TREATMENT OF MILD ENDOGENOUS DEPRESSION WITH A MONO-AMINE OXIDASE INHIBITOR: A CONTROLLED TRIAL IN GENERAL PRACTICE

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IN RECENT YEARS THE GENERAL PRACTITIONER has been presented with a large number of new drugs for the treatment of depression. These can be divided into two groups: the mono-amine oxidase inhibitors, the first of which was iproniazid (marsilid); and the amino-dibenzyl derivatives, like imipramine (tofranil) and amitriptyline (tryptizol).

Much has been written about the efficacy of these drugs in the depressions seen by psychiatrists; but, as far as we know, no attempt has been made to evaluate them under the conditions of general practice. We have attempted in this trial to remedy the defect.

The confused nomenclature of depression is a source of difficulty in organizing a trial of this kind. We have followed the classification of depression into three types: the true endogenous or psychotic depression, first described by Hippocrates as melancholia; the reactive type, precipitated by stress; and the atypical depression, described by West and Dally (1959(a)). Most cases in general practice resemble the third category and the syndrome has been well described by Watts (1957) under the name ' mild endogenous depression '. The patient is usually a young or middle-aged woman of stable personality. She comes to her doctor with complaints like: " I feel tired all the time ", " I feel low " or " I think I need a tonic "; when asked if she cries a lot she will often burst into tears and then apologize for doing so; she often suffers from insomnia; and she is frequently tense, anxious and irritable. The onset of depression is not related to environmental stress. Untreated, the illness tends to remit spontaneously in three to six months, but relapses are common.

Several workers have reported excellent results using mono-amine oxidase inhibitors in the treatment of this type of depression. In 19 out of 28 patients with atypical depression who were given iproniazid, West and Dally (1959(a)) found marked improvement; and O'Reilly

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and Hughes (1961) stated that 77 per cent of their patients with neurotic depression recovered on iproniazid, compared with 17 per cent of patients with psychotic depression. Because the patients treated by psychiatrists are inevitably selected it is difficult to apply these results to the patients seen in general practice. In the process of selection, the more severe cases are bound to gravitate to the psychiatric clinic, leaving the larger number of milder cases in the hands of the general practitioner. In this trial we were only concerned with patients not ill enough, when first seen, to need the help of a psychiatrist.

In a pilot trial which lasted a year, we treated all our cases of mild endogenous depression with phenoxypropazine (drazine). This drug has been favourably described by Imlah (1963) and by Leahy *et al.* (1963). At the time of the trial, no serious toxic effects had been reported. In this pilot trial we found that about 60 per cent of patients either recovered or were very much improved after two weeks' treatment. Having during the 12 months built up a unified concept of the syndrome of mild endogneous depression, we decided to put our results to the test of a double-blind controlled trial.

Method

The trial was conducted in two separate practices. Only women between the ages of 18 and 62 were admitted; particular care was taken to exclude patients with anaemia or hypothyroidism, or with a history suggesting unstable personality. After diagnosis, each patient was given elementary psychotherapy—consisting of explanation of the nature of their illness and reassurance—and told to collect a prescription for antidepressive tablets from the receptionist. The receptionist allotted patients to the two groups at random; those in the treated group received two tablets of phenoxypropazine twice daily; those in the control group two gr. ½ tablets of amylobarbitone twice daily. Results were assessed at the end of the first and second weeks. The short trial period was chosen for several reasons: first, because in our pilot trial we had found that most patients who recovered did so within two weeks; secondly, because the shorter the period, the lesser chance of spontaneous recovery or interference from outside factors; and thirdly, because the shorter the period the lesser likelihood of the patient failing to persevere with treatment. At the end of the second week patients were placed in one of four categories:

1. *Recovered*—complete remission of all symptoms.
2. *Partial recovery*—complete remission of some symptoms but persistence of others.
3. *Improved*—patient feeling better, but all symptoms still present.
4. *No change.*

Two patients who stopped their tablets before the end of the two

weeks were removed from the trial.

The patients

In tables I, II and III, the treated and control groups are compared. The control group contained more patients under 30 and over 50 years of age, and more with a duration of symptoms of less than four weeks. The incidence of symptoms in the two groups was closely similar.

