A STUDY OF INFLUENCE OF DEXMEDETOMIDINE PREMEDICATION ON CHANGES IN INTRAOCULAR PRESSURE FOLLOWING ADMINISTRATION OF SUCCINYLCHOLINE AND ENDOTRACHEAL INTUBATION

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ABSTRACT

BACKGROUND
Emergency surgeries for penetrating eye trauma may be complicated by elevation in intraocular pressure (IOP) caused by succinylcholine administration and endotracheal intubation. Hence, it is critical to attenuate the rise in IOP for better outcome. This study was conducted to evaluate the effect of dexmedetomidine premedication in attenuating the rise in IOP due to succinylcholine and endotracheal intubation.

MATERIALS AND METHODS
This non-randomised controlled trial was conducted on 70 American Society of Anesthesiologists (ASA) grade I-II patients, aged 18-60 years undergoing non-opthalmic surgeries under general anaesthesia (GA). The patients were divided into two groups of 35 each. Group ‘C’ (control) received 10 mL normal saline, while Group ‘D’ (study group) received dexmedetomidine (0.5 µg/kg) with normal saline added to make a total volume of 10 mL. IOP, heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded before and after premedication, after induction of anaesthesia, after succinylcholine administration immediately and 5 minutes post-intubation.

RESULTS
Data were compared using independent student ‘t’ test and chi-square test in Statistical Package for Social Sciences (SPSS) software version 22. P-value < 0.05 was considered significant. The rise in IOP, mean HR and MAP were significantly reduced after premedication in Group ‘D’. The incidence of side effects between the groups was not significantly different.

CONCLUSION
The study led to the conclusion that dexmedetomidine premedication significantly attenuates the rise in IOP in response to succinylcholine administration and endotracheal intubation without any additional side-effects and can be used in emergency ophthalmic surgeries for this purpose.

KEYWORDS
Succinylcholine, Premedication, Intraocular Pressure.


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Various techniques like self-taming and adjuvants like lidocaine, sufentanil, gabapentin, etc. have been investigated for attenuating the rise in IOP, but none was proved to be successful without drawbacks.

Dexmedetomidine, a highly selective alpha-2 adrenergic agonist, has sedative and analgesic effects as well as sympatholytic effects. These properties prompted us to evaluate the influence of dexmedetomidine premedication on changes in IOP in response to succinylcholine administration and endotracheal intubation.

MATERIALS AND METHODS
This non-randomised controlled trial was conducted after obtaining clearance from Institutional Ethics Committee and written informed consent from all the study subjects. The included subjects were 70 patients of both sexes aged between 18 and 60 years belonging to American Society of Anesthesiologists (ASA), grade I and II, undergoing elective non-ophthalmic surgeries under general anaesthesia. Patients were excluded if they had any acute or chronic ophthalmic disease, had any contraindication to study drug or were taking any medication known to alter IOP.

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The patients were divided into two study groups of 35 patients each using ‘slip in the box’ method for randomisation. Group ‘C’ received 10 mL of normal saline IV (control group) and Group ‘D’ received injection dexmedetomidine as premedication in a dose of 0.5 µg/kg body weight IV with normal saline added to make the total volume of 10 mL.

On arrival in the operation theatre, multi-parameter monitor was connected to the patient and baseline heart rate (HR), non-invasive systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP). Electrocardiogram (ECG) and oxygen saturation were noted. IOP was measured with Schiotz tonometer after instilling two drops of 4% lignocaine into each eye by an ophthalmologist who was unaware of the nature of the study. The syringes containing study solutions were prepared by a doctor not involved further in the study. The study solution was administered using an infusion pump over a period of ten minutes prior to induction.

All the patients received standard anaesthesia as follows. Patients received premedication with IV glycopyrrolate 0.2 mg and IV fentanyl 2 µg/kg. After pre-oxygenation for three minutes, general anaesthesia was induced with thiopentone sodium in a dose of 5 mg/kg. Succinylcholine was then administered in the dose of 1.5 mg/kg to achieve muscle relaxation for intubation. After one minute of giving succinylcholine when fasciculations had ceased, the trachea was intubated by a senior anaesthesiologist under direct vision laryngoscopy and position of endotracheal tube was confirmed by auscultation of chest. If intubation could not be performed successfully in the first attempt, the patient was excluded from the study. After securing the airway, anaesthesia was maintained in both the groups with mixture of oxygen, nitrous oxide and isoflurane and injection atracurium.

