A CONTROLLED CLINICAL TRIAL OF MEPROBAMATE IN THE MANAGEMENT OF DIFFICULT AND DESTRUCTIVE FEMALE MENTAL DEFECTIVES

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MEPROBAMATE is the shortened name of 2-Methyl-2-n-Propyl-1,3 propanediol dicarbamate, which is also known as Miltown or Equanil.

Previously published reports (1–5) on clinical trials of this drug have concerned its effect on patients suffering from neurotic and psychotic disorders. As far as we are aware no reports have been published of its effects on mentally defective patients.

The clinical trial was part of a long-continued search for a drug to control the behaviour disorders of mental defectives without affecting their level of consciousness. The behaviour of the patients chosen for inclusion had failed in each case to respond over the years to a large range of sedative drugs including, most recently, nine cases who had failed to respond to Largactil (chlorpromazine hydrochloride) and four cases who had failed to respond to Rauwiloid (*Rauwolfia serpentina*).

SELECTION OF PATIENTS

The sixteen patients selected for this trial all had long histories of mental instability manifesting itself in overt aggression to staff and other patients and in destructiveness of clothes and other property. They were aged between 20–54 (all but two were between 20–35) with mental ages below 6 years. No patient was included who showed evidence of any specific super-imposed psychosis, but six patients suffering from epilepsy were included.

The patients were allocated alternately to the meprobamate and control groups. This resulted in four of the epileptic patients being in the former and two epileptics in the latter group. One patient allocated to the control group developed an intercurrent infection before the trial began and was excluded. One patient in the control group developed cellulitis and was excluded after four weeks and one in the meprobamate group deteriorated mentally and was excluded after eight weeks.

PRELIMINARY INVESTIGATIONS

All patients were weighed before the beginning of the trial and at weekly intervals. The urine and blood were examined before the beginning of the trial

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and at monthly intervals. The blood pressure was measured at first weekly and later monthly. An EEG was performed on all patients except one, who was too unco-operative, before the trial was begun and repeated on the patients receiving meprobamate during its last week. A four-hourly temperature, pulse and respiration chart was kept for each patient.

Progress Reports

In an attempt to make the reports of the nursing staff as objective as possible, we devised a questionnaire in the form indicated below, which required a numerical answer to each question. Thus, deterioration or improvement in any respect was indicated as a higher or lower numerical answer to each question. The nursing staff completed this questionnaire for each patient at weekly intervals throughout the trial.

1. How many times in the past week has he/she attacked staff or other patients?
2. How many times in the past week has he/she been in seclusion?
3. In the past week how many articles of clothing has he/she deliberately damaged?
4. In the past week how many other articles has he/she deliberately damaged?
5. In the past week on how many occasions has he/she been insolent towards staff?
6. In the past week on how many occasions has he/she been noisy and excitable apart from those reported under 1–5 above:
   (*a*) during the day?
   (*b*) during the hours of sleep?

Dosage

The meprobamate tablets (400 mg.) were known to nursing staff only as tablets number 6 and the control tablets only as tablets number 5.

Patients in each group were given a commencing dosage of one tablet t.d.s. After four weeks this was increased to 5 tablets per day in divided doses and a week later to 2 tablets t.d.s. The trial was continued for seventeen weeks from its commencement.

Results

We were unable to observe any improvement in the behaviour of the patients in either group and in no case did the answers to the questionnaire reveal any sustained numerical reduction which appeared to be significant.

Physical Changes During Treatment

Except in the patients mentioned as developing intercurrent infections, there was no appreciable variation in temperature, pulse, respiration or blood pressure. No patient developed a rash.

Of the patients receiving meprobamate, two gained up to 2 pounds in weight and four lost up to 9 pounds in weight. Of those receiving the control tablets, four gained up to 8 pounds in weight and two lost up to 7 pounds in weight. No abnormality was observed in the urine. No patient developed any blood dyscrasia.

Fits

No evidence was obtained to suggest that meprobamate affected the frequency of epileptic fits.

EEG Variations

As stated above, the EEG was repeated on those patients receiving meprobamate. In each of two cases the EEG was reported more abnormal than before they received meprobamate. In one of these cases delta activity, which had been widespread, became localized in the right temporal region and in the other case delta activity which had not previously been noted was recorded from the right temporal region. In this case there was also an increase in the amplitude of delta activity.

In one case the EEG was reported as showing a very slight improvement. Delta activity previously localized in the right temporal region having disappeared.

In another case, a slight reduction in generalized delta activity was reported.

In the four remaining cases, the EEG was not repeated either because the patient had not completed the trial or because she was too unco-operative.

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