The effects of atracurium on intraocular pressure during steady state anaesthesia and rapid sequence induction: a comparison with succinylcholine

Gavin G. Lavery FFARCS,
James N. McGalliard MB BCH,
Rajinder K. Mirakhur MD PH D FFARCS FFARCSI,
William F.I. Shepherd FRCS

The effects of atracurium 0.5 mg·kg^{-1} or succinylcholine 1.0 mg·kg^{-1} on intraocular pressure (IOP) were studied in ten patients during steady state nitrous oxide-oxygen-fentanyl anaesthesia. IOP was unchanged following atracurium but, one minute after succinylcholine, it had increased significantly ($p < 0.025$) from 5.6 mmHg to 13.2 mmHg and remained significantly above control for 3 min. Twenty additional patients received either atracurium 0.75 mg·kg^{-1} or succinylcholine 1.0 mg·kg^{-1} as part of a rapid sequence induction, atracurium being administered prior to, and succinylcholine after, thiopentone. Intubating conditions were acceptable in all patients in both groups. Administration of thiopentone was associated with a significant ($p < 0.025$) decrease in IOP. Although IOP increased in both groups as a result of laryngoscopy and intubation (from 8.0 mmHg to 12.1 mmHg in the atracurium Group and from 7.5 mmHg to 14.5 mmHg in the succinylcholine group) it did not exceed pre-induction IOP in the former. In the succinylcholine group, IOP after intubation exceeded pre-induction values for 2 min, although this increase was significant ($p < 0.05$) only at the immediate post-intubation reading. It is concluded that atracurium in a dose of 0.75 mg·kg^{-1} is a suitable relaxant for use in rapid sequence induction.

Keywords
NEUROMUSCULAR RELAXANTS: atracurium, succinylcholine; EYE: intraocular pressure; ANAESTHETIC TECHNIQUES: rapid sequence induction.

From the Department of Anaesthetics and Ophthalmology, Queen's University and Royal Victoria Hospital, Belfast, Northern Ireland.

Address correspondence to: Dr R.K. Mirakhur, Department of Clinical Anaesthesia, Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA, Northern Ireland.

Despite its numerous side-effects, the ability of succinylcholine to provide excellent intubating conditions more rapidly than other agents has meant that it remains the relaxant of choice for tracheal intubation in non-fasting patients. However, the increase in intraocular pressure (IOP) caused by this agent[1–3] is particularly undesirable in patients who have sustained a penetrating eye injury. Since most nondepolarising relaxants do not cause a rise in IOP,[4–6] a rapid sequence induction using large doses of these agents has been advocated.[7,8] Although such a technique using pancuronium may produce acceptable intubating conditions fairly rapidly,[9,10] it results in a prolonged neuromuscular block.[7] The new nondepolarising relaxant, atracurium, has an onset of action which may be significantly shortened by increasing the dose but without producing an unduly prolonged neuromuscular block.[11] The effects of atracurium on IOP were assessed in the present study during steady state anaesthesia

TABLE I Classification of intubating conditions

Grade	*Description*
Excellent	Good jaw relaxation, vocal cords open and no response to intubation
Satisfactory	Good jaw relaxation, vocal cords open but minimal reaction or slight coughing on intubation
Fair	Jaw relaxed, cords closed or moving, intubation requiring firm pressure and accompanied by moderate bucking or coughing
Poor	Intubation impossible due to poor jaw or cord relaxation

and a rapid sequence induction technique. The results have been compared with succinylcholine, which is the relaxant commonly used in a rapid sequence induction.

Methods

The study, approved by the Regional Ethical Committee, involved a total of 30 fasting patients undergoing elective ophthalmic surgery. All were in good general health (ASA physical status 1), were not receiving any regular medication and had been found to have no abnormality of intraocular pressure (IOP) preoperatively. One hour prior to surgery all patients received diazepam 10 mg orally.