During intraoperative course HR, MAP and IOP were noted at following time points: Before premedication with study drug (T1), 10 minutes after premedication (T2), 30 seconds after giving thiopentone sodium (T3), 30 seconds after giving succinylcholine (T4), immediately after intubation (T5) and 5 minutes after intubation (T6).

The primary outcome variable of the study was the attenuation of intraocular pressure and the secondary outcome variables were haemodynamic parameters. Any side effects and complications were noted in both the study groups. Hypotension (MAP < 30% from the baseline) was treated with IV fluids and vasopressors and bradycardia (HR < 50 beats/min) was treated with atropine. These patients were excluded from the study. Study by convenient allocation technique since the duration of the study was few months. The patients were selected by convenience allocation technique. The sample size estimation was also done at conveniences.

**Statistical Analysis**

All observations were tabulated and analysed using independent student ‘t’ test and chi-square test in Statistical Package for Social Sciences (SPSS) software version 22. Statistically, significant difference in findings was considered when p-value was < 0.05.

**RESULTS**

There were no significant differences between the two groups with respect to age, weight, gender distribution and ASA grades. There were also no significant differences between the two groups in terms of baseline HR, MAP and IOP as shown in Table 1.

The values of HR, MAP and IOP at different time intervals in the two study groups are shown in Figures 1, 2 and 3 respectively. Differences in HR between the two groups were not significant at any time. HR increased consistently in Group ‘C’ in response to induction of anaesthesia, succinylcholine administration and endotracheal intubation, whereas in Group ‘D’, HR initially decreased after premedication but increased thereafter, though the increments were less compared to Group ‘C’. No incidence of bradycardia was reported during the study.

The values of MAP were found to be higher than the baseline after intubation in both the groups. On comparison between the two groups, Group ‘C’ consistently showed higher MAP than Group ‘D’ but this difference was not found to be significant at any point of time. One subject had hypotension in Group ‘D’ which necessitated intervention, but no such incidents were reported in Group ‘C’.

As shown in Figure 2, there was no significant difference in the baseline IOP between both the groups. After premedication IOP decreased in both the groups, but no significant change or difference between the two groups was noted. After giving thiopentone, there was further decrease in IOP but it was significantly lower in Group ‘D’ compared to Group ‘C’ (p = 0.001). Further, after giving succinylcholine and performing intubation, though IOP increased in both the groups but it remained significantly lower in Group ‘D’ when compared to Group ‘C’ (p = 0.001 and < 0.001 respectively). After 5 minutes of endotracheal intubation, IOP returned to its baseline level in both the groups with no significant difference.

Figure 4 shows the incidence of side effects in both the study groups. The only side effect warranting any intervention was single incidence of hypotension in Group ‘D’. Rest of the side effects noted were non-serious and infrequent.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group ‘D’</th>
<th>Group ‘C’</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age (Years)</td>
<td>39.17 (±11.27)</td>
<td>39.57 (±11.52)</td>
<td>0.839</td>
</tr>
<tr>
<td>Gender Ratio (Male: Female)</td>
<td>17:13</td>
<td>19:11</td>
<td>0.598</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>68.93 (±12.33)</td>
<td>68.57 (±12.43)</td>
<td>0.909</td>
</tr>
<tr>
<td>ASA Grade (Grade I: Grade II)</td>
<td>21:9</td>
<td>22:8</td>
<td>0.878</td>
</tr>
<tr>
<td>Baseline HR (BPM)</td>
<td>79.60 (±10.83)</td>
<td>80.73 (±10.67)</td>
<td>0.685</td>
</tr>
<tr>
<td>Baseline MAP (mmHg)</td>
<td>94.40 (±3.99)</td>
<td>93.67 (±4.53)</td>
<td>0.508</td>
</tr>
<tr>
<td>Baseline IOP (mmHg)</td>
<td>15.87 (±0.90)</td>
<td>15.53 (±1.14)</td>
<td>0.213</td>
</tr>
</tbody>
</table>

**Table 1. Patient Characteristics in the Two Study Groups (Data represented as Mean ± SD)**

ASA: American Society of Anesthesiologists.
<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Group 'D'</th>
<th>Group 'C'</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline (T₁)</td>
<td>15.87 (±0.90)</td>
<td>15.53 (±1.14)</td>
<td>0.213</td>
</tr>
<tr>
<td>After premedication (T₂)</td>
<td>14.73 (±0.83)</td>
<td>14.67 (±0.99)</td>
<td>0.779</td>
</tr>
<tr>
<td>After thiopentone sodium (T₃)</td>
<td>13.97 (±0.67)</td>
<td>14.63</td>
<td>0.001</td>
</tr>
<tr>
<td>After succinylcholine administration (T₄)</td>
<td>15.93 (±0.83)</td>
<td>16.73</td>
<td>0.001</td>
</tr>
<tr>
<td>Immediately after endotracheal intubation (T₅)</td>
<td>16.10 (±0.76)</td>
<td>17.73 (±0.87)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>5 minutes after endotracheal intubation (T₆)</td>
<td>15.91 (±0.93)</td>
<td>15.61 (±1.09)</td>
<td>0.207</td>
</tr>
</tbody>
</table>

