EFFECTS OF PREANESTHETIC SINGLE DOSE INTRAVENOUS DEXMEDETOMIDINE VERSUS FENTANYL ON HEMODYNAMIC RESPONSE TO ENDOTRACHEAL INTUBATION-A CLINICAL COMPARATIVE STUDY

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ABSTRACT

INTRODUCTION

Many pharmacological agents have been evaluated in regards to their efficacy of blunting the adverse cardiovascular response to laryngoscopy and tracheal intubation. The aim of this study was to evaluate the efficacy of dexmedetomidine compared to fentanyl in blunting the haemodynamic response to laryngoscopy and intubation.

METHOD

Sixty patients were randomly allocated into two groups (30 patients in each group). The group D received intravenously 1 µgm/kg dexmedetomidine infusion and group F received 2µgm/kg fentanyl infusion. The study drugs were prepared in an identical looking container and were infused fifteen minutes prior to induction of anaesthesia. The study drugs were infused over a period of ten minutes and all the patients underwent a similar anaesthetics technique. Heart rate (HR) and blood pressure (systolic, diastolic and mean blood pressure) were noted at baseline, at the end of infusion of the study drugs, after induction of anaesthesia, immediately after laryngoscopy and intubation and at 1, 3, 5, 7 and 10 minutes after laryngoscopy and intubation.

RESULTS

HR significantly decreased in the group D when compared to group F immediately after study drug infusion and there was statistically significant reduction in heart rate for up to 5 min after intubation in both the groups. Although HR increased after intubation in both the groups, the magnitude was lower in the group D. In both the groups, laryngoscopy and intubation led to an increase in systolic, diastolic and mean arterial pressure; the magnitude was lower in the group D.

CONCLUSION

Dexmeditomidine (1µ/kg) attenuates these untoward responses of laryngoscopy and intubation more effectively than fentanyl (2 µ/kg) when administered as bolus dose in the pre-induction period of general anaesthesia.

KEYWORDS

Dexmedetomidine, Fentanyl, Hemodynamics, Intubation, Intratracheal, Laryngoscopy.

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INTRODUCTION: Considering the deleterious effects of haemodynamic changes in response to laryngoscopy and tracheal intubation, many agents has been evaluated to find out the most efficacious one.[1] Among the pharmacological agents studied, local anaesthetics, calcium channel blockers, beta blockers and narcotics has been found to decrease the risk of arrhythmia associated with laryngoscopy and intubation but none of them could be labelled as the `ideal agent`.[1] Fentanyl is a commonly used narcotic in the perioperative period and is extensively used to blunt haemodynamic response to laryngoscopy and intubation.[2]

Dexmedetomidine is a highly selective α2 adrenergic receptor agonist.[3] It has many perioperative applications.[3] Its usefulness in prevention of haemodynamic response to laryngoscopy and intubation has been the interest of present research.[4-13] Propofol is the most commonly used

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induction agent and fentanyl is a commonly used agent to blunt hemodynamic response in our institute. At the time of inception of this study, no trial examined its usefulness in comparison to dexmedetomidine in patients induced with propofol.

Therefore, we proposed to compare the efficacy of bolus administration of intravenous (IV) dexmedetomidine 1mcg/kg and IV fentanyl 2mcg/kg in attenuating hemodynamic response to laryngoscopy and endotracheal intubation.

METHODS AND MATERIALS: This prospective blinded single centre randomized study was carried out after obtaining ethical committee clearance (No MC/MO/2011/Pt-11/22) and informed consent from the participants during the period of August 2011 to June 2012. Sixty (60) patients were randomly selected and enrolled in this study. The study population consisted of patients of American Society of Anesthesiology (ASA) class I and II, belonging to either sex of the age group of 18-50 years and admitted for operation under general anesthesia with endotracheal intubation. Patients with concurrent pregnancy, contraindication to any drugs used in this study, history of allergy to the drugs used, peri-operative use of calcium channel blocker, alpha or beta adrenergic blocker agents, antipsychotic medication and cardiac or neurological procedures were excluded. Patients with anticipated difficult intubation and in whom laryngoscopy and intubation required >1 attempt and/or lasted >30 seconds were excluded from the study.

