"COMPARISON OF I/V DEXMEDETOMIDINE & I/V FENTANYL TO ATTENUATE THE HAEMODYNAMIC STRESS RESPONSE TO TRACHEAL EXTUBATION"

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INTRODUCTION

Endotracheal extubation is one of the most common day-to-day performed procedure in the practice of anaesthesia. Trans laryngeal removal of a tube from the trachea via the nose or mouth is endotracheal extubation[1]. Tracheal extubation can sometimes be associated with harmful airway and hemodynamic responses[2]. Complications of extubation like bucking, breath holding, laryngospasm or pulmonary edema can occur. [3,4] Tracheal intubation and extubation may be associated with hypertension and tachycardia.[5] Many theories have been explained for sudden increase in heart rate and BP during intubation and extubation such as increased release of catecholamines[6], airway irritation, intense pain following surgery and emergence. Even though these changes are transitory, it could be a major concern for an anaesthesiologist.[7]

Extubation can be associated with various circulatory and airway responses due to reflex sympathetic activity following stimulation of epipharyngeal and laryngo-pharyngeal structures leading to coughing, agitation, bronchospasm, tachycardia, hypertension, arrhythmias, myocardial ischemia and raised intracranial and intraocular pressures. These transient but significant changes, which may be well tolerated by healthy individuals, may be deleterious in patients with hypertension, coronary artery disease or intracranial pathologies.[8] Laryngospam is found to be the most common cause of upper airway obstruction immediately after extubation.[9] Stimulation of various sites, from the nasal mucosa to the diaphragm can evoke laryngospasm.[10] Respiratory complications resulting in serious consequences like hypoxic brain injury and death following tracheal extubation have been thrice more common than those occurring during intubation.[11]

Many drugs are used to attenuate the intubation stress response like intravenous lignocaine[12], short acting opioids like fentanyl[13], esmolol[14], labetalol[15], intrathecal local anaesthetic administration[16] and Dexmedetomidine[17] which can be used during extubation also[18].Clinical research is still going on to find an ideal drug with good safety margin, which attenuates most of the hemodynamic alterations in response to airway manipulation at extubation without delaying recovery and causing adverse events (sedation, respiratory depression, hypotension, etc.)[11.]

Dexmedetomidine is a highly selective α2 adrenoreceptor agonist that induces sedation and analgesia without affecting respiratory status.[19] Administered after induction, Dexmedetomidine was found to reduce the prevalence of emergence agitation[20]. It has also been reported to reduce arterial blood pressure (BP) and heart rate (HR) dose dependently[21] and to reduce hemodynamic and plasma catecholamine responses to intubation and extubation in ophthalmic surgeries.[22] Dexmedetomidine is used for sedation and analgesia in intensive care units, where its relative lack of effect on respiration is an advantage, it is therefore theoretically appropriate for reducing airway and circulatory reflexes during emergence from anaesthesia.[23]

Fentanyl, a synthetic opioid, has been used extensively to maintain perioperative hemodynamic stability and also effective in blunting the hemodynamic changes associated with laryngoscopy and tracheal intubation.[13] This drug has also been reported to reduce the prevalence of coughing during and after extubation. It may blunt cardiovascular and airway reflexes during emergence without prolonging the recovery.[11] Fentanyl has also been reported to attenuate the cardiovascular responses to tracheal extubation in elective gynaecologic surgery.[13]

The present study is aimed at comparison of attenuation of hemodynamic response to tracheal extubation in adult patients posted for thyroidectomies, with single intravenous bolus dose of 1µg/kg body weight dexmedetomidine, given over 10 minutes, 10 minutes prior to extubation and a single bolus dose of 1µg/kg body weight fentanyl given 10 minutes prior to extubation.

Keywords : Dexmedetomidine, Fentanyl, Stress response, Extubation

OBJECTIVES

The objective of the study is to compare the efficacy of intravenous dexmedetomidine(1µg/kg) and fentanyl(1µg/kg) as regards to :

1. Variations in HR, SBP, DBP and MAP.

2. Efficacy of attenuation of above parameters in response to endotracheal extubation.

METHODOLOGY

After obtaining Institutional Ethical Committee clearance, informed written consent was taken from the patients to conduct a study on the “Comparison of I/V Dexmedetomidine and I/V Fentanyl to attenuate the haemodynamic stress response to tracheal extubation”, 60 patients of both sexes undergoing thyroidectomy under general anaesthesia were consecutively sampled and included in my study.