Table 2. Mean IOP (mmHg) at different Time Intervals in the Two Study Groups and their Comparison (Data represented as Mean ± SD)

*Considered significant (p < 0.05)

DISCUSSION

Different methods and drugs have been described to blunt the effects of succinylcholine on IOP with variable success. Clonidine has been shown to be effective in preventing the rise in IOP after succinylcholine administration and endotracheal intubation in several studies.[5,6,7,8] Dexmedetomidine, a highly selective alpha-2 adrenergic agonist was approved by the Food and Drug Administration in 1999 for use in humans as a short-term medication (<24 hours) for analgesia and sedation in the intensive care unit (ICU). It also has sympatholytic effects with minimal respiratory depression.[9,10] These unique properties make this drug suitable for sedation and analgesia during the perioperative period.[11]

Due to these properties, dexmedetomidine premedication prior to administration of local anaesthesia in ophthalmic surgery has been effective in significant reduction of the IOP in many studies, particularly with reference to day-care cataract surgeries.[12,13,14] The main observation from our study was that dexmedetomidine premedication in a dose of 0.5 µg/kg blunted the increase in IOP caused by succinylcholine administration and endotracheal intubation. The administered dexmedetomidine dose of 0.5 µg/kg in the present study was based on experience of a previous study,[15] which used 0.4 and 0.6 µg/kg dexmedetomidine and showed that in increasing the dose of dexmedetomidine to 0.6 µg/kg does not cause any
significant fall in IOP, while causing increased incidence of cardiovascular depression.

Several studies\cite{13,14,16,17} analysed the blunting of rise in IOP with succinylcholine administration and intubation using dexmedetomidine premedication and revealed observations similar to the results of our study.

The ocular hypotensive effect of dexmedetomidine can be explained by three mechanisms.\cite{17,18} First, it may have a direct vasoconstrictor effect on the afferent blood vessels of the ciliary body leading to reduction of aqueous humour production. Secondly, it may facilitate the drainage of aqueous humour by reducing sympathetically mediated vasomotor tone of the ocular drainage system. Finally, the haemodynamic properties of dexmedetomidine can add to the mechanisms responsible for reduction of IOP.

Dexmedetomidine premedication also blunted the cardiovascular sympathomimetic response to laryngoscopy and intubation in Group 'D' compared to Group 'C', which was consistent with many previous studies.\cite{11,14} The reason for this can be centrally mediated sympatholytic effects of alpha-2 agonists and thereby decreasing norepinephrine release via peripheral presynaptic alpha-2 receptors.

Some authors find the use of succinylcholine in open eye injury to be controversial and an alternative anaesthetic management based on the use of non-depolarising neuromuscular blocking agents, despite their slower onset has been suggested. Despite this debate, most authors still agree on its use in difficult airway cases with salvageable eye situations.\cite{18,19}

The present study had two major limitations. Firstly, it was performed in a small sample size and patients undergoing non-opthalmic surgeries. There is a need to replicate this study in a larger sample size and in patients undergoing ophthalmic surgeries assessing the actual outcome of such surgeries with dexmedetomidine premedication, as this is the actual group of patients going to benefit the most from the findings of the study. Secondly, as previously stated, haemodynamic action of dexmedetomidine can have a confounding causal relationship with its ocular hypotensive effect and the two effects cannot be isolated from each other. However, in practical sense, this does not limit the use of dexmedetomidine premedication in the setting of emergency ophthalmic surgeries.

Limitation of the Study
Due to short duration of study, convenience allocation technique was followed. Thus, sampling size was also calculated by convenience. The results of the study cannot be generalised due to the potential bias resulting from the allocation technique and sample size estimation.

CONCLUSION
The conclusion drawn from this study is that dexmedetomidine premedication in a dose of 0.5 µg/kg significantly blunts the increase in IOP in response to succinylcholine administration and endotracheal intubation compared to control group without causing any additional side-effects and therefore can be used in emergency ophthalmic surgeries for keeping IOP within desirable range.

REFERENCES


