Atracurium for short surgical procedures: a comparison with succinylcholine

Henry K. Gyasi MB CHB FFARCSI,
Mohamed Naguib MB, BCH MSC,
Yaw Adu-Gyamfi MB CHB FFARCS FWACS

A comparison was made between atracurium and succinylcholine in 40 patients undergoing short gynaecological procedures of 30 minutes or less.

Good intubating conditions were produced in 76.7 ± 39.3 seconds (mean $\pm$ S.D.) with succinylcholine $1 \text{ mg} \cdot \text{kg}^{-1}$ and 198 ± 84 seconds with atracurium $400 \mu\text{g} \cdot \text{kg}^{-1}$. Muscle relaxation was maintained with the initial dose of atracurium or with repeated boluses of succinylcholine. The mean time of surgery was 17.65 ± 5.3 minutes in the atracurium group and 15.2 ± 4.6 minutes in the succinylcholine group.

Residual neuromuscular block with atracurium was reversed with neostigmine $0.036 \text{ mg} \cdot \text{kg}^{-1}$ and atropine $0.018 \text{ mg} \cdot \text{kg}^{-1}$. Recovery of neuromuscular function following reversal, assessed by return of all responses to train-of-four stimulation occurred in 5.05 ± 4.6 minutes in the atracurium group but half the above doses of neostigmine and atropine were repeated in three patients.

We conclude that a single dose of atracurium $400 \mu\text{g} \cdot \text{kg}^{-1}$ is suitable for intubation and maintenance of muscle relaxation for short surgical procedures. However, the onset of action is slow, compared to succinylcholine. Residual neuromuscular block can be antagonised with standard doses of neostigmine, less than 20 minutes after the initial dose of relaxant. Atracurium appears to be a suitable alternative for short procedures where succinylcholine is unsuitable or contraindicated.

Key words

NEUROMUSCULAR RELAXANTS: atracurium, succinylcholine; INTUBATION: endotracheal.

From the Department of Anaesthesiology, King Faisal University, King Fahd Hospital, P.O. Box 2208, Al-Khobar, 31952, Saudi Arabia, where correspondence should be addressed to Dr. Gyasi.

Atracurium besylate is a new non-depolarising neuromuscular blocking agent. Initial clinical studies have shown that it has an intermediate duration of action, is easily reversed with anticholinesterase drugs and has minimal side effects.¹⁻⁴ These properties fulfill some of the criteria suggested for an ideal muscle relaxant for short surgical procedures lasting 30 minutes or less.⁵ Muscle relaxation for such procedures is usually produced with succinylcholine, given as a continuous infusion or as intermittent injection. However, succinylcholine has many side effects, including cardiovascular changes, muscle fasciculations, hyperkalaemia, increased intracranial, intragastric and intraocular pressures, postoperative muscle pains, phase II block following large doses and malignant hyperpyrexia.⁶

Previous studies have shown that vecuronium (ORG NC 45) $100 \mu\text{g} \cdot \text{kg}^{-1}$ can be used for short intra-abdominal operations but the onset of action is prolonged in comparison with succinylcholine.⁵ The non-depolarising muscle relaxants, d-tubocurarine, pancuronium, gallamine, alcuronium and fazadinium all have a slow onset, long duration of action and undesirable side effects⁷ which would make them unsuitable for short surgical procedures.

Our study was designed to compare atracurium $400 \mu\text{g} \cdot \text{kg}^{-1}$ with intermittent injections of succinylcholine in patients undergoing various gynaecological procedures lasting less than 30 minutes. Using a simple method of monitoring neuromuscular function, comparisons were made of the onset and duration of action, intubating conditions and recovery from neuromuscular activity for both drugs.

Methods

Forty women aged between 16–60 years undergoing minor gynaecological procedures were studied. All were of A.S.A. physical status I, were free from

neuromuscular, renal or hepatic disease and were not taking any drugs known to interfere with neuromuscular function. Informed consent was obtained from each patient. All patients were pre-medicated with diazepam $150 \mu\text{g}\cdot\text{kg}^{-1}$ orally one and a half hours preoperatively and atropine 0.6 mg intramuscularly, one hour before surgery.

