Frequency of train-of-four stimulation influences neuromuscular response

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SUMMARY

We have compared the effects of two different frequencies of train-of-four stimulation of the ulnar nerve (2-Hz stimulation once every 10 or 20 s) on onset time and potency of atracurium, vecuronium and mivacurium during balanced anaesthesia. The adductor pollicis EMG was recorded simultaneously in both hands of 24 children aged 2-12 yr. After administration of an ED_{50} dose of each blocker, onset times were mean 21 (SEM 10) s shorter (P < 0.05) and decreases in neuromuscular function were 22 (3) % greater (P < 0.001) in the hand which was stimulated once every 10 s. We conclude that it is not possible to compare potency estimates of neuromuscular blocking agents if different stimulation patterns have been used. (Br. J. Anaesth. 1994; 72: 686-687)

KEY WORDS


The potency of neuromuscular blocking agents is assessed commonly using either a single twitch or train-of-four stimulation at 10-20-s intervals. Previous studies have shown that a single twitch stimulation at 1-4 s intervals produces greater potency estimates than stimulation at 7-10 s intervals [1]. Train-of-four stimulation once every 10 s produces more rapid and more profound neuromuscular block than a single twitch at a similar frequency [2, 3]. There are no data to compare two frequencies of train-of-four stimuli to estimate the potency of neuromuscular blocking agents. We have compared onset and depth of neuromuscular block when train-of-four stimulation was used once every 10 or 20 s with atracurium, vecuronium or mivacurium as the neuromuscular blocking agent.

METHODS AND RESULTS

After obtaining local institutional Ethics Committee approval and parental informed consent, we studied 24 children, aged 2-12 yr and ASA I or II. Patients were undergoing elective surgical procedures requiring tracheal intubation. They did not have any diseases or were receiving any medications known to affect neuromuscular transmission.

Premedication comprised oral midazolam 0.5 mg kg⁻¹ (maximum dose 15 mg). General anaesthesia was induced with propofol 2-3 mg kg⁻¹ and alfentanil 30-50 µg kg⁻¹. The lungs were ventilated with 66% nitrous oxide in oxygen to maintain an end-tidal carbon dioxide partial pressure of 5.1-5.6 kPa. The trachea of each patient was intubated before administration of a neuromuscular blocking agent. General anaesthesia was maintained with propofol 10 mg kg⁻¹ h⁻¹, alfentanil 50-100 µg kg⁻¹ h⁻¹ and 66% nitrous oxide in oxygen. Volatile anaesthetic agents were not used. Patient monitoring consisted of ECG, non-invasive arterial pressure, end-tidal carbon dioxide, pulse oximeter and bilateral palmar skin temperature.

Neuromuscular function was monitored by adductor pollicis EMG (Relaxograph, Datex, Finland). In both hands, stimulating surface electrodes were attached over the ulnar nerve on the wrist and recording electrodes over the adductor pollicis muscle and base of a forefinger. Opposite ulnar nerves were stimulated at 10- and 20-s intervals using a synchronized, supramaximal, square wave train-of-four stimulation (2 Hz). The hands were stimulated in random order. When palmar skin temperatures and EMG calibration signals were stable, patients received a single dose of a randomly selected neuromuscular blocker (atracurium 140 µg kg⁻¹, vecuronium 40 µg kg⁻¹ or mivacurium 70 µg kg⁻¹) in a freely running infusion line located in the cubital vein. These doses were administered simultaneously with ulnar nerve stimulation and were estimated to produce 50% neuromuscular block when train-of-four stimulation was used once every 20 s [4, 5]. Thus eight pairs of hands were monitored for each drug.

Maximum neuromuscular block (depression of the first EMG response in the train-of-four series of responses) and onset times (times from administration to maximum effect) were calculated and compared between groups and between the two stimulation patterns. ANOVA and a two-tailed paired Student's t test were used, as appropriate. P < 0.05 was regarded as statistically significant. Values are expressed as mean (SEM).

Patient characteristics were similar in the three groups (table I). Palmar skin temperatures always exceeded 33 °C and were similar for both hands.

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Neuromuscular blocking agents were administered at a mean time of 19 (1) min after induction of anaesthesia. Onset times were slightly shorter for the faster stimulation pattern (Δ onset time was 21 (10) s; \( P = 0.0495 \)) and significantly shorter for mivacurium than for atracurium or vecuronium (table I). Maximum neuromuscular block was significantly greater when a faster stimulation pattern was used (Δ maximum neuromuscular block 22.5 (2.7)%; or 0.75 (0.08) probits; \( P = 0.0001 \)) (table I), without significant between-drug differences.

**COMMENT**

This study showed that when the potencies of neuromuscular blocking agents were evaluated by a train-of-four mode of stimulation, the results depended on the frequency of a commonly used stimulation pattern. When train-of-four stimulation was used once every 20 s, our preselected doses of neuromuscular blockers produced the expected degree of neuromuscular block (52 (4)%). This was significantly less than the block of 74 (5)% produced in the opposite hand when the same stimulation was used once every 10 s.

It may be assumed that the concentration of neuromuscular blocker was similar in both hands of each patient. Non-depolarizing neuromuscular blocking agents compete with acetylcholine at the postsynaptic acetylcholine receptor. We see three different mechanisms by which a short interval between series of train-of-four stimuli could produce a shorter equilibration half-life of drug with effect site (\( T_{1/2} \)) [6]. This could happen even though palmar skin temperatures were similar in both hands.

It is noteworthy that onset times were slightly shorter for faster stimulation frequency. These results are similar to those comparing a single twitch and train-of-four stimulation at the same frequency [2, 3]. Dose-response curves for different neuromuscular blockers were parallel during similar anaesthetic conditions with an average slope of 6.5 probit/log [4]. Our finding of a probit difference of 0.75 in maximal neuromuscular block produced by two stimulation frequencies corresponds to a 30% difference in ED values (10\( P^{7/6.5} \) = 1.30).

We conclude that even a commonly used difference in the frequency of train-of-four stimulation significantly influenced potency estimations of neuromuscular blocking agents. It is not justifiable therefore to compare the potency of neuromuscular blockers unless identical patterns of stimulation are used.

**REFERENCES**