TO EVALUATE AND COMPARE THE EFFECTIVENESS OF IV DEXMEDETOMIDINE AND IV LIDOCAINE ON ATTENUATION OF HAEMODYNAMIC RESPONSES AND AIRWAY REFLEXES DURING EXTUBATION

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ABSTRACT

BACKGROUND
Endotracheal intubation is an integral part of the modern anaesthesia techniques for major surgical procedures. Extubation are associated with various cardiovascular and airway responses leading to tachycardia, hypertension, arrhythmias, myocardial ischemia, coughing, agitation, bronchospasm etc., Many techniques and drugs have been proposed to attenuate airway and cardiovascular responses. This study intends to compare the effect of Dexmedetomidine & Lidocaine on hemodynamic responses and airway reflexes during tracheal extubation.

MATERIALS AND METHODS
After getting Ethical Committee clearance and written informed consent, double blinded randomised clinical trial study was conducted. 100 patients of ASA grade 1 & 2 aged between 16 to 60 years of either gender undergoing surgery under general anaesthesia were randomized into 2 groups with 50 each. Group D received Dexmedetomidine 0.75 mcg/kg and Group L received Lidocaine 1.5 mg/kg, both diluted to 10ml and given intravenously over 1min. Pulse rate, systolic, mean and diastolic blood pressure was recorded at the time of administration of the drug, at 1min, 3min, 5min after administering the drug and at extubation. Also, post extubation at 1min, 3min, 5min, 10min, 15min, 20min, 25min and 30min, it was recorded. Extubation quality was rated using extubation quality using 5-point scale. Sedation level was evaluated using Ramsay Sedation Scale. Any incidence of cough, laryngospasm, bronchospasm or desaturation was observed. Time at which the rescue analgesia was required post extubation was recorded.

RESULTS
The quality of extubation in group D was significantly better than group L (p<0.05). The sedation level was significantly higher in Group D as compared to Group L (p<0.01). The Time gap between the end of the surgery and the time of requirement of first dose of rescue analgesic was significantly higher in group D than in group L. MAP values showed a significant difference between the two groups (p<0.001) at various time intervals. The incidence of hypotension was noted during the study period was statistically significant.

CONCLUSION
Single bolus 0.75 mcg/kg dose of dexmedetomidine is an effective method to attenuate the haemodynamic response to endotracheal extubation in patients undergoing surgery under General anaesthesia and decreased the complications associated with extubation.

KEYWORDS
Extubation, Dexmedetomidine, lidocaine.


BACKGROUND
Endotracheal intubation is an integral part of the modern anaesthesia techniques for major surgical procedures. Both intubation and extubation are associated with various cardiovascular and airway responses leading to tachycardia, hypertension, arrhythmias, myocardial ischemia, coughing, agitation, bronchospasm, increased bleeding, raised intracranial and intraocular pressure. Complications of extubation like bucking (Gagging caused by involuntarily resisting positive pressure ventilation in a patient with an
Dexmedetomidine, an alpha receptor agonist has been used to attenuate the stress response to intubation. Administered after induction, Dexmedetomidine was found to reduce the prevalence of emergence agitation.\(^2\) The dose of Dexmedetomidine ranges from 0.5-1 mcg/kg.

Lidocaine attenuates the hemodynamic response to tracheal extubation by its direct myocardial depressant effect, central stimulant effect, peripheral vasodilatory effect and finally it suppresses the cough reflex, an effect on Synaptic transmission.

**Aim of the Study**

This study intends to compare the effects of Dexmedetomidine & Lidocaine on hemodynamic responses and airway reflexes during tracheal extubation.

**MATERIALS AND METHODS**

After approval by the Ethical Committee and written informed consent from the patients or their relatives, double blinded randomized clinical trial study was conducted from August 2013 to July 2016 in Department of Anaesthesiology, Institute of medical sciences, BHU Varanasi. 100 patients of ASA grade 1 & 2 aged between 16 to 60 years of either gender undergoing surgery under general anaesthesia were taken up for the study.

Demographic and clinical data, including age, gender, date of enrolment, medical or surgical condition, laboratory and radiological reports was noted down. The patients were assigned to one of two groups in equal numbers with 50 patients in each group by randomization by computer generated random numbers into 2 groups. Group D received Dexmedetomidine 0.75 mcg/kg, diluted to 10ml and Group L received Lidocaine 1.5 mg/kg, diluted to 10ml in the above-mentioned dose was given intravenously over 1min when the last skin suture towards the end of surgery.

Patients suffering from cardiac and pulmonary disease, surgeries on neck and oral cavity, with history of drug abuse or psychiatric disorder, Obese patients, with difficult airway or history of sleep apnoea, Pregnant and breast-feeding women, patients taking medications that affect the BP & HR were excluded from the study.

Patients were premedicated with tablet alprazolam 0.5mg in the evening before surgery and in the morning on the day of surgery.

