

Role of Dexmedetomidine in Attenuation of Hemodynamic Response to Laryngoscopy - A Dose-Finding Study

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ABSTRACT

Aim: Determining efficacy of pre-operative bolus dose of dexmedetomidine 0.75 and 0.5µg/kg as an infusion and compare it with placebo in attenuation of hemodynamic response to laryngoscopy and tracheal intubation (LTI).

Design: Double-blind randomized control.

Place & duration: Sindh Institute of Urology & Transplantation, Karachi, Pakistan, from August 2019 to August 2021.

Methodology: Patients were stratified into three groups. Group A received normal saline (NS), Group B received dexmedetomidine 0.5 µ/kg and Group C received dexmedetomidine 0.75 µ/kg as an infusion over 10 minutes followed by standardized general anaesthesia. Primary outcome measures were hemodynamic variables at 1, 3, 5 and 10 minutes post LTI. Secondary outcome measures were adverse effects related to dexmedetomidine.

Results: Both dexmedetomidine groups showed better attenuation of hemodynamic response to LTI than saline group. Dexmedetomidine 0.75 µg/kg attenuated hemodynamic response to LTI significantly better than dexmedetomidine 0.5 µg/kg and placebo without causing any statistically significant adverse effects.

Practical implication: The function of dexmedetomidine in attenuating hemodynamic response to laryngoscopy has several practical implications, including improved patient safety, optimal dosing, reduced anaesthetic requirements, cost-effective treatment, and enhanced patient comfort.

Conclusion: Dexmedetomidine 0.75 µg/kg efficient than 0.5 µg/kg and placebo in attenuating hemodynamic response to LTI when given as a pre-induction bolus.

Keywords: Anesthesia; Dexmedetomidine, Laryngoscopy, Intubation, Stress Response.

INTRODUCTION

Stress response to direct LTI is pronounced phenomenon in anesthesiology, demonstrated by Reid and Brace in 1940^{1,2}. During LTI, stimulation of proprioceptors at base of the tongue evokes a transient but marked rise in blood pressure instantaneously after intubation lasting for 5-10 minutes³. The corollary of these profound differences in cardiovascular physiology is well tolerated but in cardiac patients may prove detrimental⁴.

Investigators have used various techniques and different drugs regimens with varied levels of success to attenuate the stress response such as topical lignocaine spray, a deep plane of anesthesia, limiting the duration of laryngoscopy within 15 seconds, intravenous opioids^{5,7}, calcium channel blockers, vasodilators, lignocaine and beta-blocker⁸⁻¹². Besides different doses⁷⁻⁹, it has also been compared with fentanyl^{5,6}, esmolol¹¹⁻¹² sufentanil⁷ remifentanyl¹³ clonidine¹⁴.

None of the non-pharmacologic or pharmacologic measures is completely free of undesirable effects. Therefore, the search for a perfect drug and its dose is still going on. Not only intravenous but intra-nasal route has also been tried to attenuate the hemodynamic stress response of LTI without significant variations in MAP between the groups¹⁵. During the recent decade, many authors compared dexmedetomidine @ 0.5 and 1µ/kg^{9,16,17} but we found only one study in which Sebastian *et al* compared dexmedetomidine 0.5 and 0.75µ/kg¹⁸.

The significance of the study examining function of dexmedetomidine for reducing hemodynamic response to laryngoscopy stems from the fact that it addresses an essential clinical issue. Laryngoscopy is a prevalent anaesthetic procedure, but it can result in adverse hemodynamic effects such as hypertension, tachycardia, and arrhythmias. These side effects can be especially problematic for patients with cardiovascular disease. It has been demonstrated that dexmedetomidine, a highly selective 2-adrenergic receptor agonist, attenuates hemodynamic response to laryngoscopy; however, the optimal dose for this effect remains unknown.

