MODIFICATION OF MORPHINE ANALGESIA IN RATS BY ADRENERGIC BLOCKING AGENTS

By

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Since morphine analgesia in rats is modified by MAO inhibitors (2), reserpine (4, 6), reserpine and tetrabenazine (7), DOPA and 5HTP (3, 7); it is natural to expect modification of morphine analgesia by adrenergic blocking agents and 5HT blocking agents. With this in view the work was started.

MATERIAL AND METHOD

Analgesia was studied in rats as described by Gupta and Gaitonde (1). Rats were administered morphine 5 mg/kg intraperitoneally. For studying the modification of analgesic action by adrenergic blocking agents the same rats were used after 48-72 hours and were administered simultaneously morphine and the adrenergic blocking agent. Pronethalol and Tolazoline were used in doses of 15 mg and 10 mg/kg respectively. Phenoxybenzamine was, however, used in two doses-5 mg and 15 mg/kg since no discernible effect was observed with the lower dose.

RESULTS

The three drugs when used alone in doses in which they were used or in combination with morphine did not produce any analgesia.

The effects of these drugs in combination with morphine are shown in the Table 1. It is very clear that Pronethalol a beta adrenergic blocking agent blocks the analgesic action of morphine where as Tolazoline and Phenoxybenzamine both alpha adrenergic blocking agents potentiate the analgesic action of morphine.

DISCUSSION

It has been shown that reserpine antagonises the analgesic action of morphine (4,6). More recently Takagi et al (7) confirmed the antagonism of morphine analgesia by reserpine and tetrabenazine and the restoration of analgesia by 5HTP and DOPA. In the present study it is seen that the analgesic action of morphine is potentiated, by alpha adrenergic blocking agents and blocked by beta adrenergic blocking agents. All these findings could be explained if it is postulated that the analgesic action of morphine is subserved by its action on adrenergic receptors in the central nervous system and further that there are two types of receptors in the central nervous system (having

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TABLE I

Effect of morphine alone and in combination with adrenergic blocking agents

<table>
<thead>
<tr>
<th>Drugs and Doses</th>
<th>Before</th>
<th>After</th>
<th>Net increase (versus morphine alone)</th>
<th>t and value of p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine 5 mg/kg</td>
<td>4.5±0.24</td>
<td>9.0±0.29</td>
<td>4.5±0.90</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>(15)</td>
<td>(15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine 5 mg/kg</td>
<td>4.5±0.41</td>
<td>6.6±0.15</td>
<td>2.1±0.50</td>
<td>t=1.94</td>
</tr>
<tr>
<td>and Pronethalol 15 mg/kg</td>
<td>(6)</td>
<td>(6)</td>
<td></td>
<td>p=&gt;0.05</td>
</tr>
<tr>
<td>Morphine 5 mg/kg and Tolazoline 10 mg/kg</td>
<td>3.9±0.13</td>
<td>13.8±0.63</td>
<td>9.9±0.47</td>
<td>t=5.4</td>
</tr>
<tr>
<td></td>
<td>(10)</td>
<td>(10)</td>
<td></td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Morphine 5 mg/kg and Phenoxybenzamine 5 mg/kg</td>
<td>4.4±0.24</td>
<td>9.6±1.41</td>
<td>5.2±1.57</td>
<td>t=0.47</td>
</tr>
<tr>
<td></td>
<td>(6)</td>
<td>(6)</td>
<td></td>
<td>p&gt;0.50</td>
</tr>
<tr>
<td>Morphine 5 mg/kg and Phenoxybenzamine 15 mg/kg</td>
<td>4.9±0.60</td>
<td>13.6±0.54</td>
<td>8.7±0.68</td>
<td>t=3.9</td>
</tr>
<tr>
<td></td>
<td>(6)</td>
<td>(6)</td>
<td></td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

1. Before and after refers to the mean reading in seconds required for the tail to be moved before and after morphine and adrenergic blocking agent.
2. ± refers to the standard error.
3. Figures in the parentheses denote the numbers of rats used in each group.
4. Net increase is the difference between mean readings before and after drugs.

Opposing actions) similar to adrenergic receptors in the periphery. It is likely that there is a predominance of beta receptors in the central nervous system. Normally when ever morphine is administered the analgesic effect is a sum total of its action on alpha and beta receptors. Recently it has been shown that Thiopentone blocks the analgesic action of morphine (5). It is worth while to see if Thiopentone like Pronethalol has beta adrenergic blocking action peripherally.

SUMMARY

The analgesic action of morphine in rats is potentiated by Phenoxybenzamine and Tolazoline and blocked by Pronethalol. The possibility of two types of adrenergic receptors in the central nervous system is disussed.

REFERENCES


