CAN DEXMЕDЕТОМІDІNЕ PREMEDICATION OBTUND THE INTRAOCULAR PRESSURE RISE AFTER SUXAMETHONIUM AND ENDOTRACHEAL INTUBATION
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HOW TO CITE THIS ARTICLE:

ABSTRACT: BACKGROUND AND OBJECTIVES: Use of suxamethonium is associated with an increase in intraocular pressure (IOP). Laryngoscopy and endotracheal intubation further aggravates this rise in intraocular pressure. This rise in intraocular pressure is transitory, variable and may not be significant in otherwise normal individuals but may be harmful in patients with penetrating eye injuries. No method has previously been shown to abolish completely this rise in intraocular pressure. The purpose of our study was to observe the efficacy of Dexmedetomidine, a centrally acting specific alpha-2 agonist, given as premedication in prevention of rise in intraocular pressure associated with the administration of suxamethonium, laryngoscopy and endotracheal intubation.

METHODOLOGY: One hundred ASA Class I or II patients undergoing general anesthesia for elective non-ophthalmic surgery were included in this double blind, randomized, prospective, clinical study. Patients were allocated into two groups of fifty each to receive 0.6 μg/kg Dexmedetomidine (group D) or normal saline (group C) intravenously over a period of 10 minutes, 10 minutes before induction using syringe pump. IOP, heart rate and mean arterial pressure were recorded before and after the study drug administration, 0.5 minute after thiopentone sodium, 0.5 minute after suxamethonium injection, immediately after intubation and every two minutes for six minutes after endotracheal intubation.

RESULTS: After dexmedetomidine injection there was a highly significant decrease in IOP compared with the baseline (p=0.00). Suxamethonium and intubation increased IOP in both the groups. However, IOP in the Dexmedetomidine group after intubation was not significantly different from that of baseline (p = 0.834) unlike that in the control group where IOP was much higher than baseline. (p=0.000). INTERPRETATION AND CONCLUSION: Dexmedetomidine 0.6 μg/kg body weight given intravenously as premedication over ten minutes, ten minutes before induction effectively prevents the rise in IOP associated with the administration of suxamethonium, laryngoscopy and endotracheal intubation. Hemodynamic stability is an additional advantage.

KEYWORDS: Dexmedetomidine IV; Suxamethonium; Endotracheal intubation; Intraocular pressure.

INTRODUCTION: Emergency eye surgery poses a challenge to the anesthesiologist as patients with penetrating eye injury often present with full stomach. These patients require rapid sequence induction and endotracheal intubation without increasing the intraocular pressure (IOP). When the eye globe is open, any factor that increases the intraocular pressure (IOP) may cause drainage of the aqueous humour or extrusion of the vitreous humour through the wound, which can permanently damage vision.¹

Suxamethonium is used to facilitate rapid tracheal intubation in patients with high-risk for aspiration because of its fast onset time and very good intubating conditions. It is however,
associated with an increase in the IOP. Laryngoscopy and tracheal intubation further aggravate the rise in IOP.²

Various methods have been used to attenuate the effects of suxamethonium on IOP. They included self-taming, where a small dose of suxamethonium is given initially followed by the remaining amount of suxamethonium, and pretreatment with non-depolarizing neuromuscular blocking agents, lignocaine, narcotics, nifedipine, and nitroglycerine. However, no modality is devoid of drawbacks and limitations.²

Alpha-2 agonists have been used for attenuating the rise in IOP and sympathetic response to endotracheal intubation.³ Among α-2 agonists both clonidine and dexmedetomidine appear to fulfill the above criteria. But dexmedetomidine is highly specific and selective α-2 adrenoceptor agonist with α-2:α-1 binding selectivity ratio of 1620:1 compared to 220:1 for clonidine.⁴

The advantages of intravenous dexmedetomidine as premedicant and as maintenance in anesthesia include sedation, analgesia, anxiolysis and improved hemodynamic stability.⁵

Dexmedetomidine is being used in other countries since many years as premedicant. Since it has been recently introduced in India, (only in 2009) and not many studies have been done in India, especially about its intraocular pressure lowering property, there is a need to study the effectiveness of dexmedetomidine in lowering the intraocular pressure. The aim of this study is to determine the efficacy of 0.6 μg/kg of intravenous (i. v.) dexmedetomidine for prevention of rise of IOP by suxamethonium and endotracheal intubation.

**METHODOLOGY**: The study was undertaken after obtaining institutional ethical committee clearance as well as informed consent from all patients. One hundred patients of ASA class I or II, between 18 years to 60 years of age, weighing between 50-70 kgs posted for various elective non eye surgeries requiring general anesthesia were selected.

