Topical Provocation Of Fixed Drug Eruption

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To determine the usefulness of topical provocation in the diagnosis of fixed drug eruption, different drugs at various concentrations (2% & 5%) in white soft paraffin were applied on normal or affected skin of 401 patients. Reliable results were obtained with 5% ointment preparations, applied on normal skin. The results were confirmed by peroral provocation, by giving half to full therapeutic dose of the suspected drugs.
Key Words: Fixed drug eruption, topical eruption, skin.

Fixed drug eruption (FDE) is a cutaneous reaction caused by various drugs. It is characterized by one or more circular or oval erythematous macule, plaque or vesiculobullous lesions. As the lesion resolves, brownish black hyperpigmentation is left behind. On readministration of the incriminated drug, the lesion is reactivated. After frequent challenges, additional macular or vesiculobullous lesions may arise. Rarely a severe, generalized bullous type of FDE is induced. Unlike many other drug eruptions, where attempts to reproduce the eruption may be hazardous and thus contraindicated, a provocation test is indicated in FDE. The diagnosis of FDE is usually established by per oral provocation test with the suspected agent. This testing may involve risks. Topical testing of FDE, on the other hand has given conflicting results[1,2]. Positive patch tests have been obtained by some workers[3-7].

The aim of the present study was to determine the usefulness of topical provocation in the diagnosis of FDE.

Material and Methods

Four hundred and one, clinically diagnosed cases of FDE of either sex and any age were collected from the Department of Dermatology, Mayo Hospital, Lahore from November 1992 to December 1993. A detailed history and thorough clinical examination were recorded on a predesigned proforma. The diagnosis of FDE was based upon reactivation of the lesion on readministration of the drug. Written consent from the patients were taken.

All the patients were subjected to these tests, after the subsidence of the reaction and while the patients were not taking any medication. Only 3 patients were admitted in the ward for oral provocation, because of the severity of the presenting episode, rest of the patients were dealt in OPD.

The drug powder (obtained by crushing the tablet or opening up of the capsule) was mixed with white soft paraffin in 2% & 5% concentrations (Table 1 & 2). At one time, one concentration was applied on either normal skin of flexor surface of left forearm or on affected skin. The effects of provocation tests were observed for 48 hours. In case of any reaction, it was given enough time to subside.

Controls

The topical tests were repeated in:

1. Normal persons with various drug ointments.
2. Patients with white soft paraffin on normal or affected skin for 48 hours after the subsidence of reaction .

To confirm the results of topical provocation, oral provocation was done by giving half to full therapeutic dose of the suspected drugs.

Results

Age and Sex: One hundred and eighty five patients were males (mean age = 31.9 ± 17 years) and two hundred and sixteen patients were female (mean age 31.7 ± 14 years). The female to male ratio was 1.2 : 1. The youngest and the oldest patients were males with ages of two and eighty seven years respectively.

Table : 1 Topical Provocation Tests (TPTs) with 2% Ointment Preparations (n = 35)

Drug Ointment	No. of TPTs	GROUP - I Affected Skin	+ve	GROUP - II Normal Skin	+ ve
Sulphamethaxazole	14	2	1	12	5
Sulphadiazine	6	1	0	5	2
Metamizole	6	1	1	5	2
Tetracycline	6	1	0	5	5
Phenylbutazone	4	-	-	4	2
Metronidazole	4	1	1	3	0
Erythromycin	3	-	-	3	0
Chlormezanone	3	1	1	2	0
Phenobarbitone	2	-	-	2	0
Belladonna	1	-	-	1	0
Indomethacin	1	1	1	-	-
TOTAL	50	8	5	42	16

The five patients (Group 1) with positive TPTs were also positive to oral provocation. Patients (Group-II) with

negative TPTs, were subjected to oral challenge, 7 were found to be positive.

Table:2 Topical Provocation Test with 5% Ointment Preparations (n = 257).

Drug Ointment	No. of TPTs	GROUP - III		GROUP - IV	
		Affected Skin	+ ve	Normal Skin	+ ve
Sulphamethaxazole	228	1	1	227	207
Trimethoprim	75	1	0	74	53
Tetracycline	38	-	-	38	26
Metamizole	38	-	-	38	19
Paracetamol	24	-	-	24	18
Phenylbutazone	22	-	-	22	17
Sulphadiazine	19	1	0	18	13
Mefenamic acid	18	-	-	18	12
Acetylsalicylic acid	11	-	-	11	7
Erythromycin	8	-	-	8	5
Amoxycillin	7	-	-	7	3
Chlormezanone	6	-	-	6	2
Doxycycline	6	-	-	6	2
Metronidazole	4	-	-	4	1
Tinidazole	4	-	-	4	0
Ampicillin	3	-	-	3	1
Terramycin	3	-	-	3	0
Dapsone	2	-	-	2	0
Optalidon	2	-	-	2	1
Saridon	1	-	-	1	1
Allopurinol	1	-	-	1	1
Pyrental pamoate	1	-	-	1	1
Ibuprofen	1	-	-	1	1
Griseofulvin	1	-	-	1	1
Belladonna	1	-	-	1	0
Diclofenac sodium	1	-	-	1	1
Phenobarbitone	1	-	-	1	0

In 90 patients (group iv) changes were confirmed by oral provocation

Table : 3 Changes Observed in Lesions

Changes	Group-I	Group-II	Group-III	Group-IV
Itching	2	8	1	185
Burning	2	2	-	51
Pain	-	1	-	11
Pricking Sensation	-	-	-	6
Hyperpigmentation	1	3	-	256
Erythema	4	4	-	120
Swelling	-	-	-	19
New lesion formation	-	1	-	22
Local itching	-	1	-	18
Generalized pruritus	-	1	-	44

Discussion

One hundred and eighty five patients were males and two hundred and sixteen patients were female. Female to male ratio was 1.2 :1 which is in contrast to all previous studies[5-7] in which male were predominately affected.

In earlier studies, topical testing of FDE has given conflicting results[1,2], however Alanko[3] strongly recommended TPTs. He used petrolatum (1-10%), 94% ethanol or diamethyesulphoxide as vehicle. He applied drug ointment with various concentrations, in different vehicles at normal or affected sites simultaneously. He considered reaction of the lesion when erythema appeared. In our study, drug ointment of one concentration at one time, in a single vehicle was applied either on normal or affected skin. In 73%, the reactivation of the lesions which were present far from the site of application, indicates the action of drug after systemic absorption. So while performing topical provocation, one drug with a certain concentration should be used at one site on a single occasion. This will make it possible to see the effects of various drugs separately and will also minimize the false or additive effects of preparations.

In 63% of the cases, the first change noted was hyperpigmentation of the lesions (Table-3). Such lesional hyperpigmentation in response to drug ointment has not been reported earlier.

In 95% of TPTs, the lesional changes were observed within 2 hours, while in 81% of positive oral provocation, the response was noted after 4 hours of the ingestion of the drug. The oral reactions were severe and lasted longer as compared to TPTs. These TPTs with various drug ointments were found to be easy, rapid, safe and reliable in detecting the incriminated drugs. This is in contrast to the findings of many other studies[2,8]. So the oral provocation should be done if TPTs are negative.

Conclusion

Topical provocation tests with 5% drug ointments applied on normal skin were found to be quite useful in finding the incriminated drug of FDE.

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