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CROSS REACTIVITY OF CEPHALOSPORINS WITH PENICILLIN

H. L. DHAR AND D. N. KULKARNI**

**Medical Research Centre,*
Bombay Hospital Trust,
Bombay - 400 020
and
***Department of Pharmacology,*
LTM Medical College & Hospital,
Bombay - 400 022

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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

*Corresponding Author

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.

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

Type of shock	*Fall in blood pressure mm Hg*	*Fall in rectal temperature*	*Changes in respiration*
Mild	upto 20	upto 0.3°C	Hurried or irregular (+)
Moderate	20-40	0.3-0.5°C	Hurried and irregular and dyspnoea (++)
Severe	beyond 40	beyond 0.5°C	Stoppage of respiration (+++)

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 anticubital vein exposed by small incision with either cephaloridine, cephalothin, cephazolin (10 mg) or penicillin (100 I.U.) alongwith 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 ± 0.11°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 IU). N = 6 in each group.

Drugs	*Cell degranulation %*	*Measure of paw volume Mean (ml) ± SE*	
	Mean % ± SE	*Before challenge*	*30 min after challenge*
Control	16.0 ± 1.60	-	-
Cephaloridine	42.0 ± 0.77*	3.29 ± 0.09	3.75 ± 0.01
Cephalothin	41.8 ± 0.87*	3.27 ± 0.13	3.93 ± 0.06
Cephazolin	39.8 ± 1.87*	3.31 ± 0.11	3.86 ± 0.09
Penicillin	59.0 ± 1.57*	3.20 ± 0.44	4.10 ± 0.12

*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

cephalosporins. Result of mast cell degranulation was similar.

DISCUSSION

Present study demonstrated the existence of cross reaction in mice between penicillin and cephalospirins. Mice sensitised and challenged with cephaloridine exhibited mild degree of shock. Similar results have been reported when mice was sensitised and challenged with penicillin. As such the cross reaction in mice was expected as shown in the present study.

PCA with penicillin in guinea pigs sensitised with rabbit anticephaloridine serum has been reported earlier (5). Present result in addition to confirming above finding has demonstrated positive PCA reaction in guinea pig sensitised with serum from penicillin sensitive individual when challenged with cephalosporins.

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.

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