Double-blind comparison of lidocaine, tubocurarine and diazepam pretreatment in modifying intraocular pressure increases

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One hundred and sixty patients, divided randomly into four groups received normal saline (5 ml), d-tubocurarine (0.05 mg·kg⁻¹), diazepam (0.1 mg·kg⁻¹) or lidocaine (1 mg·kg⁻¹) as pretreatment, in a double blind manner, five minutes before anaesthetic induction with thiopentone and succinylcholine (1 mg·kg⁻¹). Succinylcholine caused a significant increase in IOP in all groups. However, in the lidocaine group, this increase was significantly less than that observed in the control group. The post-succinylcholine increase in IOP was further aggravated by tracheal intubation in all except the lidocaine group. A further clinical trial with higher doses of lidocaine is suggested to assess its ability to obtund the succinylcholine-induced increase in IOP. Lidocaine in a dose of 1 mg·kg⁻¹ IV prevents the rise in IOP which follows intubation.

Succinylcholine administration causes a transient but significant increase in intraocular pressure (IOP).¹ IOP is further increased following tracheal intubation.² Pretreatment with a non-depolarizing neuromuscular relaxant³ or with diazepam⁴ has been suggested to prevent succinylcholine-induced increases in IOP, although other workers have found these measures to be ineffective.⁵⁻⁷

Intravenous lidocaine reduces fasciculations following succinylcholine.⁸ It attenuates reflex circulatory responses

to laryngoscopy and intubation.⁹ It is effective against the increase in intracranial pressure which follows tracheal intubation in patients with brain tumours.¹⁰ Recently it has also been shown to attenuate the IOP response to rapid intubation facilitated by pancuronium.¹¹ This study was designed to assess the effect of lidocaine on the IOP response to succinylcholine and tracheal intubation and compare it with pretreatment with d-tubocurarine or diazepam.

Methods

The study was carried out in a double-blind fashion. One hundred and sixty patients, of both sexes, aged 15-50 yrs, ASA physical status I, without any eye ailment, scheduled for elective surgery unrelated to the eye, were selected. The procedure for measurement of IOP was explained and informed consent obtained. All patients were premedicated with meperidine 1 mg·kg⁻¹ and promethazine 0.4 mg·kg⁻¹ IM, one hour before anaesthesia and were allocated to one of the four groups, of 40 each, with the help of a random numbers chart. Pretreatment with one of the following was given intravenously 5 min before induction of anaesthesia.

Group 1	Normal saline	-5 ml
Group 2	d-Tubocurarine	-0.05 mg·kg ⁻¹
Group 3	Diazepam	-0.1 mg·kg ⁻¹
Group 4	Lidocaine	-1 mg·kg ⁻¹

The pretreatment drugs were prepared by a worker not connected with the execution of procedure. They were placed in 5 ml syringes, taped to prevent the recognition of drugs on the basis of colour, and the volume of all drugs was diluted to 5 ml. Five minutes following pretreatment, intravenous induction was carried out with sufficient thiopentone to obtund the eye lash reflex, followed by succinylcholine 1 mg·kg⁻¹. Meanwhile, ventilation was assisted/controlled with a mask, using a Bain anaesthetic breathing circuit delivering 33 per cent oxygen in nitrous oxide at a total fresh gas flow of 100 ml·kg⁻¹ body

Key words

EYE: intraocular pressure; NEUROMUSCULAR RELAXANT: d-tubocurarine; HYPNOTICS: benzodiazepine; ANAESTHETIC, LOCAL: lidocaine.

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TABLE I Mean ($\pm$ SD) resting values in each group

