Mivacurium compared with succinylcholine in children with liver disease

D. W. Green, M. Fisher and I.Sockalingham

Summary
We have compared mivacurium and succinylcholine in 27 paediatric patients with mild (Child’s A) to moderate (Child’s B) liver disease undergoing oesophagastroduodenoscopy (OGD) and injection of oesophageal varices, with 10 healthy children receiving mivacurium for ENT procedures. With mivacurium 0.2 mg kg⁻¹, the severity of liver disease did not correlate with duration of block compared with controls (time from bolus to T1 25%, P=0.74; T1 25% to T4:T1 >0.7, P=0.545). However, initial recovery (time to T1 25%, P=0.002) and overall recovery (bolus to T4:T1 >0.7, P=0.004) from mivacurium-induced neuromuscular block correlated inversely with pre-existing concentrations of plasma cholinesterase. Conditions for tracheal intubation at 2 min with mivacurium were comparable with conditions at 1 min with succinylcholine in the liver patients. (Br. J. Anaesth. 1998; 81: 463–465).

Keywords: enzymes, cholinesterase; neuromuscular block, mivacurium; neuromuscular block, succinylcholine; anaesthesia, paediatric; liver, disease

Children with moderate to severe liver disease are at risk of developing portal hypertension and oesophageal varices. To limit and prevent episodes of haematemesis necessitates regular oesophagastroduodenoscopy (OGD) to monitor progress and, if necessary, inject varices with sclerosant. To facilitate this procedure, general anaesthesia and neuromuscular block are used. As the procedure may only last a few minutes if no varices are found, succinylcholine has been the agent of choice in the absence of a non-depolarizing neuromuscular blocking drug of sufficiently short duration. Mivacurium, a short-acting, non-depolarizing benzylisoquinoline neuromuscular blocking drug, is a potentially useful agent in this context. In particular, it has a higher ED₉₅ (0.1 mg kg⁻¹), faster onset, shorter duration of action and more rapid spontaneous recovery in children than in adults. This should make it an ideal agent for this procedure.

However, the short duration of action of mivacurium results primarily from its extensive metabolism by plasma (butyryl- or pseudo-) cholinesterase (PChE). PChE concentrations may be reduced markedly in adults with liver disease and thus interfere with the metabolism of mivacurium: there is a significant negative correlation between recovery variables from mivacurium and PChE activity. The object of this study was to evaluate and compare ease of intubation, effective duration of neuromuscular block and spontaneous recovery after administration of mivacurium or succinylcholine to paediatric patients with liver disease requiring OGD. These variables were equated with the pre-existing clinical severity of the liver disease and the concentration of PChE.

Methods and results
After obtaining approval from the Ethics Committee of King’s College Hospital, we undertook a prospective, randomized, open, between-group parallel study. Groups A and B comprised 27 children, aged 2–12 yr, suffering from mild or moderate chronic liver disease (Child’s A or B, ASA II–III), necessitating OGD and possible injection of varices. Group C comprised 10 children (ASA I), aged 2–12 yr, undergoing grommet insertion. Both operations necessitated tracheal intubation. Patients were allocated to group A (Child’s A) or group B (Child’s B) according to disease severity using a modified Child’s classification in use currently at King’s College Hospital.

Groups A and B were randomized prospectively to receive succinylcholine or mivacurium in a ratio of 1:1. All patients in the control group C received mivacurium.

Anaesthesia was standardized in all cases. After induction of anaesthesia, an i.v. cannula was inserted and blood obtained for measurement of PChE concentrations and estimation of dibucaine number. Neuromuscular monitoring was then attached (Datex Relaxograph, Datex, Finland) and calibrated. The compound evoked potential of the adductor pollicis muscle was recorded after supramaximal stimulation of the ulnar nerve at a frequency of 2 Hz in a train-of-four mode every 12 s. After a 1-min control period, patients allocated randomly to group mivacurium were given a dose of 0.2 mg kg⁻¹ i.v. over 30 s and intubation was attempted 2 min after completion of the bolus dose. Patients in the succinylcholine group received glycopyrrolate 10 μg kg⁻¹ i.v. followed 30 s later by succinylcholine 2 mg kg⁻¹ over 15 s and...
intubation was attempted 1 min later. Ease of intubation was assessed as follows: grade 1 (excellent), easy passage of the tube without coughing, vocal cords relaxed; grade 2 (good), passage of the tube with slight coughing/bucking, vocal cords relaxed; grade 3 (poor), passage of the tube with moderate coughing/bucking, vocal cords moderately adducted; and grade 4 (not possible), vocal cords tightly adducted.

