Effects of Adrenergic Agonists and Antagonists on Immediate Cutaneous Reactions in Bronchial Asthma

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Asthmatic patients who showed a positive allergic reaction to house-dust antigen (HD) received an intradermal injection of 20 ng of isoproterenol (Isopr) or 2 µg of propranolol (Propr), followed by 0.02 ml of 1000 HD at various intervals of time from 0 to 4 hr. It was observed that these drugs exerted the more marked effects on the allergic skin reaction the shorter was the interval between injections of the drug and antigen.

Imbalance of the autonomic nervous system has been cited as one of the etiological factors in bronchial asthma (Cookson and Reed 1963; Shereff et al. 1973). The present study was undertaken to see whether such imbalance was corroborated in the skin of asthmatic patients by observing the effects of adrenergic agonists and antagonists on antigen-induced intradermal reactions.

Asthmatic patients who showed a positive allergic reaction to house-dust antigen (HD) received an intradermal injection of 20 ng of isoproterenol (Isopr) or 2 µg of propranolol (Propr), followed by 0.02 ml of 1000 HD at various intervals of time from 0 to 4 hr. It was observed that these drugs exerted the more marked effects on the allergic skin reaction the shorter was the interval between injections of the drug and antigen.

Then, in the next study we gave an intradermal injection of a mixture of 1000 HD and various doses of Isopr or Propr. As control an injection of 1000 HD diluted with the same volume of physiological saline (2000 HD) was also performed, and the effects of the drugs were assessed by comparing with the control 15 min after injection. The skin reaction was completely suppressed by the adrenergic effect of Isopr of 10 µg or more. An injection of 10 ng of Isopr (2.0×10⁻⁴ mM) concomitant with HD diminished the diameter of wheal by more than 50% in 62 of 75 patients (defined as positive and expressed as “I”) and by less than 20% in 6 (negative, expressed as “i”). The remaining 7 patients out of 75 the effect of Isopr was doubtful. One µg of Propr (3.4×10⁻¹ mM) increased the diameter of wheal by at least 50% in 25 of 85 patients (positive, expressed as “P”) and by less than 20% in 42 (negative, expressed as “p”). The
effect of Propr was doubtful in the remaining 18 patients. The effect of the adrenergic drugs on the allergic skin reactions was so much variable in asthmatic patients that we classified the skin sensitivities to adrenergic drugs into 4 types as follows: I-P (the effects of both Isopr and Propr were positive); I-p (Isopr suppressed the skin reaction but Propr gave a negative effect); i-P (Isopr gave a negative effect on the wheal but Propr increased the skin reaction); i-p (neither Isopr nor Propr was effective).

In the third study we examined the relation between the skin sensitivities to these drugs and the metabolic and cardio-vascular response to adrenaline in asthmatic patients. Changes of heart rate (HR), diastolic blood pressure (dBP), blood glucose (BG) and blood triglyceride (BT) were measured after intravenous injection of adrenaline hydrochloride (0.2 μg/kg of body weight/min). Blood glucose was determined by a Technicon autoanalyzer after immediate addition of sodium fluoride and BT was estimated by the acetylaceton method. The effect of adrenaline was considered to be positive if HR increased by more than 15% of the base line, dBP decreased by more than 15%, BG increased by more than 60%, and BT increased by more than 20%. The adrenaline response of asthmatic patients was classified according to the score of 4 positive adrenergic responses in the above four types of measurements as follows: (+) 4 or 3 positive responses, (±) 2 positive responses, and (−) 1 or 0 positive response. As shown in Table 1, three of four patients whose skin sensitivity to the drugs was I-P showed a positive (+) adrenaline response. On the other hand, three of four patients who were classified into i-p group showed a negative (−) adrenaline response; that is, the asthmatic patients whose skin reaction to antigen was not affected by either adrenergic agonist or antagonist tended to show reduced beta-adrenergic responses of the heart, peripheral blood vessels and blood metabolism. Thus, the sensitivity of the skin of asthmatic patients to adrenergic drugs is well correlated with the general response of the autonomic nervous system to adrenaline.

Table 1. Metabolic responses to adrenaline in different skin types classified according to the sensitivity to isoproterenol and propranolol

<table>
<thead>
<tr>
<th>Skin type</th>
<th>Adrenaline response</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td>AIP</td>
<td>+ 3</td>
<td>± 1</td>
</tr>
<tr>
<td>AIP</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>ap</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Aip</td>
<td>1</td>
<td>0</td>
</tr>
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</table>

Figures show the numbers of patients.
A, patients who showed a positive skin reaction to × 2000 HD; a, patients who showed a negative skin reaction to × 2000 HD.

References