POST-TETANIC COUNT AND PROFOUND NEUROMUSCULAR BLOCKADE WITH ATRACURIUM INFUSION IN PAEDIATRIC PATIENTS

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Atracurium degrades rapidly and, because it is difficult to quantify the train-of-four response accurately by visual or manual estimation [1], coughing, hiccup or ventilatory movements may occur on occasions, despite the use of a peripheral nerve stimulator. To avoid this, complete suppression of the train-of-four (TOF) response is sometimes required. Viby-Mogensen, Howardy-Hansen and Chraemmer-Jorgensen [2] pointed out that it is possible to quantify profound non-depolarizing neuromuscular blockade by counting the number of post-tetanic twitches after a 5-s period of supramaximal stimulation at 50 Hz. The purpose of this study was to correlate the degree of neuromuscular blockade using atracurium with the post-tetanic count (PTC).

PATIENTS AND METHODS

The study was approved by the hospital Ethical Committee; parental consent was not obtained because monitoring of neuromuscular function is commonplace in anaesthetic practice.

Thirty-eight paediatric patients undergoing a variety of surgical procedures requiring mechanical ventilation were studied. All patients were fit (ASA grade I or II) apart from their presenting condition, and were not receiving any drugs that might have interfered with neuromuscular function.

Patients younger than 8 months of age and all neurosurgical patients received atropine 0.02 mg kg⁻¹ i.m. 45 min before the induction of anaesthesia. Older children who weighed less than 15 kg were premedicated with Pethidine Com-

pound 0.06-0.08 ml kg⁻¹ (1 ml contains pethidine 25 mg, promethazine 6.25 mg and chlorpromazine 6.25 mg). Children weighing more than 15 kg received papaveretum 0.4 mg kg⁻¹ and hyoscine 0.008 mg kg⁻¹ 90 min before induction.

Anaesthesia was induced with 50% cyclopropane in oxygen or thiopentone 5 mg kg⁻¹ depending on their preference and weight. The trachea was intubated in all patients—in neonates while they were awake, and in others with the aid of suxamethonium 2 mg kg⁻¹. Anaesthesia was maintained with 0.5-1.5% halothane and 33% oxygen in nitrous oxide delivered by a paediatric T-piece and bag. The electrocardiogram, arterial pressure (Dinamap), and praecordial heart and breath sounds were monitored in all patients.

A constant current peripheral nerve stimulator (Bard Biomedical) provided supramaximal stimuli for all measurements, via surface electrodes placed over either the posterior tibial nerve behind the medial malleolus or the ulnar nerve at the wrist. Output for maximal twitch response (displayed in milliamperes on the nerve stimulator) was recorded.

SUMMARY

In 38 paediatric surgical patients given atracurium by infusion, the degree of neuromuscular blockade was monitored using the post-tetanic twitch response. This was assessed by counting the number of visible responses when single twitch stimulation was applied at 1 Hz for 30 s after a 5-s tetanic stimulation at 50 Hz. A post-tetanic count of less than 10 correlated with a single twitch height of less than 5% of control, and ensured adequate paralysis. Once the count was greater than 15, the blockade could be antagonized readily.
Neuromuscular blockade was produced initially with a single dose of atracurium 0.4 mg kg\(^{-1}\) and maintained subsequently with an infusion of undiluted atracurium (initially at 8 \(\mu\)g kg\(^{-1}\) min\(^{-1}\)) delivered by a Graeby Dynamics 16A syringe pump. Artificial ventilation was provided using a Nuffield 200 ventilator (Penlon) with a paediatric valve [3]; this converts the machine to a pressure generator and enables it to deliver small tidal volumes.

The intensity of neuromuscular blockade was monitored by assessing the visible twitch in response to the following standard sequence of stimulation, which has been modified from that described by Viby-Mogensen, Howardy-Hansen and Chraemmer-Jorgensen [2]:
(a) a train-of-four, repeated every 12 s, if necessary, for reassessment;
(b) a 30-s delay;
(c) tetanic stimulation (50 Hz) for 5 s;
(d) a 3-s delay;
(e) single twitch stimulation at 1 Hz for 30 s.
The number of visible responses was recorded. The degree of neuromuscular block was first assessed 6 min after the single dose and then at 6-min intervals, so avoiding the effect of tetanic stimulation on the subsequent cycle.

The intensity of neuromuscular blockade was varied according to the following regimen:
(a) If the bolus dose failed to obliterate the train-of-four response, incremental doses of atracurium 0.1 mg kg\(^{-1}\) were given at 6-min intervals until this was achieved.
(b) If no post-tetanic twitches were visible after 24 min, the infusion of atracurium was discontinued until the PTC had reached 5. The infusion was then restarted at its previous rate.
(c) If the PTC was decreasing, the infusion rate was halved when the count reached 5. Similarly, if the PTC was increasing, the infusion rate was doubled when it reached 15.
(d) If doubling the rate of infusion failed to bring the PTC below 15, “top up” bolus doses of atracurium 0.1 mg kg\(^{-1}\) were given as before.