The patients were visited in the wards and pre-anaesthetic assessment was performed on all the cases. The detailed history of each patient along with the findings of clinical examination and investigations were recorded. Tablet Alprazolam (0.25mg) was administered orally on the night before surgery. Patients were randomly divided (with the use of computer generated randomization table) into two groups (30 subjects each) and assigned to receive either dexmedetomidine (Group D) or fentanyl (Group F). Patients were not aware of the study group where he/she has been allocated.

A standard anaesthesia protocol was employed in all the cases. Upon shifting the patient into the operation theatre, monitor was attached and baseline (T_B) ECG (3 lead configuration, monitored lead was lead II), heart rate (HR), automated non invasive (oscillometric method) systolic, diastolic and mean blood pressure (SBP, DBP and MAP respectively) and peripheral arterial oxygen saturation (SpO_2) were recorded. A lactated ringer's solution was started at the rate of 5 ml kg^{-1} min^{-1} via an 18 gauge intravenous (IV) cannula in the left hand. Then, patients of Group D were given 1 $\mu g.kg^{-1}$ dexmedetomidine IV (prepared in 150 mL of normal saline) fifteen (15) minutes before anaesthesia induction, whereas, group F received 2 $\mu g.kg^{-1}$ fentanyl IV (prepared in 150 ml of normal saline) fifteen (15) minutes prior to induction of anaesthesia. The container of the study drug was similar in both the groups and was prepared and coded by a person not involved in the rest of the study. The study drugs were infused over 10 minutes. Decoding was done at the completion of the trial. All the patients were premedicated with Glycopyrrolate (0.2mg/kg, intramuscular) ten (10) minutes prior to induction of anaesthesia. Preoxygenation (for three minutes) was carried out with 100% oxygen, twelve (12) minutes after the commencement of IV infusion of dexmedetomidine or fentanyl. At fifteen minutes after the start of the study drug, anaesthesia was induced with intravenous propofol (2 mg/kg body wt), infused over 15 seconds or until loss of eye reflex was documented. Anaesthesia was maintained with a mixture of 67 % N_2O, 33% O_2 and 0.5% isoflurane delivered through a semi-closed circuit. The patients were then tracheally intubated with the help of appropriate sized Macintosh blade, one minute after IV administration of succinylcholine (1.5 mg/kg). Correct placement of the tube was confirmed by bilateral chest auscultation and demonstration of continuous end tidal carbon dioxide (CO_2) and normal tidal CO_2 graph and the cuff of the endotracheal tube (ETT) was inflated with air till loss of audible leak. All the intubations were carried out by consultant anaesthesiologist who was unaware of the group allocation. Subsequently muscle relaxation was achieved with inj. Vecuronium bromide (0.1 mg kg^{-1}) intravenously and was supplemented with 0.025 mg/kg when needed. The patient's lungs were mechanically ventilated with a tidal volume of 8 ml/kg, respiratory rate 14 min^{-1} and I/E ratio 1:2. HR, SBP, DBP, MAP and SpO_2 was noted at the end of infusion of the study drug (T_D), loss of eyelash reflex (T_I) following propofol administration, at the end of laryngoscopy and intubation (T_{LI0}), one minute (T_{LI1}), three minutes (T_{LI3}), five minutes (T_{LI5}), seven minutes (T_{LI7}) and ten minutes (T_{LI10}) after inflation of the cuff of the ET tube by an observer who was blinded to the group allocation. After the recording of T_{LI10}, the study was declared over and surgical draping was allowed.

STATISTICS: As we could not gather published data on the mean and standard deviation of HR and MAP following laryngoscopy and intubation using fentanyl, propofol and succinyl choline, we collected data from our clinical practice. Based on the data thus obtained, to detect a difference of 30%, with α error of 0.05 and power of 0.8, 26 samples are required in each group. Considering a dropout of 15%, we included 30 patients in each group.

