Edrophonium and plasma cholinesterase activity

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Plasma cholinesterase activity was estimated following administration of edrophonium 0.5 or 1.0 mg·kg^{-1} given for antagonism of atracurium-induced neuromuscular block. There was no inhibition of enzyme activity for up to three hours following edrophonium administration. This is in contrast to profound and prolonged inhibition of enzyme activity seen following neostigmine and pyridostigmine.

Although neostigmine and pyridostigmine are in common use for antagonism of nondepolarising neuromuscular block, edrophonium in doses of 0.5–1.0 mg·kg^{-1} has recently been advocated as an alternative on the basis of its rapid onset of action and weaker muscarinic effects.[1–5] Both neostigmine and pyridostigmine produce marked and prolonged inhibition of plasma cholinesterase activity.[6–8] In the present study plasma cholinesterase activity has been measured following administration of edrophonium for antagonism of nondepolarising neuromuscular block.

Methods

Fifteen adult patients of ASA physical status I and II, undergoing elective surgery, were included in the study after obtaining their informed consent and approval from the regional ethical committee. None was receiving any drugs or suffering from any medical conditions known to affect plasma cholinesterase activity. Following premedication with oral diazepam, anaesthesia was induced with thiopentone and maintained with nitrous oxide in oxygen, fentanyl and droperidol. Atracurium was administered for muscle relaxation in an initial dose of 0.5 mg·kg^{-1} followed by smaller increments as required. Heart rate and blood pressure were continuously monitored using an ECG and an oscillotonometer (Dinamap). Neuromuscular block was monitored by stimulating the ulnar nerve percutaneously and recording the force of thumb adduction using a force transducer and a neuromuscular function analyser (Myograph 2000).

Edrophonium was administered at the end of surgery, when neuromuscular block had recovered by at least 20–25 per cent, at two dose levels, 0.5 or 1.0 mg·kg^{-1} (selected at random) for the antagonism of neuromuscular block in seven and eight patients respectively. Atropine 10 μg·kg^{-1} was given along with edrophonium to counter its muscarinic effects. Antagonism of the block was monitored throughout. Blood samples (2.0 ml) were collected prior to induction of anaesthesia and prior to administration of edrophonium and at 1, 2, 3, 5, 7, 10, 15, 20, 30, 45, 60, 90, 120, 150 and 180 minutes later. Plasma was separated and cholinesterase activity estimated by the colorimetric method of Ellman *et al.*[9] using butyrylthiocholine as the substrate. The results in each group were subjected to analysis of variance.

We had previously reported on the plasma cholinesterase activity following neostigmine and pyridostigmine[8] but plasma cholinesterase activity in two patients each was studied again following antagonism of neuromuscular block with neostigmine 0.05 mg·kg^{-1} and pyridostigmine 025 mg·kg^{-1}. This was done primarily to ascertain the reproducibility of the results since the substrate of the test method in our laboratory had been changed from acetylthiocholine to butyrylthiocholine and the normal range of enzyme activity revised from a value of 1.9–3.8 IU·ml^{-1} to 3.8–9.0 IU·ml^{-1}.

Key words

ANTICHOLINESTERASES: edrophonium, neostigmine, pyridostigmine; ENZYMES: plasma cholinesterase.

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TABLE Plasma cholinesterase activity before and following edrophonium administration (mean ± SD)

	Plasma cholinesterase activity ($IU \cdot ml^{-1}$) following edrophonium	
	$0.5\,mg \cdot kg^{-1}$	*$1.0\,mg \cdot kg^{-1}$*
Before anaesthesia	5.7 ± 1.1	5.6 ± 1.2
Before edrophonium (control)	5.2 ± 0.9	5.2 ± 1.2
Minutes after edrophonium		
1	5.2 ± 0.9	5.0 ± 1.2
2	5.3 ± 0.9	5.1 ± 1.2
3	5.3 ± 0.8	5.2 ± 1.2
5	5.3 ± 0.8	5.2 ± 1.2
7	5.3 ± 0.9	5.4 ± 1.2
10	5.4 ± 0.8	5.5 ± 1.3
15	5.3 ± 0.9	5.3 ± 1.2
20	5.3 ± 0.7	5.3 ± 1.2
25	5.2 ± 0.7	5.3 ± 1.2
30	5.2 ± 0.9	5.4 ± 1.3
45	5.2 ± 0.8	5.3 ± 1.1
60	5.2 ± 0.6	5.3 ± 1.1
90	5.3 ± 0.8	5.1 ± 1.1
120	5.2 ± 0.8	5.2 ± 1.1
150	5.3 ± 0.7	5.3 ± 1.1
180	5.2 ± 1.0	5.3 ± 1.1

Results

The average age and weight of the patients receiving the 0.5 and 1.0 $mg \cdot kg^{-1}$ doses of edrophonium were 55 and 53 years and 79 and 73 kg respectively (p = NS).

