

COMPARISON OF THE EFFECT OF CLONIDINE AND DEXMEDETOMIDINE PREMEDICATION ON THE INTRAOCULAR PRESSURE AND HEMODYNAMIC CHANGES AFTER SUCCINYLCHOLINE ADMINISTRATION AND ENDOTRACHEAL INTUBATION IN PATIENTS UNDERGOING ELECTIVE NON-OPHTHALMIC SURGERIES UNDER GENERAL ANAESTHESIA

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ABSTRACT:

Background: Succinylecholine during anaesthesia can cause transient increase in intraocular pressure (IOP). We have assessed and compared the effect of clonidine and dexmedetomidine as IV premedication in attenuating rise in IOP following laryngoscopy and tracheal intubation following administration of succinylcholine. **Methods:** Prospective, double blind, observational study was conducted in 111 patients undergoing elective non-ophthalmic surgery under general anesthesia. Patients were randomly allocated into three groups to receive normal saline (Group I), 2 µg/kg clonidine (Group II) and 0.5 µg/kg dexmedetomidine (Group III) as premedication IV over a period of 10 min before induction. Post induction, Laryngoscopy and intubation were performed after succinylcholine 2 mg/kg IV. IOP, heart rate and mean arterial pressure were recorded. **Results:** Mean baseline IOP of all 3 groups were comparable (13.3 ± 1.2 , 13.8 ± 1.2 and 13.7 ± 1.1). The abrupt rise in IOP after succinylcholine and intubation were blunted in both Group II and III, as there was less increase in IOP from baseline as compared with the Group I and this difference was statistically significant ($p < 0.05$). In both Group II and Group III, IOP returns to baseline at just 3 min. after intubation and remains below baseline value at 6 and 9 min. after intubation while in Group I it returns to baseline only at 9 min. after intubation. **Conclusion:** Single IV dose of dexmedetomidine as premedication blunted the abrupt increase in IOP following succinylcholine administration and tracheal intubation more effectively than clonidine.

Key-words: Premedication, clonidine, dexmedetomidine, intraocular pressure, succinylcholine, laryngoscopy, intubation.

INTRODUCTION:

The key for successful outcome in ophthalmic surgeries depends on various factors including stable intraocular pressure (IOP) in the

perioperative period. Any rise in IOP can cause expulsion of ocular contents leading to loss of sight, especially in cataract surgery, removal of

foreign body, glaucoma and corneal grafting etc.(1) Inadvertent hemodynamic disturbances following laryngoscopy and intubation impose additional insult in these patients.

The goal of anaesthesia in emergency ophthalmic surgery is rapid sequence induction (RSI) and intubation without any increase in IOP. Though, succinylecholine is commonly used during RSI in patients with full stomach but it increases the IOP. Different techniques, as well as drugs have been used to attenuate these response during induction of anaesthesia. Techniques like 150 head up tilt, (2) hyperventilation (3) and anaesthetic agents like diazepam,(4) midazolam,(5) thiopental sodium,(6) propofol,(7) self-taming with succinylcholine,(8) pretreatment with non-depolarizing muscle relaxant atracurium,(9) rocuronium (10) and vecuronium,(9) potent opioids like alfentanil,(11) sufentanil,(11) fentanyl(12) and remifentanil,(13) all inhalational agents,(14) lignocaine,(15) centrally acting α_2 adrenergic agonists clonidine (16) and dexmedetomidine,(17) acetazolamide(18) etc. have been used to decrease the IOP perioperatively.

Centrally acting α_2 adrenergic agonists like clonidine and dexmedetomidine have been shown to decrease IOP following intravenous administration. In this study, we compared the efficacy of single bolus administration of

clonidine (2 μ g/kg) and dexmedetomidine(0.5 μ g/kg) as premedication in attenuating the rise of IOP after suxamethonium and tracheal intubation.

METHODS:

This study was conducted in the department of Anaesthesiology at a Tertiary Care Centre. This prospective, randomised, double-blind study included 111 patients of either sex, American Society of Anesthesiologists Grade I and II, age 25–50 years, body weight 40–70 kg who underwent elective non-ophthalmic surgical procedure under general anaesthesia. Prior ethical permission was taken from our Institutional Ethical Committee and Review Board and written informed consent was obtained from all patients enrolled for the study. Patients with history of respiratory, cardiac, hepatic, renal or metabolic disorder, convulsion, hypersensitivity to the drugs used, acute or chronic eye disease, bleeding disorder, severe neurological deficit, chronic alcohol or drug abuse, patients being treated with drugs like adrenoceptor agonist or antagonist, digoxin, anticonvulsants or psychotropic medications, medication which can alter IOP, pregnant or lactating mother, patients with bradycardia, hypertension, severe hypovolemia were excluded from the study. Patients with suspicious difficult

intubation or who required multiple attempts for intubation were also excluded from the study.

