EFFECT OF SOME $\beta$-ADRENOCEPTOR BLOCKERS AND OF $\left(\pm\right)$ PROPRANOLOL ON ADRENALINE-INDUCED PULMONARY EDEMA IN MICE

C. JAYACHANDRAN* AND N. PRAKASH**

Departments of *Pharmacology and **Biochemistry, Rajendra Memorial Research Institute of Medical Sciences, Patna - 800 007

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Summary: $\left(\pm\right)$ Propranolol is considered to prevent adrenaline-induced pulmonary edema (A.P.E.) due to the $\beta$-adrenoceptor blockade. However, local anaesthetics also are known to prevent pulmonary edema. To assess the role of $\beta$-adrenergic blockade in A.P.E., the effect of a $\beta_1$-blocker possessing local anaesthetic action ($\pm$ Metaprolol) and a $\beta_1$-blocker possessing no local anaesthetic action ($\pm$ practolol) was studied along with propranolol derivatives. The study revealed that $\left(+\right)$, $\left(-\right)$, $\left(\pm\right)$ propranolol and $\left(\pm\right)$ metaprolol completely prevented A.P.E. whereas $\left(\pm\right)$ practolol did not. This shows that local anaesthetic action but not the $\beta$-adrenergic blockade may be responsible for prevention of A.P.E.

Key words: $\beta$-blocker local anaesthetics pulmonary edema

INTRODUCTION

$\pm$ Propranolol, a $\beta$-blocker was found to protect adrenaline-induced pulmonary edema (A.P.E.) in mice (6) and in rabbits (1). In rabbits, the effect is attributed to prevention of adrenaline-induced myocardial changes, since $\left(\pm\right)$ propranolol is a potent $\beta$-adrenoceptor blocker. It is known that iv injection of local anaesthetics also prevent experimental pulmonary edema induced by various methods (4,7). To test whether the $\beta$-blocking effect or local anaesthetic effect of $\left(\pm\right)$ propranolol underlines prevention of A.P.E., several $\beta$-blockers and $\left(\pm\right)$ propranolol, an isomer without much $\beta$-blocking activity, but with a potent local anaesthetic action was studied in A.P.E.

*Present address: Department of Pharmacology, Bihar Veterinary College, Patna - 800 014
RESULTS

TABLE I: Effect of some $\beta$-adrenoceptor blockers and of (+) propranolol on pulmonary edema induced by L-adrenaline (2 mg/kg, iv) in mice.

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>L.B.I.$\pm$S.E.</th>
<th>% Haemorrhagic lung</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nil</td>
<td>1.33±0.11</td>
<td>90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(+) Propranolol</td>
<td>0.82±0.09</td>
<td>20</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>(−) Propranolol</td>
<td>0.79±0.10</td>
<td>10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(±) Propranolol</td>
<td>0.74±0.08</td>
<td>10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(±) Propranolol</td>
<td>1.21±0.15</td>
<td>80</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>(±) Metaprokol</td>
<td>0.87±0.07</td>
<td>30</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(a) L.B.I. = lung body weight index (see Methods).
(b) A lung was considered 'haemorrhagic' if haemorrhage was seen in at least one lobe of a lung. Adrenaline-induced a significant (P<0.001) rise in L.B.I. and proportion of haemorrhagic lungs (value in saline control: L.B.I. 0.71; % haemorrhagic lung 0; n=10).
Pretreatment with (+), (−) or (±) propranolol or (+) metaprolol completely prevented A.P.E. However, (+) practolol was unable to prevent A.P.E.

DISCUSSION

The observations in the present study with (+) propranolol and (−) propranolol (possessing β-adrenoceptor blocking action), (+) propranolol (possessing minimal β-blocking action), (+) practolol (a β₂-blocker possessing no local anaesthetic action) and (±) metaprolol (a β₁-blocker possessing local anaesthetic action) point out that β-blocking effect, particularly β₂-blocking effect may not be essential for prevention of A.P.E. It seems that local anaesthetic action may explain the prevention of A.P.E. observed by us, since iv injection of a local anaesthetic (procaine) prevents experimental pulmonary edema induced by various methods (4,7).

The site of action of these drugs however, is not clarified by our work. Adrenaline induced pulmonary edema has been shown to be mediated via the CNS (3,5) and "neuroedematogenic centre" responsible for pulmonary edema has been proposed (2,9). It is possible that drugs-effect observed in our work may be centrally mediated.

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REFERENCES