Effect of dexmedetomidine premedication on the intraocular pressure changes after succinylcholine and intubation

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Background. Succinylcholine is still recommended for some situations in open globe injuries. However, the use of succinylcholine is associated with an increase in intraocular pressure (IOP). This may be deleterious in open globe injuries. No method has previously been shown to abolish completely this rise in the IOP. We investigated whether dexmedetomidine, an alpha-2 agonist, could attenuate this increase in the IOP after succinylcholine and intubation.

Methods. Forty patients with no pre-existing eye disease undergoing general anaesthesia were randomly premedicated by i.v. dexmedetomidine 0.6 μg kg⁻¹, or saline. Heart rate (HR), mean arterial pressure (MAP), and IOP (using Schieotz tonometer) were measured before, after the premedication, after thiopental, after succinylcholine, immediately after intubation, and then every 2 min for 6 min.

Results. Succinylcholine and intubation increased IOP in both groups. However, in the dexmedetomidine group, the IOP rise was not different from the baseline value (P=0.65) and was significantly lower than in the saline group (P=0.003). After intubation, the MAP in the control group was higher than that in the dexmedetomidine group (P=0.041) and exceeded the baseline value (P<0.001). The HR also showed less fluctuation in the dexmedetomidine group than in the saline group.

Conclusions. We conclude that dexmedetomidine could be a beneficial premedication in open globe injuries.

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Anaesthesia for patients with open globe injury who need emergency surgical intervention may be hazardous. When the eye globe is open, any factor that increases the intraocular pressure (IOP) may possibly cause drainage of the aqueous humour or extrusion of the vitreous humour through the wound, which can permanently damage vision.1

Succinylcholine is used to facilitate rapid tracheal intubation in high-risk patients for aspiration because of its fast onset time and excellent intubating conditions.1 2 It is, however, associated with an increase in the IOP.3 4 Laryngoscopy and tracheal intubation further aggravate the rise in IOP.1 5 Various methods have been used to attenuate the effects of succinylcholine on IOP. They included self-taming, where a small dose of succinylcholine is given initially followed by the remaining amount of succinylcholine, and pretreatment with non-depolarizing neuromuscular blocking agents, lidocaine, narcotics, nifedipine, and nitroglycerin.1 However, no modality was devoid of drawbacks and limitations.

Dexmedetomidine is a highly selective alpha-2 adrenergic agonist that has sedative and analgesic effects.6 7 Alpha-2 agonists provide potentially beneficial effects in ophthalmic surgery because of their IOP lowering properties.8 9 The aim of this study is to investigate the effects of dexmedetomidine premedication on the IOP changes after succinylcholine and endotracheal intubation.

Methods

After the local research committee approval and written informed patient consent, 40 adult patients of ASA I or II,
undergoing elective non-ophthalmic surgeries under general anaesthesia, were included in the study. Patients were excluded if they were older than 60 yr, had a body weight more than 150% of their ideal body weight using Broca’s index, had acute or chronic eye disease, had any contraindication to the study drugs, or were receiving any medication known to alter IOP. Patients were randomly allocated using an online research randomizer (http://www.randomizer.org) into two equal groups (20 patients each) to receive either single bolus i.v. dose of dexmedetomidine as premedication (dexmedetomidine group) or saline (control group). Surgery was performed early in the morning to avoid diurnal variations in IOP. No other sedative premedication was given to patients.

Standard intraoperative monitoring including three-lead ECG, plethysmographic pulse oximeter, capnometry, and non-invasive arterial pressure was performed (Datex-Ohmeda S/5, ADU, Sweden). IOP was measured with a Schioetz tonometer by an ophthalmologist who was unaware of the anaesthetic technique. For this procedure, topical oxybuprocaine hydrochloride 0.4% (BNX) was applied to the cornea before measurement.

Dexmedetomidine (Precedex®, Abbott Laboratories) was prepared by diluting 1 ml of dexmedetomidine 100 μg ml⁻¹ with 49 ml of normal saline to a concentration of 2 μg ml⁻¹. Syringes containing aqueous solutions of either dexmedetomidine or saline were prepared in a double-blind fashion by a team member who was not involved in data recording. Before induction of anaesthesia, a single dose of dexmedetomidine 0.6 μg kg⁻¹ was administered i.v. using a syringe pump (Life Care 5000 Infusion System, Abbot, Ireland) over 10 min. The same amount of saline was given to the patients in the control group using the same pump.