The patients were randomized into three groups each of 37 patients by chit in box method. Medications were prepared and hidden behind drapes and administered by one anaesthesiologist, and observations were made by other anaesthesiologist who was blinded to the group to which the patient was assigned. In Group I, 37 patients received 20 ml of normal saline; in Group II, 37 patients received 2 mcg/kg body weight clonidine hydrochloride (Cloneon, Neon Laboratories) and in Group III, 37 patients received 0.5 mcg/kg body weight dexmedetomidine hydrochloride (Dexem, Themis Medicare Limited). All the drugs were prepared in identical syringes diluted with isotonic normal saline to make a total volume of 20 ml. The study solution was administered by a syringe pump over a period of 10 min before induction of anesthesia.

Patients were kept nil per oral from midnight before surgery. On day of surgery, in the operation theater, a large bore (18 G) intravenous access were obtained and Ringer lactate was started at the rate of 10 ml/kg/h. Pre-induction monitors like pulse oximeter, non-invasive blood pressure and electrocardiogram were attached and patient's baseline vitals were measured. Proparacaine hydrochloride 0.5% topical

solution was instilled on the patient's left eye and baseline IOP (T₀) was recorded with a, Schiøtz tonometer (made in Germany) by an ophthalmologist who was unaware of the nature of the study. Scaled reading noted with shiotz tonometer was converted to pressure in mm of Hg (IOP) with the help of shiotz tonometer chart. All measurements were made with the patient supine and with no tilt on the operating table. Heart rate was measured from ECG (standard lead 2), blood pressure was measured with sphygmomanometer and SpO₂ was recorded with pulse oxymeter.

All patients in the three groups received a uniform anaesthetic technique. After 3 minutes of preoxygenation with 100% oxygen, anaesthesia was induced with intravenous glycopyrrolate (4 µg/kg), midazolam (0.05mg/kg), fentanyl (2 µg/kg), and thiopental 5 mg/kg till loss of eyelash reflex. Direct laryngoscopy and tracheal intubation was performed 1 minute after intravenous succinylcholine (2 mg/kg) administration. Anesthesia was maintained with nitrous oxide-oxygen mixture (2:1) with isoflurane (1%) and intermittent dose of intravenous atracurium. Surgeon was asked to start surgery only when observation of the study was completed. All the patients were ventilated mechanically by modern anesthesia workstation to maintain the end-tidal

carbon dioxide partial pressure between 30-35 mmHg. At the end of anesthesia, the neuromuscular blockade was antagonized with neostigmine and glycopyrrolate. Trachea was extubated and the patient was observed in the postoperative recovery room.

The readings of intraocular pressure(IOP), heart rate(HR) and mean arterial pressure(MAP) were documented at following time points: -

- a) Before premedication(Baseline) = T0
- b) After completion of infusion of study drug = T1
- c) 30 seconds after administration of thiopentone sodium = T2
- d) After administration of succinylcholine = T3
- e) Immediately after intubation = T4
- f) 3 minutes after intubation = T5
- g) 6 minutes after intubation = T6
- h) 9 minutes after intubation = T7

We defined the following terms for study:

Hypotension: 30% decrease in Mean Arterial Pressure from baseline.

Bradycardia: HR < 60 beats/min.

Tachycardia: HR more than 100 beats/min.

End Point: 10 minutes after induction of anaesthesia.

Hypotension was initially treated with an IV fluid bolus of 200 ml. If hypotension persisted,

intravenous mephentermine 6 mg was administered, which was repeated if necessary. Bradycardia was treated by intravenous atropine (0.6 mg).

Statistical Analysis:

Sample size was calculated by Primer of Biostatistics software version 6.0 (by Stanton A. Glantz, © 2005 McGraw-Hill) based on a power analysis ($\alpha = 0.05$, $\beta = 0.2$), which revealed that 37 patients should be included in each group. The analysis of the statistical data was carried out by Statistical Package for the Social Sciences software version 21 (SPSS Inc., Chicago, Illinois, USA). The categorical measurements were summarized as the number and percentage, continuous measurements as the arithmetic mean and standard deviation. One-way ANOVA was used for analysis. A "p" value of less than 0.05 was considered significant.