An intravenous infusion of Ringer's Lactate in five per cent dextrose was established prior to induction. The E.K.G. was monitored continuously by an M.1 Medishield monitor and arterial blood pressure was monitored every five minutes by an electronic oscillotonometer (Dinamap).

Neuromuscular activity was assessed by observation of thumb adduction, using a Bard peripheral nerve stimulator applying supramaximal stimuli to the ulnar nerve at the wrist via surface electrodes. Observation of thumb adduction was made easier by fixing the medial four fingers with adhesive tape to an armboard and the arm abducted to approximately 90° . Train of four (TOF) stimuli of 2 msec duration and 2 hertz frequency, produced every 12 seconds were used throughout the study.

Anaesthesia was induced with fentanyl, $1 \mu\text{g}\cdot\text{kg}^{-1}$, followed by thiopentone $3\text{--}5 \text{ mg}\cdot\text{kg}^{-1}$ intravenously. For muscle relaxation, the patients were divided into two groups by random allocation. Group A, the study group, received atracurium $400 \mu\text{g}\cdot\text{kg}^{-1}$ and Group B, the control group received succinylcholine $1 \text{ mg}\cdot\text{kg}^{-1}$ following induction. In Group B, succinylcholine $0.25 \text{ mg}\cdot\text{kg}^{-1}$ was given whenever response to TOF stimulation returned during surgery.

Tracheal intubation was performed when response to TOF stimulation disappeared. Intubation conditions were compared using the method of Fahey *et al.*⁸ (Table I). Intubating conditions were assessed by the same anaesthetist who at the time was unaware of the identity of the muscle relaxant used. Anaesthesia was maintained with 66 per cent nitrous oxide in oxygen and halothane 0.5–1 per cent inspired. Ventilation was controlled manually before intubation and subsequently with a Manley "servovent" to maintain normocapnia. End tidal CO_2 was monitored by a Datex Normocap infrared carbon dioxide analyser.

At the end of surgery, halothane and nitrous oxide were discontinued and in the study group, neuromuscular block was reversed with neostigmine $0.036 \text{ mg}\cdot\text{kg}^{-1}$ and atropine $0.018 \text{ mg}\cdot\text{kg}^{-1}$.

TABLE I Scoring of intubation conditions (Fahey *et al.*)⁸

Score	Intubating conditions
0	Cords abducted, good visualisation, no patient movement.
1	Cords abducted, good visualisation, diaphragmatic movement with intubation.
2	Cords slightly abducted, poor visualisation, coughing with intubation.
3	Cords moderately abducted, poor visualisation, gross body movements with intubation.

Half of this dose of neostigmine and atropine was repeated if all four responses of TOF stimulation had not returned or if there was any visible fade of response to TOF stimulation, ten minutes following reversal.

After the return of all responses of TOF stimulation, the patients were extubated when spontaneous respiration had returned and tidal volume was assessed to be clinically adequate. Head lift in response to command was assessed every five minutes after extubation until head lift was sustained for five seconds or more.

Values are presented as mean and standard deviation. Statistical analysis was performed using Student's *t* test to compare the onset of action of both drugs. Intubating scores and time to respond to sustained head lift on command were compared using Chi square test with Yates correction factor. Differences were considered significant when $p < 0.05$.

Results

There was no statistical difference between the two groups with respect to age and body weight (Table II).

The duration of anaesthesia in all cases was less than 30 minutes and the mean time of surgery was 17.65 ± 5.3 minutes for the atracurium group and 15.2 ± 4.6 minutes for the succinylcholine group (Table II) ($P = \text{N.S.}$).

Complete twitch suppression to TOF stimulation was produced in 76.8 ± 39.3 seconds by succinylcholine and 198.3 ± 84.1 seconds by atracurium (Table III) ($p < 0.01$).