TABLE I

AGE DISTRIBUTION OF TREATED AND CONTROL GROUPS

Age	*Treated*	*Controls*
18–29	6	8
30–39	9	7
40–49	4	2
50–62	2	5
Total	21	22

TABLE II

INCIDENCE OF SYMPTOMS IN TREATED AND CONTROL GROUPS

Symptom	*Treated*	*Controls*
Feeling of depression ..	21	22
Fatigue ..	20	20
Frequent weeping ..	17	20
Insomnia ..	14	12
Irritability ..	13	18
Loss of interest	17	16
Tension symptoms ..	8	8
Diurnal variation of symptoms ..	8	7

TABLE III

DURATION OF SYMPTOMS BEFORE TRIAL IN TREATED AND CONTROL GROUPS

Duration	*Treated*	*Controls*
1–4 weeks ..	6	9
5–12 weeks ..	10	7
More than 12 weeks ..	4	5
Not recorded	1	1
Total	21	22

TABLE IV

RESULTS

	I.R. McW.		*D.C.M.*	
	Treated	*Controls*	*Treated*	*Controls*
Recovered	6	6	3	6
Partial recovery ..	2	4	4	1
Improved	2	2	1	1
No change	2	1	1	1
Total	12	13	9	9

Results

The results are shown in table IV. Taking the results from the two practices together, nine treated patients recovered, compared with 12 controls; six treated patients were partially recovered, compared with five controls; three from both groups were improved; and three treated patients and two controls were unchanged. No serious toxic effects were encountered.

Discussion

At the end of our pilot trial we were convinced that phenoxypropazine was a most valuable drug in the treatment of mild endogenous depression. Our controlled trial has now shown how cautious one must be in evaluating a new drug for this type of disorder. Not only were the results in the treated patients no better than in the controls, but more than half the latter were completely relieved of symptoms after no more than elementary psychotherapy and mild sedation.

Since our trial was carried out in general practice, it cannot be compared with trials conducted among the more serious cases attending psychiatric clinics. We believe, however, that it does show the danger of accepting the results of uncontrolled trials in any condition where the therapeutic effect of the doctor himself may be a major factor in relieving symptoms. From the results of this trial it appears that mono-amine oxidase inhibitors should not be prescribed for mild endogenous depression until psychotherapy and sedation have failed.

Summary

We describe a controlled trial, using the double-blind technique, of a mono-amine oxidase inhibitor (phenoxypropazine) in the treatment of mild endogenous depression. All the patients were women between the ages of 18 and 62. Twenty-one in the treated group received two tablets of phenoxypropazine twice daily; 22 controls received two gr. ½ tablets of amylobarbitone. The trial lasted two weeks. All patients were given elementary psychotherapy.

The results were no better in the treated group than in the controls: about half the patients in each group were cured.

We suggest that mono-amine oxidase inhibitors should not be prescribed for mild endogenous depression until psychotherapy and sedation have failed.

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CLINICAL NOTE

EPIDEMIC WINTER VOMITING IN A GENERAL PRACTICE

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EPIDEMIC WINTER VOMITING IS BECOMING a well-defined clinical entity recognized as being a commonly occurring condition. The condition is characterized by vomiting, often of sudden onset, which settles within about 36 hours. It is probably due to a virus spread by droplet transmission. The incubation period is usually about two days, but can be as long as a week. A fuller description of the disease has been given previously (Hopkins 1959). However, as there seems some disagreement in the literature as to what constitutes epidemic winter vomiting it is worth while describing some of the cases which occurred in a Liverpool practice during a four-year period. Moreover, the records illustrate the epidemiology of the condition in the general population, whereas many papers on the subject dealt with the disease as it was seen in closed communities such as boarding schools.

The fact that it was possible to record at least 24 cases occurring in sporadic incidents over a period of four years tends to confirm that epidemic winter vomiting is a common endemic disease. The recorded cases are summarized in the appendix.

Clinical picture

The picture in the first six outbreaks conforms with that of epidemic winter vomiting epidemics described by several authors (Miller and Raven, 1936; Gray, 1939; Berry, 1952; Garland, 1952; Von Harnack, 1955; Wiener, 1956; Hopkins, 1958). The seventh