The InStat 3.0 statistical software package (GraphPad Software, USA) was used for all analyses and a $P < 0.05$ was considered statistically significant. The data were examined for normality using Kolmogorov–Smirnov test. The central tendency and dispersion of normality distributed and continuous variables are expressed as mean and standard deviation respectively. Demographic data were analyzed by Student t test and Chi-square test. Intergroup comparisons for hemodynamic parameters were performed with t test. Analysis of variance was used when change of continuous data over time was analysed.

RESULTS AND OBSERVATIONS: The demographic data were comparable in both the groups and are given in Table no: 1. Heart rate decreased in comparison to baseline in both the groups after the study drug infusion and induction of anaesthesia. (Table no: 2) In both the groups, the maximum decrease, which was statistically significant, was noted after infusion of the study drug. (Table no: 2, Figure: 1)

Although statistically significant increase in HR compared to baseline was observed in both the groups immediately after laryngoscopy and intubation, this increase was more pronounced in group F (p=0.001). (Table no: 2) In group D, the increase in HR produced by laryngoscopy and intubation returned to near baseline by 5 min (p >0.05) and remained comparable to baseline (p >0.05) throughout the study period. (Table no: 2, Figure: 1)

However, in group F, the increase in HR was significantly high even at 5 min (P<0.0001) after laryngoscopy and intubation and remained significantly high from baseline throughout the study period. (Table no: 2, Figure: 1) After laryngoscopy and tracheal intubation, the HR in group D remained statistically significantly lower compared to group F. (Table no: 2, Figure: 1)

There was no statistical difference of the baseline SBP, DBP and MAP of both the study groups. (Table no: 3) Decrease in SBP, DBP and MAP was noted in the Group D, both after infusion of dexmedetomidine and induction of anaesthesia, whereas no such phenomenon was observed in the group F. (Table no: 3) Compared to baseline, although the decrease in SBP, DBP and MAP after infusion of dexmedetomidine was not statistically significant, either in intergroup or intra-group analysis, the change in SBP and MAP reached statistical significance after induction of anaesthesia. (Table no: 3) The increase in SBP peaked at 1 minute after laryngoscopy and intubation, followed by a gradual decline. (Table no: 3) The change of SBP became statistically insignificant (both inter and intra group analysis, compared to baseline) five minutes after laryngoscopy and intubation. (Table no: 3) Till this point of time, SBP in group D was statically significantly lower compared to group F. (Table no: 3) In both the groups, DBP and MAP also peaked at 1 minute after laryngoscopy and intubation and followed a similar trend as that of SBP. (Table no: 3)

During the study period, we did not observe any event of bradycardia (defined as HR <55min^{-1}), systolic hypotension (defined as SBP <90mmHg), bronchospasm, changes of ST segment in monitored ECG or any arrhythmia.

Characteristics	Group D (n=30)	Group F (n=30)
No of males	8	7
No of females	22	23
Mean age (yrs) [Mean±SD]	39.37±8.52	38.2±8.87
Mean body weight (kg) [Mean ± SD]	57.83±7.87	57.9±8.01
No of ASA I patients	24	26
No of ASA II patients	6	4

Table 1: Demographic variables of patients in both the groups

Time	Heart rate (Beats per minute) Mean±SD		P value (Intergroup comparison)
	Group D	Group F	
T_B	76.9±4.75	77.66±5.20	>0.05
T_D	72.03±5.16	74.86±5.27	0.039
T_I	72.36±4.64	75.36±4.66	0.015
T_{LI0}	80.00±4.78	93.53±6.83	<0.0001
T_{LI1}	78.83±4.27	85.96±4.62	<0.0001
T_{LI3}	76.83±4.34	81.23±4.46	0.0003
T_{LI5}	75.93±3.92	80.83±4.17	<0.0001
T_{LI7}	76.80±3.29	81.03±5.06	0.0003
T_{LI10}	77.40±3.89	80.80±4.26	0.0021

Table 2: Perioperative changes in heart rate

T_B- Baseline, T_D-at the end of infusion of the study drug, T_I- at the loss of eyelash reflex, T_{LI0}-immediately after endotracheal intubation, T_{L1}- 1 minute after endotracheal intubation, T_{LI3}- 3 minutes after endotracheal intubation, T_{LI5}- 5 minutes after endotracheal intubation, T_{LI7}- 7 minutes after endotracheal intubation, T_{LI10}- 10 minutes after endotracheal intubation.

