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Original Research Article

"A comparative study of the effect of dexmedetomidine and fentanyl on haemodynamic response in patients undergoing lumbar spine surgery under general anaesthesia - a randomized controlled study"

Rakesh D R[1] (Senior Resident), Jitendra Agrawal[2] (Associate Professor), Sourabh Shrivastava[3] (Assistant Professor), Kushal Raj Patidar [4*](Medical Officer), Preeti Goyal[5] (Professor and Head of the Department)

Department of Anaesthesiology, Gajra Raja Medical college, Gwalior, Madhya Pradesh, India.[1,2,3&5]
District hospital, Mandsour, Madhya Pradesh, India[4]
Corresponding Author*: Kushal Raj Patidar

ABSTRACT

BACKGROUND:

Spinal surgeries represent a challenge to the anaesthesiologist as they are accompanied with many perioperative problems. This study was conducted to assess and to compare the effect of intravenous Dexmedetomidine and Fentanyl on intraoperative and postoperative haemodynamics in patients undergoing lumbar spine surgery under general anaesthesia.

AIM:

To compare the efficacy of Dexmedetomidine and Fentanyl in terms of haemodynamic changes during lumbar spine surgeries under general anaesthesia.

STUDY DESIGN: prospective, double blinded, randomised controlled study.

METHODS:

Sixty four patients of either sex, aged 25-65 years with ASA I and II admitted for lumbar spine surgery under general anaesthesia were randomized into two groups. Thirty two patients received Dexmedetomidine loading dose of 0.5µg/kg over ten minutes before induction followed by infusion at the rate of 0.25µg/kg/hr throughout the surgery similarly, the remaining thirty two patients received Fentanyl loading dose of 1µg/kg over ten minutes followed by infusion at the rate of 0.5µg/kg/hr. Heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressures were noted at baseline , after loading dose of respected drugs, after induction, at intubation and throughout the surgery ,which continued in PACU upto 24hours.

STATISTICAL ANALYSIS:

Statistical tests used were unpaired t-test and Chi square test. Analyzed statistically by SPSS software version 20.0.

RESULTS:

Both Fentanyl and Dexmedetomidine attenuated the haemodynamic responses. Dexmedetomidine was more successful in reducing the heart rate and blood pressures following stress response which was statistically significant when compared to Fentanyl($p<0.001$)

Conclusion:

Dexmedetomidine proved to have better haemodynamic stability and more effective in attenuating haemodynamic response following intraoperative infusion when compared to Fentanyl.

Key words: Dexmedetomidine; Endotracheal intubation; Extubation; Fentanyl; Haemodynamics.

1. INTRODUCTION

Spinal surgeries represent a challenge to the anaesthesiologist as they are accompanied with many perioperative problems which includes fluctuation in blood pressure and severe postoperative pain. General anaesthesia is the commonly used anaesthetic modality that is more accepted by the patients.

In general anaesthesia, endotracheal intubation and time of extubation are the critical events which

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provoke transient but marked sympathoadrenal response such as hypertension and tachycardia. The mechanism in hypertension and tachycardia is the sympathetic response[1,2] which is the result of increase in catecholamine activity.[3]

Various pharmacological & non pharmacological methods have been tried to attenuate the haemodynamic response to laryngoscopy & endotracheal intubation.

Intravenous anaesthetic induction agents do not adequately or predictably suppress the circulatory responses evolved by endotracheal intubation.[4] So prior to initiating laryngoscopy, additional pharmacological measures like use of volatile anaesthetics, topical and intravenous lidocaine,[5,6] opioids,[7,8] Vasodilators – Sodium nitroprusside,[9] Nitroglycerine,[10] Calcium channel blockers[11,12] and β-blockers[13,14] have been tried by various researchers.