Mean plasma cholinesterase activity prior to induction of anaesthesia and prior to antagonism of neuromuscular block was similar in both groups receiving the two doses of edrophonium (Table). The enzyme activity showed only minor changes following administration of edrophonium and these were insignificant. ($F = 0.14$, df = 17 and 108 for edrophonium 0.5 $mg \cdot kg^{-1}$, and $F = 0.10$ df = 17 and 126 for edrophonium 1.0 $mg \cdot kg^{-1}$.)

The Figure shows the per cent change in enzyme activity following the two doses of edrophonium as well as following administration of neostigmine and pyridostigmine, each in two patients. Whereas there was no significant change following edrophonium, the enzyme activity was depressed to less than five per cent of control following neostigmine and pyridostigmine and was still only 50–60 per cent of control three hours after the anticholinesterase administration.

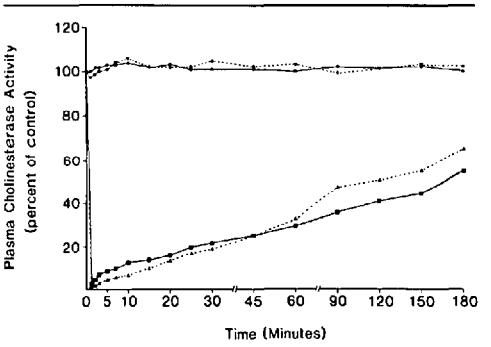

FIGURE Per cent change in plasma cholinesterase activity following administration of edrophonium 0.5 $mg \cdot kg^{-1}$ ●———●, edrophonium 1.0 $mg \cdot kg^{-1}$ ●------●, neostigmine 0.05 $mg \cdot kg^{-1}$ ▲------▲ and pyridostigmine 0.25 $mg \cdot kg^{-1}$ ■———■.

Neuromuscular block was adequately antagonised (TOF ratio of 0.7 or more) in all patients following administration of edrophonium as well as neostigmine and pyridostigmine.

Discussion

It is well-established that neostigmine and pyridostigmine produce intense and prolonged inhibition of plasma cholinesterase activity.[6–8] A previous study[10] on the effect of edrophonium in doses useful for antagonism of nondepolarising block, showed a peak inhibition in plasma cholinesterase activity of 47 per cent one minute after its administration. This is considerably less than that observed with neostigmine and pyridostigmine.[8] In addition the effect reported by Sohn *et al.*[10] lasted only about 15 minutes. The results from the present study show no inhibition of plasma cholinesterase activity, even at a dose of 1.0 $mg \cdot kg^{-1}$. It is possible that plasma cholinesterase activity in the study of Sohn *et al.*[10] was influenced by the prior administration of pancuronium, a drug known to produce marked inhibition of plasma cholinesterase,[11] whereas we used atracurium, which has negligible effects on plasma cholinesterase activity.[12] It is also possible that the different methods used for estimation of plasma cholinesterase activity could account for the difference in the results between our study and that of Sohn *et al.*[10] However, we used the same method for estimating the enzyme activity with all three anticholinesterase agents.

The absence of any inhibition of plasma cholinesterase activity following edrophonium administra-

tion may be related to its minimal inhibitory effect on acetylcholinesterase.[14-15]

In contrast to previous reports[6,13] of prolongation of a succinylcholine-induced block following administration of neostigmine or pyridostigmine, the results from the present study would suggest any such prolongation after edrophonium administration to be unlikely. Some increase in the duration of succinylcholine block reported by Sohn *et al.*[10] when it was administered after edrophonium (which had been administrated to antagonise a pancuronium-induced block) is not likely to be due to inhibition of plasma cholinesterase since the enzyme activity must be depressed by about 75 per cent before prolongation of succinylcholine block occurs.[16,17]

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Résumé

L'activité de la cholinestérase plasmatique a été estimée après administration d'édrophonium 0.5 ou 1.0 mg·kg^{-1} afin d'antagoniser un bloc neuromusculaire induit par l'atracurium. Il n'y avait aucune inhibition de l'activité enzymatique même après trois heures de l'administration de l'édrophonium. Ceci est en contraste avec l'inhibition profonde et prolongée de l'activité enzymatique observée après néostigmine et pyridostigmine.