	SBP (mmHg) Mean±SD		P value (Inter group)	DBP (mmHg) Mean±SD		P Value (Inter group)	MAP (mmHg) Mean±SD		P value (Inter group)
	Group D	Group F		Group D	Group F		Group D	Group F	
T_B	127.03±6.53	127.10±6.93	>0.05	78.76±4.16	77.36±4.18	>0.05	94.85±3.56	93.94±3.60	>0.05
T_D	124.50±6.30	126.93±6.24	>0.05	76.26±3.57	77.33±3.76	>0.05	92.34±3.39	93.86±3.93	>0.05
T_I	123.60±6.39	127.73±6.18	<0.001	75.96±2.91	77.00±2.82	>0.05	91.86±2.98	93.91±2.94	<0.01
T_{LI0}	127.76±4.58	136.23±4.41	<0.0001	79.73±2.45	87.73±4.08	<0.0001	95.74±2.21	103.90±3.29	<0.0001
T_{LI1}	132.40±5.04	138.23±4.41	<0.0001	83.76±3.46	93.83±4.15	<0.0001	99.97±3.41	110.31±3.09	<0.0001
T_{LI3}	129.86±5.15	131.26±5.95	<0.0001	78.16±3.47	86.13±4.28	<0.0001	95.40±3.39	101.17±3.58	<0.0001
T_{LI5}	126.20±4.24	127.40±5.63	>0.05	76.33±2.86	78.40±3.89	>0.05	92.95±2.09	94.73±3.08	>0.05
T_{LI7}	125.63±3.83	127.30±5.48	>0.05	76.10±2.89	77.30±2.03	>0.05	92.63±2.26	93.96±2.34	>0.05
T_{LI10}	125.56±3.82	126.50±4.71	>0.05	76.03±3.40	77.33±2.99	>0.05	92.54±2.50	93.72±2.67	>0.05

Table 3: Perioperative changes in systolic, diastolic and mean blood pressure

T_B- Baseline, T_D- at the end of infusion of the study drug, T_I- at the loss of eyelash reflex, T_{LI0}- immediately after endotracheal intubation, T_{L1}- 1 minute after endotracheal intubation, T_{LI3}- 3 minutes after endotracheal intubation, T_{LI5}- 5 minutes after endotracheal intubation, T_{LI7}- 7 minutes after endotracheal intubation, T_{LI10}-10 minutes after endotracheal intubation.

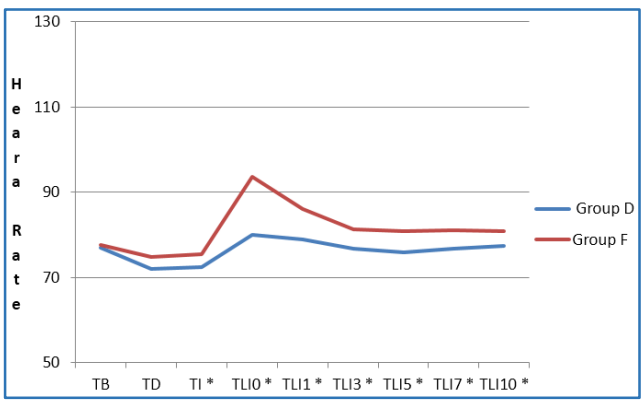

Fig. 1: Graph showing the change of heart rate over the study period in both the groups

Values are mean ± standard deviation significant. Time point of measurement and heart rate is mentioned in the X axis and Y axis respectively.