On the day of surgery, standard ASA monitors like electrocardiography (ECG), oxygen saturation (SpO\(_2\)), and non-invasive blood pressure (NIBP), end-tidal carbon-dioxide (EtCO\(_2\)) was attached to the patient. An intravenous catheter (18G) was inserted in a peripheral vein. The patients were pre-medicated Inj. Midazolam 0.025 mg/kg and Inj. Fentanyl 2 mcg/kg given intravenously. After preoxygenation, they were induced with Inj. Propofol 2 mg/kg and intubation facilitated with Inj. Vecuronium 0.1 mg/kg given intravenously. After induction with general anaesthesia, it was maintained with 66% nitrous oxide and 33% oxygen and isoflurane 1%-2% and intermittent Inj. Vecuronium and Inj. Fentanyl. Normothermia was ensured. Nitrous oxide was discontinued at the end of surgery. Residual neuromuscular blockade was reversed using Inj. Neostigmine 0.05 mg/kg and Inj. Glycopyrrolate 0.01 mg/kg given intravenously when spontaneous respiratory efforts were observed. Patients were extubated when extubation criteria were fulfilled. The Pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), oxygen saturation (SpO\(_2\)) was noted at the time of administration of the drug, at 1min, 3min, 5min after administering the drug and at extubation. Also, post extubation at 1min, 3min, 5min, 10min, 15min, 20min, 25min and 30min, it was recorded. Extubation quality was rated using extubation quality using 5-point scale (1. No coughing, 2. Smooth extubation, minimal coughing, 3. Moderate coughing (3 or 4 times), 4. Severe coughing (5 to 10 times) and straining, 5. Poor extubation, very uncomfortable (Laryngospasm and coughing >10 times).

Sedation level was evaluated using Ramsay Sedation Scale (1. Anxious and agitated, restless, 2. Co-operative, oriented, tranquil, 3. Responsive to verbal commands, drowsy, 4. Asleep*, responsive to light stimulation (loud noise, tapping),

5. Asleep, slow response to stimulation, 6. No response to stimulation). Any incidence of cough, laryngospasm, bronchospasm or desaturation was observed for a period of 30 min post extubation. Time at which the rescue analgesia was required post extubation was recorded.

Statistical analysis was done using SPSS 16. For comparing two groups, Student’s t test was used and for paired samples, Paired Student’s t test was used. For categorical variables Chi square test and Fisher’s – exact test were used. Correlations were determined by Pearson ranked correlation coefficient. p value <0.05 considered as statistically significant.

**RESULTS**

Baseline patient characteristics like age, sex and initial oxygen saturation were comparable in all the groups.

<table>
<thead>
<tr>
<th>Quality of Extubation Score</th>
<th>Group D</th>
<th>Group L</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>1</td>
<td>38</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
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<td>24</td>
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<td>3</td>
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<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>50</strong></td>
<td><strong>100</strong></td>
</tr>
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</table>

Table 1. Quality of Extubation

\(\chi^2=6.316; p=0.043\)
The quality of extubation in group D was significantly better than group L (p<0.05). In Group D, the score was 1 and 2 in 38(76%) and 12(24%) respectively whereas in group L, the scores were 1, 2 and 3 in 27(54%), 21(42%) and 2(4%) respectively (Table 1). The sedation level was significantly higher in Group D as compared to Group L (p<0.01). In group D, score of 2 was found in 18(36%) patients and 3 in 32(64%), whereas in Group L, score of 1 was found in 38(76%) patients and 2 in 12(24%) patients (Table 2). The Time gap between the end of the surgery and the time of requirement of first dose of rescue analgesic was noted which was significantly higher in group D than in group L in respect to heart rate.

* Denotes p<0.01, when group D is compared with group L with respect to MAP.

† Denotes p<0.01, when group D is compared with group L in respect to heart rate.
group L i.e., 40.66 min in group D and 10.98 in group L (Table 3).

The baseline MAP was comparable among the groups. After administration of the study drugs, a significant reduction of MAP from the baseline value was observed in Group D (at 1, 3, 5min). This was followed by a significant increase from the baseline during and for a period of time after extubation (at Ext, Posttext_1, 3, 5min) following which it decreased towards the baseline and below the baseline value (at Ext Posttext_10, 15, 20, 25, 30). In group L, after administration of study drug, there was no significant change from the baseline values (at 1, 3, 5min.) but showed a significant increase at and for a period after extubation (at Ext, Posttext_1, 3, 5min,) following which although it gradually decreased from the values at extubation it still remained above the baseline values.

Comparing the MAP values showed a significant difference between the two groups (p<0.001) at various time intervals (Table 4).

The baseline HR was comparable among the groups. After administration of the study drugs, a significant reduction of HR from the baseline value was observed in Group D (at 1, 3, 5 min). It was followed by a significant increase from the baseline during and immediately after extubation (at Ext, Posttext_1, 3, 5 min) following which it decreased towards the baseline and below the baseline value (at Ext Posttext_10, 15, 20, 25, 30). Whereas, in group L, after administration of study drug, there was no significant change from the baseline values (at 1, 3, 5min) but showed a significant increase at and for a period after extubation (at Ext, Posttext_1, 3min) following which, although it gradually decreased from the values at extubation it still remained above the baseline value.