RESULT:

A total of 111 patients were included in this randomized, double-blind trial and none excluded from final analysis. There were no significant differences in demographic profile (age, sex, weight and ASA physical status of the patients) among the groups. [Table 1] Baseline clinical parameters like HR, SBP, DBP, MAP, SpO2 and IOP of the three groups were also comparable. [Table 2]

Decrease in IOP was observed in Group II and III following infusion of study drugs (T1) and 30 seconds after administration of thiopentone (T2) as compared with baseline (T0) but it was statistically insignificant. ($p > 0.05$) [Table 3] Following succinylecholine administration (T3) IOP increased in all three Groups but it was lower in Group II and III as compared to Group I. ($P < 0.001$) IOP was also increased after intubation (T4) in all the groups but it was significantly lower in Group II and III than control group. ($P < 0.001$) [Figure 1]

IOP was more than the baseline in the Group I even after 6 min following intubation (T6) whereas it was below baseline values in Group II and Group III patients up to T7 i.e. 9 minutes after intubation. [Table 3]

After premedication, decrease in HR and MAP was observed in clonidine as well as dexmedetomidine group while significant increase in HR and MAP from baseline was recorded following intubation in control group ($P < 0.05$). [Figures 2 and 3].

No patient had bradycardia or hypotension in the study groups.

DISCUSSION:

Following observations are drawn from our study:

- Baseline intraocular pressure was between 11–16 mm Hg with mean of 13.5 mm Hg.
- Effects after premedication: A greater fall in intraocular pressure was noted after premedication in patients receiving clonidine or dexmedetomidine. Less increase in heart rate was seen after giving glycopyrrolate in patients receiving clonidine or dexmedetomidine and a greater decrease in MAP was seen in these patients compared to patients in the control group.
- Effects after thiopentone: A greater decrease in IOP was seen in patients receiving clonidine or dexmedetomidine and the increase in heart rate was less in these patients.
- Effects following administration of succinylcholine: The rise in intraocular pressure, heart rate and blood pressure were significantly less in patients receiving clonidine or dexmedetomidine as premedication than in control group.
- Effects of intubation and thereafter till ninth minute: The increase in intraocular pressure, heart rate and blood pressure were significantly less than the control group in patients given clonidine or dexmedetomidine premedication. The return of various parameters to baseline

value was also quicker in patients given clonidine or dexmedetomidine than in control group.

Succinylcholine is a depolarizing neuromuscular blocker with very rapid onset and ultra-short duration of action which is universally used during RSI. Its use is limited in patients with perforating eye injury because of significant increases in IOP. The IOP rises within 1 minute of administration, peaks at 2-4 minutes and return to normal by 6 minutes. (19) In spite of that, it is still used as no other neuromuscular blocker has been able to match the pharmacokinetic properties of succinylcholine.

The success of ophthalmic surgery largely depends on proper control of intraocular pressure in the perioperative period, especially during induction and tracheal intubation. However, no drug has been shown to be totally effective in obtunding the intraocular hypertensive effects of succinylcholine, laryngoscopy and tracheal intubation and the search of better alternatives still continues.

Clonidine causes an increase in vascular resistance and thereby reduces retinal blood flow and thus reduction in IOP follows.(20) Ghignone et al.(21) studied the effects of oral clonidine (5 µg/kg) on IOP and observed that clonidine not only effectively prevented rise in IOP but also attenuated the associated cardiovascular response

following laryngoscopy and tracheal intubation. Lemes et al.(22) reported a remarkable decrease in IOP and HR after administration of intravenous clonidine (2.5 µg/kg) in the patients undergoing cataract surgery under peribulbar block. Rajan et al.(20) evaluated the efficacy of intravenous clonidine (1 µg/kg) as premedication in obtunding the rise in IOP during laryngoscopy and intubation following administration of succinylcholine but found that clonidine did not prevent rise in IOP following succinylcholine, laryngoscopy, and intubation although it effectively attenuated hemodynamic responses to laryngoscopy and intubation. We used single bolus low dose of clonidine (2 µg/kg) in our study as there is a risk of hypotension and bradycardia if higher dose of the drug is used.

Dexmedetomidine decreases the IOP by various mechanisms. By its direct vasoconstrictor effect on the afferent blood vessels of the ciliary body, it reduces the aqueous humor production. It also facilitates the drainage of aqueous humor by reducing sympathetically mediated vasomotor tone of the ocular drainage system.(23) Moreover, the hypotension that follow dexmedetomidine administration can also result in a reduction in IOP. Mowafi et al.(24) investigated the effect of dexmedetomidine (0.6 µg/kg) on IOP following succinylcholine administration and intubation and concluded that

dexmedetomidine could be a beneficial premedication in open globe injuries. Pal et al.(25) compared the effects of two different doses of dexmedetomidine (0.6 µg/kg vs 0.4 µg/kg) and documented that both are effective in prevention of rise in IOP associated with administration of succinylcholine and endotracheal intubation. However, hemodynamic stability was better with a lower dose (0.4 µg/kg). We used single bolus low dose of dexmedetomidine (0.5 µg/kg) in our study.