T_B- Baseline, T_D- at the end of infusion of the study drug, T_I- at the loss of eyelash reflex, T_{LI0}- immediately after endotracheal intubation, T_{L1}- 1 minute after endotracheal intubation, T_{LI3}- 3 minutes after endotracheal intubation, T_{LI5}- 5 minutes after endotracheal intubation, T_{LI7}- 7 minutes after endotracheal intubation, T_{LI10}- 10 minutes after endotracheal intubation.

*time points where intergroup comparison yielded p <0.05.

DISCUSSION: The haemodynamic changes that accompany laryngoscopy and intubation are due to activation of the sympathetic nervous system. These changes may not be of much consequence for healthy patients but may be associated with significant morbidity and mortality in a cohort of high risk patients.[1] Both fentanyl and dexmedetomidine is known to decrease the manifestation of sympathetic nervous system activation.[1,4-13]

In the present study, heart rate significantly decreased in the dexmedetomidine group when compared to fentanyl group immediately after study drug infusion and there was statistically significant reduction in heart rate for up to 5 min after intubation in both the groups. Although heart rate increased after intubation in both the groups, the magnitude was lower in the Dexmedetomidine group. Unlike HR, no decrease in blood pressure was noted in the fentanyl group after its administration. In both the groups, laryngoscopy and intubation led to an increase in systolic, diastolic and mean arterial pressure, the magnitude was lower in the Dexmedetomidine group.

The changes in HR, SBP, DBP and MAP observed in our study are of similar trend to that of Gunalan et al, Kharwar et al, Laha et al, Gandhi S et al but the time duration of change of these parameter were slightly different amongst these studies.[6,7,8,9]

Gunalan et al compared the efficacy of dexmedetomidine 1µgm/kg and fentanyl 2µgm/kg in regards to their ability to blunt hemodynamic response to laryngoscopy and intubation.[6] In their study, significantly decreased heart rate was noted in the dexmedetomidine group when compared to fentanyl group immediately after study drug infusion and this trend remained for the total duration of the study.[6] In fentanyl group, heart rate increased following laryngoscopy and endotracheal intubation and returned back to normal only after 3 minutes.[6] Blunting of increase in SBP, DBP and MAP was significantly better in the dexmedetomidine group than the fentanyl group.[6] Unlike observed in our study, in the dexmedetomidine group, blood pressure did not rise significantly following laryngoscopy and endotracheal intubation.[6] Although they employed almost a similar methodology to that of ours, we used succinylcholine whereas vecuronium bromide was used in their study. The differential effect of succinylcholine and vecuronium on cardiovascular system is well known and the use of two drugs with different cardiovascular profile may have led to the differences observed in these two studies.[14]

In a study on 60 patients using dosages of the study drugs similar to us, Kharwar et al, observed a significant decrease in HR in the dexmedetomidine group compare to fentanyl group but there was more reduction of MAP in the fentanyl group compared to dexmedetomidine after induction of anaesthesia.[7] But after laryngoscopy and intubation, there was an increase of HR and MAP in both the groups, the magnitude being more in the fentanyl group.[7] It was concluded that Dexmedetomidine was more effective in attenuating the haemodynamic response to laryngoscopy and intubation.[7] It must be noted that vecuronium bromide was used as the neuromuscular blocking agent by Kharwar et al.[7]

Unlike us, Laha et al compared dexmedetomidine to placebo and all the patients in this study received fentanyl 2 µgm/kg.[8] The HR, SBP and DBP increased following intubation in both the study groups, but the rise was significantly less in the dexmedetomidine group.[8] It was concluded that dexmedetomidine attenuated but could not totally abolish the cardiovascular response to intubation after induction of anaesthesia.[8]

Gandhi S et al observed that HR was significantly lower for ten minutes in the dexmedetomidine group, but no such trend was observed in the fentanyl group.[9] After laryngoscopy and intubation, the increase was highly significant in the fentanyl group than dexmedetomidine group.[9] Although these observations are in agreement to that of ours, Gandhi et al used a much lesser dose of Dexmedetomidine (0.6 µgm/kg).[9]

Not only in non cardiac surgical patients, were similar observation also made for patients undergoing cardiac surgery.[10] Dexmedetomidine has also been compared to remifentanil, esmolol and lignocaine.[5,11,12,13] In these randomized studies, dexmedetomidine was found to be of similar efficacy to remifentanil albeit with less potentials for respiratory depression, whereas it was superior compared to esmolol or lignocaine.[11,12,13]

Bradycardia was observed in one patient each in the study by Gunalan et al and Kharwar et al.[6,7] No such adverse effect was observed in our study.