No single anesthetic technique is accepted to be completely effective in attenuating or preventing the sympathetic response. The methods used previously produced side effects or has partial effectiveness.[15]
Dexmedetomidine, is the dextro isomer and pharmocologically active component of medetomidine, high selectivity for alpha-2 adrenergic agonist with alpha-1 adrenergic receptors (selectivity ratio 1620:1) compared to 220:1 for clonidine which reduces the pressor response mediated by sympathetic nervous system during general anaesthesia. It also has anxiolytic, anaesthetic, and analgesic properties without respiratory depression and reduced postoperative shivering are noted. Termination of pain signals is controlled by pre-synaptic activation of the α2-adrenoceptor which inhibits the release of norepinephrine, fall in heart rate (HR) and blood pressure (BP) is due to postsynaptic activation of α2-receptors in the central nervous system which inhibits sympathetic activity. It decreases opioid need, helps with early postoperative recovery. Dexmedetomidine undergoes hepatic metabolism involving hydroxylation and *N*-methylation, followed by conjugation. Metabolites are excreted in the bile & urine.

Fentanyl is a phenylpiperidine derivative synthetic opioid agonist .It is structurally related to meperidine. A dose of 2 to 20 micrograms/kg IV is administered as an adjuvant to blunt circulatory responses to direct laryngoscopy for intubation of trachea or during surgical stimulation. It's analgesic potency is 50–100 times more that of Morphine. Fentanyl is a very popular anesthetic because of its short time to peak analgesic effect, cardiovascular safety and rapid termination of the effect after small bolus doses. Fentanyl undergo hepatic metabolism and renal excretion. Therefore, with the use of higher doses or prolonged infusions, fentanyl become longer acting.

The purpose of our study was to compare the effect of Dexmedetomidine and Fentanyl on haemodynamics during lumbar spine surgeries under general anaesthesia.

2. MATERIAL AND METHODS

After obtaining approval from the institutional ethics committee, the present prospective, double blinded, randomised controlled study entitled **"A COMPARATIVE STUDY OF THE EFFECT OF DEXMEDETOMIDINE AND FENTANYL ON HAEMODYNAMIC RESPONSE IN PATIENT UNDERGOING LUMBAR SPINE SURGERY UNDER GENERAL ANAESTHESIA: A RANDOMIZED CONTROLLED STUDY"** was conducted on 64 American Society of Anaesthesiologists class I &II patients after thorough pre-anaesthesia checkup and taken written informed consent.

CTRI registration number : CTRI/2021/08/035769

Institutional ethical committee number : 9/IEC-GRMC/2019

Sample size: 64

Formula used **:** $\left[Z_{\frac{\alpha}{2}}\sqrt{pq}+Z_1-\beta(\sqrt{p_1q_1}+p_2q_2)\right]^2$

$$\frac{}{(p_1-p_2)^2}$$

Where $p=\frac{p_1+p_2}{2}$

$P_1=12\%$

$P_2=48\%$[6]

@5% level of significance and 90% power of test

Inclusion criteria: Consent to participate in study**,** Age – 25 to 65 years, Gender - both male and female**,** American Society of Anaesthesiologist Grade I&II, Patients undergoing lumbar spine surgeries under general anaesthesia.

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Exclusion criteria: Patients with disorder of cardiovascular, hepatic, renal or neuromuscular systems, Patients with uncontrolled systemic diseases such as diabetes mellitus, hypertension, chronic obstructive lung disease[16], Patients on calcium channel blockers, beta blockers, chronic use of opioids, Patients with BMI>35.[17] ,Patients receiving drugs known to interact with study drugs.

Two investigators participated in the study, first investigator prepared the drugs and second investigator did monitoring and data collection and was blinded to the study. Total volume of both the drugs were 50mL each with the concentration of Dexmedetomidine as 4 micrograms/mL and Fentanyl as 2 micrograms/mL.

On the day of the surgery, routine monitors such as ECG, Pulseoximeter(spo2) and non invasive blood pressure(NIBP) monitors were attached. Patients were allocated in to 2 groups, Group D and Group F by closed envelope method.

