ADJUNCTIVE THERAPY IN DEPRESSION: A CONTROLLED TRIAL OF NIALAMIDE

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THE efficacy of anti-depressant drugs, including imipramine and the so-called monoaminase inhibitors, and their potential as a replacement for E.C.T. remain undefined. Imipramine, which has been most extensively studied, has been shown to produce an initially lower improvement rate than E.C.T. in depressives, though after six months the results are little different (Kiloh and Ball, 1961). Dewhurst and Pare (1961) have reported that the quality of improvement in the cases who improved with nialamide in their partially blind trial was comparable to that seen with electroplexy. There is still a lack of controlled trials on the monoaminase inhibitors, particularly as regards patients sufficiently disturbed to warrant hospitalization. Harris and Robin (1960) found no evidence that phenelzine influenced recovery in these patients.

METHOD

In our trial of the effect of nialamide (a hydrazine in the amine oxidase inhibitor group) on 50 severely depressed hospitalized patients, we compared this drug with chlorpromazine by a double-blind arrangement. It seemed unethical to use an inert substance and chlorpromazine has been advocated as a treatment for depression (Diethelm, 1958), though it is not so used here. Our patients received either 50 mg. of chlorpromazine or 50 mg. of nialamide t.i.d. in random sequence. The tablets were identical and specially prepared by Harvey Pharmaceuticals, who manufacture nialamide as "Niamid".

The patients were selected from 68 consecutive admissions for depression, from which 18 were excluded because of doubts regarding diagnosis, the need for immediate E.C.T., difficulty in co-operation or administrative reasons. They were rated on a five-point scale based on a structured interview from which a symptom scattergram was prepared. They were re-assessed after two weeks, and if improvement was significant we put them on a known nialamide 50 mg. tablet t.i.d., and interviewed them again at four weeks. Those who did not improve received other appropriate treatment.

RESULTS

The group showed the following characteristics: There were 33 women and 17 men. The age groups were: under 46 years, 8; 46–65 years, 26; 66 years and over, 16. Nineteen patients had shown obvious personality deviation before illness and 35 had had mental illness previously. Twenty-two had an associated physical illness and 12 showed hysterical overlay. Twenty-nine were suicidal. In 27 cases environmental stress was a precipitant and in 15 loneliness was an environmental factor. A table of catamnestic data was available to differentiate the chlorpromazine groups from those receiving the nialamide. From this we note that of 26 who received nialamide, 20 were women, 14 had physical

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illnesses, 7 had raised blood pressure and 3 hysterical overlay. In the chlorpromazine group of 24, 11 were men, 8 had organic illness, 2 raised blood pressure and 9 hysterical overlay. Sixteen in this group had paid employment compared with 8 in the other group—this is probably linked with the sex difference.

The 14-day improvement rate was 76·9 per cent. for the patients on nialamide, as compared with 66·6 per cent. for the chlorpromazine group. Following the course of the illnesses further, however, 13 patients required other specific anti-depressant treatment (electroplexy, imipramine, etc.), and the final recovery rates were 50 per cent. with nialamide (13 patients) and 42 per cent. with chlorpromazine (10 patients), when the trial was completed.

Examination of the original ratings shows that 13 of the patients who recovered on the drugs were classed as very severely depressed (nialamide 8; chlorpromazine 5). Of those who failed to improve on nialamide or required electroplexy later, 4 were markedly retarded.

The assessment of personality deviation presents difficulties, especially in patients who have had several attacks of depression when the original patterns of behaviour become obscured by the effects of illness and hospitalization. Nineteen patients showed general inadequacy, hypersensitivity or lack of confidence throughout life or sociopathic traits. Nine were in the nialamide group. Their response to drugs did not differ from the "normals". Side-effects: increase in anxiety occurred in 4 nialamide cases and in 2 on chlorpromazine; whereas 12 nialamide and 7 chlorpromazine cases experienced reduction of anxiety. One skin rash occurred in a chlorpromazine case. There were no other side-effects.

Discussion

It has been observed frequently that whereas uncontrolled trials show a high percentage of success with new drugs, controlled experiments considerably dampen enthusiasm. The difficulty in defining the type of case dealt with in psychiatric research of this kind is considerable. The overlap of both symptomatology and aetiological factors in so-called endogenous and reactive depressions is well recognized, and often becomes greater as patients are investigated more intensively. We rated our patients on severity of illness and observed the incidence of 16 symptoms and signs during the assessment. Though the patients' progress was reasonably satisfactory, we feel that further follow-up enquiries are required.

Depressive illness is frequently remittent in the wake of changes in circumstances and drugs, or even spontaneously, and it could be anticipated that some improvement would follow hospitalization alone in a series such as this where so many illnesses were precipitated by environmental stress and complicated by loneliness and personality difficulty. According to our normal hospital practice, the patients were investigated to provide an analysis of the situation and the factors predisposing to and precipitating the illness, and exploratory and supportive psychotherapy was available to the patient to the extent to which it could be accepted and utilized. Such factors in the background can be conveniently forgotten if one seeks to make a case for the efficacy of new drugs.

It may also be relevant to note the observations of Karagulla (1950), who reviewed 1,611 admissions for depression in 923 patients admitted to the Royal Edinburgh Hospital between 1930 and 1948. Having traced the patients' histories back as far as 1930 in some cases, she stated that "an unexpected finding was the relatively large number of patients with an illness of short

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duration necessitating only six weeks' stay in hospital". Of these patients only 318 had electroplexy, and amphetamine was the only anti-depressant available.

Summary

1. A controlled trial of nialamide compared with chlorpromazine is reported in 50 hospitalized depressive patients.

2. At two weeks the improvement rate was 76·9 per cent. for nialamide and 66·6 per cent. for chlorpromazine. The final improvement rates (i.e. at the completion of the trial) were 50 per cent. for nialamide and 42 per cent. for chlorpromazine. Neither the short-term nor the longer-term difference between treatment groups was statistically significant.

3. These results are discussed in relation to spontaneous recovery and the therapeutic effect of hospitalization.

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