Intubating conditions were satisfactory in all patients (intubating scores of two or less). In the atracurium group, intubating scores were graded as zero in ten patients, one in five patients and two in

TABLE II Age, body weight, dose of muscle relaxants and duration of surgery

	Age (yrs)	B.W. (kg)	Total dose of relaxant (mg)	Duration of surgery (min)
Group A, n = 20 (Atracurium)	36.0 ± 11.2	66.7 ± 9.8	26.7 ± 3.9	17.6 ± 5.3
Group B, n = 20 (Succinylcholine)	32.6 ± 8.8	66.1 ± 14.4	103.3 ± 27.1	15.2 ± 4.6

(Mean ± S.D.). There were no statistical differences between the ages, body weights, or duration of surgery between groups.

five patients. Intubating scores in the succinylcholine group were zero in 16 patients, one in one patient and two in three patients (Table III). Tracheal intubation was easily performed in all patients and there was no significant difference in intubating scores for the two groups.

The initial dose of atracurium produced adequate neuromuscular block for the duration of surgery in Group A. In Group B, the duration of action of the initial dose of succinylcholine was 6.3 ± 3.2 minutes. All patients in this group required supplemental doses of succinylcholine. The number of doses required was 2.2 ± 1.0 . The total dose of succinylcholine given was 103.3 ± 27.1 mg (Table II).

There was no response to TOF stimulation at the end of surgery in the succinylcholine group. In the atracurium group (n = 20), 17 patients showed no response to TOF stimulation prior to injection of neostigmine and in the other three patients, only the first response to TOF stimulation was present.

The time from injection of neostigmine to recovery of responses of TOF stimulation with no

fade was 5.05 ± 4.6 minutes (range 1–20 minutes, median 3.5 minutes) in the study group. In the same group, head lift to command, sustained for five seconds or more, was achieved within five minutes after extubation in 14 patients, and ten minutes in three patients. Three patients required repeat doses of neostigmine and atropine and in these patients, sustained head lift to command was achieved in 15 minutes after extubation in two patients, and 20 minutes in one patient.

In the succinylcholine group, recovery of all responses to TOF stimulation occurred in a mean time of 3.9 ± 1.4 minutes following the last supplemental dose. Sustained head lift for five seconds to command was achieved within five minutes after extubation in 12 patients, ten minutes in four patients, 15 minutes in two patients and 20 minutes in two patients. There was no significant difference between the two groups in the time to sustained head lift (for five seconds or more) on command after extubation.

Discussion

The suggested criteria for an ideal muscle relaxant for short procedures are: rapid onset of complete paralysis, early recovery and minimal side effects.⁵ None of the muscle relaxants in clinical use meet all these criteria.

Succinylcholine has a rapid onset of action but has too many side effects.⁶ The older non-depolarising muscle relaxants, d-tubocurarine, gallamine, alcuronium, and fazadinium all have a slow onset, long duration and many side effects.⁷

In a previous study, it was shown that vecuronium $100 \mu\text{g} \cdot \text{kg}^{-1}$ produced adequate muscle relaxation and was easily reversed following procedures lasting less than 30 minutes.⁵ However, the mean time taken to produce complete neuromuscular

TABLE III Time to maximum neuromuscular block (onset) and intubating scores

	Onset (sec) Mean ± S.D.	Intubating Scores		
		0	1	2
Group A. (n = 20) Atracurium $400 \mu\text{g} \cdot \text{kg}^{-1}$ B.W.	198.3 ± 84.1	10	5	5
Group B. (n = 20) Succinylcholine $1 \text{ mg} \cdot \text{kg}^{-1}$ B.W.	76.7 ± 39.3	16	1	3

Complete neuromuscular block was produced faster with succinylcholine ($p < 0.01$).

There was no significant difference in intubating scores.

block by vecuronium in that study, 230 seconds, was significantly longer than with succinylcholine. The mean time taken to produce complete paralysis by atracurium in this study was 198 seconds, which is also significantly slower than the onset time of succinylcholine. The onset time for atracurium has been found to be shorter than pancuronium.^{9,10} Therefore, in a situation where rapid intubation is required, succinylcholine remains the drug of choice.