	Group 1 (Control)	Group 2 (Tubocurarine)	Group 3 (Diazepam)	Group 4 (Lidocaine)
n	40	40	40	40
Age-range (years)	16-46	15.5-49	18-44	16-48
	27.42 $\pm$ 9.10	27.92 $\pm$ 9.29	28.77 $\pm$ 8.60	27.87 $\pm$ 8.8
Body weight (kg)	59 $\pm$ 9.42	60.97 $\pm$ 10.62	61.65 $\pm$ 10.18	58.22 $\pm$ 11.63
Thiopentone (mg)	281.25 $\pm$ 38.95	280.12 $\pm$ 60.96	254.37 $\pm$ 34.65	247.5 $\pm$ 34.27
IOP (mmHg)	15.85 $\pm$ 1.37	15.65 $\pm$ 2.17	15.96 $\pm$ 1.28	15.34 $\pm$ 1.73
Pulse rate (Beats $\cdot$ min ⁻¹)	77 $\pm$ 6.89	78.2 $\pm$ 6.26	80.9 $\pm$ 8.91	78.6 $\pm$ 5.56
Systolic BP (mmHg)	123.7 $\pm$ 10.30	122.5 $\pm$ 8.15	123.65 $\pm$ 10.49	125.75 $\pm$ 9.10

weight.¹² After the onset of apnoea, laryngoscopy and tracheal intubation was performed, taking not more than 30 seconds. Inhalational supplements or topical lidocaine spray were avoided during the induction sequence.

Measurements of IOP, systolic arterial pressure (Korotkoff's method using sphygmomanometer) and heart rate (cardiac monitor) were made with patient supine and with the operating table flat, at the following intervals:

- (i) Before pre-treatment (control value).
- (ii) Five minutes after pretreatment, just before induction.
- (iii) After injection of thiopentone and succinylcholine, immediately after the fasciculations had ceased or 45 seconds after administration of succinylcholine if no fasciculations were visible.
- (iv) Immediately after intubation and then every 2 min thereafter until the effect of succinylcholine began to wear off.

All measurements of IOP were made by an ophthalmologist, using a Schiotz tonometer (technique accurate to within ± 2 mmHg).^{13,14} In each patient, readings were taken in both the eyes following topical administration of three drops of four per cent lidocaine. The mean of the two

readings was recorded. At no time did the measurement of IOP interfere with the progress of the anaesthetic.

The patients were also monitored for intensity of fasciculations by the simple scoring system of Erkola *et al.*¹⁵ (Grade 0 – nil, Grade I – just visible fibrillations, Grade II – moderate contractions, Grade III – vigorous contractions). Conditions for intubation were based on the criteria used by Eisenberg *et al.*¹⁶ (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 ten seconds).

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

Results

All four groups of patients were comparable on the basis of age, body weight, resting IOP, pulse rate, systolic arterial pressure (SAP) and dose of thiopentone (Table I).

The changes in IOP in the various groups during the induction sequence are shown in Figure 1 and Table II. IOP rose significantly ($p < 0.001$) after administration of

TABLE II Results – Intraocular pressure (mean $\pm$ SD)

Group	Control IOP (mmHg) A	After induction drugs B	Immediately after intubation C	Change after induction drugs from control value B-A	Change after intubation from post induction value C-B
1 Control	15.85 $\pm$ 1.37	18.33 $\pm$ 1.52*	23.29 $\pm$ 2.96†	2.48 $\pm$ 1.68	4.96 $\pm$ 2.71
2 d-Tubocurarine	15.65 $\pm$ 2.17	17.38 $\pm$ 1.81*	22.42 $\pm$ 3.37†	1.73 $\pm$ 2.08	5.04 $\pm$ 3.18
3 Diazepam	15.96 $\pm$ 1.28	17.93 $\pm$ 1.68*	21.64 $\pm$ 2.70†	1.97 $\pm$ 1.61	3.71 $\pm$ 2.35‡
4 Lidocaine	15.34 $\pm$ 1.73	16.38 $\pm$ 1.79*	16.74 $\pm$ 2.15 ^{NS}	1.04 $\pm$ 1.49¶	0.36 $\pm$ 1.25§§

* $p < 0.01$ compared to control.

† $p < 0.001$ compared to postinduction.

^{NS} – $p > 0.05$ compared to postinduction.

‡ $p < 0.05$ compared with control group.

¶ $p < 0.001$ compared with control group.

§§ $p < 0.001$ compared with diazepam group.

FIGURE 1 IOP change from control values at various intervals. Significant changes in IOP are indicated.

* $p < 0.01$ compared to control.

** $p < 0.001$ compared to control.

† $p < 0.001$ compared to postinduction.

