Original Article

The effects of intravenous dexmedetomidine premedication on intraocular pressure and pressor response to laryngoscopy and intubation

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Abstract

Background and Aims: Penetrating eye injuries are a challenge for the anesthesiologists in emergency due to increase in intraocular pressure (IOP). The aim of this study was to evaluate the effects of intravenous dexmedetomidine premedication on changes in IOP and hemodynamic response following laryngoscopy and tracheal intubation.

Material and Methods: Hundred patients aged 18-60 years undergoing elective nonophthalmic surgery were divided into two groups of 50 each. Group D received a bolus dose of dexmedetomidine (0.4 μg/kg) diluted to 20 ml normal saline and Group C received normal saline (0.4 ml/kg) over 10 min as premedication. Heart rate (HR), systolic blood pressure (SBP) and IOP were measured and recorded before premedication (T1), 5 and 10 m after premedication (T2, T3), immediately after induction, intubation and then 1, 3, 5 min after intubation (T4, 5, 6, 7, 8).

Results: HR was comparable in both groups at preoperative level, but it was significantly low in the drug group when compared with the control group at T4-T8 ($P = 0.034$, $P < 0.001$, 0.001, 0.036 and 0.001, respectively). The SBP was comparable in both the groups at baseline and till before induction. At T4-T8 there was a fall in SBP in Group D compared to the Group C ($P = 0.045$, $P = 0.007$, 0.001, 0.001 and 0.001, respectively). The baseline IOP was comparable in both the groups (P = NS). There was a significant fall in the IOP in Group D, 5 min after the drug infusion compared to Group C, which was sustained till 5 min after intubation (T8) ($P < 0.001$ at all intervals).

Conclusion: Dexmedetomidine premedication in the dose of 0.4 μg/kg lowers the IOP and attenuates the pressor response to laryngoscopy and intubation.

Key words: Dexmedetomidine, hemodynamics, intraocular pressure, premedication

Introduction

Control of intraocular pressure (IOP) within the correct physiological range is necessary to maintain the anatomical conditions necessary for optimal refraction and thus vision. It normally varies between 10 and 21.7 mm Hg and is considered abnormal above 22 mmHg. If IOP is too high, it may produce opacities by interfering with normal corneal metabolism.[1]

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Access this article online

Quick Response Code:

Website: www.joacp.org

DOI: 10.4103/0970-9185.173354

The importance of IOP for anesthetists is that patients with acutely or chronically raised IOP may present for corrective surgery, nonophthalmic surgery or with open globes following penetrating eye injuries. Rise in IOP may be critical in patients with acute glaucoma, impending perforation of the eye and perforating eye injuries due to expulsion of the global contents through a surgical or traumatic opening, retinal artery occlusion and retinal ischemia.[2] Control of IOP is often important for the success of the procedure. Coughing, straining, or vomiting can increase IOP to 30-40 mm Hg similar to endotracheal intubation. Intravenous (i.v.) succinylcholine used for rapid sequence induction causes IOP to increase by 6-12 mm Hg, which lasts for 5-10 min.[3] In an open eye, these increases can lead to loss of intraocular contents, hemorrhage, and permanent vision loss.[4]

Laryngoscopy produces reflex sympathetic stimulation with an increase in plasma catecholamines resulting in tachycardia, arterial hypertension, arrhythmias, increased IOP and intra-cranial pressure.[5-7] Various pharmacologic

and nonpharmacologic methods have been tried to limit these changes following insertion of the endotracheal tube, but no ideal agent has been found and hence the search for an ideal agent continues.

Dexmedetomidine, by its central sympatholytic action, promotes hemodynamic stability when used as an adjuvant during general anesthesia. It has analgesic, potent sedative and IOP lowering properties.[8-10] We have therefore used this drug as premedication to see its effect on IOP and pressor response to laryngoscopy and intubation.

Material and Methods

After approval from the ethical committee and a valid informed written consent of the patient, this prospective, randomized, double-blind study was conducted on two groups of patients of either sex, American Society of Anesthesiologists (ASA) Grade I of 18-60 years undergoing elective nonophthalmic surgery from May 2013 to April 2014. The total (n = 100) number of patients were taken as 50 in each group after statistically analyzing the power of the study (a power of 90% with a confidence interval of 0.05). The patients who refused to be the part of the study, ASA II, III, IV, predicted difficultly airway, patients with cardio-pulmonary, hepatic, renal, ophthalmic or metabolic diseases were excluded from the study. All patients were given tablet alprazolam 25 mg and tablet ranitidine 150 mg night before the surgery.

Surgery was performed early in the morning to avoid diurnal variation in IOP. No other sedative premedication was given to the patient. The patients were divided into Group "D" and Group "C" using a computer generated random number table.