Patients less than 18 and more than 60 years of age, with Mallampatti class III and IV, obese (BMI >30), with difficult airway, patients with any contraindication to the study drug and to suxamethonium, having acute/chronic eye disease or with raised IOP, on medication known to alter intraocular pressure, having diabetes mellitus, hypertension, coronary artery disease and other co-existing diseases were excluded from the study.

A routine pre-anesthetic examination was conducted on the evening before surgery assessing the general condition of the patient, airway assessment by Mallampatti grading and rule of 1-2-3, nutritional status, body weight and height of the patient, a detailed examination of the cardiovascular system and respiratory system.

The following investigations were done in all patients including hemoglobin estimation, urine examination for albumin, sugar and microscopy, standard 12-lead electrocardiogram, X-ray chest, blood sugar, FBS/PPBS, blood urea and serum creatinine.

The population was divided randomly into 2 sub-groups of 50 patients each using simple sealed envelope method:

1) Group C (n=50), the control group.
2) Group D (n=50), the Dexmedetomidine group.

Group C patients were given 50 ml of normal saline intravenously over 10 mins, 10 mins before induction using syringe pump.
The study drug Dexmedetomidine was given to group D as a bolus in the dose of 0.6 μg/kg body weight diluted to 50 ml of normal saline intravenously over 10 mins, 10 mins before induction using syringe pump.

The double blind design of the study was assured by the fact that an anesthesiologist not further involved in the study prepared syringes immediately before administration of the study drug. The syringes were marked dexmedetomidine/placebo, together with the name of the patient. The anesthesiologist responsible for providing anesthesia and observing heart rate, blood pressure and intraocular pressure changes during the surgery, and the patient were thus kept unaware of the content of the syringes.

Standard intraoperative monitoring including pulse oximeter, ECG and noninvasive blood pressure was performed. The parameters that were compared in both the groups included intraocular pressure, heart rate, mean arterial pressure and end tidal carbon dioxide.

Intraocular pressure (IOP) was measured using Schiotz indentation tonometer, after prior instillation of local anesthetic topical lignocaine 4% eye drops. The other parameters were measured using automatic multiparameter monitor (Star plus of Larsen and Toubro).

Both the groups were premedicated with 1 mg of midazolam and fentanyl citrate 1 μg/kg intravenously before administration of the study drug.

General anesthesia was standardized in both the groups. After preoxygenation for 3 mins, anesthesia was induced with inj. thiopentone sodium 5 mg/kg and inj. suxamethonium 1.5 mg/kg. After the fasciculations had ceased, trachea was intubated with appropriate sized cuffed endotracheal tubes with gentle laryngoscopy using conventional laryngoscopic technique. Proper placement of the tracheal tube was verified by auscultation of the chest for bilateral air entry. If the trachea could not be intubated at first attempt, the patient was excluded from the study. Anesthesia was maintained with O2 + N2O + inj. vecuronium bromide + halothane 0.5% in both the groups.

Heart rate (HR), mean arterial blood pressure (MAP) and intraocular pressure (IOP) were recorded at the following time points:

† T1: 5 minutes after arrival to the operating room, before injecting the study drug.
† T2: 10 minutes after the administration of study drug.
† T3: 30 seconds after thiopentone sodium
† T4: 30 seconds after suxamethonium.
† T5: immediately after intubation.
† T6–8: every 2 minutes for 6 minutes after intubation.

After the surgical procedure patients were reversed from neuromuscular blockade using inj. neostigmine 0.05 mg/kg + inj. atropine 0.02 mg/kg given intravenously.

Sedation scoring was done as per Ramsay sedation scale.6 Side effects like hypotension (fall in mean arterial blood pressure >30% of baseline),2,7,8 bradycardia (heart rate <45 beats /min),3 post - operative nausea, vomiting and any other side effects were studied.

**STATISTICAL ANALYSIS:** Sample size was selected to detect a mean IOP difference of 30% between the two groups with type I error of 0.05 and type II error of 0.20. Power analysis was based on a pilot study of 10 patients which showed an average increase in IOP after suxamethonium and intubation of 6 mm Hg (with an SD of the highest IOP of 5.7 mm Hg).2 Minimum adequate sample size was 40 in each group. Considering the drop outs, 50 patients in each group were selected for the study.
Difference between the groups in demographic data and baseline values were analysed using unpaired t-test except for gender. For comparison of various observations within and between the groups, data were first analysed by repeated measures analysis of variance.

SPSS for windows (version 17.0) was employed for data analysis. p < 0.05 was considered as significant and p<0.01 was considered as highly significant. Data were presented in mean ± SD in the text and in the table.