Anaesthesia was standardized in all patients. After pre-oxygenation for 3 min, anaesthesia was induced with thiopental 5 mg kg⁻¹ and fentanyl 1 μg kg⁻¹. Succinylcholine was then administered at a dose of 1.5 mg kg⁻¹. When the fasciculations had ceased, the trachea was intubated under direct vision laryngoscopy and the correct position of the tracheal tube was verified by auscultation of the chest and by capnometry. If the trachea could not be intubated at the first attempt with direct laryngoscopy, the patient

Table 1 Patient characteristics (n=20 each). Data are mean (range) or mean (SD). HR, heart rate; MAP, mean arterial pressure; IOP, intraocular pressure

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Dexmedetomidine group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>29.3 (19–44)</td>
<td>28.3 (21–49)</td>
<td>0.76</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168.9 (5.5)</td>
<td>166.3 (5.9)</td>
<td>0.17</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.7 (14.0)</td>
<td>72.6 (9.5)</td>
<td>0.82</td>
</tr>
<tr>
<td>Gender (male/ female)</td>
<td>15/5</td>
<td>12/8</td>
<td>0.50</td>
</tr>
<tr>
<td>Preoperative HR (beat min⁻¹)</td>
<td>74.4 (13.2)</td>
<td>73.0 (8.8)</td>
<td>0.70</td>
</tr>
<tr>
<td>Preoperative MAP (mm Hg)</td>
<td>92.4 (11.5)</td>
<td>89.9 (13.0)</td>
<td>0.52</td>
</tr>
<tr>
<td>Preoperative IOP (mm Hg)</td>
<td>13.2 (3.0)</td>
<td>12.7 (1.7)</td>
<td>0.48</td>
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</tbody>
</table>

Fig 1 Changes in HR, MAP, and IOP in the control and dexmedetomidine groups. Measurements were recorded before premedication (T1), 10 min after premedication (T2), 30 s after thiopental (T3), 30 s after succinylcholine (T4), after intubation (T5), and 2, 4, and 6 min after intubation (T6–8). Vertical bars denote 0.95 confidence intervals. *Significance difference in comparison with T1. **Significant difference between the dexmedetomidine and the control groups.
was excluded from the study. Rocuronium 0.6 mg kg\(^{-1}\) provided the intraoperative neuromuscular block. The lung was ventilated to maintain the end-tidal carbon dioxide partial pressure between 4.3 and 4.6 kPa. Anaesthesia was maintained in both groups with sevoflurane in a mixture of oxygen and air. Fluid administration of lactated Ringer solution was standardized at 4 ml kg\(^{-1}\) h\(^{-1}\). If hypotension (MAP $\leq$ 30\% from the baseline) or bradycardia (HR $<$ 40 beat min\(^{-1}\)) occurred, it was recorded and managed according to the preference of the attending anaesthetist.

Mean arterial pressure (MAP), heart rate (HR), and IOP were recorded at the following time points:

- **T1**: 5 min after arrival to the operating room, before premedication (baseline).
- **T2**: 10 min after premedication.
- **T3**: 30 s after thiopental.
- **T4**: 30 s after succinylcholine.
- **T5**: immediately after intubation.
- **T6–8**: every 2 min for 6 min after intubation.

**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 succinylcholine and intubation of 6 mm Hg (with an sd of the highest IOP of 5.7 mm Hg). Data were tested for normal distribution using the Kolmogorov–Smirnov test. Differences between the groups in the demographic data and baseline values were analysed using unpaired t-test except for gender which was analysed using Fisher’s exact test. For comparison of different observations within and between the groups, data were first analysed by repeated measures analysis of variance, and differences were then calculated by post hoc testing (Newman–Keuls test). Analysis was performed using Statistica software version 6.0 for windows (Statsoft, Inc.). Data were presented as mean (sd) in the text and in Table 1, and as mean (95\% confidence intervals) in Figure 1.

**Results**

There were no significant differences between the two groups with regard to age, weight, height, and gender. There were also no significant differences at baseline HR, MAP, and IOP (Table 1).

The values of HR, MAP, and IOP are shown in Figure 1. No significant differences in HR between the two groups were recorded at any time. However, in the control group, the HR increased significantly after injection of thiopental, succinylcholine, and intubation. These increases in HR were not observed in the dexmedetomidine group. The MAP increased significantly compared with the preoperative value after intubation in the control group and was significantly higher than the MAP in the dexmedetomidine group (\(P=0.041\)). In the dexmedetomidine group, the MAP was not significantly higher than the preoperative value at all times. No incidence of hypotension or bradycardia requiring intervention was reported in both groups.