The lack of consensus on dose optimization of dexmedetomidine for attenuating hemodynamic response to laryngoscopy is one of the significant research gaps in this area. Even though previous studies demonstrating potency of dexmedetomidine in this regard, the doses used have differed widely; therefore, additional research is required to determine the optimal dose for this purpose. This study identified the most effective dose of dexmedetomidine and bridged this knowledge gap. Insufficient understanding of the mechanisms underlying the hemodynamic effects of dexmedetomidine during laryngoscopy is another research lacuna in this field. There is a need for additional research to clarify these mechanisms and ascertain whether other factors also contribute in its hemodynamic.

While study on role of dexmedetomidine to laryngoscopy is significant and addresses an important clinical issue, there are still research gaps that must be filled. These include an improved understanding of the underlying mechanisms and dose optimization.

METHODOLOGY

Prospective, randomized, double-blind study determined attenuation of stress response caused by LTI. After the Institutional Ethics Committee approval (Sindh Institute of Urology and Transplantation, Pakistan) written consent was acquired from 105 adult participants.

Patients were stratified into three groups. Group A received 20 mL of normal saline (NS) in infusion, Group B was administered dexmedetomidine 0.5 µ/kg diluted in 20 mL NS and Group C was given dexmedetomidine 0.75µ/kg diluted in 20mL NS. All doses were administered through a syringe pump over 10 minutes followed by induction of general anaesthesia.

Patients with preceding history of complicated or unsuccessful intubation anticipated difficult intubation with Mallampati Grade III and IV, record of hypertension, BMI>35, any cardiovascular disorders, CNS disorders, hepatic, renal, endocrine dysfunction, pregnant and lactating mothers were excluded and we included patients of different sex, age between 18-55 years undergoing elective non-cardiac surgery under general anaesthesia.

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No premedication was given in hospital ward. Once patients arrived at operating room, routine monitoring was started. After recording the baseline cardiac parameters and Ramsay sedation score (RSS), the study drug or normal saline (according to randomization) was given in 25mL syringe over 10 minutes. The study drug was constituted as 20mL solution in 25mL syringe. An independent co-investigator (anaesthesiologist) did not administered general anaesthesia or recording the study parameters prepared the study drug, either dexmedetomidine according to the body weight or NS as per group allocation. It was then handed over to the primary anaesthesiologist for administration. Vitals and sedation scores were recorded at 0,1,3,5 & 10 minutes during this infusion. We kept the atropine drawn in a syringe and ready to be given in case of HR went below 40 beats/min. Ephedrine (5mg/ml) and adrenaline 10µ/ml were also ready.

Once completing the infusion, general anaesthesia was administered using a standard protocol (Nalbuphine 0.15, Propofol 2.5 and Atracurium 0.6 mg/kg after assessing easy bag-mask ventilation in all patients. The intubating duration was kept below 15 seconds. Any patient who required more than 15 second-duration,

second try or a bougie was excluded from the study population. Hemodynamic monitoring was continued for another 10 minutes at 1, 3, 5 & 10 minutes after intubating the trachea.

Sample size: We estimated mean HR (beats/min) at 5 minutes in Group A (Normal Saline IV) is 92.87±5.08 (beats/min) and in Group B (IV dexmedetomidine 0.5 µg/kg) at 5 minutes is 79.47±4.65 (beats/min) with 95% confidence level and power 80%. We took 35 patients per group and total of 105 patients with a 10% non-response rate were included.

Statistical analysis: Gathered data was analyzed in SPSS version 20. Mean±SD were computed for continuous variables and analysis between the groups was done at students' t-test. One-way ANOVA was implied to assess group significance and variations at p<0.05.

RESULTS

All 105 patients, stratified into three groups underwent and completed the trial. All groups had comparable patients' characteristics concerning age, gender, ASA physical status, Mallampati grade, mean weight, height and BMI and time taken to perform laryngoscopy and intubation (Table 1).