Group D (n=32) Patients received a loading dose of IV Dexmedetomidine 0.5 microgram/kg over 10 minutes before induction of anaesthesia and 0.25microgram/kg/hr by continous infusion during intraoperative period and Group F (n=32) Patients received a loading dose of IV Fentanyl 1 microgram/kg over 10 minutes before induction of anaesthesia and 0.5mirogram/kg/hr by continous infusion during intraoperative period[18].

For eligible patients, demographic information collected and a physical examination was performed. A standardized anaesthesia regimen was followed. Age, weight, height, duration of surgery and ASA (I/II) were recorded and analyzed.

During the period of loading dose of the study drug, haemodynamic parameters at 0, 5 and 10 minutes were noted and supplemental oxygen was provided.

After the loading dose of study drug, induction of anaesthesia in both the groups conducted by injection propofol 2mg/kg IV, neuromuscular blocking agent, injection atracurium 0.5mg/kg IV was given following which endotracheal intubation was done after 3 min using a appropriate size cuffed endotracheal tube and connected to anaesthesia machine (Drager Fabius GS) breathing circuit. General anaesthesia was maintained by inhalational anaesthetic agent- isoflurane, oxygen and nitrous oxide and ventilation was controlled by maintaining normocapnia, $ETCO_2$ between 35 and 45 mmHg. Haemodynamic parameters such as Heart rate (HR), SBP, DBP, MAP and SpO2 were noted during induction and at the time of intubation and thereafter every 5 minutes upto 30 mins and thereafter every 10 minute till extubation. Additional doses of injection atracurium 0.1 mg/kg was given as per requirement. At the end of surgery, Dexmedetomidine/Fentanyl infusion was stopped along with isoflurane and nitrous oxide. Patients were completely reversed using mixture of Neostigmine 0.06 mg/kg IV and Glycopyrolate 0.01mg/kg IV and extubated once extubation criteria were met.

After extubation, all the patients were shifted to Post anaesthesia care unit. In PACU SBP, DBP, MAP , HR and Spo_2 were assessed on arrival and at 1, 6, 12 and 24hrs.

FOLLOW UP : Upto 24 hours.

Statistical analysis: Evaluation of study data in electronic form required performing additional statistical analysis. Data was composed in suitable spreadsheet ie; EXCEL and SPSS. After compilation of data, it was analyzed statistically by SPSS software version 20.0. Statistical tests used were unpaired t-test and Chi square test. Significance level will be 95% confidence level ($p<0.05$). Data was described as a frequency (Percentage) distribution as well as in Mean±SD. Data was presented through suitable statistical graphs.

3. Results

In our study, patients in both the groups are comparable ($p>0.05$) with respect to ASA score ,age, weight and sex distribution.

The changes in respiratory rate and SpO_2 at different time intervals in each group were within normal range and were not significant ($p>0.05$).

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TABLE 1: **Gender wise distribution of study participants**

Gender	**Dexmed**		**Fentanyl**		**p value**
	N	**%**	**N**	**%**	
Male	23	71.88%	22	68.75%	0.784
Female	9	28.12%	10	31.25%	
Total	32	100%	32	100%	

In our study, patients in both the groups are comparable (p>0.05) with respect to gender

