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PHARMACODYNAMIC BIOEQUIVALENCE : EVALUATION OF DIFFERENT BRANDS OF TERFENADINE HYDROCHLORIDE

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Abstract : Terfenadine is a selective histamine H_1 receptor antagonist which binds preferentially to peripheral receptors *in vivo* and is devoid of central nervous system depressant activity and thus has an improved adverse effect profile (1). Hence, terfenadine may be considered to be a first line agent in the treatment of allergic rhinitis and chronic urticaria. In man terfenadine is rapidly absorbed following a single oral dose and a peak terfenadine plasma concentration is reached within 1-2 hr after the drug administration (2). The present study was carried out to compare the bioequivalence of two terfenadine hydrochloride preparations marketed by Kopran Chem. Co. and Marrel Dow U.K. (Triludan) by evaluating their ability to inhibit the skin reaction to intradermally injected histamine (3).

Key words : pharmacodynamic evaluation terfenadine

METHODS

Eight healthy subjects aged between 21-32 yrs (mean age 25·62 yrs) were engaged for the study. All gave signed consent, and the protocol was approved by the Ethical Committee of the Institution. Subjects were prohibited from taking any medicines or alcoholic beverages seven days before drug administration till the end of the study.

The study was conducted as a double blind randomized two period cross trial. Each subject received either,

i) Terfenadine 60 mg formulated in India by Kopran Chemical Co. Ltd. (designated as drug A) or,

ii) Triludan (Terfenadine) 60 mg manufactured by Marrel Dow, U.K. (designated drug B).

There was a washout period of one week between the two treatment phases. Terfenadine tablets were ingested with 250 ml water in the presence of the investigator by the fasting volunteers at 0800 hrs in order to ensure comparable dosage schedules. The volunteers were given standard light breakfast 2 h later. Each volunteer was administered 2 mcg histamine phosphate (0.02 ml solution of 100 mcg/ml) into the forearm with a 1 ml tuberculin syringe (4). The injection of histamine in each subject was always made by the same investigator and at the same time of the day namely 0 h (before administration of the drug) and at 2, 4 and 6 h after drug administration. The histamine induced wheal and flare reactions were outlined on the skin 15 min after the intradermal injection of histamine. The outlines were transferred onto a transparent sheet. These outlines were again transferred on to a graph paper and the area thus measured was expressed as square millimeter.

Statistics : The data was analysed using students t-test of correlated means.

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RESULTS

The cutaneous wheal and flare response to intradermal injection of histamine phosphate is given in Tables I and II. A significant decrease in the size of both the wheal and flare response was noticed at 2 h 4 and 6 hrs the inhibition of both wheal and flare response was relatively more with drug B than with drug A. However, the difference is not significant. Two of the 8 volunteers in either treatment groups complained of mild headache, nausea and giddiness. This, however, did not incapacitate them and they continued to participate in the study.

TABLE I : Area of wheel reaction to histamine in mm^2 in healthy volunteers. Values expressed as mean±SE (n =8).

Test drug	*Time post drug (hr)*			
	0	2	4	6
Drug A	130·50 ± 16·89	90·75 ± 16·93	57·37 ± 21·16	20·37 ± 11.56
Drug B	162·00 ± 26·18	103·62 ± 19·14	40·62 ± 15.02	6·37 ± 6·37
P value	> 0·1	> 0·5	< 0·5	< 0·5

TABLE II : Area of flare reaction to histamine in mm^2 in healthy volunteers. Values expressed as mean±SE (n =8).

Test drug	*Time post drug (hr)*			
	0	2	4	6
Drug A	831·12 ± 107·63	526·87 ± 133·29	232·87 ± 40·88	213·87 ± 45.61
Drug B	800·50 ± 119·45	500·87 ± 83·12	129·25 ± 15·84	152·5 ± 24·60
P value	> 0·5	> 0·5	< 0·1	< 0·5

of administration of either of the two terfenadine 60 mg preparations. This response continued to decrease till the end of the study period of 6 h. Total disappearance of the wheal response was observed in 3 of the 8 volunteers by 4 h in each of the treatment groups. At the end of 6 h, 5 of 8 volunteers administered Drug A and 7 of the 8 volunteers administered Drug B showed a total disappearance of the wheal response. This difference in response at 6 h was, however, statistically not significant. At

DISCUSSION

Thus according to this study, it seems that the two preparations of terfenadine tested (viz formulated by Kopran Chemical Ltd., India or manufactured by Marrel Dow, U.K.) in a dose of 60 mg are equipotent and do not show any difference in their ability to inhibit intradermal histamine-induced wheal and flare response.

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