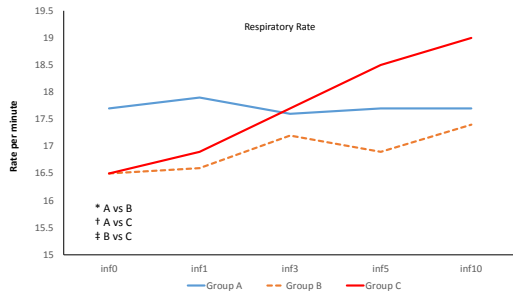
Table 1: Demographic profile

Parameters	Group A (n=35)	Group B (n=35)	Group C (n=35)	p-value
Age in years				
Mean ± S.D (Range)	34.4±9.0 (18.0 - 55.0)	34.5±11.2 (18.0 - 55.0)	33.5±10.6 (19.0 - 55.0)	0.881
Median (IQR)	35.0 (26.0 - 43.0)	32.0 (25.0 - 44.0)	31.0 (25.0 - 40.0)	
Gender n (%)				
Male	18 (51.4)	17 (48.6)	21 (60.0)	0.608
Female	17 (48.6)	18 (51.4)	14 (40.0)	
ASA n (%)				
1	26 (74.9)	24 (68.6)	25 (71.4)	0.869
2	9 (25.7)	11 (31.4)	10 (28.6)	
Malampatti score n (%)				
1	27 (77.1)	25 (71.4)	23 (65.7)	0.571
2	8 (22.9)	10 (28.6)	12 (34.3)	
Weight (kg)	61.5 ± 9.6	62.6 ± 14.5	62.1 ± 15.3	0.944
Duration of laryngoscopy & intubation (seconds)	10.9 ± 2.4	10.9 ± 2.9	11.9 ± 2.6	0.166

Table 2: Sedation score after completing dexmedetomidine infusion

Sedation score	Group A	Group B	Group C
1	4 (11.4)	1 (2.9)	2 (5.7)
2	31 (88.6)	24 (68.6)	10 (28.6)
3	0 (0.0)	10 (28.6)	21 (60.0)
4	0 (0.0)	0 (0.0)	2 (5.7)
Pair-wise significance			
	Group A vs B	Group A vs C	Group B vs C
P value	P=0.002	P<0.001	P=0.007

Figure 1: Comparing the respiratory rate

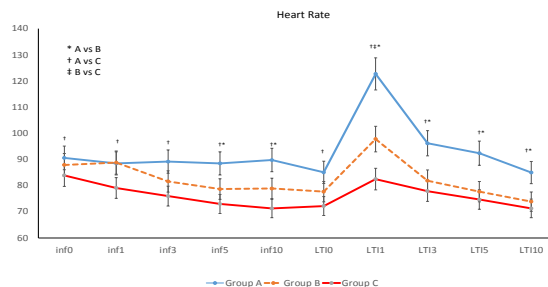


Sedation score in group C had significance (p<0.05) from 1minute onward than A whereas, Group B was significantly different from A, only at the end of infusion (Table 2). Concerning respiratory rate and oxygen saturation, no patient developed desaturation or respiratory depression at any time interval in any group. (Figure1)

Inf0: Baseline, inf1: 1 minute after starting DEX infusion, inf3: 3 minutes after starting DEX infusion, inf5: 5 minutes after starting DEX infusion, Inf10: at the end of DEX infusion,

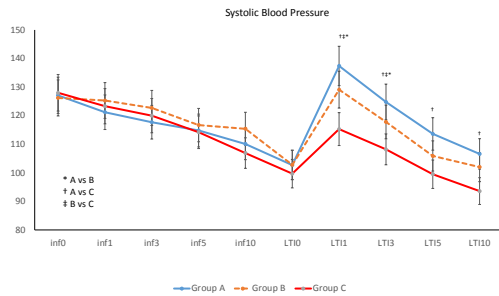
Baseline heart rate, SBP, DBP & MAP were non-significant between these groups. Commencing DEX infusion, HR gradually came down (7.73% & 10.6%) in groups B and C respectively. Final infusion, intergroup comparison showed significant difference in both Group B (DEX 0.5 µ/kg) & Group C (DEX 0.75µ/kg) compared to Group A (saline). No incidence of bradycardia (HR less than 60 bpm) was noted which could warrant the use of atropine in any individual (Figure 2,3,4,5).

