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 neuroleptanaesthesia¹. Butyrophenones including droperidol inhibit serum cholinesterases in vivo in patients² and in vitro in horses³. Droperidol also potentiated the in vitro action of the depolarising neuromuscular blocker, succinylcholine⁴, as did haloperidol⁵. 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 C using a spectrophotometric method⁶. 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 E₉₅ equation to yield the pharmacodynamic parameters E₉₅ (maximum inhibition) and IC₅₀ (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 µM (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\textsuperscript{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

<table>
<thead>
<tr>
<th>Parameter Estimate (± SEM)</th>
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<tbody>
<tr>
<td>Enzyme Source</td>
</tr>
<tr>
<td>Human Serum</td>
</tr>
<tr>
<td>Rat Serum</td>
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<tr>
<td>p (unpaired t-test)</td>
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**Figure 1** Human and rat serum cholinesterase inhibition by droperidol

**References**

1. Edmonds-Seal J, Prys Roberts C. Pharmacology of drugs used in neurolept-