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Original Research Article

Comparison of two different doses of dexmedetomidine in attenuation of haemodynamic response during endotracheal extubation

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ABSTRACT

Introduction: The data in the published literature on the use of dexmedetomidine in various dosages during extubation from India is modest. We have compared the effectiveness of intravenous dexmedetomidine 0.5 µg/Kg body weight and 0.75 µg/Kg body weight during endotracheal extubation.

Materials and Methods: Seventy-four patients aged more than 18 years posted for elective surgery under general anaesthesia were included in this randomised double-blind controlled study. Group D1 and Group D2 patients received 0.5 µg/Kg and 0.75 µg/Kg body weight intravenous dexmedetomidine respectively. The primary outcome measures were to compare haemodynamic parameters, whereas secondary outcome measures were to compare extubation quality, and post-extubation sedation.

Results: The mean heart rate at reversal, and after endotracheal extubation was considerably elevated in group D1 as compared to D2. The mean systolic blood pressure, diastolic blood pressure and mean arterial pressure after endotracheal extubation were considerably elevated in group D1 as compared to D2. The mean respiratory rate at reversal, and after endotracheal extubation were considerably elevated in Group D1 as compared to Group D2. The mean sedation score after endotracheal extubation was considerably elevated in Group D2 as compared to Group D1.

Conclusions: The haemodynamic parameters were better in Group of patients who received intravenous dexmedetomidine 0.75 µg/Kg body weight as compared to Group of patients who received dexmedetomidine 0.50 µg/Kg during endotracheal extubation.

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1. Introduction

Endotracheal extubation is one of the frequently performed procedures in the practice of anaesthesiology. Emergence from general anaesthesia and tracheal extubation is often accompanied with tachycardia and hypertension.¹ This increase in blood pressure and heart rate are transitory, variable and unpredictable. The post-operative hypertension warrants immediate assessment and treatment to reduce the risks of myocardial infarction, arrhythmias, congestive

heart failure, cerebrovascular accidents, bleeding and other end organ damage. Respiratory complications after tracheal extubation such as coughing, sore throat, laryngospasm, bronchospasm and laryngospasm are common.^{2,3}

Various methods used to attenuate these pressor response are extubation with deep anaesthesia,^{4,5} reduction of time of laryngoscopy,⁶ utilization of laryngeal mask airway,^{7,8} nitrates,⁷ prostaglandins,⁹ magnesium sulphate,¹⁰ calcium channel blockers,^{11–13} local anaesthetics topical spray,^{14–16} intravenous (IV) beta blockers,^{17–19} and IV narcotics^{15,20,21} prior to extubation. Every method used to obtund the pressor response has its advantages and disadvantages.

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An α_2 -adrenergic agonists have been introduced to clinical anaesthesia for their sympatholytic, sedative, anaesthetic sparing and haemodynamic stabilizing properties. The α_2 agonists reduce the sympathetic seepage and noradrenergic action; hence, hemodynamic fluctuations taking place at the instant of extubation due to augmented sympathetic stimulus are controlled.²² Clonidine has been studied in this aspect.¹⁹ Dexmedetomidine is an imidazoline derivative directly acting α_2 adrenoreceptor agonist. Dexmedetomidine has shown analgesic effects without significant respiratory depression.²³

The data in the published literature on the use of dexmedetomidine in various dosages during extubation from India is modest. The aim of the present study was to compare the efficacy of IV dexmedetomidine at the dosage of 0.5 $\mu\text{g/Kg}$ body weight and 0.75 $\mu\text{g/Kg}$ body weight given as an infusion over 10 minutes in attenuating haemodynamic pressor response to endotracheal extubation.

2. Materials and Methods

The present study was conducted after approval from the institutional ethics committee between April 2016 and December 2016 in the Department of Anaesthesiology, tertiary care hospital, Pune, India. Before enrolment, the patients were explained regarding the risks and benefits of the procedure. We obtained the written informed consent from all the patients. Patients more than 18 years of age posted for elective surgery under general anaesthesia, and falling into American Society of Anaesthesiologist (ASA) grades I and II were included. Patients with heart block, on beta blockers, body mass index was $> 30 \text{ Kg/m}^2$ and pregnant women were excluded.