Figure 2: Comparing the heart rate



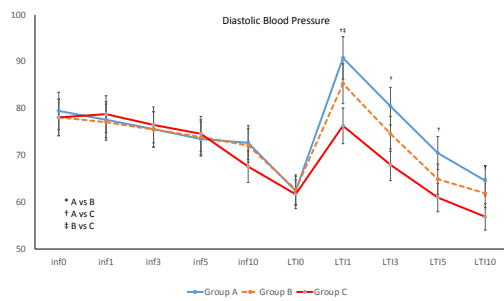
Inf0: Baseline, inf1: 1 minute after starting DEX infusion, inf3: 3 minutes after starting DEX infusion, inf5: 5 minutes after starting DEX infusion, Inf10: at the end of DEX infusion, LTI0: at the time of LTI1: 1 minute after LTI, LTI3: 3 minutes after LTI, LTI5: 5 minutes LTI, LTI10: 10 minutes after LTI.

Figure 3: Comparing systolic pressures



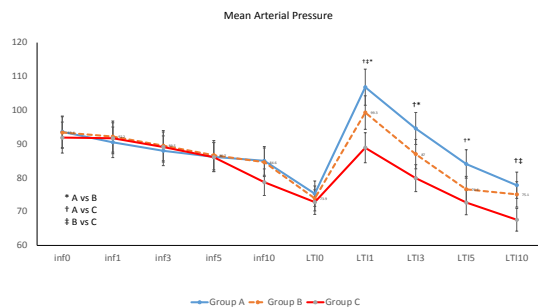
Inf0: Baseline, inf1: 1 minute after starting DEX infusion, inf3: 3 minutes after starting DEX infusion, inf5: 5 minutes after starting DEX infusion, Inf10: at the end of DEX infusion, LT10: at the time of LTI, LT11: 1 minute after LTI, LT13: 3 minutes after LTI, LT15: 5 minutes after LTI, LT110: 10 minutes after LTI.

Figure 4: Comparing diastolic pressures



Inf0: Baseline, inf1: 1 minute after starting DEX infusion, inf3: 3 minutes after starting DEX infusion, inf5: 5 minutes after starting DEX infusion, Inf10: at the end of DEX infusion, LT10: at the time of LTI, LT11: 1 minute after LTI, LT13: 3 minutes after LTI, LT15: 5 minutes after LTI, LT110: 10 minutes after LTI.

Figure 5: Comparing mean blood pressure



Inf0: Baseline, inf1: 1 minute after starting DEX infusion, inf3: 3 minutes after starting DEX infusion, inf5: 5 minutes after starting DEX infusion, Inf10: at the end of DEX infusion, LT10: at the time of LTI, LT11: 1 minute after LTI, LT13: 3 minutes after LTI, LT15: 5 minutes after LTI, LT110: 10 minutes after LTI.

During LTI, maximum stress response was evident at 1 minute post laryngoscopy in our groups. The mean HR elevation in Group A was 32.3% (38 beats/min), in Group B, 15.77% (20.3 beats/min) and in Group C, 7.44% (10.3 beats/min), Intergroup comparison was statistically significant when compared with saline (group A). One minute post laryngoscopy and tracheal intubation

(LTI) was the only time interval when HR between groups A and B was significant, otherwise, no significance was found at any other time interval. Post LTI, declined to baseline in 10 minutes in group A, 5 minutes in groups B & C, and baseline declined by 10th minute in groups B & C.

