SHORT COMMUNICATION

Serum Cholinesterase Inhibitory Effects of Droperidol

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Introduction

Droperidol is used as anaesthetic premedication for induction of anaesthesia and for neuroleptanaesthesia[1]. Butyrophenones including droperidol inhibit serum cholinesterases *in vivo* in patients[2] and *in vitro* in horses[3]. Droperidol also potentiated the *in vitro* action of the depolarising neuromuscular blocker, succinylcholine[4], as did haloperidol[5]. Droperidol thus has the potential to prolong the action of succinylcholine since it is hydrolysed *in vivo* by serum cholinesterase. This study therefore examined the *in vitro* serum cholinesterase inhibitory effects of droperidol using human and rat serum as the enzyme source.

Materials and Methods

Human and rat blood samples were collected from five human volunteers and six rats respectively and the harvested serum stored at -85° C pending enzyme assays. Serum cholinesterase activity in the absence or presence of droperidol was determined at 37° C using a spectrophotometric method[6]. This involved hydrolysis of the substrate, acetylthiocholine, to yield thiocholine with subsequent reaction with 5,5-dithiobis-2-nitrobenzoic acid yielding a yellow coloured anion (5-thio-2-nitrobenzoic acid), the formation rate of which was quantified over 10 min at 412 nm. The known serum cholinesterase inhibitor, tetra-isopropyl-pyrophosphoramide, iso-OMPA, was used as the positive control. Percent inhibition versus droperidol concentration relationships were fitted to sigmoid E_{max} equation to yield the pharmacodynamic parameters E_{max} (maximum inhibition) and IC_{50} (inhibitory concentration at half maximal inhibition). Human and rat results were compared using unpaired t-test; $P < 0.05$ was taken as statistically significant.

Results and Discussion

Droperidol showed 15 to 62 % inhibition against human and 11 to 58 % against rat cholinesterase with 2.6 to 130 μ M (1 to 50 μg/mL) of the drug. The specific serum cholinesterase inhibitor, iso-OMPA, at a concentration of 6.3 μM (2.2 μg/mL), inhibited human and rat serum cholinesterase by 39 and 34% respectively under similar conditions (figure 1). Maximum inhibition was similar for human and rat enzyme but droperidol concentration required to elicit half maximal (50%) inhibition of rat enzyme was substantially higher (Table 1). Thus sensitivity to serum cholinesterase inhibition by droperidol was different in humans and rats. Droperidol did not inhibit serum cholinesterase from human or rat serum at clinically relevant concentrations of 2.6 - 7.8 μM (1 - 3 μg/mL).

However, at higher than therapeutic concentrations (> 2.6 - 7.8 μM or > 1 - 3 μg/mL), droperidol inhibited human or rat serum cholinesterase to a significant extent. At droperidol concentrations (5-50 μM) that potentiated succinylcholine effect *in vitro* in rats[4], the enzyme was inhibited by 57% in rat serum. Droperidol is unlikely to prolong succinylcholine's effect clinically in surgical patients via serum cholinesterase inhibition.

Table 1 Serum cholinesterase inhibition by droperidol

Enzyme Source	Parameter Estimate (± SEM)		
	E_{max} (%)	EC_{50} μM	μg/mL
Human Serum	61.6 ± 1.6	35.6 ± 5.2	13.7 ± 2.3
Rat Serum	57.4 ± 2.6	53.1 ± 12.0	20.4 ± 4.7
p (unpaired t-test)	0.4	< 0.005	< 0.01

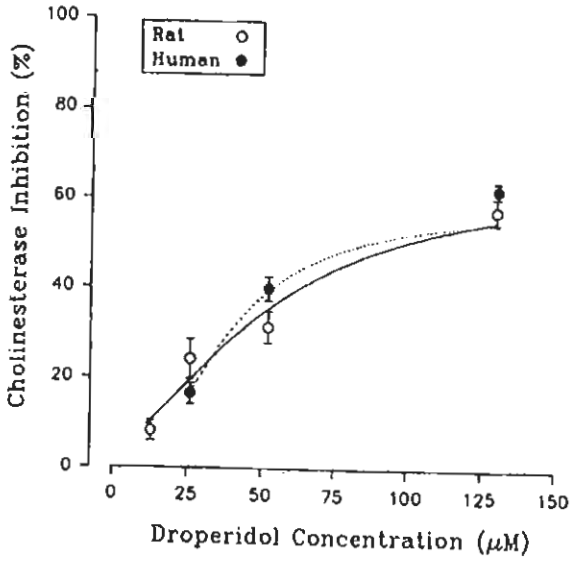

Figure 1 Human and rat serum cholinesterase inhibition by droperidol

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