RESULTS: There were no significant differences between the two groups with regard to age, weight and gender of the patients. Baseline HR, MAP and IOP were also comparable. (table 1)

<table>
<thead>
<tr>
<th>Demographic criteria</th>
<th>Group C (control)</th>
<th>Group D (Dexmedetomidine)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs.)</td>
<td>36.90 ± 9.709</td>
<td>37.02 ± 10.83</td>
<td>0.361 (NS)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>19/31</td>
<td>21/29</td>
<td>0.683 (NS)</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>56.90±4.85</td>
<td>58.12±5.69</td>
<td>0.177 (NS)</td>
</tr>
<tr>
<td>Baseline HR (beats/min)</td>
<td>90.16±12.22</td>
<td>88.06±14.00</td>
<td>0.426 (NS)</td>
</tr>
<tr>
<td>Baseline MAP (mm Hg)</td>
<td>93.48±8.91</td>
<td>91.52±4.68</td>
<td>0.171 (NS)</td>
</tr>
<tr>
<td>Baseline IOP(mm Hg)</td>
<td>17.91±1.38</td>
<td>18.46±1.52</td>
<td>0.061 (NS)</td>
</tr>
</tbody>
</table>

Table 1: Showing mean ± SD of demographic criteria, baseline heart rate (HR), mean arterial blood pressure (MAP) and intraocular pressure (IOP) between the groups

NS - Not significant (p >0.05)

<table>
<thead>
<tr>
<th>TIME</th>
<th>GROUP C</th>
<th>GROUP D</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>17.91±1.38</td>
<td>18.46±1.52</td>
<td>0.061 (NS)</td>
</tr>
<tr>
<td>T2</td>
<td>17.67±1.45</td>
<td>15.70±1.59</td>
<td>0.000 (HS)</td>
</tr>
<tr>
<td>T3</td>
<td>15.73±1.78</td>
<td>13.97±1.76</td>
<td>0.000 (HS)</td>
</tr>
<tr>
<td>T4</td>
<td>19.07±1.62</td>
<td>16.17±1.45</td>
<td>0.000 (HS)</td>
</tr>
<tr>
<td>T5</td>
<td>21.00±1.18</td>
<td>18.43±1.52</td>
<td>0.000 (HS)</td>
</tr>
<tr>
<td>T6</td>
<td>20.54±1.24</td>
<td>18.30±1.53</td>
<td>0.000 (HS)</td>
</tr>
<tr>
<td>T7</td>
<td>19.48±1.28</td>
<td>17.33±1.52</td>
<td>0.000 (HS)</td>
</tr>
<tr>
<td>T8</td>
<td>19.09±1.37</td>
<td>16.77±1.49</td>
<td>0.000 (HS)</td>
</tr>
</tbody>
</table>

Table 2: Showing the intergroup comparison of mean intraocular pressure (IOP in mmHg) changes in response to succinylcholine, laryngoscopy and intubation between control group and dexmedetomidine group

NS – not significant (p>0.05), HS- highly significant (p<0.01)
The mean baseline IOP were comparable in both groups (p=0.061). In the dexmedetomidine group initially there was a decrease in IOP after dexmedetomidine bolus which was statistically highly significant (p=0.000). After thiopentone sodium administration IOP decreased further from the baseline. After suxamethonium there was a rise in IOP, but however it remained below baseline.

At intubation there was a rise in IOP which almost reached the baseline value. Even at 6 mins after intubation, the IOP remained below baseline unlike in the control group where the IOP raised above baseline after suxamethonium and intubation and remained so till 6 min after intubation which was statistically highly significant compared to mean IOP in group D (p=0.000).

![Figure 1: Changes in intraocular pressure between the groups](image1)

After premedication with dexmedetomidine, decrease in HR was observed in group D. The mean HR remained below basal value at intubation and even at 6 minutes after intubation. The mean HR increase observed at intubation and 2, 4 and 6 minutes after intubation in group C was statistically highly significant compared to mean HR in group D (p=0.000).

![Figure 2: Changes in heart rate between the groups](image2)

The MAP increased significantly compared with the baseline value after intubation in the control group and was significantly higher than the MAP in the dexmedetomidine group (p=0.000). In group D MAP was not significantly higher than baseline at all times.
Statistical evaluation showed no difference in the sedation score between the two groups (p>0.05). No incidence of hypotension or bradycardia requiring intervention was reported in both groups.

