ORIGINAL ARTICLE

A STUDY ON COMPARISON OF INTRAVENOUS DEXMEDETOMIDINE WITH INTRAVENOUS FENTANYL FOR SUPPRESSION OF HEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION DURING GENERAL ANAESTHESIA

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ABSTRACT

Background: Laryngoscopy and intubation is the Gold standard for airway management but this evokes a stress response which is exhibited in the form of changes in heart rate, blood pressure and arrhythmias. This study was prospective, randomized, double blind study to determine whether the fentanyl 2μg/Kg or dexmedetomidine 1μg/Kg would decrease the attenuation of hemodynamic response during laryngoscopy and tracheal intubation during general anaesthesia.

Methodology: The patients were randomly allocated into two groups. In Group D cases (n=30) received injection Dexmedetomidine 1μg/kg diluted to 10ml NS IV over 10min using syringe pump prior to intubation and 5ml of NS 5 min. prior to intubation. In Group F cases (n=30) received 2μg/kg diluted to 5ml NS 5min. prior to intubation and 20ml NS in infusion pump over 10 min., prior to intubation.

Results: The age and weight of the cases in both the groups are comparable. It was observed that mean HR increased in both groups D and F immediately after endotracheal intubation. The systolic blood pressure was highly significant in group F as compared to group D during laryngoscopy and intubation, 1, 3, 5 and 10 min after intubation ($p<0.000$). Ramsay sedation score was ≥ 4 in all patients in group D and was ≤ 3 in group F. Dexmedetomidine has higher sedation score but no respiratory depression.

Conclusion: We concluded that dexmedetomidine in dose 1μgm/kg i.v. is more effective in attenuating the hemodynamic pressor responses to laryngoscopy and intubation than Inj. Fentanyl 2μgm/kg i.v. when given as pre-medicant without significant side effects.

Keywords: Dexmedetomidine, Fentanyl, laryngoscopy, endotracheal intubation

INTRODUCTION

In 1940, Reid and Brace first described hemodynamic response to laryngoscopy and intubation.[1] Till today, laryngoscopy and intubation is the Gold standard for airway management. But this evokes a stress response which is exihibited in the form of changes in heart rate, blood pressure and arrhythmias. Various pharmacological methods like volatile anaesthetics, topical and intravenous lignocaine, opioids, vasodilators nitroglycerine, nifedipine, β blockers have been tried but none is proved to be ideal.[2]

Fentanyl is an opioid analgesic and is popular to be used as premedicant to provide cardiovascular stability during laryngoscopy and intubation and during intraoperative period also. The clinically effective dose of fentanyl to attenuate hemodynamic responses to laryngoscopy intubation starts at 2μg/Kg and its comparison has been done with other groups.[2]

Wijeysundera et al., investigated the effects of α_2 adrenoreceptor agonists, dexmedetomidine, clonidine and mivazerol, on perioperartive cardiovascular complications and mortality in adults undergoing cardiac surgeries.[3] During cardiac and vascular surgeries, α_2 –adrenoceptor agonists reduced the

number of ischemic episodes and were associated with a reduced risk of myocardial infarction and trend toward decreased mortality. Sagiroğlu et al., conducted a study with different doses of dexmedetomidine and found that to control the hemodynamic responses to tracheal intubation, dexmedetomidine 1μg/Kg is more effective than 0.5μg/Kg without any side effect.[4]

With this in background we planned prospective, randomized, double blind study was planned to determine whether the fentanyl 2μg/Kg or dexmedetomidine 1μg/Kg would decrease the attenuation of hemodynamic response during laryngoscopy and tracheal intubation during general anaesthesia.

METHODOLOGY

This was the randomized, double blind study conducted in two groups of cases who were scheduled for various elective surgical procedures belonging to ASA grade 1 and 2. The patients belonged to both gender and within 18 to 60 years of age. The patients were randomly allocated into two groups by computer generated random numbers. In Group D - Dexmedetomidine (n=30) received injection dexmedetomidine 1μg/kg diluted to 10ml NS IV over 10min using syringe pump prior to intubation and 5ml of NS 5 min. prior to intubation. In Group F-Fentanyl (n=30) received 2μg/kg diluted to 5ml NS 5min. prior to intubation and 20ml NS in infusion pump over 10 min., prior to intubation.

