SHORT COMMUNICATION

EFFECT OF SOME PSYCHOACTIVE AGENTS ON PENTOBARBITONE ANAESTHESIA IN RATS

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Summary: Several psycho-active agents were investigated for their influence on pentobarbitone anaesthesia time in rats. It was found that prior administration of haloperidol, methaqualone and triflupromazine reduced the duration of anaesthesia. An increase in duration was noted after diazepam. The probable mechanism has been discussed.

Key words: pentobarbitone anaesthesia psychoactive agents

INTRODUCTION

Kato and Chiesara (7) reported that many centrally active agents may produce tolerance to barbiturates as a result of induction of liver microsomal enzymes involved in drug metabolism. Haloperidol and promethazine have also been reported to influence the enzyme activity (6). As there is lack of information concerning the effect of various psycho-active agents on metabolic mechanisms, it was thought of interest to study the influence of some of the commonly used agents on pentobarbitone anaesthetic time and if possible to attempt to correlate the data obtained with the results on enzyme activity reported in the literature.

MATERIALS AND METHODS

This study was conducted on 69 albino rats (100-200 g) of either sex. Groups of animals received an intraperitoneal injection of a psychoactive agent for three consecutive days. On the fourth day, all the animals were given pentobarbitone sodium (Abbott) 20 mg/kg (ip) and the interval between loss of righting reflex and its subsequent recovery was noted by the method of Dandiya and Cullumbine (4).

Diazepam (Sigma) 10 mg/kg, methaqualone (Boots) 15 mg/kg, promethazine HCl (M&B) 10 mg/kg, chlorpromazine HCl (M&B) 5 mg/kg, thioproprazine mesylate (M&B) 10 mg/kg, triflupromazine HCl (Squibb) 10 mg/kg, imipramine HCl (Geigy) 10 mg/kg and haloperidol (Searle) 10 mg/kg (in suspension with 2 per cent methylcellulose in normal saline) were used. The control group of the animals were pretreated with saline (2 ml/kg ip). The experiments were carried at a room temperature of 15-20°C.

The mean anaesthetic time prolonged the time was reduced after haloperidol, methaqualone and triflupromazine. The results are presented in Table I.

**Table I: Influence of Drugs (mg/kg, i.p.)**

<table>
<thead>
<tr>
<th>Drugs (mg/kg, i.p.)</th>
<th>Control (Saline 2 ml/kg)</th>
<th>Methylcellulose (2%) in normal saline</th>
<th>Promethazine (10.0 mg)</th>
<th>Chlorpromazine (5.0 mg)</th>
<th>Triflupromazine (10.0 mg)</th>
<th>Thioproperazine (10.0 mg)</th>
<th>Haloperidol (10.0 mg)</th>
<th>Methaqualone (15.0 mg)</th>
<th>Diazepam (10.0 mg)</th>
<th>Imipramine (10.0 mg)</th>
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<tbody>
<tr>
<td>Influence of Drugs</td>
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</table>

The results obtained after pretreatment with observations made by Kato and Chiesara (7) for a result since prior administration in the duration of anaesthesia barbitone sleeping time (1) caused a reduction only in case of diazepam. The ability of drugs is paralleled in vivo by changes noted in the duration of anaesthesia barbitone sleeping time (1) caused a reduction only in case of diazepam after haloperidol. It has been argued that the induced by drugs which changes noted in the duration of enzyme induction/repression.
RESULTS

The mean anaesthetic time in the control group was 53.7 ± 5.70 min. Prior diazepam administration prolonged the duration of anaesthesia significantly (P < 0.01). The anaesthetic time was reduced after haloperidol, methaqualone and triflupromazine. Chlorpromazine, promethazine, imipramine and thioproperazine were devoid of any action. The results are presented in Table I.

<table>
<thead>
<tr>
<th>Drugs (mg/kg, i.p.)</th>
<th>Number of animals</th>
<th>Mean anaesthesia time ± SE (min)</th>
<th>t'</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Saline 2 ml/kg)</td>
<td>8</td>
<td>53.7 ± 5.70</td>
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</tr>
<tr>
<td>Methylcellulose (2%) in Normal saline (2 ml/kg)</td>
<td>5</td>
<td>47.4 ± 6.32</td>
<td>0.74</td>
<td>&gt;0.10</td>
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<tr>
<td>Promethazine (10.0 mg)</td>
<td>8</td>
<td>40.3 ± 6.01</td>
<td>1.63</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Chlorpromazine (5.0 mg)</td>
<td>6</td>
<td>56.2 ± 12.70</td>
<td>0.17</td>
<td>&gt;0.10</td>
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<tr>
<td>Triflupromazine (10.0 mg)</td>
<td>7</td>
<td>28.2 ± 4.81</td>
<td>3.50</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Thioproperazine (10.0 mg)</td>
<td>9</td>
<td>45.7 ± 9.45</td>
<td>0.76</td>
<td>&gt;0.10</td>
</tr>
<tr>
<td>Haloperidol (10.0 mg)</td>
<td>7</td>
<td>15.5 ± 2.82</td>
<td>6.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Methaqualone (15.0 mg)</td>
<td>7</td>
<td>27.7 ± 5.40</td>
<td>3.40</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diazepam (10.0 mg)</td>
<td>7</td>
<td>80.9 ± 7.21</td>
<td>3.06</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Imipramine (10.0 mg)</td>
<td>5</td>
<td>41.0 ± 6.81</td>
<td>1.79</td>
<td>&lt;0.10</td>
</tr>
</tbody>
</table>

DISCUSSION

The results obtained reveal that there was change in pentobarbitone anaesthetic time after pretreatment with diazepam, methaqualone, triflupromazine and haloperidol. The observations made by Kato and Chiesara (7) with chlorpromazine are at variance with the present result since prior administration of chlorpromazine failed to produce any significant change in the duration of anaesthesia. Thiothiazepine and imipramine did not significantly influence pentobarbitone anaesthesia. Promethazine which has been earlier reported to reduce pentobarbitone sleeping time (6) was observed to be devoid of any action. The foregoing observation is in conformity with that of Kato and Chiesara (7). A significant increase was noted only in case of diazepam. Methaqualone which has been reported to increase barbiturate oxidation (1) caused a reduction in pentobarbitone anaesthetic time. A similar result was noted after haloperidol.

The ability of drugs to stimulate or repress the microsomal metabolizing enzymes is paralleled in vivo by changes in the rates of metabolism and variations in duration of drug action (2,3,8). Several workers (5, 3, 7, 8) have tried to correlate the changes induced in the metabolism of pentobarbitone by pretreatment with other agents, with the duration of sleep. It has been argued that the metabolic enzyme systems which inactivate hypnotic barbiturates are induced by drugs which are known to induce microsomal enzymes (2). The foregoing changes noted in the duration of pentobarbitone anaesthesia may be explained on the basis of enzyme induction/repression (2) or change in the activity of metabolic enzymes (10) or inter-
ference by the psychoactive agent with the feed-back regulatory role of the breakdown products of enzymes (9).

ACKNOWLEDGEMENTS

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REFERENCES


Summary: The effect of 30-3 studied in rats. The results ological investigations carry significant observation which had low total lipid levels in comparison to non-piperazine.

Key words: piperazine

Piperazine is widely used for worm infestation in man and were in use until about the important reasons for its wide toward effects have been obs made to study the biochem. This becomes all the more si requires administration of the infestation.

Some preliminary bioch.

Twelve Sprague-Daw the study. They were fed lghout the 30-day experiment were observed as controls f were given a solution of piparatna Pharmaceuticals, E give a concentration of 30% content in the different ti Laboratory Methods and