Study setting : Department of Anaesthesiology, Government medical college, Thrissur, Kerala, India.

Study design : Comparative cross sectional study

Study period : 1 year

Study population : ASA physical status 1 and 2 patients aged between 18 to 60 years

undergoing thyroid surgeries under general anaesthesia in Government Medical College, Thrissur.

Inclusion criteria :

1. ASA 1 and ASA 2 groups
2. Between 18-60 years, of both sexes
3. Undergoing thyroid surgeries

Exclusion criteria :

1. Patient allergic to dexmedetomidine or fentanyl
2. Patients with difficult airway
3. Patients with severe obesity
4. Patients undergoing emergency surgeries
5. Patients with hypertension, cardiorespiratory abnormalities, renal insufficiency, liver dysfunction, pregnant and nursing mothers.
6. Patient refusal.

Sample size :

Sample size was calculated by the formula

$$\mathbf{n = \frac{(Z_\alpha + Z_\beta)^2\, 2S^2}{(\mu 1 - \mu 2)^2}}$$

Standard deviation of heart rate is used for sample size calculation

$S_1 = 11$

$S_2 = 9$

$$\mathbf{n = \frac{7.84 \times 2 \times 10 \times 10}{(91\text{-}83)^2}}$$

$$\mathbf{n = 24.5}$$

To conduct the study sample size is taken as **30** in each group.

Study procedure :

All patients were explained in detail about the study and informed consent taken after that. Patients were randomly designated as Group D and Group F for study purpose. Baseline systolic blood pressure, diastolic blood pressure, mean arterial blood pressure and heart rate were recorded before induction of anaesthesia.

Groups F and D received intravenous bolus infusion of 1mcg/kg of Fentanyl, and 1mcg/kg of Dexmedetomidine respectively, infused over a period of 10 minutes starting 10 minutes prior to extubation. Patients were extubated when the extubation criteria is fulfilled. HR, SBP, DBP and MAP were recorded at reversal, at extubation, every 2 min for 10 minutes, every 5 min for first 30 minutes, and every 30 min for next 1 hour 30 minutes after extubation.

Study tool :

Self-prepared proforma with structured questionnaire.

Statistical analysis :

Standard deviation and mean calculated and compared statistically using T test for quantitative variables and chi-square test for qualitative variables.