The patients with past or present history of hypertension (BP>140/90mmHg), ischemic heart disease, ECG abnormalities, hypotension (MAP<80mmHg), bradycardia (PR<50/min), liver and renal disease, asthma, lactating and pregnant female, patients with predicted difficult intubation and obese patients (BMI>30) and endocrine diseases like hyperthyroidism, hypothyroidism, diabetes mellitus were excluded from the study. The study was conducted after ethical committee clearance for the study and patients were enrolled in the study only after obtaining informed written consent from them.

The procedure was explained and written consent was taken from the patients prior to the surgery. Patients were kept nil per orally for 8 hrs prior to surgery. Intravenous line was started with DNS. Heart rate, systolic, diastolic and mean arterial blood pressure, rate pressure product (RPP) was recorded just prior to premedication and was taken as baseline. Airway of patients that were likely to be anticipated for difficult intubation was evaluated. Patients were subjected to routine investigations like complete blood count (CBC) blood sugar, renal and liver function tests and electrocardiogram (ECG). All patients were premedicated with Inj. Glycopyrrolate 0.04 mg/kg i.v., Inj. Midazolam 0.04 mg/kg i.v., Inj. Ondansterone 0.1mg/kg i.v. and Inj. Tramadol 2mg/kg i.v. 10 min. before induction. Patients in group D received Dexmedetomdine 1 μg/kg diluted in 10ml NS IV using syringe pump and 5ml NS 5min. prior to induction. Patients in group F received Fentanyl 2μg/kg diluted in 5ml NS Patients were preoxygenated with 100% oxygen with facemask for 3 min.

Anaesthesia was induced with 2.5% sodium thiopentone till the eyelash reflex was lost, followed by succinylchoine 2mg/kg i.v. to facilitate intubation. After the disappearance of fasciculation, laryngoscopy and intubation was done using standard Macintosh laryngoscope. All intubations were completed within 20 seconds by the experienced laryngoscopist. The cases in which intubation required more than 20 seconds, were excluded from the study.

Immediately after intubation; systolic, diastolic and mean arterial blood pressure and rate pressure product were recorded as 0 minute and these readings were repeated at intervals of 2, 3, 5 and 10 min. from 0 min. reading. Anaesthesia was maintained using isoflurane (0.4% v/v) and sevoflurane (0.8%v/v) 60% nitrous oxide and 40% of oxygen. After recovered from the effects of succinylcholine further neuromuscular blockade was maintained with vecuronium 0.05mg/kg bodyweight. No surgical stimulus was given during the 10 min. study period. Isoflurane concentration was adjusted to maintain systolic blood pressure within 20% of preoperative values.

At the end of surgery residual neuromuscular block will be antagonised with Inj. Neostigmine 50 μgm/kg i.v. & Inj. Glycopyrrolate 10 μgm/kg i.v. Patients were observed for any side effects like hypotension, bradycardia, arrhythmias and bronchospasm intraoperative. Sedation score before induction was done using Ramsay sedation score. The results were expressed as mean± SD. Statistical analysis was done using paired t-test and p value less than 0.05 was considered as significant.

RESULTS

Demographic profile of the cases is as shown in table 1.

Table 1: Demographic profile of cases

Groups	Age (in years)	Number of patients		Weight (in kgs)
		Male	Female	
Group D (Dexmetomidine)	31.39 ±11.82	16	14	53.7 ±7.63
Group F (Fentanyl)	34.92 ±10.80	14	16	50.6 ±6.23

Table 2: Distribution of heart rate in both the groups

Duration (in minutes)	Heart rate			
	Group F		Group D	
	Mean	Sd	Mean	Sd
Baseline	92.67	16.7	88.57	12.34
2 min	93.23	16.87	89.2	12.23
5min	91.43	15.89	83.34	12.84
8min	90.23	15.02	76.45	13.08
Before induction	89.13	14.87	69.57	13.81
0 min	109.35	15.46	89.68	20.92
1 min	100.91	15.86	86.43	17.93
3 min	94.304	12.4	81.04	17.37
5 min	82.21	20.31	72.96	15.61
10 min	82.88	12.12	69.25	13.55

Table 3: Distribution of Systolic blood pressure in both the groups

Duration (in minutes)	Systolic blood pressure			
	Group f		Group d	
	Mean	Sd	Mean	Sd
Baseline	125.04	10.84	127.82	9.63
2min	126.45	10.92	126.12	10.12
5min	126.23	10.86	124.23	12.23
8min	122.67	12.23	120.23	13.21
Before induction	120.47	14.49	110.12	15.8
0 min	149.23	20.23	131.61	30.31
2min	128.67	13.47	105.96	27.11
3min	119.03	23.65	100.79	26.31
5min	107.29	21.72	97.54	24.07
10min	99.167	12.44	91.54	22.71

