CLINICAL TRIAL OF DIMETHOTHIAZINE ('BANISTYL') IN PRURITUS ASSOCIATED WITH DERMATOLOGICAL DISORDERS AND URTICARIA

By

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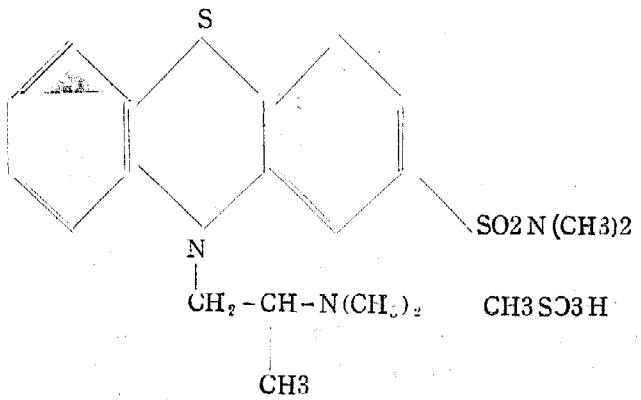
INTRODUCTION

Pruritus is a characteristic dermatoiogical symptom distinct from other sensory modalities (Shelley and Arthur, 1957; Keele, 1957). Rothman (1954) believes that itching is identical in quality with and varying only in intensity from protopathic agents and is mediated by the 'C' group of nerve fibres. Pruritus is the commonest symptom of skin disease and is a disagreeable sensation which excites the desire to scratch for its relief. It is produced by the excitation of nerve endings immediately beneath the epidermis and from intra-epidermal endings as well. It does not occur after the epidermis has been completely removed. Although pruritus is localised to the surface epithelium and is usually due to involvement of the covering epithelium, itching is also encountered in obstructive jaundice, Hodgkin's disease, etc. This type of itching is due to central causes and without any evidence of cutaneous disease. It is frequently termed as 'essential pruritus'.

The mechanism of pruritus is not yet precisely known. However, release of histamine or 'H'-substance and other similar substances is known to be associated with pruritus. Histamine release in urticaria not only causes itching but also contributes to the hyperalgesia due to severe tissue damage. It is probable that itching results from stimulation of the nerve endings which are below the epidermis and from stimulation of deeper dermal nerve endings. (Samson Wright, 1965).

Dimethothiazine is 2-dimethylsulphamoyl-10-2'-dimethylaminopropylphenothiazine and is available as mesylate which contains 83% of the active base. It has the following structural formula :



Molecular Weight = 487.7

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On the basis of the above, the use of antihistamine agents for the management of pruritus and urticaria appears to be rational. Antihistaminics are frequently used orally for the treatment of pruritus due to urticaria or other skin diseases. Dimethothiazine, though an antihistamine agent par excellance, yet possesses a distinct anti-pruritic effect irrespective of the pathogenic mechanism. Thus, it seems to be a broad-spectrum anti-pruritic agent. Therefore, I undertook a trial to evaluate it in diverse pruritic dermatoses.

The results of the initial clinical trials of dimethothiazine have clearly indicated the value of the drug in the symptomatic control of hay fever, allergic rhinitis and in the relief of puritus associated with many skin conditions. Besides, minimal soporific effect of dimethothiazine renders it more suitable for day-time use.

Pharmacologically, dimethothiazine possesses powerful antihistamine activity, and experimental studies in laboratory animals indicate that the antihistamine properties of dimethothiazine are equipotent with promethazine ('Phenergan').

Other laboratory studies have shown that dimethothiazine has a marked antiserotonin action 2 to 3 times greater than promethazine) and significant anti-bradykinin effect.

Material and Methods

26 cases (males 14, femaels 12) suffering from pruritus were selected, at random, for the trial. Their ages varied from 10 to 55 years. It is worthwhile to note that these cases failed to respond to locally applied ointments/lotions and oral corticosteroids. A daily dosage of three dimethothiazine tablets 20 mg in divided doses was used for a period of two to three weeks according to the response of the patients. Concomitantly, nothing except a bland soothing agent with negligible anti-pruritic activity was used. Of these 26 cases, 21 (males 11, females 10) received dimethothiazine for the treatment of pruritus associated with dermatological conditions and 5 (males 4, female 1), for the management of urticaria.