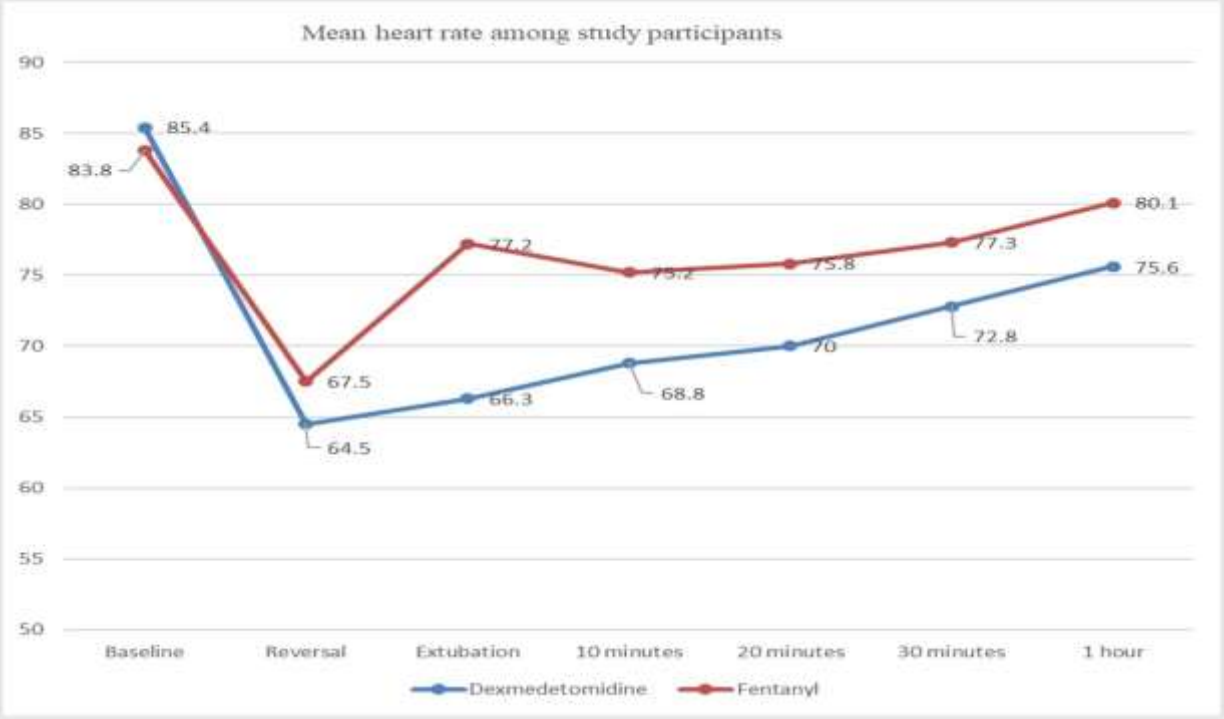
RESULTS

A total of 60 participants were recruited with 30 in each group. Group D received iv Dexmedetomidine while group F received iv Fentanyl and both were compared for hemodynamic parameters following tracheal extubation.

Comparison of heart rate (HR) among the participants of both groups at various time points (N=60)

Unpaired t test was used to assess the association between both the groups. The mean HR was lower at baseline in Fentanyl group but it was statistically insignificant (p value 0.65). However following extubation the mean HR of Fentanyl group was higher compared to Dexmedetomidine after 30 minutes and 1 hour of extubation but this was statistically insignificant (p value 0.06 & 0.08 respectively). The mean HR at extubation in the Fentanyl group was higher than the Dexmedetomidine group and this difference was statistically significant (p value <0.001). The mean HR at 10 and 20 minutes following extubation were also significantly different with the Fentanyl group having a higher HR than the dexmedetomidine group (p value 0.003 & 0.016) respectively.

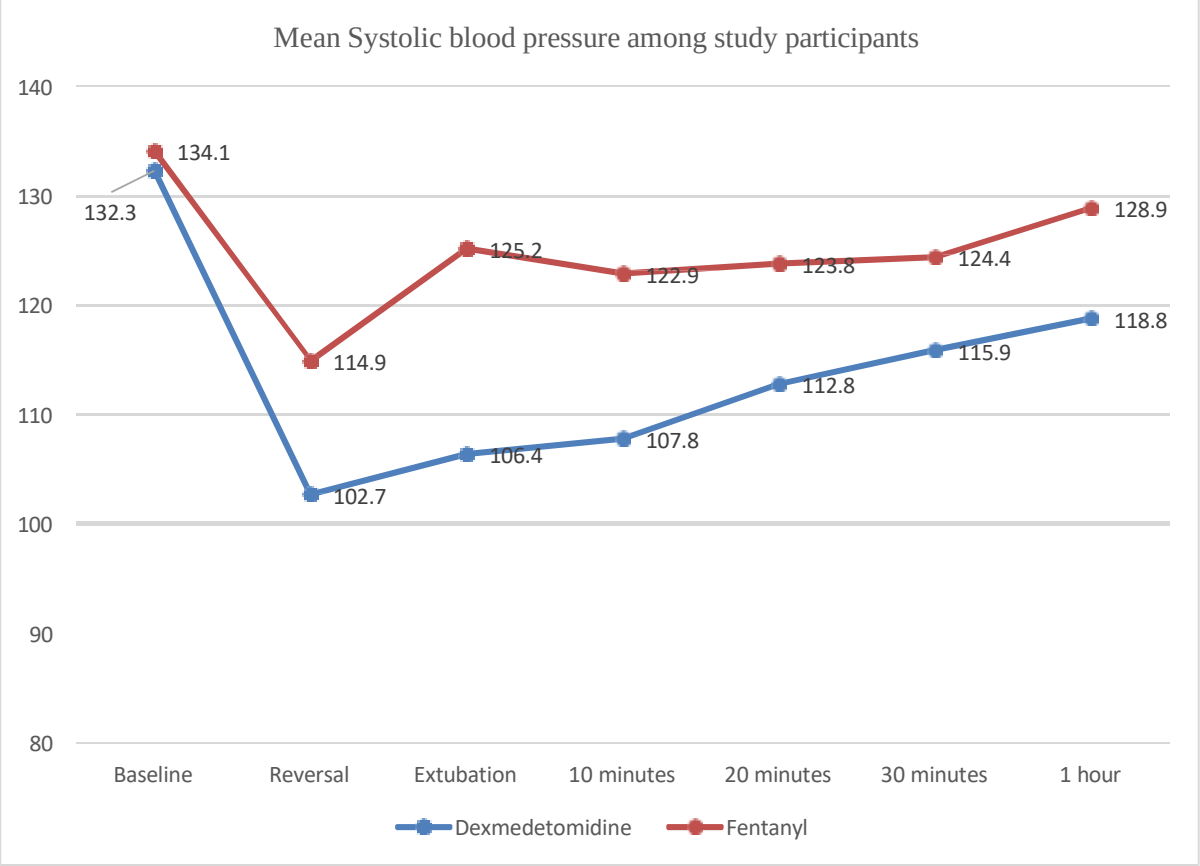
Figure 1 shows the mean HR among the participants in Dexmedetomidine Group and Fentanyl group (N=60).