Out of 80 patients assessed for eligibility, after exclusion, 74 patients were randomly divided into two equal groups of 37 each with the help of www.randomizer.org (Diagram 1). The program was known as research randomizer. The program produced two sets of random numbers out of the range of numbers provided (for e.g. 1- 74) by taking user input on having uniqueness of the numbers to be generated. For the present study, the program produced two sets of 37 unique numbers per set. The sheet of the random numbers was ready before the study was started. Group D1 and Group D2 patients received 0.5 $\mu\text{g/Kg}$ and 0.75 $\mu\text{g/Kg}$ body weight IV dexmedetomidine respectively. Both, the patients and researcher were blind for D1 and D2 group.

Pre-anaesthetic evaluation was done on the evening before surgery and patient was kept nil per orally for solids from night 10 p.m. before surgery. An IV line was obtained with 20 G cannula. Patient was connected to multi-parameter monitor for recording heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR), SPO_2 , and ECG. The baseline HR, SBP, DBP, MAP, RR, and SPO_2 were recorded. The patient was premedicated with

IV glycopyrrolate 0.004 mg, IV midazolam 0.04mg/Kg, IV fentanyl 2 $\mu\text{g/Kg}$ and IV Ondansetron 0.08 mg/Kg. Anaesthesia was induced with Inj propofol 2 mg/Kg followed by IV vecuronium 0.1 mg/Kg for muscle relaxation and cuffed endotracheal tube was passed smoothly. Intra-operatively patient's HR, SBP, DBP, MAP, RR, and SPO_2 were monitored. Patients were extubated by the anaesthesiologist when the following criteria are fulfilled: sustained head lift for 5 seconds, sustained hand grip for 5 seconds, and adequate level of consciousness.

HR, SBP, DBP, MAP, RR, and SPO_2 readings baseline (just prior to test drug infusion), 1, 3, 5, 7 and 10 minute during infusion, following reversal administration, just before extubation, after-extubation 1, 3, 5, 7, 10, 15, 45, 75, and 105 minute were recorded. A 5 point rating Extubation Quality Score was used to evaluate the quality of extubation.⁶ A 6 point Ramsay Scale was used to assess the post-operative sedation.⁷ The sedation score was recorded at 3, 5, 7, 10, 15, and 45 minutes post-extubation.

The primary outcome measures were to compare haemodynamic parameters such as HR, SBP, DBP, MAP, whereas secondary outcome measures were to compare extubation quality and post-extubation sedation. The previously published study was used to find the sample size.²⁴ A formula $N = \{2SD^2(Z_{\alpha} + Z_{\beta})^2\} / \Delta^2$ was used to calculate the sample size.²⁵ We have taken Z_{α} a standard normal variate at 5% type I error (1.96) and Z_{β} the standard normal deviate for β power 80% at type II error (0.84). Total sample size of 37 was calculated by above method.

3. Results

Of 80 patients assessed for eligibility, 6 were excluded because of patients on beta blockers (3), body mass index was $> 30 \text{ Kg/m}^2$ (3). Seventy-four patients were randomized into two groups of 37 each, Group D I and Group D 2 (Diagram 1). The mean age, gender, mean weight and ASA grades were comparable between the two groups (Table 1).

The mean HR at baseline, 5-min, 7-min 10-min during infusion, at extubation, 45-min, 75-min, 105-min and 135-min after extubation were comparable between two intervention groups. The mean HR at 1-min and 3-min during infusion were considerably elevated in group D2 as compared to D1, whereas the mean HR at reversal, 1-min, 3-min, 5-min, 7-min, 10-min and 15-min after extubation were considerably elevated in group D1 as compared to D2 (Figure 1).

