

TRIAL OF A NEW ANTIHISTAMINE (MEBROPHENHYDRAMINE) IN GENERAL PRACTICE

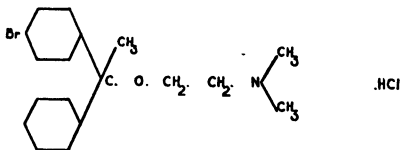
M. EMIL HOLZER, MED. DIPL., M.D.
London, E.1

Von Pirquet, in 1906, invented the word "allergy" to describe an altered reaction of the body to foreign proteins. Since then the term has been used to include more and more conditions in which a reaction develops to agents where none existed previously. These include such diverse conditions as asthma, perennial rhinitis, contact dermatitis, eczema, migraine, and colitis, although these do not always have an allergic basis. It is thought that the common factor is the excessive local release of histamine or histamine-like substance on exposure to a chemical agent or allergen. It has been shown that many of these effects can be reduced by certain substances of varying chemical structure, which have been grouped together as the antihistamines, (Loew, 1947; Goodman and Gilman, 1955).

During recent years, there has been an increase in the incidence of allergic conditions associated with the introduction of new chemical preparations for commercial, domestic, and therapeutic purposes. This has led to an increasing demand in general practice for a drug which will produce rapid and effective relief without interfering with normal activities.

Numerous antihistamines have become available but their use has been limited by inadequacy of response or undesirable side effects. It was therefore, considered worthwhile to investigate a new antihistamine, mebropfenhydramine, to determine whether this would prove superior to those already available.

The chemical structure of this drug is:



The results of animal pharmacology studies carried out by Votava and his colleagues, (Votava, Metysova, and Horakova, 1959; Metysova, Votava, and Horakova, 1959; Votava, Metysova, and Horakova, 1961), indicate that mebropfenhydramine, when compared with diphenhydramine (Benadryl), has a significantly stronger antihistaminic effect with a more rapid onset of action and a longer period of effectiveness. It was also shown that it is a weaker inhibitor of activity of the central nervous system, suggesting a less sedating

effect than diphenhydramine.

Unpublished results of investigations undertaken in this country show that mebropfenhydramine has nearly three times the antihistaminic activity of diphenylpyraline, (Histyl), and is less sedating.

The continental and British studies demonstrate that mebropfenhydramine is considerably less toxic than diphenhydramine and diphenylpyraline. An oral dose of ten times the effective antihistamine level did not produce acute or chronic toxic effects.

Material and Methods

Selection of Patients. Fifty patients were included in the trial. All complained of symptoms which were considered allergic in origin. In general, those with acute conditions, i.e. with history that did not exceed 2 to 3 weeks were chosen and chronic cases excluded. The only exceptions to this were patients with chronic allergic rhinitis and some of those with hay fever. The diagnostic categories are shown in table I.

TABLE I
ANALYSIS OF RESULTS

Diagnosis	Number of Patients	Results			
		Excellent	Good	Fair	Poor
Hay fever	14	7	5	—	2
Urticaria	10	4	5	1	—
Contact dermatitis ..	15	8	7	—	—
Angioneurotic oedema ..	4	3	1	—	—
Chronic allergic rhinitis ..	3	2	—	1	—
Neurodermatitis	4	3	1	—	—
TOTAL	50	27	19	2	2

Dosage. The maximum period of treatment was two weeks. For the first three days, the patient took one 25 mg. tablet every 12 hours. If there was a satisfactory response, the dose was reduced to one tablet a day for the next four days. If necessary, a maintenance dose of one tablet every other day was given for the second week.

Assessment of results. Each patient was seen regularly twice a week. The results were assessed as follows:

Excellent: Where there was a rapid (i.e. within 3 days) and complete remission of all symptoms.

Good: Where remission of symptoms was delayed but complete.

Fair: Where there was only slight improvement of symptoms of doubtful therapeutic value.

Poor: Where there was no response or where side-effects were sufficient to require withdrawal of the drug.

Results

The *therapeutic results* are summarised in table I.

The results have been uniformly good in the conditions treated, with a virtual absence of side-effects. Forty-six of the 50 patients had a complete remission of symptoms, twenty-seven of these within three days. There were only two poor results. One of these was a patient with hay fever, who gained complete relief of the rhinitis but the treatment had to be withdrawn because of drowsiness and loss of energy. Reducing the dosage from 50 to 25 mg. a day prevented the side-effects but the rhinitis was not then controlled. The other poor result was also in a patient with hay fever, who responded well during the first week, but apparently became resistant to the drug subsequently. On the basis of speed of response, the best effects were seen in the patients suffering from hay fever and contact dermatitis, in whom there was an improvement within half-an-hour of taking the drug, which continued rapidly during the first 24 hours. The maximum effect was achieved during the first three days and in 14 of the patients in these groups no further treatment was required and there were no remissions.

One patient who showed marked improvement, complained that he did not feel well on very hot days, which he ascribed to the drug, but this did not cause him to stop treatment.

In contact dermatitis, the patients generally presented with a rash and pruritus of sudden onset, suggesting an allergic factor. Mebropenhydramine was supplemented in these cases by the topical application of calamine.

From the speed of the initial response and effect during the first three days it was possible to predict the eventual outcome. In general, the more rapid the response, the quicker and more complete was the remission of symptoms. If there was no change in the patient's condition in the first three days, none occurred even if treatment was continued for the full fortnight.

Side effects were minimal. The only one encountered was drowsiness. This occurred in four of the 50 patients treated but in only two instances was this sufficient to warrant withdrawal of the drug. In the other two, drowsiness was prevented by reducing the doses from 50 mg. to 25 mg. a day, with continued benefit to the patients.

Discussion

The results indicate that mebropenhydramine is a potent antihistaminic in a selection of allergic conditions common in general practice. In a trial of this nature it is impossible to make a direct

comparison with other antihistamines, but the impression of the patients and myself suggest that mebropenhydramine is superior to others currently available. This is based on the speed and completeness of response in a large proportion of allergic patients, the scope of the conditions satisfactorily treated and the small incidence of side effects.

The results obtained in the four patients with neurodermatitis warrants a fuller investigation of the treatment of this troublesome condition which is often refractory to other forms of therapy.

Apart from its therapeutic value, it is considered that this drug may have a place in unravelling dermatological conditions in which the allergic factor is probably more important than previously realized.

Summary and Conclusions

1. Fifty patients with varying allergic conditions were treated for periods up to two weeks with a new antihistamine, mebropenhydramine.

2. The results indicate that it is a powerful antihistamine with a rapid onset of action and effecting a speedy relief of symptoms in the majority of patients.

3. Of the fifty patients, 46 had a complete remission of symptoms, 27 within three days of starting treatment.

4. The only side effect was drowsiness in four patients. In only two instances was this sufficiently severe to warrant withdrawal of the drug.

5. Mebropenhydramine is a useful addition to the antihistamine group of drugs and is probably better than those currently available.

Acknowledgment

I wish to thank Messrs. Smith, Kline and French Laboratories Ltd., for the supplies of the drug used in this trial.

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TWO CASES OF NEUROSYPHILIS IN GENERAL PRACTICE

K. G. HEYMANN, B.Sc., M.B., CH.B. N.Z.

London, W.11

When we think back to our student days we are probably reminded of some aphorisms pertaining to the *Treponema pallidum*. Yet, in