There was no significant difference in the baseline IOP between both groups. After dexmedetomidine injection, there was a significant decrease in IOP, compared with baseline (\(P=0.017\)). Thiopental decreased IOP significantly in both groups (\(P<0.001\)). Succinylcholine and intubation increased IOP in both groups. However, IOP in the dexmedetomidine group after intubation was not significantly different from that at baseline (\(P=0.65\)), unlike that in the control group (\(P<0.001\)).

**Discussion**

The main finding in this study was that dexmedetomidine premedication in a dose of 0.6 \(\mu\)g kg\(^{-1}\) over 10 min blunted the rise in the IOP caused by succinylcholine and intubation. In addition, dexmedetomidine attenuated the haemodynamic response to laryngoscopy and intubation.

The intraocular hypotensive effect of dexmedetomidine in the present study is consistent with previous several researches on alpha-2 agonists. Clonidine was effective in preventing the rise of the IOP in response to succinylcholine and tracheal intubation.

Dexmedetomidine infusion as an adjunct to local analgesia in ophthalmic surgery was effective in reduction of the IOP significantly. The drug was also found to reduce the IOP by 34\% after a single i.v. dose of dexmedetomidine 0.6 \(\mu\)g kg\(^{-1}\). Similar effects were shown in elderly patients during cataract surgery. On the contrary, when Lee and colleagues infused dexmedetomidine as a supplement to isoflurane anaesthesia, they found no IOP lowering effect. However, the loading dose of dexmedetomidine used in their study was lower than that in the present study. No previous study examined the effect of dexmedetomidine on the succinylcholine-induced ocular hypertension.

The effect of dexmedetomidine on the IOP may be caused by a direct vasoconstrictor effect on the afferent blood vessels of the ciliary body, which results in reduction of aqueous humour production. Moreover, it could increase outflow of the aqueous humour caused by a reduction of the sympathetically mediated vasomotor tone of the ocular drainage system. Additionally, its associated haemodynamic response could contribute to the IOP lowering effect.

In the present study, HR and MAP increased significantly after intubation in the control group. On the
contrary, in patients who received dexmedetomidine premedication, this response was attenuated. Several previous studies have reported the blunting effect of dexmedetomidine on this sympathetic response to laryngoscopy and intubation.\(^1\)\(^2\)\(^9\)\(^20\)\(^21\) This could be due to the centrally mediated sympatholytic effects of alpha-2 agonists and by its decreasing norepinephrine release via peripheral presynaptic alpha-2 receptors.\(^22\)\(^23\)

The dose of dexmedetomidine premedication administered in the present study (0.6 μg kg\(^{-1}\)) was based on a previous clinical study,\(^9\) where the selected dose resulted in a significant reduction in IOP and prevented the rise in the IOP in response to intubation. In addition, the pressor response to laryngoscopy and endotracheal intubation was also significantly attenuated. Higher doses of dexmedetomidine were associated with an additional reduction in the arterial pressure and HR without any further decrease in the IOP.\(^14\)\(^15\)

Some authors find that the use of succinylcholine in open ocular trauma is controversial and an alternative anaesthetic management based on the use of non-depolarizing neuromuscular blocking agents, despite its slower onset, was suggested.\(^1\) Various methods have been tried to speed up this onset, including priming,\(^24\) administering the non-depolarizing relaxant before the induction agent,\(^1\) and high-dose regimen.\(^25\) Despite these strategies, non-depolarizing neuromuscular blocking agents can still result in non-ideal intubation conditions: increases in the IOP from mask application and longer time with insecure airway and prolonged paralysis.\(^1\) Although sugammadex may overcome the prolonged effects of large doses of rocuronium or vecuronium, the drug is not launched yet for routine clinical use.\(^26\) Despite this debate about the use of succinylcholine in open globe injury, most authors still agree on its use in difficult airway cases with salvageable eye situations.\(^1\)

A limitation of this study is that the effect of dexmedetomidine on the IOP changes after succinylcholine and intubation cannot be isolated from its action on the haemodynamics since both effects are parallel and a causal relationship cannot be denied. However, this limitation should not decline the potential advantage of using dexmedetomidine as an alternative agent to obtund the IOP changes of succinylcholine and intubation.

We conclude that the rise of IOP with succinylcholine and endotracheal intubation can be blunted with i.v. dexmedetomidine premedication. The haemodynamic stability is an additional advantage.

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