CONCLUSION: From this randomized comparative study undertaken to evaluate the effectiveness of single dose dexmedetomidine versus fentanyl in attenuating the haemodynamic responses to laryngoscopy and intubation, it can be concluded that dexmeditomidine (1µ/kg) attenuates these untoward responses of laryngoscopy and intubation more effectively than fentanyl (2 µ/kg) when administered as bolus dose in the pre-induction period of general anaesthesia.

REFERENCES:

1. Khan FA, Ullah H. Pharmacological agents for preventing morbidity associated with the haemodynamic response to tracheal intubation. Cochrane Database Syst Rev. 2013;7:CD004087.
2. Kim JK, Park JM, Lee CH, et al. Dose fentanyl injection for blunting the hemodynamic response to intubation n increase the riskof reflex bradycardia during major abdominal surgery? Korean J Anesthesiol. 2012;63(5):402-8.
3. Anju Grewal. Dexmedetomidine: New avenues. J Anaesthesiol Clin Pharmacol. 2011;27(3):297–302.
4. Scheinin B, Lindgren L, Randell T, et al. Dexmedetomidine attenuates sympathoadrenal responses to tracheal intubation and reduces the need for thiopentone and peroperative fentanyl. Br J Anaesth. 1992;68(2):126-31.
5. Yavascaoglu B, Kaya FN, Baykara M, et al. A comparison of esmolol and dexmedetomidine for attenuation of intraocular pressure and haemodynamic responses to laryngoscopy and tracheal intubation. Eur J Anaesthesiol. Jun 2008;25(6):517-9.
6. Gunalan S, Venkatraman R, Sivarajan G, et al. Comparative Evaluation of Bolus v Administration of Dexmedetomidine and Fentanyl for Stress Attenuation During Laryngoscopy and Endotracheal Intubation. J Clin Diagn Res. 2015;9(9):UC06-9.
7. Kharwar DRK, Kumar DM, Tiwary DPK, et al. A Comparison Of Intravenous Dexmedetomidine V/S Inj. Fentanyl For Attenuation Of Hemodynamic Responses During Laryngoscopy And Intubation After Propofol Induction. National Journal of Integrated Research in Medicine 2014;5(3):71-5.
8. Laha A, Ghosh S, Sarkar S. Attenuation of sympathoadrenal responses and anesthetic requirement by dexmedetomidine. Anesth Essays Res. 2013;7(1):65-70.
9. Gandhi S, Goyal V, Radhakrishnan K, et al. Comparison of Dexmedetomidine with Fentanyl in Attenuation of Pressor Response during Laryngoscopy and Intubation. IOSR Journal Of Pharmacy. 2014;4(2):28-3.
10. Menda F, Köner O, Sayin M, et al. Dexmedetomidine as an adjunct to anesthetic induction to attenuate hemodynamic response toendotracheal intubation in patients undergoing fast-track CABG. Ann Card Anaesth. 2010;13(1):16-21.
11. Li C, Li Y, Wang K, et al. Comparative Evaluation of Remifentanil and Dexmedetomidine in General Anesthesia for Cesarean Delivery. Med Sci Monit. 2015;21:3806-13.
12. Srivastava VK, Nagle V, Agrawal S, et al. Comparative evaluation of dexmedetomidine and esmolol on hemodynamic responses during laparoscopic cholecystectomy. J Clin Diagn Res. 2015;9(3):UC01-5.
13. Gulabani M, Gurha P, Dass P, et al. 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. Jan-Apr 2015;9(1):5-14.
14. Appiah-Ankam J, Hunter JM. Pharmacology of neuromuscular blocking drugs. Contin Educ Anaesth Crit Care Pain 2004;4(1):2-7.