Table 4: Distribution of Diastolic blood pressure in both the groups

Duration (in minutes)	Diastolic blood pressure			
	Group F		Group D	
	Mean	Sd	Mean	Sd
Baseline	80.21	7.79	80.92	9.51
2min	80.23	8.01	80.02	9.42
5min	80.12	8.34	77.02	9.23
8min	78.23	7.79	73.23	9.51
Before induction	74.23	9.88	68.02	12.36
0 min	96.54	11.09	86.63	22.89
2min	84.54	11.44	74.46	26.63
3min	82.23	12.4	72.38	25.22
5min	73.08	9.74	68.35	18.11
10min	71.08	12.31	65.88	16.7

The basal heart rate was comparable in both groups (p=1.000). Groups showed significant fall in HR in group D after 10 min. of drug administration and before induction. It was observed that mean HR increased in both groups D and F immediately after endotracheal intubation. The heart rate started to return to normal values at the end of 10 min. post intubation. The increase was significant in group F compared to group D during laryngoscopy and after intubation ($p<0.001$)

Baseline SBP of all patients in both groups F and D are comparable to each other and there is no statistical difference between them (p value<0.05). The systolic blood pressure was highly significant in group F as compared to group D during laryngoscopy and intubation, 1, 3, 5 and 10 min after intubation ($p<0.000$).

After 10 min. of drug administration, there is decrease in diastolic blood pressure in all patients of both groups but significant fall in group D as compared to group F. It was observed that DBP increased significantly from baseline during laryngoscopy and after intubation and returned to normal after 10 min. post intubation in all patients. Baseline diastolic blood pressure of all patients of both groups F and D are comparable to each other and there is no statistical difference between them (p value>0.05). Increase was highly significant in group F as compared to group D during laryngoscopy and after intubation ($p<0.001$)

It was observed that mean blood pressure was increased significantly from the baseline during laryngoscopy and intubation in both groups and returned to normal at the end of 10 min after intubation in all patients. Baseline Mean Arterial Blood Pressure are comparable to each other in all patients of both groups D and F and there is no statistical difference between them (p value>0.05). The increase was highly significant in group F compared to group D during laryngoscopy and after intubation ($p<0.001$).

We found that rate pressure product was decreased below the baseline value after the drug infusion and increased above the baseline after the intubation and return to normal values after 10 min. of intubation. Baseline Rate Pressure Product values are comparable in both groups with no statistical significant difference (p value < 0.001). It was significantly less in group D as compared to group F after laryngoscopy and intubation.

Ramsay sedation score was ≥ 4 in all patients in group D. In group F, Ramsay sedation score before induction was ≤ 3.

Table 5: Distribution of Mean blood pressure in both the groups

Duration (in minutes)	Mean blood pressure			
	Group F		Group D	
	Mean	Sd	Mean	Sd
BASELINE	92.29	8.54	94.5	10.45
2min	91.96	8.67	94.12	10.23
5min	91.16	8.26	90.02	10.67
8min	90.78	10.02	86.43	11.05
Before induction	88.14	11.6	83.13	11.96
0 min	104.25	24	96.23	25.27
2min	96.25	12.32	88.03	21.11
3min	93.67	10.96	84.55	21.09
5min	90.67	9.09	80.02	20.18
10min	88.23	8.68	74.35	19.78

Table 6: Distribution of rate pressure product in both the groups

Duration (in minutes)	Rate pressure product			
	Group F		Group D	
	Mean	Sd	Mean	Sd
Baseline	11587.45	181.021	11325.45	118.83
2min	11788.93	184.22	11249.9	123.76
5min	11541.2	172.57	10353.33	157.03
8min	11068.51	183.69	9191.58	172.79
10min	10737.49	215.47	7661.05	218.19
After intubation	16318.3	312.76	11802.78	634.08
1min	12984.08	213.63	9158.12	486.08
3min	11225	293.26	8168.2	457
5min	8820.31	441.13	7116.51	375.73
10min	8218.96	150.77	8169.95	307.72

Dexmedetomidine has higher sedation score but no respiratory depression. SPO_2 was continuously monitored during 10 min. of infusion during laryngoscopy and intubation after 10 min. after intubation for all patients. SPO_2 was maintained between 98-100 % in both groups. We calculated that the mean dose of thiopentone sodium required for induction was less in group D as compared to group F.