End-tidal carbon dioxide and isoflurane were maintained at 3.5–4.5% and 0.5–1%, respectively, in all patients.

The following measurements were made from the Datex Relaxograph: percentage block at time of intubation (1 min with succinylcholine, 2 min with mivacurium); time from completion of administration of the first bolus dose to 25% recovery of T1; time from 25% recovery of T1 to T4:T1 >0.7 (mivacurium only); and time from administration of the bolus dose to T4:T1 >0.7 (mivacurium only). Neuromuscular function was allowed to recover spontaneously in all patients.

All statistical significance tests were two-sided at the 5% level.

Mean age of the patients was 6.4 (range of 2.2–11) yr. There were no significant differences between groups.

Mean concentrations of PChE (normal range 600–1400 iu litre⁻¹, measured using the method of Kalow and Lindsay⁹) in the three groups were: group A, 700 (SD 170), (range 282–991) iu litre⁻¹; group B, 510 (201), (239–991) iu litre⁻¹; and group C, 932 (165), (734–1224) iu litre⁻¹. Mean PChE concentration was significantly greater (P<0.05) in healthy children compared with the liver patients.

Grade of intubation with succinylcholine at 1 min and mivacurium at 2 min showed no significant differences in the specified comparisons. In the 16 patients who received succinylcholine, intubation conditions were 14 grade 1, one grade 2 and one grade 3. In the 21 patients who received mivacurium, intubation conditions were 20 grade 1 and one grade 4.

There were no significant differences between the controls (group C) and the mivacurium-treated patients (groups A and B) for: time (min:s) from bolus to T1 25% (group C, 10:48 (3:45) vs group A, 9:50 (2:58) and group B, 12:44 (2:46) (P=0.74) and T1 25% to T4:T1 >0.7 (group C, 5:59 (1:22) vs group A, 6:28 (1:42) and group B, 8:18 (2:57) (P=0.545). Thus there was no evidence of prolongation in the overall recovery of mivacurium between Child’s A and B and the control group. Recovery was faster in both groups with succinylcholine: time (min:s) from bolus to T1 25% (group A, 7:48 (3:45) and group B, 8:31 (1:51) (P=0.0007) and time from T1 25% to T4:T1 >0.7 (group A, 2:02 (3:00) and group B, 1:11 (1:11) (P=0.0001).

Correlations between recovery variables and baseline PChE concentrations were calculated for mivacurium patients. Figure 1 shows a scatterplot of the predicted time, expressed as natural log from bolus dose to 25% recovery of T1 in the mivacurium patients. Stratified correlation coefficient = −0.81, 95% confidence interval −0.94, −0.35, P=0.002.

Comment

In our study of 10 healthy adult patients and 25 patients with cirrhosis of the liver who received a bolus dose of mivacurium 0.15 mg kg⁻¹, we found that patients with hepatic cirrhosis may be sensitive to mivacurium, which could be explained, at least in part, by lower PChE activity.⁷ Our study has shown that in children with liver disease undergoing OGD and possible injection of oesophageal varices, duration and recovery from neuromuscular block with mivacurium 0.2 mg kg⁻¹ did not correlate with the pre-existing clinical severity of liver disease (Child’s A or B). However, recovery significantly correlated inversely with pre-existing concentrations of PChE. Conditions for tracheal intubation at 2 min with mivacurium were comparable with conditions at 1 min with succinylcholine. This implies that mivacurium is a suitable neuromuscular blocking drug in this group of patients which may be used instead of succinylcholine.

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References

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