Two solutions for infusion were prepared by a colleague who labeled the solutions as solution "X" and "Y". Instructions regarding content for the preparation of the solution were given by the guide keeping the anesthetist blind about nature of the solution.

Group D (n = 50): Received the bolus dose of dexmedetomidine (0.4 μg/kg) diluted to 20 ml with normal saline over 10 min as premedication (solution "X").

Group C (n = 50): Received the bolus dose of normal saline (0.4 ml/kg) over 10 min as premedication (solution "Y"). Baseline hemodynamic parameters (heart rate [HR], systolic blood pressure [SBP], diastolic blood pressure, mean blood pressure [MBP], and oxygen saturation) were noted. Baseline IOP was measured using Schiotz tonometer after instillation of lignocaine. After dexmedetomidine or normal saline bolus, patient was premedicated with fentanyl 1 μg/kg in each group. Each patient was given oxygen via nasal cannula throughout the study drug infusion in each group. Anesthesia was induced with propofol 2 mg/kg and rocuronium 1 mg/kg. IOP and hemodynamic changes were noted at predefined intervals after induction.

The parameters were recorded at different predefined intervals as T1 - Before premedicaton, T2 - 5 min after premedication,T3 - 10 min after premedication, T4 - Immediately after induction, T5 - Immediately after intubation, T6 - 1 min after intubation, T7 - 3 min after intubation, T8 - 5 min after intubation.

Statistical analysis

Sample size - With reference to the previous study in literature it was found that mean ± standard division (SD) of IOP was 14.55 ± 1.79 and 16.36 ± 1.78 in Group D and Group C respectively. Assuming same minimum sample size of 50/group was calculated based on a mean difference of 1.81 in IOP after medication between the two groups at a two-sided alpha of 0.05 and a power of 90%.

Statistical testing was conducted with the statistical package for the social science system version SPSS Statistical package (version 17.0; SPSS Inc, Chicago, IL, USA). Results are expressed as mean ± SD, numbers and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student's t-test and within the groups at different time points from Baseline was compared using Paired t-test. Nominal categorical data between the groups were compared using Chi-square test or Fisher's exact test as appropriate. $P < 0.05$ was considered as statistically significant.

Results

The mean age was comparable in the 2 groups (Group D 47.4 ± 11.63, Group C 46 ± 12.06). The groups were equally distributed for gender.

The mean baseline HR in the 2 groups was comparable.

HR decreased significantly from the baseline at T1 to T3 ($P < 0.001$) and at T7 ($P = 0.02$) time intervals [Table 1]. However, in the control Group HR was comparable to the baseline up to T3 time interval but there was a fall in HR at T4 ($P < 0.001$) and T5 ($P = 0.002$) time intervals. In dexmedetomidine group, the mean preoperative baseline HR (90.48 ± 17.54 bpm) was comparable with the mean preoperative HR (85.04 ± 14.71 bpm) of the control group ($P = 0.096$). Similarly comparable HR was observed in both the groups at T2 and T3 intervals. However at induction

(T4), the mean HR in the dexmedetomidine group (78.20 ± 11.24) was significantly low as compared to the control group (82.26 ± 7.26, $P = 0.034$). Immediately after intubation (T5), HR increased to statistically significant values in the control group (102.18 ± 13.42) as compared to the dexmedetomidine group (86.34 ± 9.91) ($P < 0.001$). Similarly, the increase in HR was statistically significant at 1, 3 and 5 min after intubation ($P = 0.001$, 0.036 and 0.001 respectively) as shown in Table 1.

In dexmedetomidine group the mean SBP was comparable at T1, T2 and T3 time intervals. However, the SBP showed a fall from baseline at T4 ($P < 0.001$), and 1, 3 and 5 min ($P < 0.001$) after intubation. In the control group also the SBP was comparable at T1, T2 and T3 time intervals. There was statistically significant fall in SBP from the baseline values at induction (T4) ($P < 0.001$), however at rest of the time intervals the SBP was comparable to the baseline [Table 3]. SBP showed a significantly greater fall in group D when compared to group C at T4 ($P = 0.045$), T5 ($P = 0.007$), T6 ($P = 0.001$), T7 and T8 time intervals ($P < 0.001$).

The baseline values of IOP were comparable in both the groups (15.3 ± 1.22 vs. 15.31 ± 1.19, $P = 0.957$).

There was a significant fall in the IOP from the baseline value (15.32 ± 1.22) in dexmedetomidine group throughout the study period, that is, 5 min after giving the drug to 5 min postintubation ($P < 0.001$). However in the control group, the baseline IOP (15.31 ± 1.19), started rising after intubation that is, at T5 (17.71 ± 2.12, $P < 0.001$), T6 (17.10 ± 1.90, $P < 0.001$), T7 (16.33 ± 1.62, $P < 0.001$) and T8 (15.84 ± 1.55, $P = 0.007$) time intervals and remained higher than the baseline value till 5 min postintubation as shown in Table 2.

