RECOVERY OF ATRACURIUM AND VECURONIUM NEUROMUSCULAR BLOCK IN THE ISOLATED FOREARM

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SUMMARY

The duration of recovery from neuromuscular block after a 3 × ED₉₀ dose of atracurium or vecuronium is similar in spite of their three-fold difference in elimination half-lives. We have investigated simultaneous spontaneous recovery from equipotent doses of atracurium and vecuronium in the isolated forearms of volunteers in order to attempt to explain this paradox. Simultaneous administration of the two drugs, one in each of the subject's forearms, allowed direct comparison of recovery to be made against the same plasma concentration of drug. The recovery index of atracurium was found to be significantly longer than that of vecuronium. We suggest that this observation, when considered with the different plasma concentrations after a 3 × ED₉₀ dose, helps to explain the similar duration of action of the two drugs during the recovery phase after a large systemic bolus. (Br. J. Anaesth. 1993; 71: 730-731)

KEY WORDS

Neuromuscular relaxants, atracurium, vecuronium, isolated forearm, recovery rate.

METHODS AND RESULTS

We studied spontaneous recovery from equipotent doses of atracurium and vecuronium administered simultaneously, one drug in each of the two isolated forearms of volunteers. This technique allowed us to compare the recovery from neuromuscular block produced by the drugs against the same minimal non-blocking plasma concentration. In this way, recovery from neuromuscular block can be separated from the effect of changes in plasma concentration of the drug.

METHODS AND RESULTS

We studied the spontaneous recovery of atracurium and vecuronium neuromuscular block in the isolated forearm in eight investigations in six volunteers (29-61 yr). Ethics Committee approval for the study was obtained.

A vein at the back of each hand was cannulated. Bilateral forearm tourniquets were applied. The ulnar nerve at the wrist was stimulated via surface electrodes. Supramaximal pulses of 0.2 ms duration were delivered by a nerve stimulator at a frequency of 0.2 Hz. The resultant force of thumb adduction was monitored by a force displacement transducer preloaded to 200 g.

After a period of stabilization of 10 min the forearm tourniquets were inflated simultaneously to 300 mm Hg pressure. Vecuronium 0.3 mg diluted in saline 20 ml was injected i.v. into the back of one hand and atracurium 1.5 mg diluted in saline 20 ml into the other hand. These are equipotent doses and each drug produced the same degree of neuromuscular block in the isolated forearm. The forearm tourniquets were released simultaneously after 3 min. In all experiments, greater than 90% twitch depression was achieved. We excluded from the results any experiment in which a block greater than 99% occurred. The recovery indices (RI) (time from 25% to 75% recovery) for both drugs were measured, as was the time from 0% to 25% twitch recovery. The mean RI of atracurium and vecuronium were compared using Student's paired t test.

All volunteers were healthy and none was receiving any medication influencing neuromuscular conduction. Similar degrees of block were produced in both arms. The block for vecuronium was 97.6 (sd 1.4)% and that for atracurium 94 (1.8)%.

Mean (sd) time from maximum block to 25% recovery was 17.6 (6.8) min for atracurium and 13.3 (2.7) min for vecuronium. Mean 25-75% RI for
Atracurium 1.5 mg  
Vecuronium 0.3 mg  

Drugs injected  
Tourniquets off  

**Fig. 1.** Typical trace of onset and recovery of neuromuscular block in the two arms of a volunteer after simultaneous administration of atracurium 1.5 mg in saline 20 ml (upper trace) in one isolated forearm and vecuronium 0.3 mg in saline 20 ml (lower trace) in the other. The tourniquet was released at 3 min. The RI of vecuronium is shorter than that of atracurium.

Vecuronium was 7.9 (0.85) min (range 6.9–9 min) and for atracurium 10.6 (1.8) min (range 8.3–13.6 min) \( (P = 0.004) \).

**COMMENT**

Bevan, Bevan and Donati [4] asked “why are the duration of action and rate of recovery from atracurium and vecuronium similar when their elimination half-lives differ threefold?” It is this question that we have examined.

The previous suggested explanation, that the metabolism of atracurium in the effect compartment could explain this paradox, is improbable as the effect compartment is of small size and Ericksson and colleagues [6] have demonstrated that Hofmann degradation does not occur to any extent at the neuromuscular junction.

In these experiments, we have demonstrated that vecuronium is associated with a significantly shorter time to spontaneous recovery from neuromuscular block than atracurium (7.9 vs 10.6 min) in the isolated forearm. By using simultaneous administration of the two drugs, we subjected each arm to similar circulation changes and to the same plasma concentration of both drugs. If any degradation of atracurium had occurred during the period of tourniquet occlusion, when the biophase concentration would have been great, the recovery of atracurium block recorded would have underestimated the effect of the drug.

We have demonstrated previously that the systemic effect of doses of neuromuscular blocking drugs of this magnitude do not affect recovery in the isolated arm. It has been demonstrated that, when drugs of similar clinical duration of action and similar pharmacokinetic profiles are compared in the isolated arm there is no difference in their RI. It has been proposed that different recovery times revealed in the isolated arm reflect different affinities with biophase binding sites.

We can now suggest an explanation as to why the recovery times of atracurium and vecuronium are similar after systemic 3 × ED\textsubscript{90} doses. If the plasma concentrations of both drugs were similar during the elimination half-life, one would expect vecuronium to recover more quickly than atracurium (indeed there is evidence that this occurs following 1 × ED\textsubscript{90} to 1 × ED\textsubscript{96} of both drugs). However, if the plasma–biophase concentration gradient of vecuronium were reduced by a greater concentration of drug in the plasma, the spontaneous recovery rate would be slower and likely to approach that of atracurium. Thus the inherently faster spontaneous recovery of vecuronium neuromuscular block in the isolated forearm is offset by the effect of the greater plasma concentration of drug during the elimination phase. We suggest that this mechanism explains the similar duration of action of these two drugs when used in clinical doses as bolus injections.

**ACKNOWLEDGEMENT**

N. Campkin was supported by the Westminster and Charing Cross Hospital Trustees.

**REFERENCES**