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Atracurium besylate in paediatric anaesthesia

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Summary

Atracurium was evaluated in clinical anaesthesia in 50 children undergoing elective surgery. The time to onset of maximum block (182 seconds) was similar to that of vecuronium but shorter than that of pancuronium as previously reported. The duration of clinical relaxation (33 minutes) is between those of vecuronium and pancuronium. The antagonism of block at 25% recovery was easy. There were no untoward cardiovascular effects but skin reactions were observed in over 30% of patients.

Key words

Neuromuscular relaxants; atracurium.
Anaesthesia; paediatric.

Atracurium and vecuronium are two non-depolarising agents recently introduced into clinical practice. Both drugs have been reported to be associated with excellent cardiovascular stability and a medium duration of action.[1–4]

Clinical experience with atracurium, mostly in adult patients, has shown this drug to be safe and effective[4] and an alternative to the established relaxants.[5,6] It has a relatively rapid onset of action,[5] short intermediate duration [7,8] and a low tendency to cumulation.[9] Cardiovascular side effects are minimal in clinical dosage[5,8,10] and neuromuscular block is easily antagonised. The present paper describes our clinical experience with the drug in paediatric patients and some comparisons are made with our previously published work on vecuronium, used in children under similar conditions.[11]

Method

Following approval by the local ethical committee, 50 children aged 1–14 years, generally fit, undergoing elective abdominal or ophthalmic surgery requiring the use of non-depolarising muscle relaxants were studied. Premedication, given 60 min pre-operatively, consisted of trimeprazine 3 mg/kg and atropine 0.02 mg/kg orally. Anaesthesia was induced using either thiopentone 5 mg/kg intravenously or inhalation of nitrous oxide, oxygen and halothane. At the loss of the eyelash reflex, atracurium 0.5 mg/kg was given intravenously. Manual ventilation of the lungs with 60% nitrous oxide and 0.5% halothane in oxygen was carried out for 90 seconds, at which point tracheal intubation was performed. Anaesthesia was maintained with nitrous oxide, oxygen and halothane in the porportions mentioned above, along with supplements of pethidine.

Monitoring of neuromuscular blockade was accomplished using a peripheral nerve stimulator (Myotest, Biometer Ltd) delivering a train-of-four stimulus, at 2 Hz every 10 seconds, to the ulnar nerve via skin electrodes. The technique involved counting the number of contractions in a slightly abducted thumb in response to train-of-four stimulation as described by Viby-Mogensen[12] and previously used in this unit.[11] The time to 100% block was measured from the end of injection until loss of all four twitches. Duration of clinical relaxation was measured as the period from the same zero point until return of all four twitches. This is equivalent to 25% recovery of original twitch height.[13] Cardiovascular monitoring comprised an electrocardiograph (ECG), an oscillotonometer with recorder (Dinamap, Critikon Ltd) measuring heart rate and blood pressure respectively.

Intubating conditions were assessed using a four point scale described previously.[14] Conditions termed excellent or satisfactory were clinically acceptable; those described as fair or poor were not.

Additional increments (0.125 mg/kg) of atracurium were administered at 25% recovery and the duration of clinical relaxation (recovery to 25%) of each increment noted. Antagonism of the block was performed

using a mixture of neostigmine 50 μg/kg and glycopyrronium 10 μg/kg at the end of surgery whenever at least three twitches in the train-of-four sequence were present. Antagonism was deemed satisfactory when all four contractions in response to train-of-four stimulation appeared to be of similar amplitude and a tetanic contraction was well sustained without significant post-tetanic facilitation or fade. Clinical assessment of reversal by head lifting or ability to cough were also used, whenever applicable.

Results

Table 1 shows the physical characteristics of the patients. Thirty-three received an intravenous induction (thiopentone), the remaining 17 having anaesthesia induced by inhalation of a mixture of 60% nitrous oxide and halothane in oxygen.

Table 1. Physical characteristics of patients in the study

Number	50
Sex M:F	30:20
Mean (SD) age, years	6.8 (3.0)
Mean (SD) weight, kg	22.6 (7.9)

Intubating conditions, assessed at 90 seconds after administration of the relaxant, were clinically acceptable in 94% of patients, being graded as excellent in 72% (Fig. 1). In no patient was there an inability to intubate at this time.

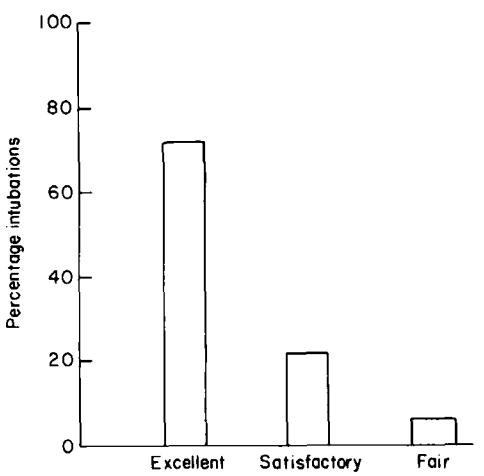

Fig. 1. Intubating conditions 90 s after atracurium 0.5 mg/kg.

The overall time to achieve 100% block was 182 seconds (Table 2). When analysed separately there was no difference in this time between those receiving an inhalational induction and those receiving an intravenous one.