The mean SBP at baseline, 10-min during infusion, at reversal, at extubation, 45-min, 75-min, 105-min and 135-min after extubation did not differ significantly between two intervention groups. The mean SBP at 1-min, 3-min, 5-min and 7-min through infusion were significantly elevated in group D2 as compared to D1, whereas the mean SBP at 1-min, 3-min, 5-min, 7-min, 10-min and 15-min after extubation were considerably elevated in group D1 as

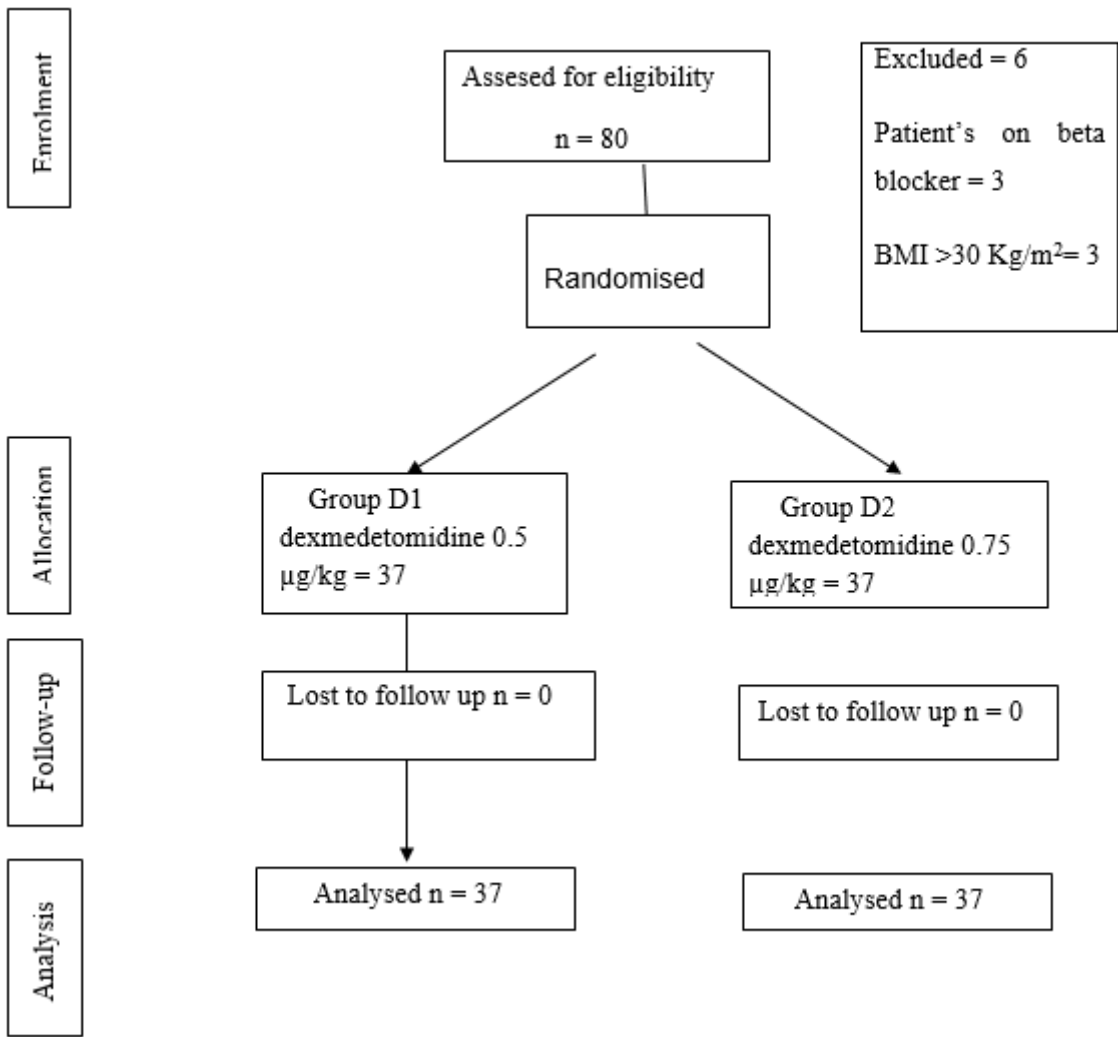


Diagram 1: Consort diagram

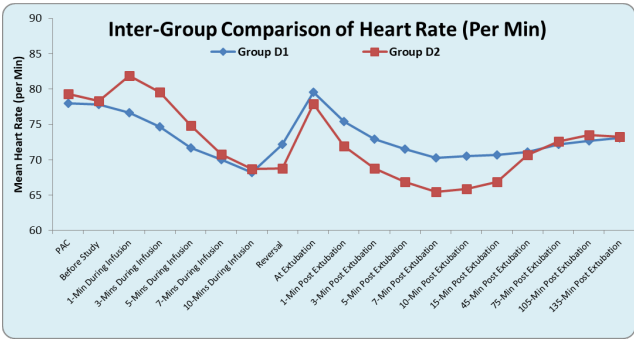


Fig. 1:

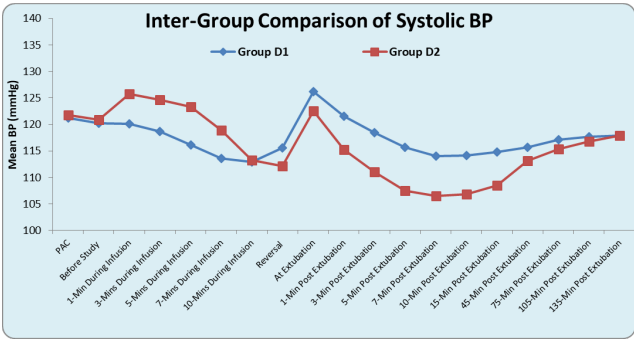


Fig. 2:

compared to D2 (Figure 2).

The mean DBP at baseline, 1-min, 3-min, 5-min, 7-min 10-min during infusion, at reversal, 1-min, 75-min