DISCUSSION: Patients with penetrating eye injury may present with full stomach. Goal of anesthesia in this scenario is to secure the airway by rapid sequence induction technique without increasing the IOP. Suxamethonium, the most commonly used muscle relaxant for rapid sequence airway management increases the IOP.8

Although rocuronium, an intermediate acting non-depolarizing muscle relaxant provides good intubating condition after 1–1.5 minutes, it is not preferred in patients with anticipated difficult airway.8

This is by far the most important indication for attenuation of hike in IOP and hemodynamic response to laryngoscopy and endotracheal intubation in patients posted for eye surgeries and in patients with raised IOP.

Clonidine was effective in preventing the rise in IOP in response to suxamethonium and endotracheal intubation.9,10 Dexmedetomidine has been found by various authors to blunt the rise in IOP associated with suxamethonium and intubation,2,3,8,11 and also the hemodynamic response to laryngoscopy and endotracheal intubation.2,3,5 Dexmedetomidine infusion as an adjunct to local analgesia in eye surgery was effective in reduction of the IOP significantly.12 The drug was also found to reduce the IOP by 34% after a single i.v. dose of dexmedetomidine 0.6 µg/kg.13 Similar effects were shown in elderly patients during cataract surgery.14,15

On the contrary, when Lee and colleagues16 infused dexmedetomidine as a supplement to isoflurane anesthesia, they found no IOP lowering effect. However, the loading dose of dexmedetomidine used in their study was lower than that in the present study. Dexmedetomidine administered intravenously in the dose of 0.6 µg/kg before induction as a premedicant significantly obliterated the rise in IOP following suxamethonium and endotracheal intubation.2 Palck and colleagues8 used dexmedetomidine in two doses 0.4 µg/kg and 0.6 µg/kg intravenously as premedicant and found that both doses lowered the IOP but hemodynamic stability was better with 0.4 µg/kg.
The effect of alpha-2 agonists on the IOP may be due to its direct vasoconstrictor effect on the afferent blood vessels of the ciliary body leading to reduction of aqueous humour production.\(^{17}\) It may also facilitate the drainage of aqueous humour by reducing sympathetically mediated vasomotor tone of the ocular drainage system.\(^{18}\) Finally, the hemodynamic effect of dexmedetomidine can be responsible for reduction of IOP.\(^{19}\)

Since most of the authors\(^{2,3,8}\) found dexmedetomidine is effective at the dose of 0.6 µg/kg body weight in attenuating the rise in IOP following suxamethonium, laryngoscopy and endotracheal intubation, 0.6 µg/kg body weight dose was chosen for our study. Higher doses of dexmedetomidine were associated with episodes of severe hypotension and bradycardia without further decrease in IOP.\(^{14,15}\)

In the present study dexmedetomidine was diluted in 50 ml of normal saline and given intravenously over 10 minutes using syringe pump. Administration of bolus dose of dexmedetomidine rapidly, initially results in transient hike in blood pressure and reflex decrease in HR. The initial reaction is due to peripheral α-2 adrenoceptors stimulation of vascular smooth muscle and can be attenuated by a slow infusion over 10 minutes using infusion pump.\(^{4,20}\) Hence in our study we administered the bolus dose over 10 minutes.

From the pharmacokinetic profile, it is seen that the rapid distribution half-life of intravenous dexmedetomidine is approximately 6 minutes.\(^{4}\) Many authors have administered the drug 10 mins before induction as premedicant.\(^{2,3,8}\) In view of the above, in the present study dexmedetomidine was administered 10 minutes before induction as premedicant to blunt the rise in IOP.

The main finding in our study was that dexmedetomidine premedication in the dose of 0.6 µg/kg body weight given over 10 mins before induction as a premedicant blunted the rise in IOP caused by suxamethonium, laryngoscopy and endotracheal intubation. Our study correlates with the studies done by Jaakola et al,\(^{3}\) Mowafi et al\(^{2}\) and Pal CK et al,\(^{8}\) as in all of their studies there is a reduction in IOP in dexmedetomidine group at various time intervals.

Dexmedetomidine premedication also produced significant fall in arterial pressure and HR. Even after intubation MAP remained below baseline unlike the increase in MAP seen in control group. The present series also observed significant attenuation of pressure response related to laryngoscopy and endotracheal intubation, which supports the statements made by previous workers.\(^{3,13}\)

**CONCLUSION:** Dexmedetomidine in the dose of 0.6 µg/kg body weight intravenously can be used for obtundation of rise in IOP associated with suxamethonium, laryngoscopy and endotracheal intubation in patients where rise in IOP can be detrimental. It also attenuated the hemodynamic response to laryngoscopy and tracheal intubation without significant side effects.

**REFERENCES:**


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Date of Submission: 21/06/2014.
Date of Peer Review: 23/06/2014.
Date of Acceptance: 30/06/2014.
Date of Publishing: 03/07/2014.