The incidence of hypotension was noted during the study period and was present in 8(16%) in the D group and 1(2%) in the L group. which is statistically significant. No significant differences were found between the groups for incidence of bradycardia.

**DISCUSSION**

Endotracheal intubation is an integral part of the modern anaesthesia techniques for major surgical procedures. Dexmedetomidine offers a unique pharmacological profile with sedation, sympatholysis, analgesia, cardiovascular stability and with great advantage to avoid respiratory depression.\(^4\) In previous studies dexmedetomidine as a single pre-anaesthetic dose has been used in dose ranges from 0.5 to 2.0 mcg/kg. In our study we used a dose of 0.75 mcg/kg (Group D). We compared this with the use of Lignocaine 1.5 mg/kg (Group L).

Dexmedetomidine helps in attenuation of airway reflexes like coughing, bucking during extubation and thus improving the extubation quality score.\(^4\) In vitro studies states α2 stimulation can cause smooth muscle relaxation thereby preventing bronchoconstriction. We found that a score of 1 and 2 were obtained in 80% and 20% patients of Group D respectively. Whereas in group L, 55 % patients had score 1 and 45% with score 2.

The sedative properties of dexmedetomidine are well documented.\(^5,6\) The hypnotic and sedative action of dexmedetomidine is thought to be mediated primarily by post synaptic α2 adrenergic receptors. These effects differ depending on receptor location; in the locus caeruleus. Decreased noradrenergic output from the locus coeruleus allows for increased firing of inhibitory neurons including the γ-amino butyric acid system resulting in anxiolysis and sedation.\(^7\) In healthy volunteers, IV dexmedetomidine 0.5 to 1 mcg/kg caused sedation within 5 min and reached maximum effects at 15 min. Higher degree of sedation (score 3 in 64% and Score 2 in 36% in group D compared to score 1 in 76%, 2 in 24% of patients) were obtained in this study.

The activation of α2 adrenoceptors, imidazoline preferring receptors, or both in the ventrolateral medulla and especially in the solitary nucleus tract by dexmedetomidine causes bradycardia. In our study, 6 out of 50 patients of group D had bradycardia compared to 0 out of 50 in Group L. This may be due to a higher dose of dexmedetomidine used in our study (0.75 mcg/kg v/s 0.50 mcg/kg). Vivek et al 2015, found only one case of bradycardia in his study.\(^8\)

In our study, Patients of both groups showed a significant rise in HR and BP during and after extubation possibly because of light planes of anaesthesia due of discontinuation of volatile agents and N2O just before extubation. In our study, Lesser rise in HR during Ext and Post Ext 1min was observed in group D compared to group L (P<0.05) which is due to dexmedetomidine induced central inhibition of sympathetic outflow by activation of receptors in vasomotor center, reducing catecholamine levels, reducing nor epinephrine turnover, resulting in alterations in sympathetic function enhanced vagal activity and decreased HR and BP through.\(^9\)

Hypotension was observed in 8 out of 50 patients in Group D and 1 out of 50 patients in Group L which was statistically significant. Similarly, incidences of Bradycardia were also significant. This shows the need to excise caution using a single bolus dose of dexmedetomidine as an anaesthetic and analgesic adjuvant.

This effect of Dexmedetomidine on haemodynamics has been seconded by various studies. Jaakola et al, in their study concluded that dexmedetomidine attenuates the increase in heart rate and blood pressure during intubation.\(^10\) Scheinm et al studied the effect of dexmedetomidine on tracheal intubation. They concluded that the drug attenuated the hemodynamic response to intubation. Xuexin et al compared the effect of pre-anaesthetic single dose dexmedetomidine given in a dose of 0.6 mcg/kg with similar infusion of normal saline in 60 patients who underwent gynaecological laparoscopy and they reported that a single dose of dexmedetomidine given before induction of general anaesthesia significantly decreased the stress hormone response to endotracheal intubation and kept haemodynamics more stable and contributed to perioperative safety.\(^11\)
The administration of dexmedetomidine before the completion of major surgery significantly reduced the early post-operative need for morphine. We found that patients of group D, required rescue analgesia after 41 min post extubation whereas in group L, the requirement of rescue analgesia was at 11 min and thus was statistically significant (p<0.05).

Our study has too limitations. We used a single dose and didn't take the dose response into consideration.

CONCLUSION

We concluded that a single bolus 0.75 mcg/kg dose of dexmedetomidine is a safe and effective method to attenuate the haemodynamic response to endotracheal extubation in patients undergoing surgery under General anaesthesia and decreased the complications associated with extubation and had excellent recovery profiles. However, the single dose may not be so efficacious in decreasing the postoperative analgesic requirement in the first 24 hr postoperative period. Further studies can be carried out in this domain before concluding the use of dexmedetomidine for post op analgesia.

REFERENCES