Chlorpromazine, Clotiapine and Thioridazine– A Comparative Clinical Trial on Bantu Psychotic Patients*

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SUMMARY

In a non-blind assessment of 3 neuroleptic drugs, chlorpromazine (Largactil), thioridazine (Melleril) and clotiapine (Etomine), we found Etomine to be the drug of choice when the diagnosis is in doubt between a toxic psychosis or schizophrenia. This drug also offered the highest discharge rate, 77·7% at 12 weeks compared with 73·5% in the thioridazine group, and 55·5% in the chlorpromazine group.

No clouding of consciousness was seen in the clotiapine group, whereas it was troublesome in the chlorpromazine group in patients having received high parenteral doses.

No side-effects were seen with thioridazine and extrapyramidal side-effects caused by the other two drugs were easily controlled by dose reduction.

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Early in 1968, the drug clotiapine (Etomine, Wander) became available in South Africa for clinical trials. At that stage the available literature[1,2] indicated that because of its quick action, it might be useful in increasing patient turnover rate, especially in the Bantu wards where we have a high admission rate.

It was decided to launch a clinical investigation, comparing its effects with chlorpromazine and thioridazine, two well-known and often used neuroleptics in the Bantu wards.

METHOD

Because of the administrative and staff shortage problems we could not introduce any 'blind' procedures into the trial. However, we hoped that by using a fair number of patients and following them through until discharge, we might nevertheless be able to gather enough data for a global evaluation of the 3 drugs.

All patients were physically healthy adult Bantu males suffering from acute psychoses. No epileptic or depressive psychoses were included and on subsequent analysis it was found needful to divide all patients into two broad diagnostic groups, e.g. schizophrenia and toxic psychosis (Table I).

TABLE I. NUMBER OF PATIENTS

Treatment	Schizophrenia	Toxic psychosis	Total
Clotiapine (Etomine)	**28**	**8**	**36**
Thioridazine (Melleril)	**21**	**10**	**31**
Chlorpromazine (Largactil)	**25**	**9**	**34**

Allocation to either of the 3 drug groups was at random and all patients were handled by the same staff and the same clinical investigator throughout the trial. Diagnoses were confirmed before final diagnostic grouping.

Psychosis ratings were done before treatment and thereafter weekly for 12 weeks or until discharge. The psychosis rating scale was a very simplified tabulation of the usual important psychiatric signs and symptoms with which Bantu patients present. All patients were scored from 1 (normal) through 5 (severely disordered) on 5 diagnostic criteria, e.g. orientation, insight, delusions, hallucinations and general behaviour.

No patients received concurrent electroconvulsive or antiparkinsonism therapy during the trial.

Dosage

All patients received an initial maximum recommended dose of each drug. Dosage was reduced when improvement or side-effects began to occur.

Clotiapine: 40 mg *t.d.s.* **orally.** Because of restlessness and agitation in 11 patients the initial treatment was limited to a single dose on the first day (120 mg), given intravenously, to be followed only on the second day with the normal daily dosage orally.

Chlorpromazine: 200 mg *t.d.s.* **orally.** Due to agitation and restlessness, 4 patients received an initial dose of 100 mg intramuscularly, followed after 8 hours and 16 hours with oral medication, to make up the total daily dosage of 600 mg.

Thioridazine: 200 mg *t.d.s.* **orally.** 10 patients received 300 mg *t.d.s.* on the first day to alleviate agitation and restlessness.

Medication was discontinued when patients rated 'symptom free' for 2 consecutive weeks, and only when they remained symptom free for the following 4 weeks, were they discharged. No patients were discharged on medication but a letter to the district surgeon stating the treatment which had been received, was given to all discharged to be handed in to their district surgeon on arrival home.

RESULTS

Figs. 1 and 2 show the differences in action in the two main diagnostic categories.

