SHORT COMMUNICATION

Serum Cholinesterase Activity in Spontaneously Hypertensive Rats

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Introduction

Succinylcholine, a depolarising neuromuscular blocker, is used routinely to facilitate endotracheal intubation and provide muscle relaxation in surgery including in hypertensive patients[1]. Succinylcholine being an ester drug is dependent entirely on hydrolysis by serum-(pseudo-or butyryl) cholinesterase for termination of its action[2]. In spontaneously hypertensive rats (SHR), abnormalities in a number of hepatic enzymes have been noted[3]. Serum cholinesterase enzyme activity may thus be altered in spontaneously hypertensive rats (SHR) and in hypertension in general. The objective of this study was to examine the serum cholinesterase activity in SHR and in the related normotensive Wistar-Kyoto (WKY) rats. Specifically the hydrolysis rate of a model substrate of serum cholinesterase (acetylthiocholine) was determined[4] in serum from SHR and WKY rats. In addition, the inhibition profile of a specific serum cholinesterase inhibitor, tetraisopropyl pyrophosphoramide, iso-OMPA[5], was also examined in serum from these two groups of rats.

Materials and Methods

Two groups (n = 6) of rats were used: spontaneously hypertensive rats (SHR) and the related normotensive Wistar-Kyoto (WKY) counterparts. Blood was obtained from these rats under brief ketamine/xylazine (50/3 mg/kg i.p.) anaesthesia and the harvested serum served as the source of the serum cholinesterase enzyme whose activity was estimated using a spectrophotometric technique[4]. Briefly this involved hydrolysis of a model substrate (acetylthiocholine) to yield thiocholine which reacted with a colour reagent (5,5-dithiobis-2-nitrobenzoic acid, DTNB) to form a yellow complex which was quantified at 412 nm. The rate of hydrolysis of the substrate over 10 min was thus a measure of the enzyme activity. The hydrolysis was carried out under various conditions as assay variables influence enzyme activity[7]. Inhibition profile of the enzyme from SHR and WKY rats was determined in the presence of 10, 100, 500 and 1000 μM of the specific serum cholinesterase inhibitor, iso-OMPA; concentration eliciting 50 % inhibition (IC_{50}) was then calculated. Mean ± SEM of the results are presented and $P < 0.05$ were considered statistically significant.

Results

One day prior to withdrawal of the blood sample for enzyme assay the blood pressure in SHR and WKY rats was 175 ± 4 and 146 ± 4 mm Hg respectively ($P < 0.001$). The hydrolysis of acetylthio-

choline was substantially faster in serum from SHR compared to WKY rats both at pH 7.4 and pH 8.0 (Table 1); thus the serum cholinesterase activity was higher in SHR. The elevated serum cholinesterase activity in SHR was not due to a novel or altered cholinesterase enzyme in SHR as the iso-OMPA inhibition profile of the enzyme was identical in SHR and WKY rats; iso-OMPA IC_{50} from SHR and WKY rats did not differ (600 ± 52 μM vs 620 ± 47μM, $P > 0.05$).

Discussion

Spontaneoulsy hypertensive rats (SHR) had elevated serum cholinesterase activity compared to normotensive Wistar-Kyoto rats. This finding is similar to a published report where SHR rats had double the serum cholinesterase activity of WKY rats[6]. Thus the *in vivo* degradation of the ester depolarising neuromuscular blocker, succinylcholine, is likely to be faster leading to a greater requirement for this blocker. If these results are extrapolated to human hypertensive patients, then a resistance (higher dose requirements or more rapid recovery from paralysis) to the neuromuscular effects of succinylcholine and similar ester neuromuscular blockers like mivacurium may be expected. Clinical studies in hypertensive surgical patients undergoing anaesthesia and receiving succinylcholine or mivacurium are warranted to determine the clinical significance of this *in vitro* finding.

Table 1 Acetylthiocholine hydrolysis by serum cholinesterase from spontaneously hypertensive (SHR) and normotensive (WKY) rats

Assay Condition	Hydrolysis rate (mole/ L/min x 10^{-6})		
	SHR	WKY	p
pH 7.4 (37 ^{0}C)	3.60 ± 0.12	2.63 ± 0.07	< 0.001
pH 8.0 (37 ^{0}C)	4.19 ± 0.18	3.06 ± 0.11	< 0.001
pH 8.0 (25 ^{0}C)	3.33 ± 0.11	2.46 ± 0.08	< 0.001

Values are mean ± SEM, n = 6 rats in each group (mean of 3 determinations in each rat)

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