In ten patients, anaesthesia was induced using thiopentone 5 $mg \cdot kg^{-1}$ and fentanyl 4–5 $\mu g \cdot kg^{-1}$. Tracheal intubation was performed without the aid of a muscle relaxant and anaesthesia was maintained with 33 per cent oxygen in nitrous oxide. Ventilation was adjusted to maintain an end-tidal carbon dioxide concentration between 4.5 and 5.0 per cent. An electrocardiogram and oscillotonometer (Dinamap, Critikon Ltd) were used to monitor heart rate and arterial pressure. When these parameters had been stable for at least 10 min IOP was measured using a Perkins hand-held applanation tonometer.[12] The patients then received either atracurium 0.5 $mg \cdot kg^{-1}$ (Group I) or succinylcholine 1.0 $mg \cdot kg^{-1}$ (Group II) as dictated by a computer-generated random sequence. IOP was subsequently measured at 1, 2, 3, 4, 5 and 10 min after administration of relaxant. The study ended, and surgery was commenced, after the 10 min observation.

The remaining 20 patients were pre-oxygenated for 5 min, received fentanyl 2–3 $\mu g \cdot kg^{-1}$ and had baseline IOP measured. Patients then received, at random, atracurium 0.75 $mg \cdot kg^{-1}$ (Group III) or thiopentone 5 $mg \cdot kg^{-1}$ followed immediately by succinylcholine 1.0 $mg \cdot kg^{-1}$ (Group IV). Group III patients received thiopentone 5 $mg \cdot kg^{-1}$ as soon as they showed any sign of muscle weakness, such as drooping eyelids. Cricoid pressue was applied in both groups at the loss of the eyelash reflex and tracheal intubation and cuff inflation performed 30 seconds later. Intraocular pressure, heart rate and mean arterial pressure were measured after thiopentone, after intubation and then at one minute intervals for 5 min. Intubating conditions were graded on a four point scale (Table I) as used previously by the authors.[11,13]

All measurements of IOP were performed on the eye *not* scheduled for surgery by one of the authors (WFIS) who was unaware of which relaxant had been administered and was prevented from watching for the presence of fasciculations. All patients were in a horizontal supine position while IOP was measured and care was taken to avoid external compression of neck veins. The data for IOP, heart rate and arterial pressure were analysed using paired t tests within each group and Student's t test between Groups I and II and Groups III and IV. A Chi-squared test with Yates' correction was used to compare intubating conditions.

Results

There were no statistical differences in the mean ages and weights of those patients who received the relaxants during steady state anaesthesia (Groups I and II), or in those who received the two agents as part of a modified rapid sequence induction (Groups III and IV) (Table II).

The changes in IOP following administration of atracurium and succinylcholine during steady state anaesthesia are shown in Figure 1. There was no

TABLE II Physical characteristics of patients (mean ± SEM)

	Age (years)	*Weight (kg)*
Group I	45.4 ± 7.8	76.0 ± 7.0
Group II	41.6 ± 8.5	63.2 ± 5.5
Group III	51.4 ± 5.2	68.3 ± 2.5
Group IV	44.2 ± 5.1	66.4 ± 5.1

Groups I and II refer to patients given atracurium and succinylcholine during steady state anaesthesia and Groups III and IV during the rapid sequence induction respectively.

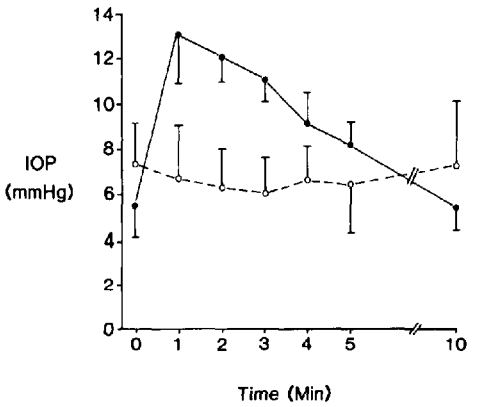

FIGURE 1 IOP during steady state anaesthesia after administration of atracurium 0.5 mg·kg^{-1} or succinylcholine 1.0 mg·kg^{-1}. o– – –o atracurium group (I). ●——● succinylcholine group (II). Vertical bars represent one standard error of the mean.