At the end of the operative procedure, the infusion was discontinued and neuromuscular transmission allowed to recover spontaneously. When at least one response was visible on the TOF, the anaesthetic agents were discontinued and any residual neuromuscular blockade was antagonized with neostigmine 0.05 mg kg\(^{-1}\) (plus atropine 0.02 mg kg\(^{-1}\)). The times taken from the injection of the reversal agents to the return of the fourth response of the TOF and to the patient making an adequate clinical recovery (as assessed by regular ventilation and purposeful movements) were recorded.

Student’s \(t\), Chi-squared and Wilcoxon Rank

| Table I. Demographic details of patients studied. Standard deviation shown in parentheses |
|---------------------------------------------|-----------------|-----------------|------------------|
| Infants (wt < 5 kg)                        | Small children (5-15 kg) | Older children (> 15 kg) |
| Number studied                             | 8               | 11              | 19               |
| Age: Mean                                  | 55 (47) days    | 1.5 (1) yr      | 8.3 (4) yr       |
| Range                                      | 2-120 days      | 3 month-3 yr    | 4-16 yr          |
| Weight (kg) (mean)                         | 2.9 (0.8)       | 10.1 (2.8)      | 29 (13)          |
| Time of premedication (min before operation)| 52 (19)         | 68 (22)         | 96 (35)          |
| Duration of anaesthesia (min)              | 95 (58)         | 76 (34)         | 93 (40)          |
| Range                                      | 16-181          | 33-165          | 47-180           |
| Type of surgery                            |                 |                 |                  |
| Ophthalmic                                 | —               | 1               | 2                |
| Abdominal                                  | 8               | 4               | 4                |
| Neurosurgical                              | —               | 3               | 4                |
| Orthopaedic                                | —               | 1               | 1                |
| Urological                                  | —               | 1               | 2                |
| Bone marrow harvest                        | —               | 1               | 1                |
| Plastic surgery                            | —               | —               | 4                |
| Cardiac catheterization                    | —               | —               | 1                |
Sum tests were used for statistical analysis and a $P$ value of less than 0.05 was considered significant.

**RESULTS**

The age, weight, time of premedication, duration and type of surgery in the 38 patients studied are shown in table I.

In three patients, the infusion of atracurium was withheld because of unexpected changes in the surgical procedure.

In the 12 patients whose posterior tibial nerve was used for monitoring, a maximum twitch response was obtained with a mean output of $20 \pm 7.8$ mA from the stimulator while a mean stimulus of $33 \pm 17$ mA was required ($P < 0.05$) in those in whom the ulnar nerve was used.

The patients were divided into three groups according to weight (< 5 kg, 5-15 kg, > 15 kg), but there were no differences between the groups in the mean initial bolus dose of atracurium required to obliterate the train-of-four response. The overall mean initial bolus dose required was $0.56 \pm 0.14$ mg kg$^{-1}$.

The mean infusion rates used throughout the procedures for the three groups are shown in table II. The older children required a significantly higher rate of infusion when compared with the younger groups, between whom the different rates were not significant. Three of the 19 older children (> 15 kg) required an additional dose of atracurium compared with five out of the 19 smaller children (> 15 kg). The mean additional single dose was $0.22 \pm 0.1$ mg kg$^{-1}$, administered an average of 50(SD ± 6) min after the initial bolus, and did not vary between the three groups. The duration of anaesthesia in those patients who required an additional dose was $116 \pm 15$ min and this was significantly longer ($P < 0.05$) than in patients who did not require an extra dose (mean duration of anaesthesia $80 \pm 7$ min).

The increase in PTC with time as neuromuscular function recovered spontaneously with and without the effect of the infusion is shown in figure 1. Recovery was similar up to 36 min, after which time the infusion significantly slowed the return of function.

Figure 2 illustrates the relationships between the increasing PTC and the return of the response to train-of-four stimulation. The return of the full

| TABLE II. Mean (SD) infusion rates in three patient groups.  
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<tr>
<td>Infants (&lt; 5 kg)</td>
<td>Small children (5-15 kg)</td>
<td>Older children (&gt; 15 kg)</td>
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<td>7.9 (0.63)</td>
<td>7.4 (0.74)</td>
<td>8.6* (1.25)</td>
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* $P < 0.05$ compared with younger groups.

**Fig. 1.** The PTC (mean ± SEM) increasing as neuromuscular function recovers spontaneously (X) and under the effect of the infusion (O).
TOF and clinical recovery took longer than 5 min from injection of the reversal agents in one patient. This patient received a total initial dose of 0.8 mg kg$^{-1}$, since some of the atracurium was suspected of being administered extravascularly by accident. Reversal was attempted only 18 min after this dose. The patient made a full recovery 8 min after the administration of the anticholinesterase.