and 105-min after extubation were comparable between two intervention groups. The mean DBP at extubation, 3-min, 5-min, 7-min, 10-min, 15-min, 45-min and 135-min

after extubation were considerably elevated in group D1 as compared to D2 (Figure 3).

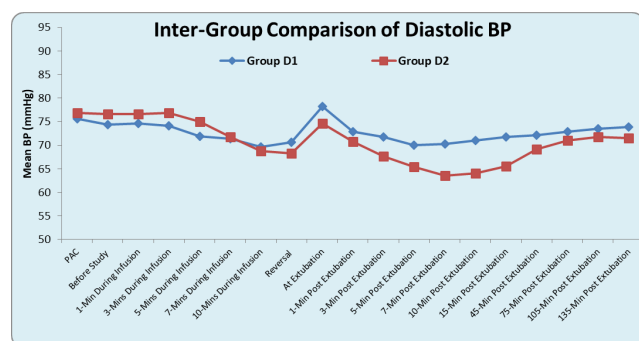


Fig. 3:

The mean MAP at baseline, 7-min, 10-min during infusion, at reversal, 1-min, 75-min, 105-min and 135-min after extubation were comparable between two intervention groups. The mean MAP at 1-min, 3-min and 5-min during infusion were considerably elevated in group D2 as compared to D1, whereas the mean MAP at extubation, 3-min, 5-min, 7-min, 10-min, 15-min and 45-min after extubation were considerably elevated in group D1 as compared to D2 (Figure 4).