% - Percentage

N – Number of participrnts

TABLE 2 : Side effects/complication in two study groups

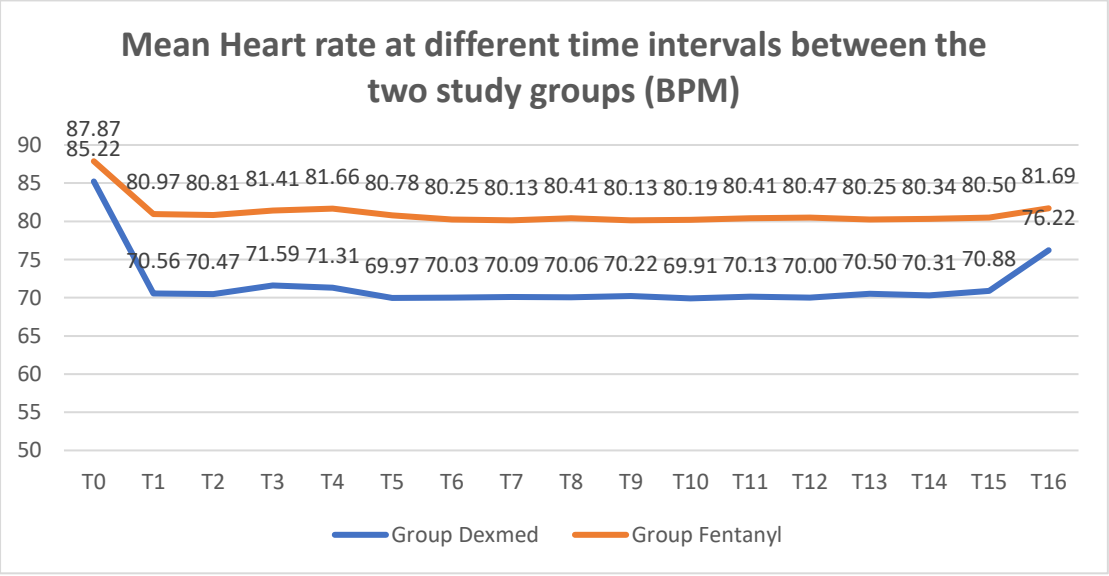
Side effect	**Group Dexmed (N-32)**		**Group Fentanyl (N-32)**	
	N	**%**	**N**	**%**
Nausea	0	0%	2	6.25%
Vomiting	0	0%	2	6.25%
Hypotension	1	3.13%	0	0%

Nausea and vomiting seen in 6.25% patients in Group F and Hypotension seen in 3.13% patient in Group D.

% - Percentage

N – Number of participents

GRAPH 1 : **Statistical analysis of changes in Mean Heart rate (beats per min) at different time interval between two study groups**



In both the groups, statistically significant (p=0.000) attenuation of Heart rate seen at all the time intervals as compared to baseline. When the two groups were compared, Highly significant(p=0.000) reduction in heart rate was observed in group D as compared to group F at all time intervals.

BPM – Beats per minute

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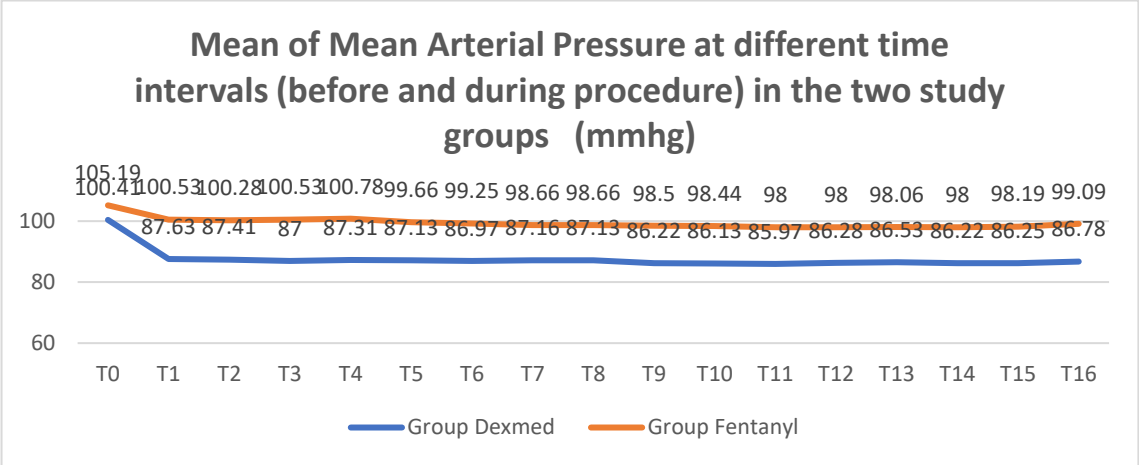
GRAPH 2 : **Statistical analysis of changes in Mean of Mean Arterial Pressure at different time intervals**



(before and during procedure) in the two study groups

In both the groups, statistically significant (p=0.000) attenuation of MAP seen at all the time intervals as compared to baseline. When the two groups were compared, Highly significant(p=0.000) reduction in MAP was observed in group D as compared to group F at all time intervals.