Comparison of systolic blood pressure (SBP) among the participants of both groups at various

Unpaired t test was used to assess the association between both the groups. The mean SBP was lower at baseline in Dexmedetomidine group compared to Fentanyl group but it was statistically insignificant (p value 0.59). However, the SBP dropped at reversal, raised at extubation in both the groups. Following reversal the raise in the SBP was higher in Fentanyl group compared to Dexmedetomidine at extubation and this was statistically significant (p value <0.001). The SBP dropped in the Fentanyl group following extubation and again raised at 1 hour after extubation. On the contrary the SBP at extubation in Dexmedetomidine group slowly raised following extubation till 1 hour following it. However the difference in the mean SBP values of both groups were statistically significant at reversal, extubation, 10 minutes, 20 minutes, 30 minutes and till 1 hour following extubation.

Figure 2 shows the mean SBP among the participants in Dexmedetomidine Group and Fentanyl group (N=60).



Comparison of diastolic blood pressure (DBP) among the participants of both groups at various time points (N=60)

Unpaired t test was used to assess the association between both the groups. The mean DBP was lower at baseline in Fentanyl group compared to Dexmedetomidine group but it was statistically insignificant (p value 0.28). However, the DBP dropped at reversal, raised at extubation in both the groups. Following reversal the raise in the DBP was higher in Fentanyl group compared to Dexmedetomidine at extubation and this was statistically significant (p value <0.001). The DBP dropped in the Fentanyl group following extubation at 10 minutes and again raised at 1 hour after extubation. On the contrary the DBP at extubation in Dexmedetomidine group slowly raised following extubation till 1 hour following it. However, the difference in the mean DBP values of both groups were statistically significant at

extubation, 10 minutes, 20 minutes, 30 minutes and till 1 hour following extubation.

Figure 3:shows the mean DBP among the participants in Dexmedetomidine Group and Fentanyl group (N=60).