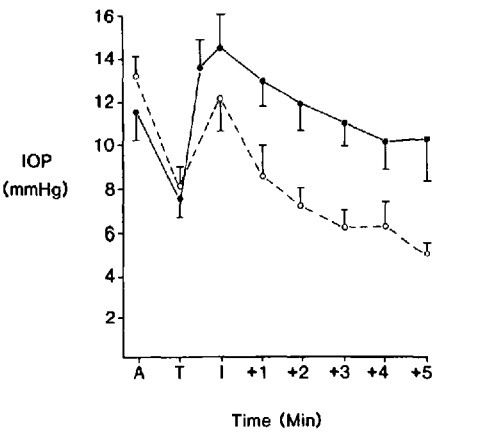

FIGURE 2 IOP during rapid sequence induction using atracurium 0.75 mg·kg^{-1} or succinylcholine 1.0 mg·kg^{-1}. o– – –o atracurium group (III). ●——● succinylcholine group (IV). Vertical bars represent one standard error of the mean. A = awake; T = after thiopentone; I = after intubation.

significant change in IOP after administration of atracurium whereas it was greater than control for 5 min following administration of succinylcholine, being significantly elevated ($p < 0.05$) for the first 3 min.

Heart rates in both Groups I and II did not vary significantly during the study (Table III). Systolic blood pressure in Group I decreased by up to six per cent (from 104 to 98 mmHg) and increased by up to 13 per cent (from 115 to 130 mmHg) in Group II. However, these changes were not statistically significant.

The changes in IOP during induction and intubation in Groups III and IV are shown in Figure 2. IOP decreased significantly ($p < 0.025$) after thiopentone in both groups. IOP immediately after intubation was significantly elevated ($p < 0.005$) in both groups when compared to IOP following thiopentone. In those patients given atracurium (Group III) the maximum IOP after intubation (12.1 mmHg) did not exceed the pre-induction value (13.1 mmHg) and IOP at 1, 2 and 3 min after intubation was significantly lower ($p < 0.01$) than pre-induction IOP. However, in patients who received succinylcholine (Group IV) IOP immediately after intubation (14.5 mmHg) was significantly greater ($p < 0.05$) than the pre-induction IOP (11.5 mmHg) and did not return to the pre-induction value until 3 min after intubation. When IOP in Groups III and IV is compared, there was no significant difference before induction, following thiopentone or immediately after intubation. However, when measured at 1, 2 and 3 min after intubation, IOP was significantly lower in Group III.

TABLE III Heart rate and systolic arterial pressure after administration of atracurium (I) or succinylcholine (II) during steady state anaesthesia (mean ± SEM)

Time	*Heart rate (beats·min^{-1})*		*Systolic arterial pressure (mmHg)*	
(min)	*Group I*	*Group II*	*Group I*	*Group II*
0	56 ± 3.4	62 ± 3.8	104 ± 10.1	115 ± 10.9
1	57 ± 3.6	61 ± 3.6	103 ± 13.7	115 ± 12.0
2	61 ± 5.3	64 ± 3.6	100 ± 11.9	128 ± 12.3
3	59 ± 4.7	62 ± 3.2	98 ± 10.7	130 ± 11.1
4	58 ± 3.7	60 ± 3.8	100 ± 12.0	117 ± 9.2
5	58 ± 4.3	59 ± 3.4	101 ± 14.4	120 ± 9.3
10	58 ± 3.6	58 ± 2.9	99 ± 13.0	118 ± 10.5

In Group III the average time between administration of atracurium and thiopentone was 28 seconds (range 20–50 sec.). Thirty seconds after loss of the eyelash reflex, all ten patients in each group had clinically acceptable intubating conditions – eight in Group III and seven in Group IV being graded as "excellent."

Heart rate increased significantly in both Groups

TABLE IV Heart rate and systolic arterial pressure during rapid sequence induction with atracurium (III) and succinylcholine (IV) (mean ± SEM)

Time (min)	Heart rate (beats·min^{-1})		Systolic arterial pressure (mmHg)	
	Group III	Group IV	Group III	Group IV
Control (awake)	73 ± 4.8	72 ± 5.2	150 ± 7.8	143 ± 4.7
T	85 ± 3.8	81 ± 6.2	140 ± 8.4	123 ± 5.1
I	96 ± 6.1	84 ± 6.5	155 ± 8.0	139 ± 7.7
+1	91 ± 5.3	84 ± 6.5	155 ± 7.3	144 ± 7.9
+2	86 ± 5.0	86 ± 10.2	144 ± 7.3	148 ± 9.3
+3	82 ± 4.9	83 ± 7.7	137 ± 6.4	142 ± 9.7
+4	73 ± 4.9	83 ± 8.2	123 ± 5.0	136 ± 9.0
+5	74 ± 0.9	86 ± 10.4	116 ± 5.8	136 ± 9.4

T = after thiopentone.
I = after intubation.