**DISCUSSION**

The mean initial dose of atracurium 0.56 mg kg$^{-1}$ for infants and children was higher than might be expected; however, it agrees with the findings of Nightingale and Bush [4] whose paediatric patients required 0.6 mg kg$^{-1}$ for intubation when assessed on clinical grounds. When more sensitive monitors of neuromuscular function such as twitch tension and electromyography were used, smaller bolus doses were reported (for example 0.3 mg kg$^{-1}$ [5] and 0.4 mg kg$^{-1}$ [6]). The incremental method used in this study, in which each additional dose of atracurium was given at 6-min intervals, will tend to increase the dose required for a given effect.

Goudsouzian and colleagues [7] reported a mean infusion rate of atracurium during halothane, oxygen and nitrous oxide anaesthesia as 8.3 μg kg$^{-1}$ min$^{-1}$—a value which agrees closely with our findings. The concentration of atracurium at steady state is given as:

$$C^{ss} = \text{infusion rate} \times \text{clearance}$$

As no statistical differences in atracurium clearance have been reported between small and older children [8], the lower rate of infusion in children weighing less than 15 kg in the present study would imply that a lower concentration of atracurium was required to achieve the same degree of neuromuscular blockade, and may reflect increased sensitivity, as shown by Goudsouzian, and colleagues [9].

The number of patients who required an additional single dose at some time during anaesthesia was the same in infants and young children weighing less than 15 kg and those children weighing more. This would suggest that the intensity of neuromuscular blockade was similar in both groups and that the different infusion rates reflected a genuine difference in sensitivity.

The patients who required an additional dose did have a significantly longer anaesthetic and this suggests that the infusion rates in this study were not the most suitable for procedures lasting more than 80 min. This is also reflected in the fact that the recovery of the PTC was only marginally slowed by the infusion in the first 30 min, at which time the PTC had reached 15. Although recovery of blockade after this was delayed more markedly by the infusion, at 30 min the level of neuromuscular function was 10–20%.

The larger supramaximal stimulus required when stimulating the ulnar nerve compared with the posterior tibial nerve may be a reflection of the

**Fig. 2.** The relationship between the PTC (mean±95% confidence limits) and the train-of-four response.
deeper position of the ulnar nerve at the wrist compared with that of the posterior tibial at the ankle.

The spontaneous degradation of atracurium occurs rapidly and, once recovery of neuromuscular function has begun, it continues to improve rapidly. Goudsouzian and co-workers [9], studying infants anaesthetized with halothane, oxygen and nitrous oxide, and given a bolus of atracurium 0.4 mg kg\(^{-1}\), showed that once recovery had started the single twitch response moved from 5% to 25% of its control value in a mean of 8.5 min. Unless the single twitch is kept at less than 10% of its control value or the train-of-four response kept to 25% [10] ventilatory movements, cough and hiccup may occur [11].

In the present study the spontaneous recovery of neuromuscular function took longer than was found by Goudsouzian and colleagues [9]. The time taken to recover from 5% twitch height (equivalent to one response on the TOF) to 25% twitch height (three out of four in the TOF) was approximately 12 min. The use of the infusion plus the bolus dose may explain the longer recovery time obtained in the present study.

Heisterkamp, Stansted and Cohen [12] described enhancement of the post-tetanic twitch tension (post-tetanic facilitation) in partially curarized patients. Viby-Mogensen, Howard-Hansen and Chraemmer-Jorgensen [2] demonstrated that this still occurred with profound neuromuscular blockade and that the response to post-tetanic twitch stimulation after injection of non-depolarizing neuromuscular blockers appeared earlier than the pre-tetanic twitch or train-of-four response. These investigators showed that the time of return of train-of-four responses could be derived from the number of post-tetanic twitch responses when pancuronium was used.

Figure 2 shows that when the PTC was less than 10, all the responses of the train-of-four were obliterated. If the PTC was kept in single figures, the height of the single twitch was less than 5% of its control value and cough, hiccup and ventilatory movements could be avoided. This is particularly important in neurosurgery and ophthalmic surgery, where the duration of surgery is hard to predict and movements of the patient could be disadvantageous. A decreasing PTC indicates an increasing intensity of neuromuscular blockade and so allows appropriate action to be taken. Similarly, towards the end of surgery, the intensity of blockade may be adjusted by simply counting the PTC rather than endeavouring to estimate the train-of-four ratio which is difficult without complex monitoring equipment. This allows easy antagonism of the neuromuscular blockade.

Our results suggest that following an initial bolus of 0.5 mg kg\(^{-1}\), an infusion rate of 8 \(\mu\)g kg\(^{-1}\) min\(^{-1}\) will lead to a gradual decrease in the intensity of neuromuscular blockade, especially in children weighing more than 15 kg. Using this basic infusion rate as a guideline, and adjusting it to keep the PTC between 5 and 10, will ensure adequate paralysis throughout the period of surgery. Complete antagonism of neuromuscular blockade can be expected within 6 min of injection of the anticholinesterase.

REFERENCES