Low-dose mivacurium supplementation of prilocaine i.v. regional anaesthesia

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Summary
We have compared in two groups of five healthy volunteers, the motor effect of prilocaine i.v. regional anaesthesia of the forearm with and without addition of mivacurium 0.6 mg. Although addition of mivacurium might, theoretically, provide the benefit of increased neuromuscular block with rapid plasma cholinesterase degradation in the isolated limb, we observed prolonged forearm weakness in the mivacurium group using tests of grip strength (median recovery to 90% of control, 80 min (range 60 min to >8 h) vs control median recovery to 90% of 16 (8–24) min) and bead transfer (median recovery to 90% of control 36 (24–48) min vs control median recovery to 90% of 12 (8–16) min). This weakness was considerably in excess of that predicted by rapid systemic degradation of mivacurium. The mivacurium group experienced symptoms of local anaesthetic toxicity which did not occur in the control group and which could not be replicated by administration of mivacurium alone. (Br. J. Anaesth. 1997; 78: 222–223).

Key words
Neuromuscular block, mivacurium. Anaesthetic techniques, regional. Anaethetics local, prilocaine.

Methods and results
We studied 10 healthy, fasted and consenting volunteers in a double-blind, controlled study that was approved by the Wellington Ethics Committee. I.v. cannulae (22-gauge) were sited in the dorsum of both hands and the IVRA was performed on the non-dominant arm. The limb was elevated for 1 min and an upper arm tourniquet inflated to 300 mm Hg. Volunteers were allocated randomly to one of two groups of five subjects (age and weights were not significantly different, one female in each group) to receive either 0.5% prilocaine 40 ml (control) or 0.5% prilocaine 40 ml with mivacurium 0.6 mg (mivacurium group). The tourniquet remained inflated for 20 min after injection of local anaesthetic.

Immediately before drug injection, baseline

Forearm fractures are commonly reduced as outpatient procedures using i.v. regional anaesthesia (IVRA). These fractures often cause muscle spasm which increases bone impaction and the traction that is required for fracture reduction; IVRA with local anaesthetic alone provides poor neuromuscular block. Paralysing the arm by adding a small dose of neuromuscular blocking agent to the local anaesthetic has been shown to facilitate fracture reduction, decrease the pain experienced by the patient both during and after the procedure, and may obviate the need for hospital admission and general anaesthesia in some muscular young patients.1–3

Many different neuromuscular blocking agents have been used in small doses with few reported side effects other than transient diplopia and difficulty with accommodation. These include tubocurarine 1 mg, gallamine 10 mg, atracurium 2–5 mg, suxamethonium 4 mg and decamethonium 0.2 mg.2 3 Ideally, to limit the systemic effects of the neuromuscular blocking agent on deflation of the cuff, the blocker should have a shorter duration of action than the duration of cuff inflation. Atracurium undergoes Hoffman degradation under mild alkaline conditions and should decay spontaneously in the isolated limb. However, most studies have demonstrated that atracurium produces prolonged paralysis when used to supplement IVRA, which may in part be caused by decreased Hoffman degradation related to the acidic environment of the ischaemic limb.1 2 4

Mivacurium is hydrolysed by plasma cholinesterase and may therefore be degraded in the isolated limb provided there is sufficient plasma cholinesterase activity after exsanguination of the limb which must inevitably be incomplete. In this study mivacurium was added to IVRA with 0.5% prilocaine and its effect on the development of motor block and on the return of motor function was investigated. Earlier studies with suxamethonium, which is also degraded by plasma cholinesterase, have yielded conflicting results.3 4 If degraded in the isolated arm, mivacurium would confer the benefits of ease of reduction and decreased pain with a low risk of systemic effects.

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neuromuscular strength and co-ordination were assessed and these were repeated every 4 min until the test variables had returned to baseline or 2 h had elapsed. Crude grip strength was measured by recording the maximum pressure generated by asking the subject to maximally compress a rubber bulb connected to a pressure gauge. The number of beads transferred from one container to another in 15 s with a pair of forceps was used as a test of fine motor skills. Complete neuromuscular block was defined as complete loss of all voluntary movement in the fingers, hand and arm below the cuff.

Complete forearm muscle paralysis occurred in none of the controls and in only two subjects in the mivacurium group and then only after 18 min of limb ischaemia. Muscle strength decreased rapidly in both groups while bead transferral decreased more rapidly in the mivacurium group.

Time to recovery of grip strength to baseline, after deflation of the tourniquet, was significantly more rapid in the control group than in the mivacurium group. When mivacurium 0.6 mg was injected i.v. the tourniquet deflation, was significantly more rapid in the mivacurium group. Although not specifically tested, there appeared to be no qualitative difference in return of sensation between the two groups.

All volunteers who had received mivacurium in the prilocaine ischaemic arm block spontaneously volunteered symptoms of light headedness, dizziness, perioral paraesthesia, tinnitus, diplopia, blurred vision, altered hearing or slurred speech. These symptoms began 1–2 min after deflation of the tourniquet and lasted for 5–15 min. No adverse effects were volunteered by subjects in the control group. When mivacurium 0.6 mg was injected i.v. into one of the volunteers who had experienced these adverse effects, none of these symptoms of presumed local anaesthetic toxicity was experienced, apart from diplopia which lasted for 10 min.

Two of the five volunteers who received mivacurium developed urticarial weals on the arm several minutes after cuff deflation. One had experienced some pruritus while the cuff was inflated. Neither had a history of atopy.

Comment

Our results demonstrated that supplementation of prilocaine IVRA with mivacurium resulted in prolonged muscle weakness on cuff deflation, as has been reported with other non-depolarizing neuromuscular blocking agents. This slow recovery suggests that mivacurium is not broken down in the ischaemic limb and that recovery of neuromuscular function is not dependent on plasma concentration, which would be expected to decrease rapidly with washout and dilution on reperfusion of the limb to concentrations too small to affect recovery of the block. Recovery from a drug effect is dependent on plasma concentration only if the plasma concentration decreases slowly; however, if the plasma concentration decreases rapidly, then recovery of neuromuscular function is related to the transfer of mivacurium from the biophase to the plasma.

All volunteers who received the combination of mivacurium and prilocaine displayed symptoms of local anaesthetic toxicity that were absent in the control volunteers. Apart from diplopia, none of the symptoms was reproduced when mivacurium 0.6 mg was given i.v. to a volunteer who had demonstrated these side effects. Despite the small numbers, these symptoms were a consistent finding and occurred with a far greater incidence than the 1–2% incidence of minor adverse reactions reported in the literature for IVRA. This interaction has not been reported in previous studies and may warrant specific investigation.

Development of urticarial weals would suggest an increase in vascular permeability. The fact that normal intravascular hydrostatic pressure only occurs on deflation of the tourniquet would explain the delayed development of the urticarial weals.

In summary, mivacurium increases the degree of paralysis of the forearm when added to IVRA, although as with other blocking agents, the neuromuscular blocking effect has a duration well in excess of that of tourniquet inflation.

References