NS – $p > 0.05$ compared to postinduction.

the induction drugs in all groups. However, in group 4 (lidocaine) this increase was significantly less than the increase observed in the control group ($p < 0.001$). Tracheal intubation caused a further increase in IOP ($p < 0.001$ compared to postinduction values) in groups 1, 2, and 3. In the lidocaine group, there was no change in IOP following intubation.

Systolic arterial pressure rose significantly above postinduction values in groups 1, 2, and 3 (Figure 2) while in group 4 (lidocaine), the change was not significant ($p > 0.05$).

The intensity of fasciculations (Table III) were significantly less in the d-Tc and lidocaine groups, as compared to the control group. Diazepam pretreatment also reduced fasciculations but to a lesser extent. Intubating conditions (Table IV) were significantly worse in d-Tc group when compared to the control group.

Discussion

Although a number of studies have revealed that succinylcholine causes a rise in IOP,^{1,2,6} the exact mechanism

FIGURE 2 SAP change from control values at various intervals. Significant changes in SAP are indicated.

* $p < 0.01$ compared to control.

† $p < 0.01$ compared to postinduction.

‡ $p < 0.001$ compared to postinduction.

remains uncertain. Contracture of extraocular muscles¹⁷ and dilatation of choroidal blood vessels¹⁸ have been suggested as being responsible. This rise in IOP following succinylcholine is further aggravated by tracheal intubation,^{2,19} may be secondary to a sudden increase in arterial pressure,¹³ straining²⁰ or reflex venospasm.²¹

To avoid the use of succinylcholine, some authors¹¹ advocate a pancuronium, thiopentone and atropine drug sequence for rapid intubation in children with full stomachs in whom an increase in IOP is undesirable. However, the need to search for methods to make the use of succinylcholine safe in cases with penetrating eye injuries continues because succinylcholine still remains the drug of choice for rapid intubation.^{22,23}

Miller *et al.*³ suggested non-depolarising neuromuscular relaxant pretreatment to abolish the succinylcholine-induced rise in IOP. However, these workers did not intubate their patients. Subsequent studies⁵⁻⁷ have disputed the effect of non-depolarizer pretreatment on the

TABLE III Between-group analysis of intensity of fasciculations (n = 40 in each group)

Intensity	Group 1 (control)	Group 2 (d-tubo- curarine)	Group 3 (diazepam)	Group 4 (lidocaine)
Grade 0	0	25	6	22
Grade I	15	12	16	16
Grade II	20	3	17	2
Grade III	5	0	1	0

NS - $p > 0.05$

IOP rise associated with succinylcholine and tracheal intubation. In our study also, we could not demonstrate a protective effect.

Since an IOP rise was seen in spite of a reduced incidence and intensity of succinylcholine fasciculations in group 2 (dTe, Table III), it can be inferred that the succinylcholine-induced rise in IOP is independent of fasciculations. Similar findings have been described by Feneck and Cook.⁷ In our study d-tubocurarine pretreatment affected the intubation conditions adversely (Table IV), a finding in agreement with previous workers.²⁴ We suggest that pretreatment with a non-depolarizer is not only undesirable but may be hazardous when a smooth induction sequence is required.

While pretreatment with diazepam has been suggested to prevent the rise in IOP following succinylcholine and tracheal intubation,⁴ others dispute this.⁷ Examination of our own data reveals that diazepam failed to prevent the rise in IOP after succinylcholine and also after endotracheal intubation (Table II, Figure 1). Although less than that in the control group, the postintubation rise in the diazepam group was significant (Table II). Cunningham *et al.* used $0.1 \text{ mg} \cdot \text{kg}^{-1}$ of diazepam and concluded that it was effective in preventing the IOP rise following succinylcholine and intubation. In their study, the IOP measurements were taken two minutes after intubation,

TABLE IV Between-group analysis of intubating conditions (n = 40 in each group)

Conditions for intubation	Group 1 (control)	Group 2 (d-tubo- curarine)	Group 3 (diazepam)	Group 4 (lidocaine)
Excellent	32	19	35	36
Good	4	11	4	2
Fair	3	7	1	2
Poor	1	3	0	0

NS - $p > 0.05$

while it has been shown that the increase in IOP following intubation maintains its peak for one minute² only, to decrease thereafter and becoming insignificant by two minutes after intubation.⁷ Thus the measurement of IOP two minutes after intubation will miss the peak values.

