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TOPICAL TIMOLOL PREVENTS INTRAOCULAR PRESSURE RESPONSE TO SUCCINYLCHOLINE AND TRACHEAL INTUBATION

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The effect of topical timolol on intraocular pressure response to succinylcholine and tracheal intubation was studied in 40 adult patients, divided randomly into two groups of 20 each. These groups received normal saline (one drop) and timolol (one drop, 0.5%) as pretreatment in a double blind manner, thirty minutes before anaesthetic induction with thiopentone and succinylcholine 1.5 mg/kg. Topical timolol caused a significant decrease in intraocular pressure.

Succinylcholine and tracheal intubation caused a significant increase in intraocular pressure in the control group (normal saline) whereas intraocular pressure remained below basal levels throughout the period of study in the trial group (timolol). In conclusion, topical timolol pretreatment administered 30 minutes prior to induction of anaesthesia offers protection against succinylcholine and tracheal intubation initiated increases in intraocular pressure without causing any significant cardiovascular effects. Bahrain Med Bull 1995;17(4):

Rapid sequence induction of anaesthesia for patients with penetrating eye injury continues to be a matter of concern because no clear and reliable methods for avoiding increases in intraocular pressure (IOP) have been agreed upon[1]. Succinylcholine, the relaxant of choice for rapid intubation, causes a transient but significant increase in IOP[2]. IOP is further increased after tracheal intubation[3,4]. Several methods of pretreatment have been suggested, but none has been found to be consistently and completely effective in preventing succinylcholine and tracheal intubation induced increase in IOP[1,5-8,9-11].

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Timolol, a B-blocking agent is an effective drug against a variety of glaucomas[12]. Though the exact mechanism of action is not known, it is believed to alter the production of aqueous humor. It has been used to lower the IOP during perioperative period in patients undergoing cataract surgery and Nd-YAG laser capsulotomies[13,14]. The aim of the present study was to test the efficacy of topical timolol, to suppress the IOP response after succinylcholine and tracheal intubation.

METHODS

The study was carried out in a double blind fashion. Forty patients of both sexes, aged 15-50 years, and categorised in accordance to criteria of American Society of Anaesthetists as physical status 1 were selected. The patients had

no eye ailment and were scheduled for elective surgery unrelated to the eye. The study was approved by and carried out according to the instructions of the ethics committee of the institute. The patients were informed about the procedure for measurement of IOP and consent obtained. All patients were premedicated with meperidine 1.5 mg/kg and promethazine 0.4 mg/kg IM, one hour before anaesthesia and were allocated to one of the two groups, of 20 each, with the help of a random number chart. Pretreatment with one of the following was given topically 30 minutes before induction of anaesthesia.

Group - 1 Normal Saline, 1 drop
Group - 2 Timolol (0.5%), 1 drop

Thirty minutes following pretreatment, intravenous induction was carried out with sufficient thiopentone to obtund the eye lash reflex, followed by succinylcholine 1.5 mg/kg. Meanwhile, ventilation was assisted/controlled with a face mask, using a Bain anaesthetic circuit delivering 33% oxygen in nitrous oxide at a total fresh gas flow of 100 ml/kg body weight/ min[15]. After the onset of apnoea, laryngoscopy and tracheal intubation was performed, taking not more than 30 seconds. Inhalational supplements and/or topical local anaesthetic spray were avoided during the induction sequence.

Measurements of IOP, systolic arterial pressure (indirect), and heart rate (Horizon 2000, Mennen Medical Inc.) were made with patient supine and with the operating table flat, at the following intervals:

1. Before pretreatment (basal value)
2. Thirty minutes after pretreatment, just before induction.
3. After injection of thiopentone
4. One minute following intubation and then every 2 min thereafter until the effect of succinylcholine began to wear off.

All measurements of IOP were made by the same worker (RK), using a perkins hand held applanation tonometer (technique accurate to within0.5 ˚ mm Hg)[16,17]. In each patient, the readings were taken in both eyes following topical administration of three drops of 4% lidocaine. The mean of the two readings was recorded. At no time did the measurement of IOP interfere with the progress of the anaesthetic. In addition, conditions for intubation were assessed in each patient according to criteria used by Eisenberg et al (Excellent - easy passage without coughing, Good - easy passage with slight cough, Fair - easy passage with more than one cough, Poor - difficult passage or/with coughing more than 10 seconds)[18].

The data were analysed using t-test for paired and non-paired parametric data and the chi-square test for non-parametric data.

RESULTS

The two groups of patients were comparable on the basis of age, body weight, resting IOP, heart rate, systolic arterial pressure (SAP) and dose of thiopentone (Table 1). Conditions for intubation were either excellent or good in all the patients and were comparable in the two groups ($p > 0.05$).