In this study, we used Schiotz tonometer (an indentation tonometer) to measure IOP which is commonly available and easy to use. But, it is considered less accurate as it doesn't take into account corneal thickness and viscoelasticity. Study of changes of IOP with Goldmann applanation tonometry would be more appropriate and precise as it is considered as the gold standard nowadays.

CONCLUSION:

Thus, Single bolus dose of either clonidine or dexmedetomidine is a good choice as premedication to attenuate the rise in intraocular pressure and hemodynamic changes following succinylcholine administration and tracheal intubation. Though both the drugs are effective but dexmedetomidine was found to be better than clonidine.

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Table 1: Demographic Profile [mean \pm SD]:

Variables	Group I	Group II	Group III	p value
Age (years)	34.6 \pm 8.6	33.8 \pm 8.1	35.1 \pm 8.4	0.79
Weight (kg)	55.2 \pm 7.4	57.9 \pm 6.5	58.2 \pm 7.5	0.14
Sex(male : female)	20 : 17	19 : 18	20 : 17	0.89
ASA (I : II)	30 : 7	28 : 9	32 : 5	0.67

SD = Standard Deviation, Group I = control group, Group II = clonidine group, Group III = Dexmedetomidine group

Table 2: Baseline clinical Parameters [mean \pm SD]:

Variables	Group I	Group II	Group III	p value
IOP	13.3 \pm 1.2	13.8 \pm 1.2	13.7 \pm 1.1	0.155
SBP	119.8 \pm 8.7	119.9 \pm 9.1	123.3 \pm 9.5	0.175
DBP	79.8 \pm 7.1	79.5 \pm 6.3	82.3 \pm 6.8	0.151
MAP	93.1 \pm 6.5	92.9 \pm 6.3	96.0 \pm 6.9	0.081
Pulse Rate	82.4 \pm 6.1	81.4 \pm 10.6	83.8 \pm 13.3	0.611
SpO ₂	99.5 \pm 0.6	99.7 \pm 0.6	99.8 \pm 0.5	0.074

SD = Standard Deviation, Group I = control group, Group II = clonidine group, Group III = Dexmedetomidine group, IOP = Intraocular Pressure, SBP = Systolic Blood Pressure, DBP = Diastolic Blood Pressure, MAP = Mean Blood Pressure

Table 3: Changes in IOP over different time intervals:

Time event	Group I	Group II	Group III	p value
T ₀	13.3 ± 1.2	13.8 ± 1.2	13.7 ± 1.1	0.155
T ₁	13.0 ± 1.3	12.8 ± 1.4	12.3 ± 1.8	0.128
T ₂	12.2 ± 1.4	11.8 ± 1.6	12.1 ± 2.0	0.570
T ₃	14.3 ± 1.4	13.3 ± 1.5	13.0 ± 1.7	0.019
T ₄	16.4 ± 1.1	15.0 ± 1.5	14.1 ± 1.5	< 0.001
T ₅	15.0 ± 1.1	13.4 ± 2.3	13.4 ± 1.4	< 0.001
T ₆	13.9 ± 1.2	12.3 ± 2.0	12.4 ± 1.7	< 0.001
T ₇	13.1 ± 1.3	11.6 ± 1.7	11.5 ± 1.8	< 0.001

SD = Standard Deviation, Group I = control group, Group II = clonidine group, Group III = Dexmedetomidine group