During stress response at 1-minute post-LTI, there was a 35.23%, 26.93% & 15% rise in mean SBP, 17.3%, 13.98% & 9% elevation in mean DBP and 23.87%, 18.77% & 11.72% rise in mean MAP for A, B & C groups, respectively. Comparing hemodynamic variables (HR, SBP, DBP & MAP), for 10 minutes post LTI, significant distinction prevailed between group A and B than C.

DISCUSSION

Although SBP, DBP & MAP were declined, yet we did not observe the phenomenon of transient increase in HR and MAP which has been mentioned in many studies, typically during the initial phase of injecting dexmedetomidine infusion¹⁹. The lack of this sympathetic effect might be due to low dose, slow infusion rate and or study populace of normotensive individuals in our study. Not only that we neither needed atropine to combat any such incidence nor did we use any prophylactic antisialagogue as it might mask the incidence of bradycardia.

Another study done by Gulabani et al used two doses of dexmedetomidine (0.5 & 1 µg/kg) given as slow pre-induction bolus and compared it with lignocaine 1.5mg/kg⁹. They found dexmedetomidine 1 µg/kg was more effective than 0.5 µg/kg. They did not find any side effects with DEX 1µg/kg. Our study denoted the same finding regarding DEX 0.5µg/kg as we did not find any significant difference when compared with saline (Group A).

Keshari et al described that 0.5µg/kg dexmedetomidine is valuable in obtunding pressor response¹⁶. Whereas dexmedetomidine 1 µg/kg was bear significant attenuation of tracheal intubation-related cardiovascular responses, however declined BP and HR were also evident pre- and post intubation. In our study, hemodynamic parameters have shown no statistical difference between the saline group and DEX 0.5µ/kg group¹⁶.

Selvaraj et al compared impact of dexmedetomidine and esmolol 0.5 mg/kg on hemodynamic response LTI in ASA I patients. In their study, dexmedetomidine was highly effective than esmolol²⁰. Contrary to their findings, we found DBP better controlled than SBP in both DEX groups as there was a 26.93% & 15% elevated SBP as compared to 13.98% & 9% elevated DBP in groups B & C respectively.

A study corroborated our results that dexmedetomidine (diluted in NS) declined heart rate, and mean blood pressure after intubation. It indicated that single dose dexmedetomidine attenuated hemodynamic response to LTI in patients with controlled hypertension²¹.

Our findings were defended by a study reporting distinct concentrations of dexmedetomidine (0.5 and 1.0 g/kg) in attenuating the hemodynamic pressor responses while monitoring bispectral index (BIS). 120 patients with ASA physical status I or II received dexmedetomidine 0.5, 1.0 g/kg, or saline over 15 minutes. Change in hemodynamics was the primary outcome measure. In both dexmedetomidine groups, the mean HR, SBP, DBP, and MAP remained substantially lesser than in control group. Moreover, mean HR, SBP, DBP, and MAP were substantially lower in group D2 than in group D1 (P<0.05). In groups treated with dexmedetomidine, the propofol induction dose was significantly lower than in the control. RSS score was significantly increased in D1 and D2 groups and hence dexmedetomidine was reported more²².

Mahiswar et al. studied fentanyl 2g/kg in conjunction with dexmedetomidine 0.5 g/kg and reported that dexmedetomidine 0.5 g/kg was as efficacious as fentanyl 2g/kg in attenuating hemodynamic response in LTI²³. Another study found significant impact of preoperative dexmedetomidine nebulization (1g/kg) than saline on HR responses following LTI. In addition to reducing intraoperative anaesthetic and analgesic consumption, preoperative dexmedetomidine nebulization was also effectual²⁴.