Results

The accompanying table indicates the results of the trial of dimethothiazine in dermatological practice and is quite significant even for the limited trial.

Dimethothiazine was generally very well tolerated by all the patients except one who complained of retrosternal burning sensation and heaviness. However withdrawal of dimethothiazine was not necessary.

Discussion

Gomez and Gomez (1967) reviewed the results of collaborative studies in which 13 general practitioners carried out double blind trials to compare the clinical effectiveness and side-effects of dimethothiazine and chlorpheniramine marched capsules containing the equivalent of dimethothiazine 20 mg or chlorpheniramine maleate in matched capsules of 4 mg. was used, the dosage being one capsule twice daily for one week. A change being made to the atternative drug. The

two treatment periods were separated by a 2 days gap to allow for excretion of the drug. A total of 147 patients who had hay fever, allergic rhinitis, or urticaria completed the trial. No difference was found between the two drugs in their ability to relieve allergic symptoms; drowsiness occured less frequently with dimethothiazine.

Marshall (1967) assessed the value of dimethothiazine in the treatment of various allergic skin conditions encountered in general practice His series consisted of 16 male and 33 female patients: 46 suffering from dermatitis accompanied by itching and three from allergic rhinitis. Dimethothiazinne was used at a dosage of 20 mg. 3 times daily. Excellent results (complete alleviation of symptoms) were noted in 37 patients (75.5%), and much improved in six and negative (no effect) in the remaining six cases. He, therefore, concluded that 'Banistyl' was one of the best anthistaminics for day-time use and was of particular value for the relief of pruritus in patients with itching skin conditions who have to continue working.

In our series, 3 dimethothiazine 20 mg. tablets were used daily for 2 to 3 weeks in the management of pruritus associated with varicus dermatological conditions and urticaria. 7 patients (26.9%) suffering from urticaria or pruritus were completely cured. In 11 patients (42.3%) considerable improvement of their complaint was noted. No improvement was noted in 3 patients (11.5%) only. Dimethothiazine was well tolerated by all the patients except one, in whom retrosternal burning in the chest, not amounting to withdrawal of the drug, were noted. Follow-up of patients necessitating in this series was not possible.

Although the series was relatively small the results of the study indicate that dimethothiazine appears to be useful in symptomatic control of allergic conditions of the skin associated with pruritus. Drowsiness was not encountered in any of the patients in this series.

Summary and Conclusions

1. 26 patients were included in this study, only 21 patients could be followed up.

2. Three dimethothiazine 20 mg. tablets were used in divided doses per day in the management of urticaria and pruritus associated with other dermatological conditions.

3. Out of 21 cases who were fully assessed only 3 patients failed to obtain relief from dimethothiazine therapy. Beneficial effects of dimethothiazine were noted in 18 cases.

4. Dimethothiazine was well tolerated by all patients except one who experienced retrosternal burning sensation and heaviness in the chest; however, no treatment for burning or withdrawal of dimethothiazine was necessary. Drowsiness was not complained of by any patient in this series.

5. It is, therefore, concluded that dimethothiazine, which appears to have powerful anti-allergic actions, has no soporific effects, is a valuable addition to the list of pharmacological agents for use in dermatology, especially in combating pruritus due to any cause.

Acknowledgement

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References

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TABLE SHOWING DETAILS OF RESPONSE OF THE CASES TO DIMETHOTHIAZINE

Diagnosis	No. of Cases		Dosage of 'Banistyl'	Duration of Treatment	Side-effects	RESULTS				
	M	F				Cured	Much improved	Improved	No. improve-ment	Not turned up for clinical assessment
Pruritus associated with various dermatological conditions	11	10	1x20 mg. t.d.s.	2 – 3 weeks	1*	5	6	4	3	3
Urticaria	4	1	1x20 mg. t.d.s.	2 - 3 weeks	—	2	1	—	—	2

*Retrosternal burning sensation and heaviness in the chest not necessitating to withdrawal of 'Banistyl'.