III and IV after intubation, reaching peak values of 32 and 20 per cent respectively above pre-induction values (Table IV). The corresponding figures for the peak systolic blood pressure was three and four per cent respectively above pre-induction readings. There were no statistically significant differences between the two groups in terms of heart rates or systolic pressure.

When questioned on the first postoperative day, none of the patients remembered any unusual sensation prior to losing consciousness, although when prompted, two who received a rapid sequence induction using atracurium did claim to recall a "heaviness" in their limbs.

Discussion

Atracurium has previously been reported to have no significant effect on IOP.[14] Since, in addition, its use is not associated with any significant cardiovascular effects,[15–17] we considered it a suitable relaxant for use in a modified rapid sequence induction technique – an induction technique which allows smooth rapid tracheal intubation, as required in non-fasting patients, yet avoids the use of succinylcholine.

Although Maharaj *et al.*[14] detected no significant effect on IOP after administration of atracurium 0.45 mg·kg^{-1}, their observation times (5, 10 and 15 min) were such that any immediate changes in IOP could have been missed. The first part of the present study, therefore, investigated immediate changes in IOP after both atracurium and succinylcholine during steady state anaesthesia using a method similar to that advocated by Al Abrak and co-workers.[18] Central venous pressure (CVP) was not measured as insertion of a CVP line was considered to be not justifiable ethically. However, all patients were in a horizontal, supine position, ventilated to normocapnia and great care was taken to prevent any external compression of the neck veins. Our findings with atracurium confirm those of Maharaj *et al.*[14] and with succinylcholine are similar to those reported by Pandey *et al.*[19] and by Cook.[3]

During induction of anaesthesia, the reduction of IOP with thiopentone was similar to that reported by previous workers.[20,21] After administration of succinylcholine, IOP returned to a level which exceeded the pre-induction value. This differs from the findings of Joshi and Bruce[20] and is surprising since we used a much larger induction dose of thiopentone. However, their results could have been influenced by the use of Shiotz indentation tonometry which can result in apparently lower IOP's on successive measurements at short intervals. We also found that intubation was associated with an additional increase in IOP, even if this had already been increased by succinylcholine, as has been previously reported.[19,20] Although patients given atracurium in the present study also exhibited a rise in IOP after intubation, this was much less and of a shorter duration than after succinylcholine, with the result that IOP never exceeded the pre-induction value during rapid sequence induction.

When choosing the dose of atracurium for use in a modified rapid sequence induction, we tried to balance rapid onset of action and early acquisition of good intubation conditions with the risk of serious side-effets. Our previous work[11] suggested 0.75 mg·kg^{-1} would be most appropriate since increasing the dose beyond this neither decreased the onset time nor improved intubating conditions significantly. While atracurium, 0.75 mg·kg^{-1} has been shown to produce complete neuromuscular block in just over 2 min,[11] intubation in the modified rapid sequence induction presented in this paper occurred, approximately 80 seconds after atracurium 0.75 mg·kg^{-1} (this assumes approximately 20 seconds for administration of thiopentone 5 mg·kg^{-1}). However, previous work with atracurium has shown that excellent intubating conditions can be achieved before the onset of complete block

even with doses of 0.5 $mg \cdot kg^{-1}$.[22,23] The changes in IOP with this technique were similar to those reported when intubation was performed 2 min after administration of thiopentone 5 $mg \cdot kg^{-1}$ and alcuronium 0.25–0.30 $mg \cdot kg^{-1}$.[21] Although we found an overall fall in IOP between awake and post-intubation readings, there was a rise in IOP at intubation. This might be attenuated by using an induction agent such as di-isopropylphenol with a greater tendency to lower IOP than thiopentone[24] and by using divided doses of muscle relaxant in such a way as to improve the intubating conditions further.[25]

As has previously been reported[26,27] we observed no significant changes in heart rate or arterial pressure after administration of atracurium. Although the changes in heart rate and arterial pressure during induction and intubation were greater in the atracurium group (III) than in the succinylcholine group (IV), these were clinically acceptable during what is widely acknowledged to be an extremely stressful stimulus.