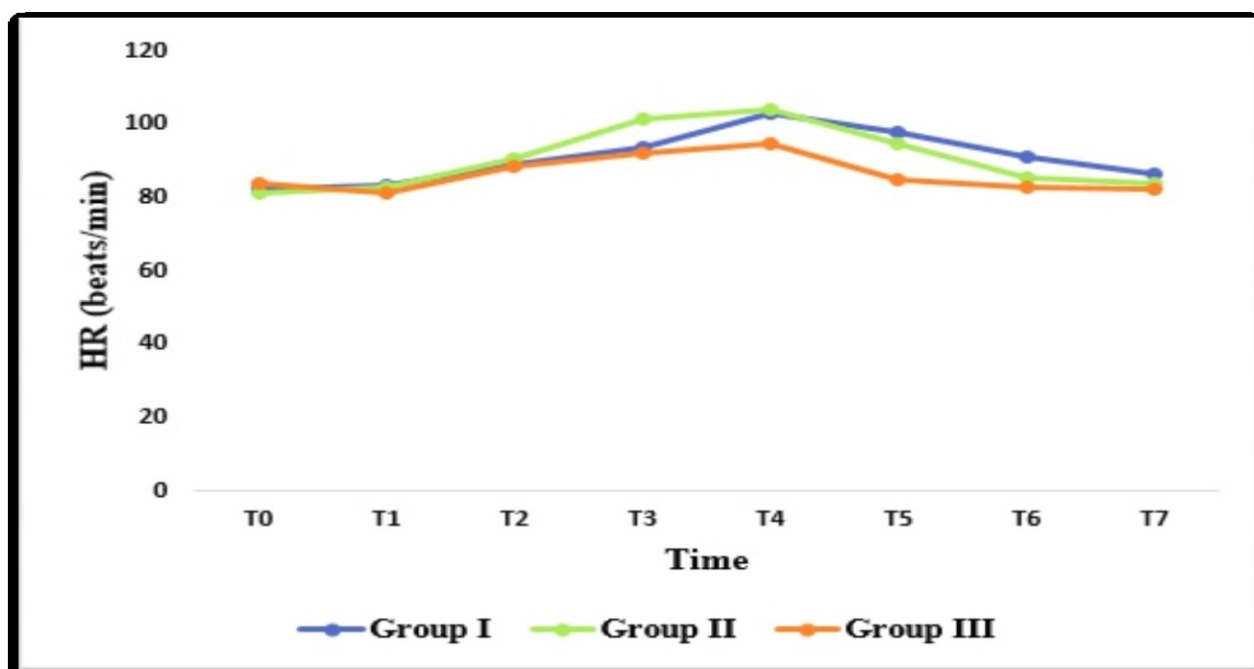
Figure 1

Figure 2:

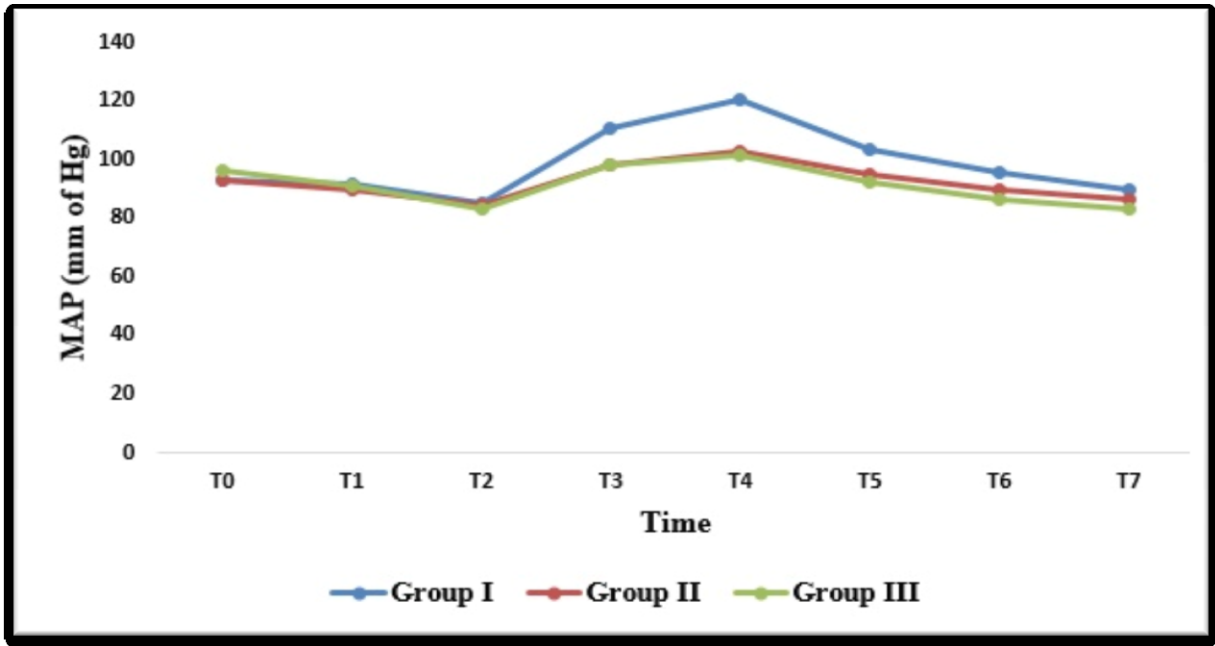


Figure 3:

