A CLINICAL TRIAL OF 'STELAZINE' IN THE TREATMENT OF CHRONIC SCHIZOPHRENIA

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Introduction

The problem of the treatment of the chronic schizophrenic in the mental hospitals of this country is still most pressing. It is this group which contributes more than any other to the large and mounting number of occupied beds and to the nursing difficulties in any hospital today. Therapy with pharmaceutical agents in the last few years has produced results better than previously used methods. Unfortunately, in spite of gratifying successes, the problem still remains. When the opportunity arises for the trial of a new psychotropic drug, an investigation into its possibilities must obviously be worthwhile.

The present trial was devoted to the study of 'Stelazine,' a phenothiazine derivative which differs from prochlorperazine in having a trifluoromethyl group in the place of a chlorine atom in the 2 position of the nucleus. It is claimed that animal experiments have shown that 'Stelazine' was approximately nine times as potent as chlorpromazine and four times as potent as prochlorperazine in blocking conditioned responses in rats.

Methods

Patients Selected

Forty female patients were chosen for the trial. All occupied beds in the same ward, which was an advantage in that the same staff were continuously in charge; and occupational therapy was carried out by the same members of the staff. It was thus thought that the environmental factors would be kept constant. All other therapy was stopped and the patients were given inert tablets at the commencement of the trial. At the end of 14 days those who improved on the inert tablets were eliminated from the trial. Those in whom the symptomatology increased or remained constant proceeded to trial with 'Stelazine.' There were 32 patients left for trial.

Results of administering the drug were assessed as follows:

- (a) On the patient's insight and touch with reality.
- (b) On the loss of affective incongruity.
- (c) On the thought block and hallucinations and delusions associated with this.

The assessment was made independently by the physician-in-charge, and the nursing staff.

Endocrine Tests

Thyroid function was assessed by tracer tests with I^{131} . I^{131} was administered intravenously in all cases in doses of 28 microcuries and the uptake measured at the end of the first hour, and then at the end of the first 24 hours; together with excretion rates at the end of 24 and 48 hours. The reason for not giving I^{131} by mouth, as is usually done, and for using a larger dose, is that it has already been shown that the absorption rate in psychotic patients is slower than in the normal.

Urinary 17 ketosteroids and total corticoids excretion was measured in every patient. These measurements were made at the beginning of the trial, and then at an interval of 14 days. 17 ketosteroids and total corticoids were estimated according to the method of Norymberski *et al.* (1953).

Dosage

The routine adopted was to give 5 mg. of 'Stelazine' three times a day as the initial dose. If no improvement was apparent after the first three days of treatment, 'Stelazine' was increased by 5 mg. per dose to a total of 30 mg. per 24 hours; and later at suitable intervals to 15 mg. and finally 25 mg. three times a day. Experience showed that if no improvement had occurred when 75 mg. was given per day there was no point in increasing the dose further. This method of administering 'Stelazine' was not entirely in accordance with that suggested by other investigators where the dose administered was raised more slowly and by only 5 mg. increases per day on each occasion.

TABLE 1.—RESULTS OF TREATMENT OF CHRONIC SCHIZOPHRENIC FEMALE PATIENTS WITH 'STELAZINE'

Number of patients	Average age Years	Average duration of disease Years	Onset of improvement Average number of days	Average daily dose 'Stelazine' mg.	Results of treatment		
					Excellent: Marked improvement	Good: Moderate improvement	No change
32	37.8	12	17	25	6	21	5

Results

Table 1 presents the results obtained in all the patients investigated as assessed on the three factors noted above. Of the 32 patients the ages varied from 15 to 67 years, with an average of 37.8 years. Of these, eight were below 25, 19 were between 26 and 50 years and five were over 50 years. The duration of illness was not always easy to assess in some cases. The duration varied from 1 to 33 years, with an average of 12 years.

The improvement in six cases was far in advance of that which had been obtained when the patients were on other drugs of a similar type. In one case a patient who for years was unable to leave the ward unattended by staff was sufficiently well to be allowed home for week-end visits. The nursing staff and the therapist in charge of occupational therapy in the ward were of the opinion that the quality and quantity of work output had gone up considerably, although no efforts had been made to encourage special attention to this group. The rate of improvement in the condition of the patients was shown in an average of 17 days, although some had displayed lessening of symptoms before this.

The majority of the patients showed improvement between 4 to 57 days, with an average of 17 days for all the patients. There was no correlation between the size of the dose and the degree of improvement when it was seen.

Endocrine Function

The results showed no alteration in the thyroid function as measured by the I^{131} tests. All the values for urinary 17 ketosteroid and urinary total corticoids were within normal limits. There were thus, in the tests done, no significant endocrine changes noted.

Side-Effects

All the patients were examined for blood changes. There were no demonstrable abnormalities throughout the period of the trial. Similarly, all liver function tests were within normal limits. Dermatitis or any other signs of allergic responses in the patients, or the staff, were not noted. Onset of the Parkinson-like syndrome was noted in many cases. Seventeen of the 32 patients showed

evidence of extra-pyramidal symptoms which were readily controlled with Artane and by diminishing the dose of the drug. Restlessness was present in 12 patients, but was not sufficiently noteworthy to justify discontinuation of the drug. It was interesting to note that when Parkinsonism developed in a patient, and when the drug was stopped and the symptoms disappeared, re-introducing the drug did not always produce the recurrence of Parkinsonism. The same was true where restlessness developed.

Discussion

Although the number of cases in this trial is small it is clear that, as only five patients out of the 32 did not improve, 'Stelazine' must be considered a most useful pharmacological product in the treatment of chronic schizophrenia. No endocrine changes were noticed. Ayd (1958) enumerated not less than nine endocrinological changes associated with the use of chlorpromazine and reserpine, and it was suggested that the action of psychotropic drugs was associated with the hypothalamic pituitary axis. In this trial, with the three special tests involved, no endocrine changes could be demonstrated.

It would seem that with the relatively high doses administered in this trial extra-pyramidal symptoms may appear rapidly with the use of 'Stelazine.' There is no correlation in regard to the age of the patients and the production of side-effects. Reiss (1957) observed that there may be a correlation between age and chlorpromazine therapy. With 'Stelazine' therapy it is clear that the dose must be related specifically to each individual patient. There is no evidence that the improvement in mental state went hand in hand with the extent of Parkinsonism, but it may be that in the chronic schizophrenic this is a part of the price one must pay for improvement in the patient. All side-effects can be reasonably controlled by administering Artane or by temporarily reducing the amount of the drug, and it is considered that the side-effects are not of great importance with this form of therapy. In a recent article, Forrester (1958) stated that side-effects in her series of 25 cases were marked, and she enumerated symptoms such as mask-like faces,

tremor, salivation, rigidity, flushing, pallor and restlessness. In our opinion, many of these symptoms are normally seen in the chronic schizophrenic, and are not necessarily due to administering a drug.

It is interesting to note that 28 of the 32 patients had received some other form of tranquillizing drug as a routine treatment in the period preceding this trial. In this respect, therefore, a comparison was possible between the effects of 'Stelazine' and other earlier treatment. In this trial one gains the impression that 'Stelazine' in chronic schizophrenia may yield better results than other phenothiazines.

Summary

1. A clinical trial of 'Stelazine' was carried out on 32 female chronic schizophrenic patients.
2. Twenty-seven patients improved to such an

extent that it is believed that 'Stelazine' will prove a valuable drug in psychiatric practice. Further work will be done in the study of side-effects and the mechanisms of the psychotropic activity of 'Stelazine.'

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BIBLIOGRAPHY

- AYD, F. J. (1958), *Psychiat. Quart.*, **32**, 48.
 FORRESTER, M. E. (1958), *Brit. med. J.*, **ii**, 90.
 NORBYNBERSKI, J. K., STUBBS, R. D., and WEST, H. F. (1953), *Lancet*, **i**, 1276.
 REISS, M. (Ed.) (1957), 'Psycho-endocrinology,' p. 182, Grune and Stratton Inc., New York.

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