In conclusion, when administered during steady state anaesthesia, atracurium had no significant effect on IOP. Under identical conditions, succinylcholine produced a significant increase in IOP, which returned to baseline value after 5 min. When used in a rapid sequence induction technique, atracurium 0.75 $mg \cdot kg^{-1}$ produced similar intubation conditions but a smaller increase in IOP when compared with succinylcholine 1.0 $mg \cdot kg^{-1}$ and would be a suitable relaxant for use in a rapid sequence induction in situations, where an excessive increase in IOP is undesirable.

Acknowledgements

We thank the surgical, nursing and other staff of the eye operating theatres at the Royal Victoria Hospital, Belfast for their cooperation with the study. Doctor Lavery was in receipt of a Royal Victoria Hospital Research Fellowship from the Endowment and Gifts Fund of the hospital. Miss S. Connery and Mrs. A. Quinn are thanked for typing the manuscript.

References

1 *Lincoff HA, Ellis CH, Devoe AG et al.* The effect of succinylcholine on intraocular pressure. Am J Ophthalmol 1955; 40: 501–10.

2 *Wynands JE, Crowell DE.* Intraocular tension in association with succinylcholine and endotracheal intubation: a preliminary report. Can Anaesth Soc J 1960; 7: 39–43.

3 *Cook JH.* The effect of suxamethonium on intraocular pressure. Anaesthesia 1981; 36: 359–65.

4 Litwiller RW, Difazio CA, Ruslian EL. Pancuronium and intraocular pressure. Anesthesiology 1975; 42: 750–2.

5 *George R, Nursingh A, Downing JW, Welsh NH.* Nondepolarising neuromuscular blockers and the eye: a study of intraocular pressure (pancuronium versus alcuronium). Br J Anaesth 1979; 51: 789–92.

6 *Sia RL, Rashkovsky OM.* Org NC45 and intraocular pressure during anaesthesia. Acta Anaesthesiol Scand 1981; 25: 219–21.

7 *Brown EM, Krishnaprasad D, Smiler BG.* Pancuronium for rapid induction technique for tracheal intubation. Can Anaesth Soc J 1979; 26: 489–91.

8 *Couch JA, Eltringham RJ, Magauran DM.* The effect of thiopentone and fazadinium on intraocular pressure. Anaesthesia 1979; 34: 586–90.

9 *Lerman J, Kiskis AA.* Effects of high dose pancuronium and endotracheal intubation on intraocular pressure in children. Anesthesiology 1984; 61: A434.

10 *Lerman J, Kiskis AA.* Lidocaine attenuates the intraocular pressure response to rapid intubation in children. Can Anaesth Soc J 1985; 32: 339–45.

11 *Mirakhur RK, Lavery GG, Clarke RSJ, Gibson FM, McAteer E.* Atracurium in clinical anaesthesia. Effect of dosage on onset, duration and intubating conditions. Anaesthesia 1985; 40: 801–5.

12 *Perkins ES.* Hand held applanation tonometer. Br J Ophthalmol 1965; 49: 591–3.

13 *Mirakhur RK, Ferres CJ, Clarke RSJ, Bali IM, Dundee JW.* Clinical evaluation of Org NC45. Br J Anaesth 1983; 55: 119–24.

14 *Maharaj RJ, Humphrey D, Kaplan N et al.* Effects of atracurium on intraocular pressure. Br J Anaesth 1984; 56: 459–63.

15 *Basta SJ, Savarese JJ, Ali HH, Moss J, Gionfriddo M.* Histamine releasing potencies of atracurium, dimethyl tubocurarine and tubocurarine. Br J Anaesth 1983; 55: 105S–106S.

