THERAPY

A CLINICAL TRIAL OF DIMETHOTHIAZINE IN PRURITIC DERMATOSES

By

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Since the introduction of histamine antagonists into medicine, undoubted progress has been made in providing compounds with greater potency. The increased activity, however, has often been accompanied by an increased incidence and intensity of side-effects and even the recently-introduced antihistamine preparations are still not completely satisfactory. The varied response of patients to antihistaminics and the high incidence of drowsiness produced by most of these drugs have indicated a need for further potent anti-allergic drugs which produce little or no soporific effect.

The phenothiazine derivative (dimethothiazine: 'Banistyl') was selected for detailed examination on the basis of its potent antihistamine, antiserotinin and anti-bradykinin activities. The results of the initial clinical trials of dimethothiazine have amply confirmed the product's value in the symptomatic relief of hay fever, allergic rhinitis and the pruritus associated with many skin conditions. Moreover, the minimal soporific effect of dimethothiazine appears to make it particularly suitable for day-time administration.

Because dimethothiazine had been found in earlier studies to be a potent histamine antagonist and to have a minimal soporific effect, it was decided to evaluate it clinically in out-patients suffering from pruritic dermatoses.

Pharmacology of Dimethothiazine

In acute toxicity tests in the mouse, dimethothiazine has been found to be some what less toxic than promethazine and after longer term (one month) administration to laboratory animals its general tolerance was very good. Reproduction studies have revealed no evidence of teratogenic effect in the chick embryo, the mouse and the rat; in the rabbit there was similarly no teratogenic effect and no resorption sites were recorded

In the laboratory, dimethothiazine has been found to be a potent histamine antagonist with marked antiserotonin action (2–3 times greater than that of promethazine) and significant anti-bradykinin activity. Studies of the cardiovascular, sympathetic and parasympathetic systems of experimental animals after administration of dimethothiazine and promethazine have indicated very little difference in the effects of the two drugs. Dimethothiazine is, however, about half as active as promethazine in enhancing the action of anaesthetics, in enhancing morphine analgesia and in hypothermic activity. Moreover, it has an antiemetic activity ten times greater than that of promethazine as measured by apomorphine-induced vomiting in the dog.

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Clinical Study–Material and Methods

The patients in this clinical trial were suffering from urticaria, neurodermatitis, pruritus, scabies, exogenous eczema and atopic dermatitis; they were randomly selected from the out-patients department of dermatology at Safdarjang Hospital. The study was concerned with ascertaining the antihistaminic and antipruritic effects of dimethothiazine and also in assessing the drowsiness potential relating to its administration. The dimethothiazine was administered to adults in a dosage of 20 mg. (1 tablet) three time daily for from 4 days to 15 days; in children dosage was reduced proportionately according to bodyweight.

The results were assessed subjectively and objectively and classified as follows:—

A. Excellent–when there was complete alleviation of itching. B. Good–when itching was much improved. C. Fair–when itching was slightly improved. D. Negative-when no improvement occurred.

Outline of Trial

Twenty–four male patients and 11 female patients were included; their ages ranged from $2\frac{1}{2}$ to 70 years.

The number of patients in the age groups specified are detailed below

0 to 9 years 3, 10 to 19 years 11, 20 to 29 years 9, 30 to 39 years 6, 40 to 49 years 3, 50 to 59 years –, 60 to 69 years 2, 70 to 79 years 1 Total 35

The detailed history of each patient was taken and relevant routine investigations were carried out. With a view to assessing the antihistaminic effect of dimethothiazine it was decided to try it on different aetiological varieties of urticaria and to assess its combined antihistamine and antipruritic effects in cases of neurodermatitis, exogenous eczema, atopic dermatitis, pruritus and scabies. Details are given below:—

I	*Urticaria*	19
	A. Aucte urticaria	6
	(a) Drugs	2
	(b) Infections	1
	(c) Cause not known	3
	B. Chronic urticaria	13
	(a) Drugs	1
	(b) Infections	1
	(c) Physical	1
	(d) Atopic	5
	(e) Cause not known	5
II	*Neurodermatitis*	5
III	*Pruritus and Scabies*	6
IV	*Eczema*	5
	(a) Exogenous eczema	3
	(b) Atopic dermatitis	2

Observations

Acute urticaria. Out of 6 cases of acute urticaria treated with dimethothiazine, 4 became completely asymptomatic, 1 improved considerably and the other did not appear to benefit from the treatment. The dimethothiazine was excellently tolerated, no side-effects (including drowsiness) being reported.

Chronic urticaria. In this group there were 13 patients and the results of treatment are listed below :—

(a) Seven patients became completely symptom free,

(b) Three patients showed considerable improvement, the intensity and frequency of attacks being greatly reduced,

(c) Two patients showed some improvement, the intensity and frequency of attacks being reduced slightly,

(d) One patient failed to responed.

Two of the patients complained of slight drowsiness and 1 patient developed a photosensitisation reaction.

Neurodermatitis. Out of 5 patients, 4 showed a good response and there was no improvement in 1. There were no side-effects in this group.

Pruritus and Scabies. Out of 6 patients, 5 showed good response and in one there was no improvement. No side-effects were recorded.

Exogenous eczema Out of 3 patients, 2 had a good response and one showed no improvement. No side-effects were reported.

Atopic dermatitis. Out of 2 patients an excellent result was obtained in one and a good result in the other; the product was product was well tolerated and no side-effects occurred.

Summary of Results

	Diagnosis	Excellent	Good	Fair	Negative	Side-Effects
I.	Urticaria	11	4	2	2	3
II.	Neurodermatitis	—	4	—	1	—
III.	Pruritus and Scabies	—	5	—	1	—
IV.	Exogenous Eczema	—	2	—	1	—
V.	Atopic Dermatitis	1	1	—	—	—

Conclusions

A short term clinical trial of the recently introduced dimethothiazine ('Banistyl') has been carried out in out-patients suffering from (a) various pruritic dermatoses and (b) acute and chronic urticaria. In aduits, oral dosage of 20 mg. three times daily was given. Out of 35 patients excellent results were obtained in 12, good results in 16, fair in 2 and in 5 patients there was no improvement. Two patients experienced mild drowsiness and one patient developed photosensitisation. Under

the conditions of this trial dimethothiazine was found to be highly effective in pruritic conditions and to be extremely well tolerated; drowsiness was rare and of a mild degree.

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