Table 1: Intragroup and intergroup comparison of HR

HR	Group D		Group C		*P*
	Mean ± SD	*P*	Mean ± SD	*P*	
T1	90.48±17.54	<0.001	85.04±14.71	1.000	0.096
T2	81.68±15.14	<0.001	84.04±12.32	0.554	0.395
T3	79.38±15.62	<0.001	82.88±10.72	1.000	0.194
T4	78.20±11.24	0.473	82.26±7.26	<0.001	0.034
T5	86.34±9.91	0.124	102.18±13.42	0.002	<0.001
T6	84.70±11.80	0.167	94.08±14.70	1.000	0.001
T7	84.32±11.76	0.020	89.90±14.33	0.473	0.036
T8	82.56±11.96		90.82±11.74		0.001

HR = Heart rate, SD = Standard deviation

Table 2: Intragroup and intergroup comparison of IOP between the groups

IOP	Group D		Group C		*P*
	Mean ± SD	*P*	Mean ± SD	*P*	
T1	15.32±1.22	<0.001	15.31±1.19	0.064	0.957
T2	14.17±1.08	<0.001	15.13±1.40	0.320	<0.001
T3	13.65±0.91	<0.001	15.20±1.55	<0.001	<0.001
T4	10.45±2.03	<0.001	13.36±1.58	<0.001	<0.001
T5	14.25±1.81	<0.001	17.71±2.12	<0.001	<0.001
T6	13.29±1.70	<0.001	17.10±1.90	<0.001	<0.001
T7	12.92±1.89	<0.001	16.33±1.62	0.007	<0.001
T8	13.36±1.72		15.84±1.55		<0.001

IOP = Intraocular pressure, SD = Standard deviation

Table 3: Intergroup and intragroup comparison of SBP

SBP	Group D		Group C		*P*
	Mean±SD	*P*	Mean±SD	*P*	
T1	123.94±12.01	0.478	126.22±9.21	0.561	0.289
T2	122.78±16.91	0.154	125.92±7.87	0.138	0.235
T3	120.72±10.96	<0.001	125.06±6.50	<0.001	0.071
T4	108.50±14.58	1.000	113.96±12.32	1.000	0.045
T5	120.76±16.30	0.001	130.24±17.97	0.930	0.007
T6	113.62±16.19	<0.001	126.02±18.59	0.287	0.001
T7	102.92±11.24	<0.001	124.02±15.28	0.056	<0.001
T8	102.32±12.52		122.34±14.20		<0.001

SBP = Systolic blood pressure, SD = Standard deviation

Discussion

Postoperative visual loss (POVL) is a rare, unexpected but a disastrous complication, which can occur in nonocular surgery. The main causes of visual loss after nonocular surgery are retinal vascular occlusion and ischemic optic neuropathy. Incidence of POVL has been reported as 1/60,000-1/125,000.[11,12]

Although the incidence of POVL is low, the permanent disability cripples the patient to lifelong handicap. This concern has raised the awareness regarding maintaining IOP intraoperatively. Steep trendelenberg position in robotic surgeries, prone position in spine surgery, open heart procedures with prolonged hypotension, etc. has increased the incidence of POVL. Open globe injuries if subjected to raised IOP can lead to loss of intraocular contents.[3] So maintaining IOP intraoperatively to low-normal values is of utmost importance. Avoiding laryngoscopy and intubation is an alternative to intubation for maintaining airway intraoperatively but can not be used in all cases. So in cases where intubation is imperative, pharmacological measures have been sought to reduce and maintain IOP. Among these pharmacologic measures local anesthetics, opioids, vasodilators, beta blockers, calcium channel blockers, etc. have been used in the past. These agents either were not effective as required or had untoward side effects. Newer agents then were explored, and work has been done on agents like dexmedetomidine, clonidine, gabapentin, etc.

Dexmedetomidine, the pharmacologically active d-isomer of medetomidine, is a highly selective and specific α2-adrenoceptor

agonist. Dexmedetomidine, by its central sympatholytic action, promotes hemodynamic stability when used as an adjuvant during general anesthesia. The effect of dexmedetomidine on the IOP may be due to its direct vasoconstrictor effect on the afferent blood vessels of the ciliary body. It leads to a reduction of aqueous humor production. It may also facilitate the drainage of aqueous humor by reducing sympathetically mediated vasomotor tone of the ocular drainage system. Finally, the hemodynamic effects of dexmedetomidine can be responsible for the reduction of IOP.[13,14]

Mowafi *et al.*[10] studied the effect of dexmedetomidine premedication (0.6 μg/kg) on the IOP changes after succinylcholine and intubation on patients undergoing elective nonophthalmic surgeries under general anesthesia. They concluded that dexmedetomidine premedication blunted the rise in the IOP caused by succinylcholine and intubation. In addition, dexmedetomidine attenuated the hemodynamic response to laryngoscopy and intubation.