Mmhg – millimeters of mercury

4. DISCUSSION

In spine surgery under general anaesthesia, Laryngoscopy, tracheal intubation , prone positioning and extubation are considered as the most critical events as they provoke transient but marked sympathoadrenal response manifesting as hypertension and tachycardia.These responses are transient, variable and may not be significant in otherwise normal individuals. But in patients with cardiovascular compromise these transient changes in haemodynamics can result in potentially harmful effects.A drug which can blunt both the heart rate and blood pressure response to laryngoscopy and intubation, without having any adverse effects like respiratory depression and post-operative nausea and vomiting (PONV) was required for the purpose.

The study population consisted of 64 patients in the age group of 25- 65 belonging to ASA grade I and II were randomly divided into 2 groups. Each group consisting of 32 patients. Group D patients received IV inj Dexmedetomidine loading dose of 0.5µg/kg over 10 minutes before induction of anesthesia, followed by infusion of 0.25µg/kg/hr till the end of the surgery. Group F patients received IV inj Fentanyl loading dose of 1µg/kg over 10 minutes before induction of anesthesia, followed by 0.5µg/kg/hr till the end of the surgery.

This randomized controlled study was done to compare the efficacy of Dexmedetomidine and Fentanyl in terms of haemodynamic changes during lumbar spine surgeries. There was no statistically significant difference in the distribution of age, gender, weight or ASA physical status between the two groups.Heart rate, systolic pressure, diastolic pressure and mean blood pressure were measured in all the patients at baseline, after loading dose of the drug, at intubation, after that every 5 minutes upto 30 minutes and thereafter every 10minutes till extubation and also in PACU at 0hr,1hr,6hr,12hrs,24hrs.

The baseline heart rate in the Dexmedetomidine group was 85.22 ± 8.49 bpm and in the Fentanyl group was 87.87 ± 10.03 bpm. In group D after Dexmedetomidine loading dose HR reduced to 70.56 ± 6.36 bpm and in group F after Fentanyl loading dose HR reduced to 80.97 ± 9.74 bpm. When two groups were compared ,statistically significant reduction HR in group D as compared to group F (p=0.000). The fall in heart rate was less than 20% in both the groups throughout the procedure.In correlation with the current study, a study conducted by **Bajwa SJS et al[19]** assessed the effect of 1mcg/kg of Dexmedetomidine given preoperatively on the perioperative hemodynamic parameters and compared them to a Fentanyl control. The rise of mean heart rate and MAP following laryngoscopy and intubation in the Fentanyl group was higher compared with the Dexmedetomidine group (P<0.001). The return of the haemodynamic parameters to baseline was faster in the Dexmedetomidine group and was highly significant (P<0.001).

Dexmedetomidine reduces heart rate by reducing the sympathetic tone and increasing the vagal tone.

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Additionally the initial increase in the biphasic blood pressure response would result in baroreceptor mediated bradycardia. This explains the effectiveness of Dexmedetomidine over Fentanyl in attenuating the rise in heart rate, in response to laryngoscopy and intubation.

The baseline MAP in group D was 100.41±7.6 and in group F was 105.19±5.78 which was reduced to 87.63±8.59 in group D and 100.53±5.04 in Group F after loading dose and remain below baseline level throughout the procedure and in postoperative period ,when compared between the group , statistically significant attenuation in MAP in group D compared to group F.