16 *Basta SJ, Ali HH, Savarese JJ et al.* Clinical pharmacology of atracurium besylate (BW33A). A new nondepolarising muscle relaxant. Anesth Analg 1982; 61: 723–9.

17 *Sokoll MD, Gergis SD, Mehta M, Ali HH, Lineberry*

C. Safety and efficacy of atracurium (BW33A) in surgical patients receiving balanced or isoflurane anaesthesia. Anesthesiology 1983; 58: 450–5.

18 *Al-Abrak MH, Samuel JR*. Further observations on the effects of general anaesthesia on intraocular pressure in man: halothane in nitrous oxide and oxygen. Br J Anaesth 1974; 46: 756–9.

19 *Pandey K, Badola P, Kumar S*. Time course of intraocular hypertension produced by suxamethonium. Br J Anaesth 1972; 44: 191–5.

20 *Joshi C, Bruce DL*. Thiopental and succinylcholine action on intraocular pressure. Anesth Analg 1975; 54: 471–5.

21 *Balamoutsos NG, Tsakona H, Kanakoudes PS, Iliadelis E, Georgiades CG*. Alcuronium and intraocular pressure. Anesth Analg 1983; 62: 521–3.

22 *Gergis SD, Sokoll MD, Mehta M, Kemmotsu O, Rudd GD*. Intubating conditions after atracurium and suxamethonium. Br J Anaesth 1983; 55: 83S–86S

23 *Foldes FF, Nagashima H, Boros M, Tassonyi E, Fitzal S, Agoston S*. Muscular relaxation with atracurium, vecuronium and Duador under balanced anaesthesia. Br J Anaesth 1983; 55: 97S–103S.

24 *Mirakhur RK and Shepherd WFI*. Intraocular pressure changes with propofol (diprivan): comparison with thiopentone. Postgrad Med J 1985; 61 (Suppl 3): 41–4.

25 *Mirakhur RK, Lavery GG, Gibson FM, Clarke RSJ*. Intubating conditions with atracurium administered in divided doses. Eur J Anaesthesiol 1986; 3: 60–1.

26 *Katz RL, Stirt J, Murray AL, Lee C*. Neuromuscular effects of atracurium in man. Anesth Analg 1982; 61: 730–4.

27 *Ramsay FM, White PA, Stulliken EH, Lineberry CG, Allen LL*. Clinical use of atracurium during N_2O/O_2, enflurane anesthesia regimens. Anesthesiology 1984; 61: 328–31.

Résumé

Les effets de 0.5 mg·kg^{-1} d'atracurium ou de succinylcholine 1.0 mg·kg^{-1} sur la pression intraoculaire (IOP) ont été étudiés chez les patients lors d'une anesthésie stable au protoxyde d'azote-oxygène-fentanyl. La IOP a été inchangée suite à l'administration d'atracurium mais après une minute de l'administration de succinylcholine elle augmenta significativement ($p < 0.025$) de 5.6 mmHg à 13.2 mmHg et demeura significativement supérieure au contrôle après 3 minutes. 20 patients additionnels ont reçu soit de l'atracurium 0.75 mg·kg^{-1} ou du succinylcholine 1.0 mg·kg^{-1} lors d'une induction à séquence rapide; l'atracurium étant administré avant et la succinylcholine après, thiopentone. Les conditions d'intubation étaient acceptables chez tous les patients des deux groupes. L'administration de thiopentone était associée avec une diminution significative de l'IOP ($p < 0.025$). Même si la IOP a augmenté dans les deux groupes suite à la laryngoscopie et l'intubation (de 8.0 mmHg à 12.1 mmHg pour le groupe atracurium et de 7.5 mmHg à 14.5 mmHg pour le groupe succinylcholine) elle n'a pas surpassé la valeur pré-induction pour le groupe atracurium. Dans le groupe succinylcholine la IOP après intubation a excédé les valeurs pré-inductions pour deux minutes, même si cette augmentation n'était significative ($p < 0.05$) qu'immédiatement après l'intubation. Il est conclut que l'atracurium à des doses de 0.75 mg·kg^{-1} est une bloqueur neuromusculaire convenable pour l'utilisation lors d'induction à séquence rapide.