Our results show that in the lidocaine group the post-succinylcholine rise in IOP was significant (Table II, Figure 1). However the increase was the smallest amongst the groups and was significantly less than the increase observed in the control group. The observed efficacy of lidocaine in reducing the post-succinylcholine IOP rise may be explained on the basis of the proposed peripheral actions of lidocaine.²⁵

We found intravenous lidocaine to be the only effective pretreatment in preventing the rise in IOP following tracheal intubation. This might have been due to an obtunded haemodynamic response,⁹ suppressed cough reflex,²⁶ and increased depth of anaesthesia following lidocaine pretreatment. Lerman and Kiskis¹¹ used $1.5 \text{ mg} \cdot \text{kg}^{-1}$ of lidocaine to attenuate IOP response to intubation in children. However, in adults, we have been able to produce similar results with lesser doses ($1 \text{ mg} \cdot \text{kg}^{-1}$). Our results are in contradiction to Smith *et al.*²⁷ who concluded that lidocaine in doses of $1-2 \text{ mg} \cdot \text{kg}^{-1}$ is ineffective in preventing the increase in IOP following succinylcholine and/or tracheal intubation. In their study, IOP readings were not taken between succinylcholine administration and tracheal intubation, making it difficult to define whether the increase was because of succinylcholine or tracheal intubation or both.

We were unable to monitor arterial carbon dioxide tension. Changes in arterial carbon dioxide may alter IOP²⁸ but these were probably unimportant during the short period of this study throughout which the patients were ventilated adequately, using a Bain circuit.¹²

Correlating systolic AP and IOP, it is evident from Figures 1 and 2 that the extent of IOP and SAP changes after succinylcholine is poorly related, AP changes were minimal while IOP rose significantly in all the groups. However, after tracheal intubation there was a significant rise in both IOP as well as SAP in groups 1, 2 and 3. Since in group 4 (lidocaine) the rise in both IOP and SAP following tracheal intubation were blunted, we are of the opinion that a sudden rise in arterial pressure following tracheal intubation can lead to acute IOP changes.

Finally, we conclude that pretreatment with lidocaine is more effective than either d-tubocurarine or diazepam in preventing an IOP rise following succinylcholine and/or tracheal intubation. Although a further clinical trial with higher doses (more than $1 \text{ mg} \cdot \text{kg}^{-1}$) of lidocaine is required to evaluate its ability to obtund succinylcholine-induced IOP changes, this drug in doses of $1 \text{ mg} \cdot \text{kg}^{-1}$ is sufficient to prevent the IOP rise associated with tracheal intubation.

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Résumé

Cent soixante patients divisés d'une façon randomisée en quatre groupes ont reçu du salin physiologique (5 ml), de la d-tubocurarine ($0.05 \text{ mg} \cdot \text{kg}^{-1}$), du diazépam ($0.1 \text{ mg} \cdot \text{kg}^{-1}$) ou de la lidocaïne ($1 \text{ mg} \cdot \text{kg}^{-1}$) comme pré-traitement à double insu, cinq minutes avant l'induction de l'anesthésie avec du thiopentone et de la succinylcholine ($1 \text{ mg} \cdot \text{kg}^{-1}$). La succinylcholine a provoqué une augmentation significative de la pression intraoculaire chez tous les groupes. Cependant, pour le groupe lidocaïne, cette augmentation était significativement moindre que celle observée chez le groupe contrôle. L'augmentation de la pression intraoculaire post succinylcholine était davantage aggravée par l'intubation trachéale chez tous les groupes à l'exception du groupe lidocaïne. Un essai clinique ultérieur avec de plus fortes doses de lidocaïne est suggéré afin d'évaluer sa capacité de diminuer l'augmentation de la pression intraoculaire induite par la succinylcholine malgré qu'elle est suffisante aux doses de $1 \text{ mg} \cdot \text{kg}^{-1}$ pour prévenir l'augmentation de la pression intra-oculaire après l'intubation.