CONCLUSION

Dexmedetomidine is an effective and safe medication for reducing hemodynamic response to LTI. As pre-induction bolus, 0.75 g/kg of dexmedetomidine is efficacious than 0.5 g/kg and placebo in reducing the hemodynamic response to LTI, according to the study. The study also emphasized the practical implications of dexmedetomidine in anaesthesia practice, such as improved patient safety, optimal dosing, reduced anaesthetic requirements, cost-effective treatment, and increased patient comfort. The study's findings have significant implications for managing patients of hypertension, ischemic and cerebrovascular disease, in whom an elevated BP response to LTI may have fatal consequences.

Limitations: It has limitations of small sample size, lack of blinding, lack of comparative data, short follow-up period and lacking assessment of adverse effects.

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Authors' contributions: All authors were responsible for the conception and design of the study. Abbas SM designed and conducted the study analyzed data, searched the literature, and wrote the manuscript. Siddique M helped to supervise the study and gave a critical review of the study. Abbas MQ and Farooq F helped to conduct the study, search literature, and revised the manuscript. Malik S helped to conduct the study, collect, analyze and interpret data and draft the manuscript. Siddique M helped to collect the data. All authors have read and approved the final manuscript.

Conflict of interest: We declare no conflict of interest

REFERENCES

- Reid LC, Brace DE. Irritation of respiratory tract and its reflex effect on heart surgery. *Surg Gynaecol Obstet.* 1940;70:157-62
- Sarkar J, Anand T, Kamra SK. Hemodynamic response to endotracheal intubation using C-Trach assembly and direct laryngoscopy. *Saudi J Anaesth.* 2015;9:343-7.
- Sharma S, Suthar OP, Tak ML, Thanvi A, Paliwal N, Karnawat R. Comparison of esmolol and dexmedetomidine for suppression of hemodynamic response to laryngoscopy and endotracheal intubation in adult patients undergoing elective general surgery: A prospective, randomized controlled double-blinded study. *Anesth Essays Res.* 2018;12:262-6.
- De Cassai A, Boscolo A, Geraldini F, Zarantonello F, Pettenuzzo T, Pasin L, *et al.* Effect of dexmedetomidine on hemodynamic responses to tracheal intubation: A meta-analysis with meta-regression and trial sequential analysis. *J Clin Anesth.* 2021 Sep;72:110287.
- Sunil BV, Neeta S. A prospective randomized controlled trial comparing the effects of dexmedetomidine and fentanyl on attenuation of pressor response during laryngoscopy and intubation. *Anaesth Pain Intensive Care.* 2018;22(1):62-66.
- Kataria AP, Attri JP, Kashyap R, Mahajan L. Efficacy of dexmedetomidine and fentanyl on pressor response and pneumoperitoneum in laparoscopic cholecystectomy. *Anesth Essays Res.* 2016;10:446-50.
- Su P, Li Z, Jia X, Peng X, Liu D, Xiao J, Tu Y, Gao F. A Response Surface Analysis of the Combination of Dexmedetomidine and Sufentanil for Attenuating the Haemodynamic Response to Endotracheal Intubation. Dose-Response. 2022 Apr 5;20(2):15593258221092367.
- Varshney RK, Prasad MK, Garg M. Comparison of Nitroglycerin versus Lignocaine Spray to Attenuate Haemodynamic Changes in Elective Surgical Patients Undergoing Direct Laryngoscopy and Endotracheal Intubation: A prospective randomised study. *Sultan Qaboos Univ Med J.* 2019;19(4):e316-e323.
- Gulabani M, Gurha P, Dass P, Kulshreshtha N. Comparative analysis of efficacy of lignocaine 1.5 mg/kg and two different doses of dexmedetomidine (0.5 µg/kg and 1 µg/kg) in attenuating the hemodynamic pressure response to laryngoscopy and intubation. *Anesth Essays Res.* 2015;9:5-14.