Similar findings were observed in study conducted by **Parikh DA et al[20]** where intraoperative heart rate and mean arterial pressure following dexmedetomidine therapy were lower than the baseline values and the corresponding values in the Midazolam-Fentanyl therapy (P Value < 0.05) during tympanoplasty.These results corresponds to the study conducted by **Feld JM et al[21]**, who studied twenty bariatric patients undergoing surgery for open gastric bypass. They used Fentanyl 0.5µg/kg bolus followed by 0.5µg/kg/hr infusion and Dexmedetomidine 0.5µg/kg bolus followed by 0.4µg/kg/hr infusion. They found that MAP and heart rate were lower in the Dexmedetomidine group compared to Fentanyl group.

The primary outcome of this study was that intraoperative infusion of Dexmedetomidine significantly attenuates the pressor response to intubation, noxious stimuli, extubation and recovery as shown by that the heart rate, systolic, diastolic and mean arterial pressure which were significantly lower throughout the intraoperative period in the Dexmedetomidine group compared to the Fentanyl group.

In the present study most commonly observed side effect was nausea and vomiting. 0(0%) patients in Group D and 4(12.5%) patients in Group F had post operative nausea and vomiting. The less incidence of PONV in group D may be due to direct anti emetic properties of alpha-2 agonists. Nausea and vomiting may be induced by high catecholamine concentrations, a decrease of sympathetic tone could explain the antiemetic effect of dexmedetomidine.This findings were similar to the study conducted by **Turgut N et al[22]** where 12% patients in dexmedetomidine group and 48% in fentanyl group had postoperative vomiting. Another study by **Neil L et al[23]** observed PONV in 6% in dexmedetomidine and 10% in fentanyl group.In our study the group D 1(3.13%) patient had episode of hypotension in postoperative period.This finding was similar to the study conducted by **Jain V et al[24]** where 1 patient had episode of hypotension and none in fentanyl group.

LIMITATIONS

1. Lack of BIS monitor to assess the depth of anesthesia .
2. Postoperative opioid consumption was not assessed. Hence the effect of dexmedetomidine in reducing the opioid consumption could not be assessed.

5. CONCLUSION

Dexmedetomidine and Fentanyl can be used safely to attenuate the haemodynamic response without significant side effects, whereas Dexmedetomidine proved to have better haemodynamic stability and more effective in attenuating haemodynamic response following intraoperative infusion when compared to Fentanyl.

6. REFERENCES

1. Kayhan Z, Aldemir D, Metler H, Ogus E. Which is responsible for the haemodynamic response due to the laryngoscopy and endotracheal intubation? Catecholamines, vasopressin or angiotensin? European Journal of Anaesthesiology 2005;22:780-5.
2. Morin AM, Gelbner G, Schwarz U, Kahl M, Adams HA, Hulf H, et al. Factors influencing pre-operative stress responses in coronary artery bypass graft patients. BMC Anaesthesiology 2004;4.
3. Kovac AL. Controlling the haemodynamic response to laryngoscopy and endotracheal intubation. Journal of Clinical Anaesthesia 1996;8:63-79.
4. Stoelting RK, Stephan F Dierdorf. Anaesthesia and co-existing disease. 4th ed.2002.
5. Thompson KR, Rioja E. Effects of intravenous and topical laryngeal lidocaine on heart rate, mean arterial pressure and cough response to endotracheal intubation in dogs. Veterinary Anaesthesia and Analgesia. 2016;43:371-8.
6. Xue FS, Liu HP, He N, Xu YC, Yang QY, Liao X, Xu XZ, Guo XL, Zhang YM. Spray-as-

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you-go airway topical anesthesia in patients with a difficult airway: a randomized, double-blind comparison of 2% and 4% lidocaine. Anesthesia & Analgesia. 2009;108:536-43.