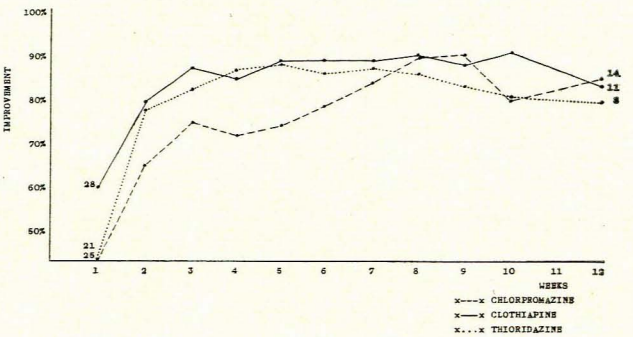
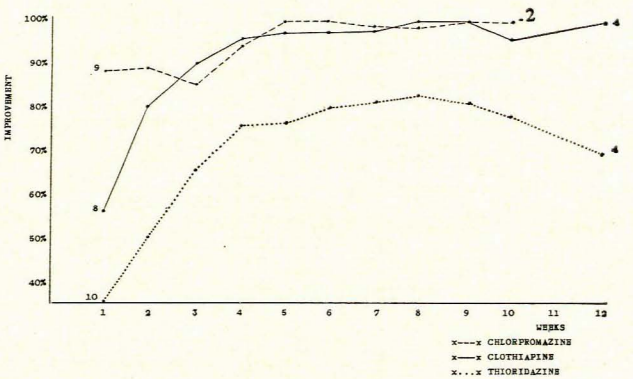


Fig. 1. Results in schizophrenia.



Toxic

Fig. 2. Results in toxic psychosis.

It is interesting to note, in the schizophrenic group, a definite lag in the chlorpromazine curve below the other two drugs. Also in the toxic group there is a definite lag in the thioridazine curve below the other two drugs.

When calculating a discharge rate after 12 weeks treatment we obtained the results shown in Table II.

TABLE II. PERCENTAGE PATIENTS DISCHARGED

Treatment	Toxic psychosis	Schizophrenia	Total discharged
Chlorpromazine	**26·1%**	**29·4%**	**55·5%**
Clotiapine	**16·7%**	**61·0%**	**77·7%**
Thioridazine	**21·2%**	**52·3%**	**73·5%**

DISCUSSION

The total rating of all symptoms before beginning treatment (x) was computed for each patient. In addition, their total rating of all symptoms after 1, 2 and more weeks of observation in hospital was determined. (yi, i = 1, 2, ...). To obtain the measure of improvement under drug therapy we computed the rate $\bar{z}_i = \frac{(x - iy).100}{x - \bar{5}}$. In the graphs are represented the mean values of $\bar{z}_i$ computed from all patients observed in week 1. The differences between mean values $\bar{z}_i$ of the 3 drug groups were then tested by Student's *t*-test. The small numbers at the beginning and at the end of the curves represent the number of patients from which the mean was computed.

This method has the disadvantage that patients who are cured and discharged from hospital fall out of the calculation. Their ratings after discharge are not known, and it would be wrong to assess them with the minimal rating for all following weeks. So those discharged early have a negative influence upon the improvement-curves. However, this factor remains approximately the same for all drug groups.

In the schizophrenic group a general tendency for each drug is apparent in Fig. 1, although statistically there are no significant differences. This can be explained by the fact that at 9 weeks and longer, the numbers of patients in each group were too small.

In the toxic psychosis group statistically significant differences (at the level $2\alpha = 0{\cdot}05$) were found between the groups chlorpromazine—clothiapine and chlorpromazine—thioridazine.

Taking into consideration the large number of Bantu patients admitted in a toxic state with an underlying schizophrenia discovered only when toxicity is clearing up, we think that the clotiapine would be an ideal neuroleptic to increase our patient turnover rate. This conclusion is reinforced by Figs. 1 and 2, where it is evident that clothiapine (Etomine, Wander) gives rapid response in both schizophrenia and toxic psychoses. By using either of the other two drugs at the time when exact diagnosis is still in doubt, one might find an unsatisfactory response.

Furthermore, an advantage of clotiapine over the other two drugs is the availability of a safe parenteral solution. In none of the 11 patients treated with 120 mg clotiapine intravenously did we notice untoward clinical side-effects either locally or systemically. They all promptly calmed down and were put to bed.

We did notice an upsetting degree of mental clouding in all 4 patients 24 hours after the intramuscular chlorpromazine injection. It was so severe that it was only with difficulty that any information could be obtained from them the next day.

This clouding of consciousness was not present at all in patients that had received clothiapine intravenously the previous day. Although they were heavily sedated, they could give a good account and assessment of psychosis was therefore much easier with them.

No extrapyramidal side-effects were noticed in the thioridazine group. This is in accordance with the observations of other workers.[3,4] However, extrapyramidal side-effects did occur in several patients in the other two groups but because they were easily controlled by dose-reduction, we did not find it necessary or practical to rate side-effects separately.

Because of practical and administrative problems no follow-up studies could be carried out.

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