2009 Jun 1;70(3):197-208.
23. Ibraheim OA, Abdulmonem A, Baaj J, Zahrani TA, Arlet V. Esmolol versus dexmedetomidine in scoliosis surgery: study on intraoperative blood loss and

hemodynamic changes. Middle East J Anaesthesiol. 2013 Feb 1;22(1):27-33.
24. Massad IM, Mohsen WA, Basha AS, Al-Zaben KR, Al-Mustafa MM, Alghanem SM. A balanced anesthesia with dexmedetomidine decreases postoperative nausea and vomiting after laparoscopic surgery. Saudi Med J. 2009 Dec 1;30(12):1537-41.
25. Dereli N, Tutal ZB, Babayigit M, Kurtay A, Sahap M, Horasanli E. Effect of intraoperative esmolol infusion on anesthetic, analgesic requirements and postoperative nausea-vomitting in a group of laparoscopic cholecystectomy patients. Revista brasileira de anestesiologia. 2015 Mar;65:141-6.