Table 2 Time (s) to 100% block

Group	Time (SD) to 100% block
Inhalation	178 (48)
Intravenous	184 (47)
All patients	182 (47)

Table 3. Duration of clinical relaxation of intubating dose and subsequent increments

	Mean (SD) duration to 25% recovery (min)				
	Intubating dose	Increment number 1	2	3	4
	33 (4.7)	17	19	19	20
n	50	17	5	2	1

n = number of patients receiving the dose. Standard deviation not given for incremental doses due to small numbers involved.

The average duration of clinical relaxation (Table 3) was 33 min. Seventeen patients (34%) received at least one additional increment of relaxant and five (10%) received further increments. Although the numbers are small, the duration of action of these increments was 17–20 minutes in every case.

No untoward cardiovascular effects were experienced at any time in any of the patients. Under stable anaesthesia, i.e. more than 10 minutes after intubation, pulse rates and systolic blood pressure readings were similar to pre-induction values (Fig. 2).

Reversal of neuromuscular block was assessed as excellent in 44 (88%) cases and good in five cases (10%). In both these groups a sustained contraction in response to a tetanic stimulation was achieved within two min of administration of neostigmine. One patient who had 25% recovery at 31 min and whose surgery ended at 56 min without further administration of relaxant, did not receive any neostigmine. At this stage spontaneous respiration had resumed and there were four twitches in response to a train-of-four stimulus with no fade during tetanic contraction.

Sixteen children (32%) exhibited a cutaneous reaction on administration of atracurium. Of these, 12 (24%) had a generalised truncal erythema or erythematous

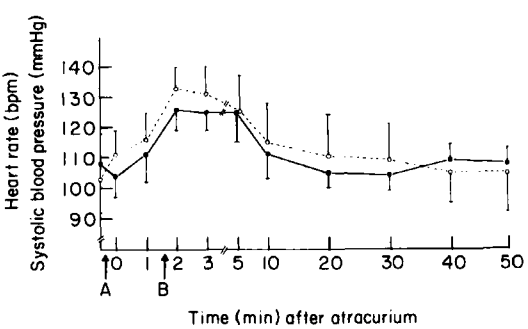

Fig. 2. Mean (SD) pulse rate (-○-) and systolic blood pressure (-●-) during anaesthesia. A, induction; B, intubation.

macular rash (most marked on the upper, anterior thoracic wall) and four (8%) had erythema along the course of the vein used to administer atracurium. Three (6%) of these cutaneous reactions occurred after inhalational induction while 13 (26%) occurred subsequent to induction with thiopentone. However, no patient in the present series exhibited any associated bronchospasm, hypotension or other histaminoid response.

Discussion

The ideal neuromuscular blocking agent has been described as one possessing a non-depolarising mode of action, a short duration, no cumulation, easy antagonism and absence of undesirable cardiovascular effects.[15] It is clear that pancuronium, long popular in paediatric anaesthesia[16–18] lacks some of these desirable features. Atracurium is now in clinical use and has been the subject of a number of studies.[3,4,7,8] A recently published study[19] showed it to be a useful agent for use in paediatric anaesthesia.

The time of onset of maximum block (182 seconds) in the present study using atracurium 0.5 mg/kg is comparable to that of vecuronium 0.1 mg/kg (173 seconds) and marginally better than pancuronium 0.1 mg/kg (208 seconds) under identical conditions,[11] these doses being considered equipotent in adults.[20] The quicker onset is also reflected in intubating conditions, with atracurium producing conditions superior to pancuronium and equivalent to those produced with vecuronium. When compared with our experience in adults, the onset of maximum block after atracurium 0.5 mg/kg is significantly faster in children (182 seconds as compared to 224 seconds in adults). This has also been reported previously with vecuronium.[4,11] Again, intubating conditions reflect this faster onset by being significantly better in children.

The duration of clinical relaxation (33 minutes) confirms atracurium to be a moderately long-acting agent. It is significantly shorter-acting than pancuronium (48 minutes), but when compared with vecuronium using a similar anaesthetic technique, the latter has a significantly shorter duration of action (20 minutes).[11] The duration of action of atracurium is only slightly, though significantly shorter in children (33 minutes) when compared with that of adults (39 minutes) under similar conditions (unpublished observations).

No evidence of cumulation was observed in the small number of children given repeated doses of atracurium.

Our data support the view that, in clinical dosage, atracurium has little, if any, cardiovascular effects.[4,21] Antagonism of neuromuscular blockade is rapid and effective.

Early work suggested that this agent was free from histamine releasing activity.[4,8] However, a 32% incidence of cutaneous reactions indicates some histamine releasing effect. The incidence is more or less similar to that reported in adults.[22] These cutaneous manifestations were not, however, accompanied by other signs of histamine release. Histamine levels with atracurium (0.6 mg/kg) have been reported to be about one-half of those observed with tubocurarine (0.5 mg/kg).[23] This may be the reason why no other effects of histamine release such as bronchospasm or hypotension were observed in the present study. Only rarely are such phenomena observed when using tubocurarine in children, although the histamine releasing potential of that drug is in no doubt. The higher incidence of reactions in those patients induced with thiopentone may point to some form of thiopentone/atracurium interaction when injected in quick succession.

In conclusion, atracurium produces neuromuscular blockade in children which is shorter than that produced by pancuronium but longer than that with vecuronium. The relatively rapid onset of action is reflected in better intubating conditions at 90 seconds. Lack of cardiovascular effects, especially lack of vagolytic action, appear advantageous. There is no tendency to cumulation and antagonism of the block is easy as carried out in the present study, although difficulties may arise if antagonism is attempted soon after administration of the relaxant or in the presence of an intense block.[24]

Acknowledgments

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