- Seangrung R, Pasutharnchat K, Injampa S, Kumdang S, Komonhirun R. Comparison of the hemodynamic response of dexmedetomidine versus additional intravenous lidocaine with propofol during tracheal intubation: a randomized controlled study. *BMC Anesthesiol.* 2021 Oct 30;21(1):265.
- Li Z, Xu L, Zheng J, Wang Q. Comparison of Intravenous Dexmedetomidine versus Esmolol for Attenuation of Hemodynamic Response to Tracheal Intubation after Rapid Sequence Induction: A Systematic Review and Meta-Analysis. *Biomed Res Int.* 2019 Apr 17;2019:6791971..
- Singh D, Jagannath S, Priye S, Mudassar AS. The comparison of dexmedetomidine, esmolol, and combination of dexmedetomidine with esmolol for attenuation of sympathomimetic response to laryngoscopy and intubation in patients undergoing coronary artery bypass grafting. *Ann Card Anaesth.* 2019;22:353- 7.
- Modir H, Yazdi B, Moshiri E, Mohammad beigi A, Afshari S. Efficacy of dexmedetomidine versus remifentanyl to blunt the hemodynamic response to laryngoscopy and orotracheal intubation: A randomized clinical trial. *Med Gas Res.* 2018;8(3):85-90.
- Hussain SY, Karmarkar A, Jain D. Evaluation and comparison of clonidine and dexmedetomidine for attenuation of hemodynamic response to laryngoscopy and intubation: A randomized controlled study. *Anesth Essays Res.* 2018;12:792-6.
- Niyogi S, Biswas A, Chakraborty I, Chakraborty S, Acharjee A. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with dexmedetomidine: A comparison between intravenous and intranasal route. *Indian J Anaesth.* 2019;63:915-23.
- Keshri RK, Prasad MK, Choudhary AK, Jheetay GS, Singh Y, Kapoor K. Comparative evaluation of different doses of intravenous dexmedetomidine on hemodynamic response during laryngoscopy and endotracheal intubation in geriatric patients undergoing spine surgeries: A prospective, double-blind study. *Anesth Essays Res.* 2018;12:897-902.
- Sharma N, Mehta N. Therapeutic efficacy of two different doses of dexmedetomidine on the hemodynamic response to intubation, the intubating conditions, and the effect on the induction dose of propofol: A randomized, double-blind, placebo-controlled study. *Anesth Essays Res.* 2018;12:566-71.
- Sebastian B, Talikoti AT, Krishnamurthy D. Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine: A comparison between two doses. *Indian J Anaesth.* 2017;61:48-54.
- Lee S. Dexmedetomidine: present and future directions. *Korean J Anesthesiol.* 2019 Aug;72(4):323-330..
- Selvaraj V, Manoharan KR. Prospective randomized study to compare between intravenous dexmedetomidine and esmolol for attenuation of hemodynamic response to endotracheal intubation. *Anesth Essays Res.* 2016;10:343-8.
- Ismail EA, Mostafa AA, Abdelatif MM. Attenuation of hemodynamic response to laryngoscopy and endotracheal intubation with single dose dexmedetomidine in controlled hypertensive patients: prospective randomized double-blind study. *Ain-Shams J Anesthesiol.* 2022;14:57.
- Jain K, Sethi SK KN, *et al.* Efficacy of dexmedetomidine in attenuating pressor response to laryngoscopy and endotracheal intubation under bispectralindex controlled anesthesia: a prospective randomized double-blinded study. *Ain-Shams J Anesthesiol.* 2023;15:15.
- Mahiswar AP, Dubey PK, Ranjan A. Comparison between dexmedetomidine and fentanyl bolus in attenuating the stress response to laryngoscopy and tracheal intubation: a randomized double-blind trial. *Brazilian J Anesthesiol.* 2022;72(1):103-109.
- Misra S, Behera BK, Mitra JK, Sahoo AK, Jena SS, Srinivasan A. Effect of preoperative dexmedetomidine nebulization on the hemodynamic response to laryngoscopy and intubation: a randomized control trial. *Koran J Anesthesiol.* 2021 May;74(2):150-157.