The degree of residual neuromuscular block with atracurium at the end of surgery in this study, as shown by the absence of response to TOF stimulation or the presence of only the first response to TOF stimulation, corresponds to more than 90 per cent depression of first twitch height¹¹ and would provide adequate surgical relaxation.¹² From this state of intense neuromuscular block with atracurium, recovery of all responses to TOF stimulation was achieved in a mean time of 5 ± 4.6 minutes following administration of neostigmine. Thus the neuromuscular effect of atracurium $400 \mu\text{g}\cdot\text{kg}^{-1}$ can be reversed with standard doses of neostigmine, less than 20 minutes after injection of relaxant. In contrast, with pancuronium and d-tubocurarine, such profound neuromuscular block may be difficult to reverse, even with larger doses (5 mg) of neostigmine.¹³

Atracurium may be easy to reverse because of its unique mode of elimination from the body. It is metabolised by Hofmann elimination, a non-enzymatic process which is pH and temperature dependent^{1,3,14} but is independent of renal or hepatic factors.^{15,16} Spontaneous recovery from neuromuscular block with atracurium occurs more rapidly than following pancuronium, d-tubocurarine and gallamine.¹⁷ Since the antagonism of neuromuscular blocking drugs may be considered as an acceleration of spontaneous recovery,¹⁸ anticholinesterase-induced recovery can be expected to occur more rapidly after atracurium.

Successful reversal of neuromuscular block following atracurium in this study occurred despite the presence of 90–100 per cent residual block at the time of reversal with neostigmine. Similarly in a previous study, neuromuscular block from vecuronium was successfully reversed when residual block was assessed to be more than 90 per cent in 19 out of 20 patients.⁵ Therefore, it would seem that reversal of the new non-depolarising muscle relax-

ants vecuronium and atracurium with neostigmine, from more than 90 per cent twitch depression, is possible, unlike the older non-depolarising relaxants, d-tubocurarine and pancuronium.¹⁷ However, close monitoring of neuromuscular function is required in order to ensure complete reversal of neuromuscular block following short procedures.

We conclude that atracurium in a dose of $400 \mu\text{g}\cdot\text{kg}^{-1}$ is suitable for short surgical procedures lasting for less than 30 minutes. Good intubating conditions are achieved in about three minutes. Full neuromuscular block is produced and this can be reversed with standard doses of anticholinesterase drugs less than 20 minutes after the initial dose of muscle relaxant. Monitoring of neuromuscular function is recommended. When succinylcholine is regarded as unsuitable or contraindicated, atracurium may be the drug of choice for short surgical procedures.

Acknowledgements

The authors thank Professor Richard I. Bodman, Department of Anesthesiology and Dr. Sundar Rao, Department of Biostatistics for their advice and Mr. Emmanuel I. Lapak for typing this manuscript.

References

- 1 Stenlake JB, Waigh J, Urwin J, Dewar GH, Coker GG. Atracurium: conception and inception. *Br J Anaesth* 1983; 55: (Suppl. 1) 3S–10S.
- 2 Hughes R, Payne JP. Clinical assessment of atracurium using the single twitch and tetanic responses of the adductor pollicis muscles. *Br J Anaesth* 1983; 55: (Suppl. 1) 47S–57S.
- 3 Hughes R, Chapple DJ. The pharmacology of atracurium: a new competitive neuromuscular agent. *Br J Anaesth* 1983; 53: 31–44.
- 4 Basta SJ, Ali HH, Savarese JJ et al. Clinical pharmacology of atracurium besylate (BW 33A). A new non-depolarising muscle relaxant. *Anaesth Analg* 1982; 61: 723–9.
- 5 Gyasi H, Williams A, Melloni C, Bevan DR. ORG NC 45 for short intra-abdominal operations: a comparison with succinylcholine. *Can Anaesth Soc J*, 1983; 30: 132–5.
- 6 Durant NN, Katz RL. Suxamethonium. *Br J Anaesth* 1982; 54: 195–208.
- 7 Feldman SA. Muscle relaxants. 2nd Ed. W.B. Saunders Co. 1979; pp 190–205.
- 8 Fahey MR, Morris RB, Miller RD, John YJ,