DISCUSSION

Dexmedetomidine is a highly selective α2 receptor agonist having eight times high affinity and α2 selectivity compared to clonidine and has a shorter duration of action than clonidine. It provides anxiolysis, co-operative sedation and analgesia without respiratory depression.

Scheinin et al., studied the effect of dexmedetomidine on tracheal intubation, required dose of induction agent and preoperative analgesic requirements.[5] They concluded that required dose of thiopentone was significantly lower in dexmedetomidine group and the drug attenuated the hemodynamic responses to intubation. The concentration of noradrenaline in mixed venous plasma was lesser in the dexmedetomidine group.[5] Lawrence et al. found that a single dose of 2μg/kg of dexmedetomidine before induction of anaesthesia attenuated hemodynamic response to intubation as well as etubation.[6] Bradycardia was observed at 1st and 5th min. after administration. This might have been due to bolus administration. Sulaiman, et al. studied the effects of dexmedetomdine on attenuation of stress response to endotracheal intubation in patients undergoing elective off pump coronary artery bypass grafting (CABG). They concluded that pre-treatment with dexmedetomidine at a dose of 0.5μg/kg as 10 min. infusion prior to induction of anaesthesia attenuate the hemodynamic response to laryngoscopy and intubation.[7] Dexmedetomidine can be considered in patients undergoing myocardial revascularization, even if the patients are receiving beta-blocker.

Tanskanen et al. studied that the continuous infusion of 0.2-0.4 μg/kg of dexmedetomidine in patients of craniotomies started 15 min. before induction of anaesthesia and continued till the end of surgeries had increased peri-operative hemodynamic stability and fast recovery without respiratory depression.[8] Jaakola and co-workersfood that dexmedetomidine 0.6μg/kg given 10 min. before induction reduces intraocular pressure and anaesthetic requirement in patients undergoing ophthalmic surgeries.[9] Varshali M Keniya et al. also studied that dexmedemidine infusion in dose of 1μg/kg given over 10min before induction of anaesthesia and continued in a dose of 0.2-0.7μg/kg/hr until skin closure, is effective in attenuating sympathoadrenal response to tracheal intubation. It has significant anaesthetic and opioid sparing effect.[10] R. Saraf et al also found that the dexmedetomidine (0.6μg/kg) given 10 min before induction effectively attenuate the pressor response to laryngoscopy and intubation without any side effect.[11]

In our present study, we observed a difference of decrease in mean heart rate, systolic, diastolic and mean blood pressure by 3bpm, 5mmhg, 6mmHg and 4mmHg in group F while 19bpm, 17mmhg, 12mmHg and 10mmHg in group D from baseline after 10 min of drug infusion and before induction. The mean increase in heart rate, systolic diastolic and mean blood pressure after intubation was 19 bpm, 15 mmhg, 16 mmhg and 12 mmhg in group F while 1 bpm, 4 mmHg, 6 mmHg and 2 mmHg in group D. This difference in increase after intubation is highly significant. The increase in rate

pressure product during laryngoscopy and intubation was 4731.43 in group F as compared to 477.13 in group D which is highly significant and difference in values 1 and 3 min after intubation was 3157.25 and 362.45 in group F and -2167.33 and -3157.25 in group D from baseline values. The difference in Ramsay Sedation Score values which is 2.26 in group F and 4.46 in group D which is higher in group D is also significant while SPO2 was maintained between 98-100%. As for the adverse effects ,we observed bradycardia(pulse rate<50/min) in 2 patients, which was treated with intravenous atropine 0.6 mg and then patient remain stabilized and ventricular premature contractions in 2 patients which was resolved within 3min. without treatment in group D and hypotension in 1 patient in group F which was treated by giving intravenous fluids. It was not statistically significant.

The limitations regarding this study are that we did not measure the plasma norepinephrine levels. We have not calculated the dose of isoflurane and total dose of vecuronium bromide required during surgical procedures in all patients of both groups.

CONCLUSION

Based on the results of our study, we concluded that dexmedetomidine in dose 1μgm/kg i.v. is more effective in attenuating the hemodynamic pressor responses to laryngoscopy and intubation than Inj. Fentanyl 2μgm/kg i.v. when given as premedicant without significant side effects. Dexmedetomidine provides all anxiolysis, sedation, analgesia, anaesthetic sparing and hemodynamic stability without respiratory depression during general anaesthesia.

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