7. Adachi YU, Satomoto M, Higuchi H, Watanabe K. Fentanyl attenuates the hemodynamic response to endotracheal intubation more than the response to laryngoscopy. Anesthesia & Analgesia. 2002;95:233-7.
8. SHAN XUE FU, PENG LIU KU, Liu Y, CHAO XU YA, Liao X, ZHANG GH, LI CW, YONG YANG QU, SUN HT. Assessment of small-dose fentanyl and sufentanil blunting the cardiovascular responses to laryngoscopy and intubation in children. Pediatric Anesthesia. 2007;17:568-74.
9. Stoelting RK. Attenuation of blood pressure response to laryngoscopy and tracheal intubation with Sodium Nitroprusside. Anesthesia Analgesia. 1979; 58:116-9.
10. Mikawa K, Hasegawa M, Suzuki T, Maekawa N, Kaetsu H, Goto R, Yaku H, Obara H. Attenuation of hypertensive response to tracheal intubation with nitroglycerin. Journal of Clinical Anesthesia. 1992;4:367-71.
11. Puri GD, Batra YK. Effect of Nifedepine on cardiovascular response to laryngoscopy and intubation. Br J Anaesth. 1988;60:579-81.
12. Nishikawa T, Naiki A. Attenuation of the pressor response to laryngoscopy and tracheal intubation with IV Verapamil. Act Anaesthesiologica Scandinavica 1989;33:232-5.
13. Prys-Roberts C, Foex P, Biro GP. Studies of anaesthesia in relation to hypertension versus adrenergic β receptor blockade. Br J Anaesth 1973; 45:671-80.
14. Mc Cammon RL, Hilgenberg JC, Stoelting RK. Effect of Propranolol on circulatory responses to induction of diazepam- nitrous oxide anesthesia and to endotracheal intubation. Anesthesia Analgesia 1981;60:579-83.
15. Mondal S, Mondal H, Sarkar R, Rahaman M. Comparison of dexmedetomidine and clonidine for attenuation of sympathoadrenal responses and anesthetic requirements to laryngoscopy and endotracheal intubation. Int J Basic ClinPharmacol 2014;3:501-6
16. Fox EJ, Sklar GS, Hill CH, Villanue Var, King BD. Complications related to the pressor response to endotracheal intubation. Anaesthesiology. 1977; 47:524-5.
17. Ronald D Miller. Miller's Anesthesia volume 2 Seventh edition 2010.
18. Karl et al- Insertion of LMA in place of endotracheal intubation to attenuate the cardiovascular response. IJA, 1999;43:30-35.
19. Bajwa SS, Kaur J, Singh A, Parmar SS, Singh G, Kulshrestha A, et al.Attenuation of pressor response and dose sparing of opioids and anaesthetics with pre-operative dexmedetomidine. Indian J Anaesth 2012;56:123-8.
20. Parikh DA, Kolli SN, Karnik HS, Lele SS, Tendolkar BA. A prospective randomized double-blind study comparing dexmedetomidine vs combination of midazolam-fentanyl for tympanoplasty surgery under monitored anesthesia care. J Anaesthesiol Clin Pharmacol 2013;29:173-8.
21. Feld JM, Hoffman WE, Stechert MM, Hoffman IW, Ananda RC. Fentanyl or dexmedetomidine combined with desflurane for bariatric surgery. Journal of clinical anesthesia. 2006;18:24-8.
22. Turgut N, Turkmen A, Gokkaya S, Altan A, Hatiboglu MA. Dexmedetomidine-based versus fentanyl-based total intravenous anesthesia for lumbar laminectomy. Minerva anestesiologica. 2008;74:469.
23. Neil L, Patel A. Effect of Dexmedetomidine Versus Fentanyl on Haemodynamic Response to Patients Undergoing Elective Laparoscopic Surgery: A Double Blinded Randomized Controlled Study. Journal of clinical and diagnostic research: JCDR. 2017;11:UC01.
24. Jain V, Chandak A, Ghosh A, Golhar M. Comparison of dexmedetomidine and fentanyl for attenuation of the hemodynamic response to laryngoscopy and tracheal intubation. Ain-Shams Journal of Anaesthesiology. 2015;8:236.