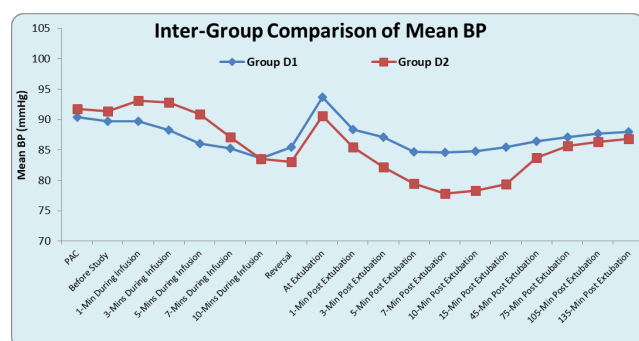


Fig. 4:

The mean SPO₂ throughout the procedure were comparable between two intervention groups. The mean RR at baseline, 1-min., 3-min, 5-min, 7-min, 10-min during infusion, 1-min, 3-min, 5-min 7-min after extubation were comparable between two intervention groups. The mean RR at reversal, at extubation, 10-min, 15-min, 45-min, 75-min, 105-min and 135-min after extubation were considerably elevated in Group D1 as compared to Group D2 (Figure 5).

The mean sedation score at 3-min, 5-min, 7-min and 10-min after extubation were considerably elevated in Group D2 as compared to Group D1, whereas the mean sedation score at 15-min and 45-min after extubation were comparable between two intervention groups (Table 2).

In Group D 1, the extubation quality score 1 and 2 was observed in 28/37 (75.7%) and 9/37 (24.3%) patients

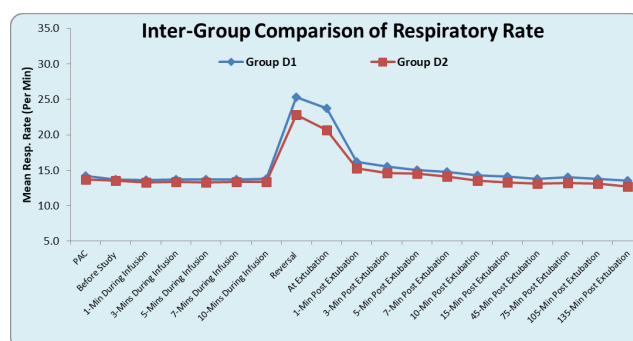


Fig. 5:

respectively whereas in Group D2, the extubation quality score 1 and 2 was observed in 27/37 (73.0%) and 10/37 (27.0%) patients in respectively (p-value = 0.999).

4. Discussion

For the major surgical procedures, endotracheal intubation is an essential element of the current anaesthesia techniques. Tachycardia, hypertension, arrhythmias, myocardial ischemia, coughing, agitation, bronchospasm, increased bleeding, raised intracranial and intraocular pressure are linked with intubation and extubation.¹ Various anaesthetic methods and drugs are used to control haemodynamic response to the endotracheal extubation, The technique or drug of choice depends on the necessity and duration of operation, choice of anaesthetic technique, route of administration, and medical condition of the patient.

Recently dexmedetomidine, a potent α_2 -adrenoreceptor agonist has been used to facilitate extubation in surgical intensive care unit. The role of dexmedetomidine in the reduction of hemodynamic and airway reflexes during extubation in general anaesthesia is limited. During extubation a single dose of dexmedetomidine has been found to be effective in decrease of the airway and circulatory reflexes.

In a study conducted by Jain D et al.²² to evaluate the effect of dexmedetomidine on stress response to extubation, it is reported that there was considerable drop in pulse rate 7-10 minutes after the start of bolus dose of dexmedetomidine (p-value < 0.05). It was further reported that the pulse rate remained below the pre-dexmedetomidine values at all time intervals subsequent extubation. There was no considerable change in blood pressure. The authors concluded that bolus dose of dexmedetomidine can provide hemodynamic stability associated with extubation.