Later on Pal *et al.*[15] studied two doses of dexmedetomidine, 0.4 μg/kg and 0.6 μg/kg and compared with saline and studied their effects on IOP, HR and MAP on laryngoscopy and intubation with succinylcholine. They concluded that dexmedetomidine (0.6 μg/kg, as well as 0.4 μg/kg body weight,) effectively prevents rise of IOP associated with administration of suxamethonium and endotracheal intubation. However, dexmedetomidine 0.6 μ/kg may cause significant hypotension and bradycardia without further decrease in IOP. Thus, dexmedetomidine 0.4 μg/kg may be preferred for prevention of the rise in IOP Even in hypertensive patients administration of dexmedetomidine before anesthesia blunts the hemodynamic response to tracheal intubation and reduces the thiopental dose.[16]

Previous researchers used succinylcholine for rapid sequence induction, which lead to increase in IOP as observed in studies done by Mowafi *et al.*[10] Suxamethonium use for intubation is controversial in penetrating eye injury due to the risk of extrusion of vitreous contents, which can be avoided by substituting it with rocuronium when a rise in IOP is undesirable.[17]

Thus to curb this rise in IOP by succinylcholine for laryngoscopy and intubation, we have used rocuronium, a nondepolarizing neuromuscular blocking agent as there was evidence from another previous study done by Larsen *et al.*[18] where he substituted rocuronium in place of succinylcholine and got ideal intubating condition for rapid sequence induction with a definite benefit in terms of stable IOP.

Based on the above findings a randomized, double-blind study was designed by us to study the effect of dexmedetomidine premedication on IOP and hemodynamic changes in response to laryngoscopy and intubation.

HR in the dexmedetomidine group showed that there is no incidence of significant bradycardia during the infusion of the drug or even later on. The findings were similar to the observations in the previous study by Pal *et al.*[15] where he found that at 0.4 μg/kg body weight dexmedetomidine does not lead to any untoward side effects whereas in a dose of 0.6 μg/kg body weight, it leads to significant bradycardia.

Dexmedetomidine given as a continuous infusion at a rate of 0.4 μg/kg/h intraoperatively also helped to alleviate the IOP increase in patients undergoing robot-assisted laparoscopic radical prostatectomy in the steep trendelenburg position.[19]

In our study, HR remained at values lower than the baseline preoperative values in the dexmedetomidine group (*P* values at T2-T1, T3-T1 and T4-T1 <0.001). HR values in dexmedetomidine premedicated patients were significantly low as compared to the control group starting from the induction, intubation and 1, 3 and 5 min after intubation (*P* values of 0.034, <0.001, 0.001, 0.036 and 0.001respectively) as shown in Table 1.

The SBP was comparable in the two groups till the induction, after induction there was statistically significant fall in SBP in Group D compared to the control group ($P = 0.045$). At intubation, there was no significant rise SBP in the drug group compared to the control group. It remained low even at 1, 3 and 5 min after intubation ($P < 0.001$, $P < 0.001$, $P < 0.001$ respectively). Statistically low IOP was recorded at all times as compared to the preoperative baseline values in the dexmedetomidine group ($P < 0.001$). It never increased above the baseline even at intubation. Whereas, in the control group, the IOP was significantly above the baseline at intubation and at 1, 3 and 5 min after intubation ($P < 0.001$, <0.001, <0.001, =0.007 respectively) [Table 2].

Above findings suggest that pressor response to intubation following the laryngoscopy has been attenuated by dexmedetomidine premedication effectively. On contrary, findings in the control group confirmed the sympathetic haemodynamic response to laryngoscopy and intubation was observed to a statistically significant values that could be detrimental in certain group patients.

Conclusions

Dexmedetomidine premedication (0.4 μg/kg infused over 10 min i.v.) attenuates the pressor response of laryngoscopy and intubation. It lowers the IOP and maintains it lower

than the baseline values even after laryngoscopy and intubation without any untoward effects like bradycardia and hypotension.

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How to cite this article: Chandra A, Ranjan R, Kumar J, Vohra A, Thakur VK. The effects of intravenous dexmedetomidine premedication on intraocular pressure and pressor response to laryngoscopy and intubation. J Anaesthesiol Clin Pharmacol 2016;32:198-202.
Source of Support: Nil, **Conflicts of Interest:** None declared.