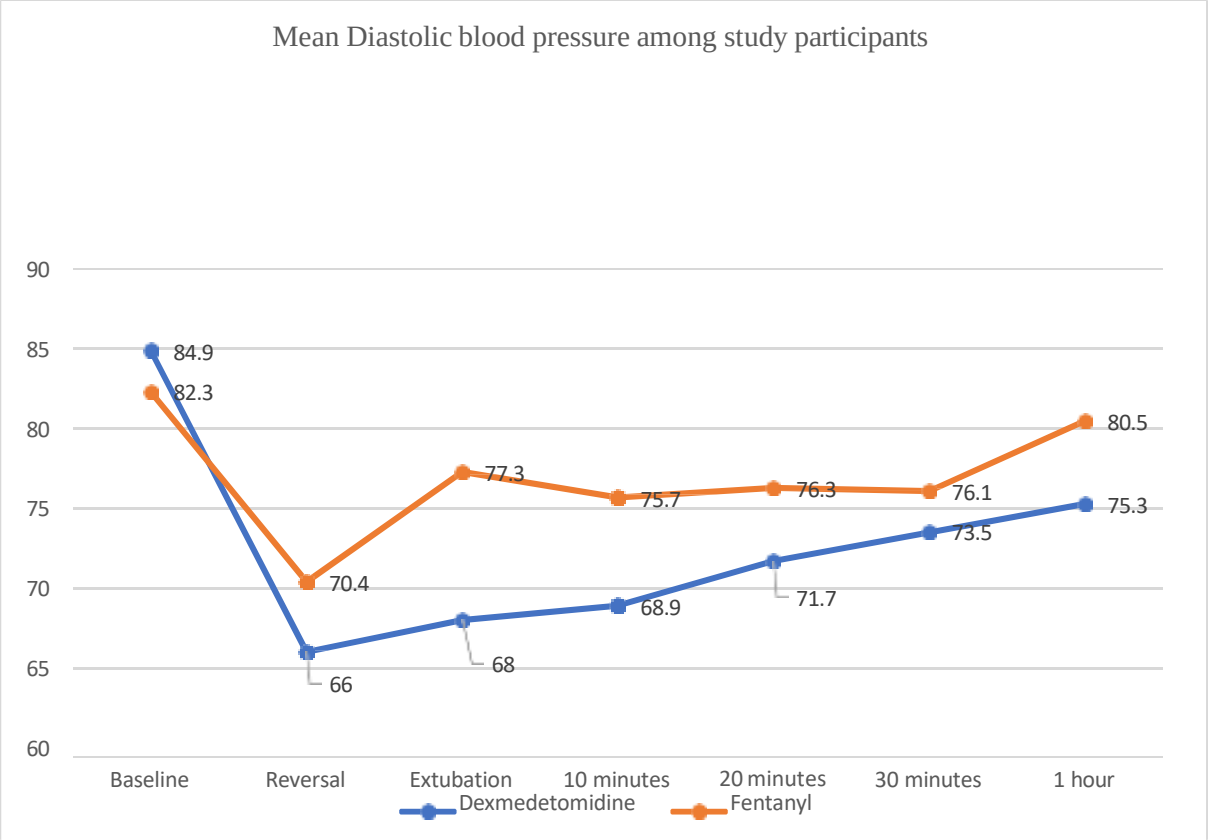


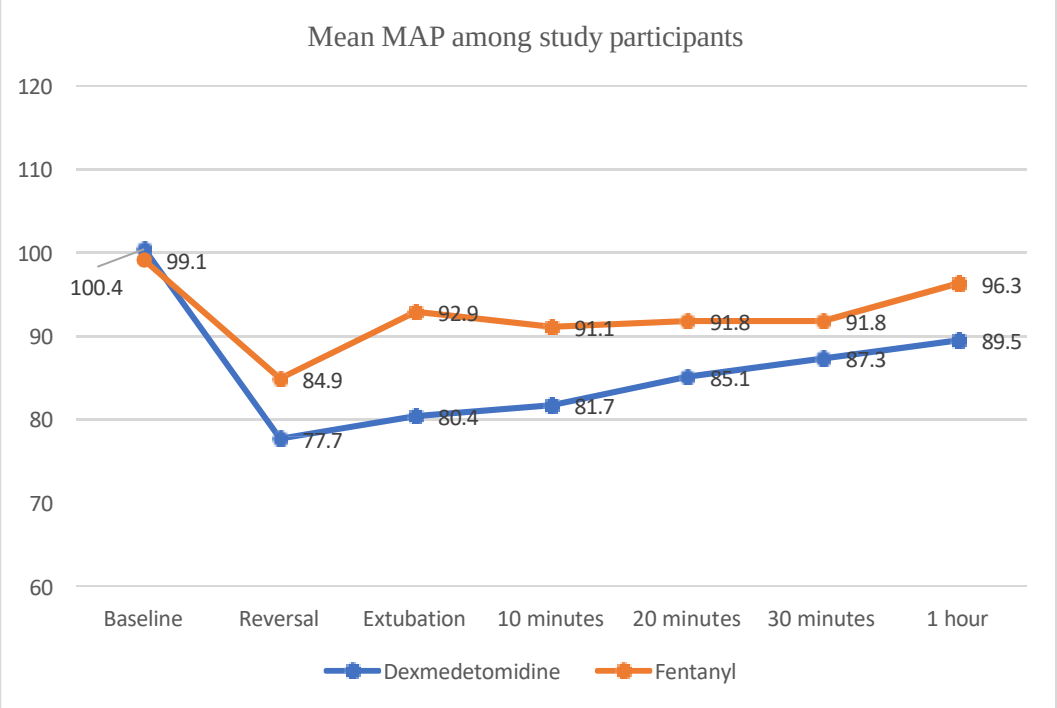
Table 1: Comparison of mean arterial pressure(MAP) among the participants of both groups at various time points (N=60)