Seo KH et al.²⁶ reported that HR, SBP and DBP after drug administration were significantly lower in all three dexmedetomidine groups compared with controls. They concluded that IV infusion of 0.5 μ g/Kg dexmedetomidine 30 min before the end of surgery attenuated the haemodynamic responses during emergence. The study

Table 1: Baseline characteristics

Characteristics	Group D1 n = 37	Group D2 n = 37	Total	p- value
Age (years), mean $\pm$ SD	37.4 $\pm$ 12.7	38.3 $\pm$ 11.3		0.790*
Gender				
Male	21 (56.8)	18 (48.6)	39 (52.7)	0.485**
Female	16 (43.2)	19 (51.4)	35 (47.3)	
Weight (Kg), mean $\pm$ SD	56.4 $\pm$ 8.3	55.6 $\pm$ 7.4		0.680*
ASA grade (%)				
Grade I	19 (51.4)	22 (59.5)	41(55.4%)	0.483**
Grade II	18 (48.6)	15 (40.5)	33 (44.6%)	

*Unpaired t-test was used, **Chi square test was used

ASA - American Society of Anaesthesiologist

SD- Standard deviation

Table 2: Inter-group comparison of mean sedation score

Post-extubation in minutes $\pm$ SD	Group D1 n = 37	Group D2 n = 37	p- value
3	2.1 $\pm$ 0.3	2.9 $\pm$ 0.3	0.001
5	2.0 $\pm$ 0.2	2.8 $\pm$ 0.4	0.001
7	2.0 $\pm$ 0.2	2.6 $\pm$ 0.5	0.001
10	2.0 $\pm$ 0.3	2.2 $\pm$ 0.4	0.002
15	2.0 $\pm$ 0.2	2.0 $\pm$ 0.2	0.999
45	2.0 $\pm$ 0.3	2.0 $\pm$ 0.2	0.999

Unpaired t-test was used

SD- Standard deviation

further reported that dexmedetomidine doses higher than 0.5 $\mu\text{g/Kg}$ did not exert additional positive effects on cardiovascular responses.

Sim JH et al.²⁷ studied the effects of different loading doses of dexmedetomidine on sedation. The study was designed to investigate the clinical effects and complications of different loading doses, 0.5 and 1.0 $\mu\text{g/Kg}$. They found that Ramsay score was significantly lower in 0.5 $\mu\text{g/Kg}$ group as compared to 1.0 $\mu\text{g/Kg}$ group. The study concluded that higher loading dose (1.0 $\mu\text{g/kg}$) of dexmedetomidine can lead to faster sedation without any severe complications.

Bindu B et al.²⁴ concluded that dexmedetomidine 0.75 $\mu\text{g/Kg}$ administered 15 min before extubation, stabilized hemodynamics and facilitated smooth extubation. The mean HR, SBP, DBP and MAP were significantly lower in dexmedetomidine group of patients as compared to placebo (normal saline). Extubation quality score was 2 and 3 in 21/25 (84.0%) and 4/25 (16.0%) patients in dexmedetomidine group respectively, whereas extubation quality score was 2 and 3 in 4/25 (16.0%) and 21/25 (84.0%) patients in placebo group respectively (p-value 0.04). Ramsay sedation scale was 2 and 3 in 4/25 (16.0%) and 21/25 (84.0%) patients in dexmedetomidine group respectively, whereas Ramsay sedation scale was 2 and 3 in 21/25 (84.0%) and 4/25 (16.0%) patients in placebo group respectively (p-value 0.017).

5. Limitations

The study was conducted in a single center with small sample size which included only stable ASA class I or II patients. Therefore, our findings cannot be extrapolated to the patients with significant co-morbidities. Adverse events such as arrhythmias, hypotension, hypertension, vomiting and dry mouth were not recorded during post-operative period. Multicentric studies with a large sample size should be undertaken to substantiate the research findings described in this paper.

6. Conclusions

The mean heart rate at reversal, and after extubation was considerably elevated in group D1 as compared to D2. The mean systolic blood pressure, diastolic blood pressure, and mean arterial pressure after extubation were considerably elevated in group D1 as compared to D2. The mean respiratory rate at reversal, and after extubation was considerably elevated in Group D1 as compared to Group D2. The mean sedation score after extubation was considerably elevated in Group D2 as compared to Group D1. The extubation quality score between the two groups was comparable.

7. Source of Funding

None.

8. Conflict of Interest

None.

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