Table 1
Summary of patient data in two groups, Mean (SEM)

	Group 1 (control) (n=20)		Group 2 (Timolol) (n=20)	
Age, year	28.80	(1.93)	28.35	(2.81)
Body weight, kg	52.55	(1.85)	54.78	(1.71)
IOP, mm Hg	14.55	(0.54)	13.70	(0.61)
Heart rate (Bears min-1)	80.10	(2.17)	87.20	(2.99)
SAP, mm Hg	124.40	(2.57)	125.00	(2.71)
Dose of thiopentone, mg	256.25	(8.09)	271.25	(6.36)

Figure 1 shows the sequential changes in IOP in the two groups. IOP decreased significantly below basal value after pretreatment in group 2 (timolol) by an average of 18.25% of basal value (P<0.001). Following thiopentone, IOP decreased significantly in both the groups, however, in patients pretreated with timolol (group 2), this decrease was greater (48.6%) than in patients pretreated with normal saline (40.5%). IOP increased significantly in group 1 (Saline) immediately following succinylcholine and tracheal intubation (P<0.001) and continued to remain above basal values even at 3 and 5 minutes. In group 2 (timolol) IOP remained lower than the basal value following succinylcholine and tracheal intubation through out the period of study.

Table 2
Heart rate and systolic arterial pressure (SAP) in two groups, Mean (SEM)

		Basal	After pretre-atment	After thiope-ntone	Minutes 1	After 3	Intubation 5
Heart rate beats min-1	Group 1	80.10 (2.17)	79.60 (2.29)	85.35# (2.35)	99.65* (3.45)	91.95* (3.97)	87.35# (4.04)
	Group 2	87.20 (2.99)	76.95# (3.18)	83.30 (3.32)	95.70@ (3.10)	91.10 (2.72)	87.90 (2.73)
SAP, mm Hg	Group 1	124.40 (2.57)	126.75 (2.73)	112.70* (2.60)	139.00* (3.86)	133.85* (2.97)	132.20# (3.01)
	Group 2	125.00 (2.71)	128.30 (2.74)	120.55 (4.18)	140.75* (3.66)	134.30# (4.28)	129.50 (3.13)

* P<0.001 as compared to basal value
# P<0.01 as compared to basal value
@ P<0.05 as compared to basal value

Timolol pretreatment produced a significant decrease in heart rate (P<0.01) in group 2 (Table 2). This fall occurred in 17 out of 20 patients in the present study. Following thiopentone the heart rate increased by 5.25 bpm (P<0.01) in group 1 whereas it remained below basal rate by 3.9 bpm in group 2. However, tracheal intubation caused a significant increase in heart rate in both group 1 (24.4%, P<0.001) and group 2 (9.74%, P<0.05).

Tracheal intubation also caused a significant increase ($P<0.001$ at 1 min) in systolic arterial pressure in both groups (Table 2). However, it returned to values, comparable with basal values within 5 minutes of tracheal intubation in group 2.

DISCUSSION

A number of studies showed that succinylcholine causes an increase in IOP[2-4,19], but the exact mechanism remains uncertain. Contraction of extraocular muscles, dilatation of choroidal blood vessels, axial shortening of globe and relaxation of orbital smooth muscles were suggested as being responsible[20]. This increase in IOP following succinylcholine, which is aggravated further by tracheal intubation, may be secondary to a sudden increase in arterial pressure[21], reflex venospasm[22] or straining[23].

A number of methods of pretreatment have been suggested in an attempt to prevent the succinylcholine induced increase in IOP. These include small doses of competitive neuromuscular relaxants 'self taming' small doses of succinylcholine and drugs such as hexafluorenium, acetazolamide, diazepam, nitroglycerine and lignocaine but none of these methods has been universally accepted in clinical practice[5, 6, 7, 8, 9, 10,11 24-30].

Timolol is a potent, long acting B-adrenergic blocking drug which decreases IOP by decreasing the production of aqueous humor[12]. It has little systemic effects when instilled locally. The drug has been reported to be present in aqueous humor within 12 minutes and drug effects are evident in 20 minutes[12,31]. We instilled the drug 30 minutes before induction to ensure adequate latent period for the drug action. In our study the ocular hypotensive effect was evident within half an hour i.e. IOP dropped significantly below basal values. Since thiopentone has different mechanism for decreasing IOP, the two drugs have a synergistic effect on IOP[32]. Further, the administration of succinylcholine and tracheal intubation increased the IOP in the control group but it remained below basal values at all time intervals in the trial group.

Our results show that pretreatment with topical timolol 30 minutes prior to induction of anaesthesia offers complete protection against succinylcholine and tracheal intubation induced increase in IOP.

We were unable to monitor arterial carbondioxide tension. Changes in arterial carbondioxide may alter IOP, but these were probably not important during the short period of this study, throughout which the patients were ventilated using a Bain anaesthetic breathing circuit[33,15].

The study also showed that tachycardia due to laryngoscopy and tracheal intubation was significantly attenuated by pretreatment with topical timolol. However, timolol failed to prevent rise in systolic arterial pressure following tracheal intubation. This implies that changes in arterial pressure do not necessarily cause changes in IOP themselves.

CONCLUSION

Topical timolol administered 30 minutes prior to induction of anaesthesia is sufficient to prevent the IOP increase associated with succinylcholine and tracheal intubation. Since it has been reported that topical timolol instillation in one eye also causes decrease in IOP in the contralateral eye, further studies are in progress to assess the efficacy of topical timolol instilled in one eye to prevent IOP increase in opposite eye following tracheal intubation.

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