Variables	Dexmedetomidine (n=30) mean (sd)	Fentanyl (n=30) mean (sd)	p value*
Baseline	100.4(11.6)	99.1(8.1)	0.62
Reversal	77.7(10.1)	84.9(8.8)	0.005
Extubation	80.4(9.1)	92.9(7.3)	<0.001
10 minutes	81.7(8.3)	91.1(7.7)	<0.001
20 minutes	85.1(7.6)	91.8(7.9)	0.001
30 minutes	87.3(7.4)	91.8(7.6)	0.02
1 hour	89.5 (7.1)	96.3(6.5)	<0.001

Table 1: shows the MAP measured at various time points following tracheal extubation in both groups. Unpaired t test was used to assess the association between both the groups. The MAP was lower at baseline in Fentanyl group compared to Dexmedetomidine group but it was statistically insignificant (p value 0.62). However, the MAP dropped at reversal, raised at

extubation in both the groups. Following reversal the raise in the MAP was higher in Fentanyl group compared to Dexmedetomidine at extubation and this was statistically significant (p value <0.001). The pressure dropped in the Fentanyl group following extubation at 10 minutes and again raised at 1 hour after extubation. On the contrary the MAP at extubation in Dexmedetomidine group slowly raised following extubation till 1 hour following it. However, the difference in the mean MAP values of both groups were statistically significant at reversal, extubation, 10 minutes, 20 minutes, 30 minutes and till 1 hour following extubation.

Figure 4:shows the mean MAP among the participants in Dexmedetomidine Group and Fentanyl group (N=60).



DISCUSSION

The present study was undertaken to compare the effect of intravenous Fentanyl 1mcg/kg versus intravenous Dexmedetomidine 1mcg/kg on attenuation of hemodynamic responses following tracheal extubation.

Tracheal extubation is crucial step following emergence from general anaesthesia. Following extubation there is a sudden increase in the HR and BP which are attributed to factors such as catecholamine release, airway irritation during suction, pain arising out of surgical wounds and emergence. Smooth extubation requires inhibition of the above.The commonly used adjuvant following general anasthesia is fentanyl. It is shown to reduce the hemodynamic responses which occur following a nociceptive stimuli triggered by intubation and extubation.

Nishina et al in their study showed that the optimal dose of fentanyl of 2mcg/kg given at the end of surgery reduces the cardiovascular changes associated with extubation and emergence without prolonging the time of recovery.[12] Dexmedetomidine is an alpha-2 agonist which decreases sympathetic activity with added sedative and anxiolytic properties. Numerous studies have shown that single dose of 0.5-1mcg/kg dexmedetomidine administered prior to extubation attenuates the hemodynamic changes which occur following extubation.[24]

In our study we have chosen the dose of 1mcg/kg for Fentanyl and Dexmedetomidine because we aimed at comparing the efficacy of the drug in attenuating the hemodynamic changes at a same dose and to avoid dose dependent variation in action of the drug.

In this study majority of the study participants belonged to 31-45 year age group and almost two third were females. Majority had ASA grade of I.The overall female participants in this study were more because only patients of thyroid surgery were included in this study and since thyroid abnormalities are more common in females that resulted in a higher female population.

In this study the mean HR at reversal was lowest compared to baseline in the Dexmedetomidine group and slowly started rising at extubation and the time following it. However, in the fentanyl group the mean HR dropped at reversal and rised at extubation. It again dropped at 10 mins following extubation and started rising in the subsequent time period.

Rani et al in their study also showed a similar finding where the HR in the Dexmedetomidine group was lower at all time interval following extubation compared to baseline value.[7] The rise in the HR at extubation was lower in the Dexmedetomidine group compared to the Fentanyl group and similar findings were obtained in the study by Nikhila et al.[25]

Turan et al[26] in their study showed that HR at extubation was higher than the post extubation values but the overall increase in HR was lower in Dexmedetomidine group. The rise in HR was about 20bpm which was higher compared to our study. The cause for such discrepancy is because a lower dose of 0.5 mcg/kg was used in that study compared to our study wherein 1mcg/kg was used. Similar results were obtained in study by Guler et al[23] and Goyal et al[27].

There was a rise in HR in the fentanyl group at extubation compared to Dexmedetomidine group in our study. Aksu et al[28] in their study also obtained a similar finding but they showed a rise in HR at extubation of both groups attributed to low dose dexmedetomidine used in that study. The sedative property of Dexmedetomidine contributes to the decrease in HR at extubation compared to Fentanyl group.

In our study the mean HR in the Dexmedetomidine group fell upto 20 bpm compared to baseline value and 16bpm in Fentanyl group. At extubation there was a rise of 2bpm in the Dexmedetomidine group and 10bpm in the Fentanyl group. Nikhila et al[25] in their study showed that mean HR rised upto 8bpm in the dexmedetomidine group and 21bpm in the Fentanyl group. Since they used Dexmedetomidine at a dose of 0.4mcg/kg and Fentanyl of 0.5mcg/kg it resulted in a greater mean HR at extubation compared to our study findings.

Nishina et al in their study showed that the optimal dose of Fentanyl in the reduction of HR occurring at extubation was 2mcg/kg.12 Since we used a lower dose of 1mcg/kg it resulted in an increased HR at extubation in Fentanyl group.

The mean SBPand DBP of the Dexmedetomidine group dropped at reversal and rised at extubation and subsequent time period following extubation in this study. However, in the Fentanyl group there was a drop at reversal and rise at extubation. Following extubation there was a fall in the BP and it began to rise subsequently.

Nikhila et al62 in their study showed that when Dexmedetomidine was given at a dose of 0.4mcg/kg there was an increase in SBP at extubation and returned to normal after 2 mins. Whereas when Fentanyl was given at a dose of 0.5mcg/kg the increase in SBP at extubation was more compared to Dexmedetomidine group. The rise in the DBP at extubation was more in the Fentanyl group compared to Dexmedetomidine group. These findings were consistent with our study findings.

In our study the SBP fell upto 30 mmHg in Dexmedetomidine group and 20 mmHg in the Fentanyl group. At extubation there was a rise of 4 mmHg in Dexmedetomidine group and 11 mmHg in Fentanyl group. Nikhila et al6 in their study showed that the SBP at extubation rised upto 14 mmHg in Dexmedetimidine group and upto 29 mmHg in Fentanyl group. The mean DBP in our study fell upto 19 mmHg compared to baseline in Dexmedetomidine group and 12mmHg in Fentanyl group. At extubation there was a rise of 2 mmHg in Dexmedetomidine group and 7 mmHg in Fentanyl group. In the study by Nikhila et al62 at extubation the rise in the DBP was 7mmHg in Dexmedetomidine group and 16mmHg in the Fentanyl group. The rise was higher in that study compared to our finding because a lower dose of Dexmedetomidine and Fentanyl were used in that study.

Nikhila et al[25] in their study showed that the MAP of Dexmedetomidine group rised upto 8mmHg and Fentanyl group rised upto 17mmHg. This rise was more compared to our study findings because lower dose drug were used in that study compared to our study. Liyakhath et al[11] in their study showed that MAP in the Dexmedetomidine group and Fentanyl group rised at reversal and extubation. The rise was 13mmHg in the Fentanyl group and 11 mmHg in the Dexmedetomidine group. These findings were close to that obtained in our study.

In our study the HR, SBP, DBP and MAP dropped at reversal and rised at extubation in both groups. All the hemodynamic variables were around the baseline value at extubation in the Fentanyl group and remained the same throughout the study period. In the

Dexmedetomidine group all the hemodynamic variables decreased below the baseline at extubation and remained same till end of the study. These findings were similar to that obtained by Liyakhath et al.[11]

Strengths of the study include use of optimal dose of Dexmedetomidine 1mcg/kg and measurement of baseline, reversal values and till 1 hour following extubation for comparison of hemodynamic parameters at various time points.

Limitations of the study is that we have done the study as a comparative cross sectional study, but the study design as a randomised controlled trial would be an appropriate study design to see the effectiveness of a drug and long term outcomes. The optimal dose of Fentanyl is 2mcg/kg but a dose of 1mcg/kg was used in this study. Extubation quality scales are available which can be used to grade the quality of anaesthesia and sedation post extubation.

CONCLUSION

This study was carried out to determine if intravenous Dexmedetomidine at the dose of 1mcg/kg infusion over 10 minutes prior to extubation is advantageous over intravenous Fentanyl 1mcg/kg 10 minutes before extubation to attenuate the hemodynamic stress response to tracheal extubation.

The results clearly confirm that both Dexmedetomidine and Fentanyl attenuates the hemodynamic stress response to extubation. Use of Dexmedetomidine prior to extubation is superior compared to Fentanyl in attenuating hemodynamic parameters such as HR, SBP, DBP and MAP.

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