CROSS REACTIVITY OF CEPHALOSPORINS WITH PENICILLIN

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Abstract: Cross antigenicity of cephalosporins with penicillin has been studied experimentally and also by using serum from penicillin sensitive individuals.

Definite hypersensitivity reaction was observed in all the animals sensitised with cephalosporins and challenged with penicillin except in rats.

Cephalosporins could elicit reaction in tissues sensitised passively with serum obtained from penicillin sensitive individuals.

Key words: cephalosporins immediate hypersensitivity cross antigenicity

INTRODUCTION

Cephalosporins are a group of antibiotics which were developed to replace penicillin in therapeutics. Initially these were thought to be drugs of choice in penicillin sensitive individuals and hence were used in such patients. Besides being useful in penicillin sensitive patients, there are other advantages over penicillin such as broader spectrum of activity resistance to Beta-lactamase and longer half life (1).

In view of sporadic incidences of either mild or severe hypersensitivity reactions in penicillin sensitive patients due to cephalosporins (2) and also absence of it reported earlier (3) detailed study about cross reaction between cephalosporins and penicillin has been undertaken in the present work.

METHODS

Rats and mice were sensitised based on the method reported earlier (4) and challenged with cephaloridine (10 mg) or penicillin (10,000 I.U.) administered i.v. (vol. 0.2 ml). In control animals challenge was given with distilled water (0.2 ml). The effect was studied in terms of change in blood pressure, respiration and rectal temperature using multichannel polyrite. Assessment of shock in rats on challenge was done as shown in Table I while that in mice was done as reported by Dhar and Sanyal (4).

Passive Cutaneous Anaphylaxis (P.C.A.) : The method described by Bandriss et al (5) with minor modification was as follows. Guinea pigs sensitised passively with anticephaloridine serum obtained from rabbits sensitised with cephaloridine, in various
dilutions, were challenged with either penicillin (1000 I.U.) or cephaloridine (10 mg). Sera samples obtained from individuals with the history of hypersensitivity to penicillin were used to sensitise guinea pigs passively with 0.1 ml of serum in different dilutions. The animals were subsequently challenged with either cephaloridine, cephalothin, cephazolin or penicillin to assess cross reactivity using following tests.

### RESULTS

**Table I**: Criteria for assessment of shock in rats (2 out of 3 parameters should be fulfilled).

<table>
<thead>
<tr>
<th>Type of shock</th>
<th>Fall in blood pressure (mm Hg)</th>
<th>Fall in rectal temperature (°C)</th>
<th>Changes in respiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>up to 20</td>
<td>up to 0.3</td>
<td>Hurried or irregular (+)</td>
</tr>
<tr>
<td>Moderate</td>
<td>20-40</td>
<td>0.3-0.5</td>
<td>Hurried and irregular and dyspnoea (++)</td>
</tr>
<tr>
<td>Severe</td>
<td>beyond 40</td>
<td>beyond 0.5</td>
<td>Stoppage of respiration (+++ )</td>
</tr>
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</table>

**Passive cutaneous anaphylaxis (PCA)**: Guinea pig skin was passively sensitised with 0.1 ml of 4 fold dilutions of serum from penicillin sensitive patients. The sera dilutions used were 1:16, 1:64, 1:256 and 1:1024 prepared in normal saline. After 10 hours guinea pigs were challenged i.v. through antecubital vein exposed by small incision with either cephaloridine, cephalothin, cephazolin (10 mg) or penicillin (1000 I.U.) along with 0.5 ml Evans blue dye solution (0.5%). The bluing reaction was read 30 min after challenge and compared with control.

**Mast cell degranulation**: Method described by Schwartz et al (6) was used. Passively sensitised mast cells were challenged with cephalosporins (i.e.) cephaloridine, cephalothin, cephazolin (5 mg) or with penicillin (1000 I.U.).

**Passive Paw Anaphylaxis (PPA)**: Hind paws of adult rats were passively sensitised with 0.1 ml of serum from penicillin sensitive patients.

Eight hours after sensitisation, the rats were challenged with one of the cephalosporins (cephaloridine, cephalothin or cephazolin 5 mg) or with penicillin (100 I.U.) i.v., paw volume was measured by plethysmometer before and 30 min after challenge. The challenged paws were observed for development of erythema compared with control.

### RESULTS

The mice sensitised with cephaloridine when challenged with cephaloridine exhibited mild shock. But rats sensitised with cephaloridine and challenged with penicillin did not show any effect on blood pressure, respiration and body temperature. The findings were similar when rats sensitised with penicillin and challenged with cephaloridine. However, rats sensitised and challenged with cephaloridine exhibited mild shock as per the criteria fixed. Fall in B.P. was 19.3 ± 6.5 mm Hg and fall in rectal temperature 0.3 ± 0.1°C. PCA reaction was positive at a dilution of 1:80 with penicillin as compared to 1:320 dilution of cephalosporin.

**Table II**: Correlation of percent degranulation of mast cell with paw volume of rats passively sensitised with serum from penicillin sensitive individuals challenged with cephalosporins (10 mg) or penicillin (1000 I.U.). N = 6 in each group.

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mean % ± SE Before challenge</th>
<th>30 min after challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>16.0 ± 1.60</td>
<td>-</td>
</tr>
<tr>
<td>Cephaloridine</td>
<td>42.0 ± 0.77*</td>
<td>3.29 ± 0.09</td>
</tr>
<tr>
<td>Cephalothin</td>
<td>41.8 ± 0.87*</td>
<td>3.27 ± 0.13</td>
</tr>
<tr>
<td>Cephazolin</td>
<td>39.8 ± 1.87*</td>
<td>3.31 ± 0.11</td>
</tr>
<tr>
<td>Penicillin</td>
<td>59.0 ± 1.57*</td>
<td>3.20 ± 0.44</td>
</tr>
</tbody>
</table>

*P < 0.001

Rat paws sensitised passively with serum from penicillin sensitive individuals showed significant increase in volume on challenge with cephalosporins compared with prechallenge control (Table II). However, the rat paws sensitised passively with antipenicillin human serum when challenged with penicillin exhibited more severe reaction than that with
mast cells passively sensitised with serum from penicillin sensitive individuals showed degranulation on challenge with cephalosporins (Table II). Mast cell degranulation in allergic reaction has been shown to be of IgE type (9). The present result indicates possible development of hypersensitivity reaction in these individuals on administration of cephalosporins.

It has been reported that most individuals have antipenicillin antibodies in their serum (10) and that penicillin sensitive individuals are more susceptible to cephalosporins (8). Present results show that animals sensitised with human serum sensitive to penicillin react more severely with cephalosporins than penicillin giving conclusive evidence to just clinical observation. It is suggested that replacement of penicillin with cephalosporins should be generally avoided or done with caution.

REFERENCES