- Cronelly R, Gencarelli P. Clinical pharmacology of ORG NC45 (Norcuron): a new non-depolarising muscle relaxant. *Anesthesiology*, 1981; 55: 6–11.
- 9 Gramstad L, Lilleaasen P, Minsas B. Onset time and duration of action for atracurium, ORG NC45 and pancuronium. *Br J Anaesth* 1982; 54: 827–30
 - 10 Schiller DJ, Feldman SA. Comparison of intubating conditions with atracurium, vecuronium and pancuronium. *Anaesthesia* 1984; 39: 1188–91.
 - 11 Lee, C. Train-of-4 quantitation of competitive neuromuscular block. *Anesth Analg* 1975; 54: 639–53.
 - 12 Viby-Mogensen J. Clinical assessment of neuromuscular transmission. *Br J Anaesth* 1982; 54: 209–23.
 - 13 Lee C, Katz RL. Neuromuscular pharmacology: A clinical update and commentary. *Br J Anaesth* 1980; 52: 173–88.
 - 14 Neill EAM, Chapple DJ, Thompson CW. Metabolism and kinetics of atracurium: an overview. *Br J Anaesth* 1983; 55: (Suppl. 1) 23S–25S.
 - 15 Ward S, Neil EAM. Pharmacokinetics of atracurium in acute hepatic failure (with acute renal failure). *Br J Anaesth*; 55: 1169–72.
 - 16 Gyasi HK, Naguib M. Atracurium and severe hepatic disease: a case report. *Can Anaesth Soc J* 1985; 32: 161–4.
 - 17 Donati F, Bevan JC, Bevan DR. Neuromuscular blocking drugs in anaesthesia. *Can Anaesth Soc J* 1984; 31: 324–35.
 - 18 Bevan DR. Neuromuscular blocking drugs. *Can Anaesth Soc J* 1983; 30: 556–61.

Résumé

Lors des procédures gynécologiques de courte durée (30 minutes ou moins), l'atracurium a été comparé à la succinylcholine chez 40 patientes. La fonction neuromusculaire a été évaluée par observation de la réponse de l'adducteur du pouce après stimulation avec une ondée de quatre (T.O.F.).

Des bonnes conditions d'intubation ont été produites après 76.7 ± 39.3 secondes avec la succinylcholine $1 \text{ mg} \cdot \text{kg}^{-1}$ et 198 ± 84 secondes avec l'atracurium $400 \mu\text{g} \cdot \text{kg}^{-1}$. Le relâchement musculaire a été maintenu avec la dose initiale d'atracurium ou des doses répétées de succinylcholine. Le temps chirurgical moyen était de 17.65 ± 5.3 minutes pour le groupe atracurium et 15.2 ± 4.6 minutes pour le groupe succinylcholine.

Le bloc neuromusculaire résiduel avec l'atracurium a été antagonisé avec de la néostigmine $0.036 \text{ mg} \cdot \text{kg}^{-1}$ et de l'atropine $0.018 \text{ mg} \cdot \text{kg}^{-1}$. La reprise de la fonction neuromusculaire après antagonisme, évaluée par le retour des réponses à la stimulation du T.O.F. et survenue après 5.05 ± 4.6 minutes pour le groupe atracurium. Il faut cependant noter que la moitié des doses d'antagoniste sus-mentionnées a été répétée pour trois patientes. Dans la période post opératoire aucune complication ne fut notée dans les deux groupes.

On conclut qu'une dose unique d'atracurium de $400 \mu\text{g} \cdot \text{kg}^{-1}$ est convenable pour l'intubation et le maintien du relâchement musculaire lors des procédures chirurgicales de courte durée. Cependant le début d'action est lent comparativement à la succinylcholine. Un bloc neuromusculaire résiduel peut être antagonisé avec des doses standard de néostigmine moins que 20 minutes après la dose initiale de relaxant. L'atracurium apparaît comme étant une alternative convenable pour des procédures de courte durée lorsque que la succinylcholine est contre-indiquée ou déconseillée.