CHLORPROMAZINE IN THE TREATMENT OF THE CHRONIC DISTURBED SCHIZOPHRENIC PATIENT

By

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INTRODUCTION

The pharmacology of chlorpromazine (Anton-Stephens, 1954; Hopkin, 1955) and its use in psychiatric practice (Garmany et al., 1954; Elkes et al., 1954; Charatan, 1954; Labhardt, 1954) have been described in several recent papers. The present paper briefly describes a controlled experiment on the use of the drug in a group of chronic disturbed schizophrenic patients, the object being to introduce as few variables as possible into the experimental situation, with a view to making the results as objective as is ever possible in a psychiatric investigation.

THE EXPERIMENT

In a disturbed male ward of 60 patients, about 40 patients were in the age group 29–50 (average age 35) suffering from schizophrenia, mostly classified as paranoid, of at least ten years’ duration. For the purposes of the experiment, these patients were divided into two numerically equal groups, surnames beginning A to L in one group and the remainder in the other, the division, therefore, being clinically random.

The names of the patients were recorded on a large wall-chart in the ward office, and daily against each name was recorded the number of “aggressive” outbursts that the patient had shown and which the nursing staff noted in the course of their normal duties. In order to simplify matters as far as possible for the observers, “aggressiveness” was divided into four categories, A, B, C and D. “A” was defined as being a short verbal outburst, not sufficiently prolonged to merit interference by a nurse; “B” was a more prolonged verbal outburst, which required interference; “C” was a short physical outburst, such as a sudden blow, the physical equivalent of “A”; and “D” was a prolonged physical outburst requiring interference by the nursing staff. It was not expected that every “aggressive” outburst could be recorded, but deficiencies in this respect would be of no practical significance in the comparisons between the two groups.

After a preliminary control period of recording of six weeks’ duration, each individual of one group was given 50 mg. three times daily of chlorpromazine and of the other group the same number of identical-appearing but inactive tablets. The tablets were administered for six weeks and the recording continued as before.

There was then a rest period of twelve weeks, after which a precisely similar experiment was carried out, with the exception that the dosage used was 100 mg. three times daily and the tablets were administered for ten weeks. The personnel of the groups in the second experiment did not exactly correspond to that of the first, due to unavoidable transfers.

In both experiments the identity of the active and inactive tablets was known only to the hospital pharmacist.
Apart from the giving of the tablets, the normal ward routine remained completely unchanged throughout. The patients were not interviewed any more often than usual by the medical or nursing staff, nor was any alteration made in any regular medication that the patients might have been having previously. The weights of the patients were those recorded normally.

RESULTS

The results are summarized in Tables I and II. Groups $X_1$ and $X_2$ received the active tablets, whilst groups $W_1$ and $W_2$ were the controls. It will be seen that there is no significant change in the recorded aggressive incidents of any type in groups $X_1$ and $X_2$ following a dosage of 150 mg. or 300 mg. daily of chlorpromazine orally, respectively. There is, however, in each group a significant increase in body weight, not shown in the control groups.

### TABLE I

*Patients Given 150 mg. Daily of Chlorpromazine or Equivalent Control Tablets*

<table>
<thead>
<tr>
<th>Group</th>
<th>Period</th>
<th>Number of &quot;Aggressive&quot; Incidents</th>
<th>Average Weight Change at End of Experiment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Type</td>
<td>Type</td>
</tr>
<tr>
<td>$W_1$</td>
<td>40 days prior to tabs.</td>
<td>160</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>40 days on tabs.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>$X_1$</td>
<td>40 days prior to tabs.</td>
<td>83</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>40 days on tabs.</td>
<td>.</td>
<td>.</td>
</tr>
</tbody>
</table>

### TABLE II

*Patients Given 300 mg. Daily of Chlorpromazine or Equivalent Control Tablets*

<table>
<thead>
<tr>
<th>Group</th>
<th>Period</th>
<th>Number of &quot;Aggressive&quot; Incidents</th>
<th>Average Weight Change at End of Experiment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Type</td>
<td>Type</td>
</tr>
<tr>
<td>$W_2$</td>
<td>14 days prior to tabs.</td>
<td>74</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>70 days on tabs.</td>
<td>.</td>
<td>.</td>
</tr>
<tr>
<td>$X_2$</td>
<td>14 days prior to tabs.</td>
<td>46</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>70 days on tabs.</td>
<td>.</td>
<td>.</td>
</tr>
</tbody>
</table>

### DISCUSSION

The difficulty of finding adequate controls, the lack of objectivity and the inability to make quantitative measurements, are only a few of the problems inherent in the investigation of the effectiveness of a drug in psychiatric conditions.
Without control groups, it is impossible to be certain that any change found in the patient is not due partly or totally to the altered environmental factors inherent in an experimental set-up. For example, a series of detailed psychiatric interviews in patients previously neglected, or an awareness amongst the nursing staff and patients that some new drug is being tried, are important changes that cannot be disregarded (Bickford, 1955). Unfortunately, many of the reported experiments on the effect of chlorpromazine seem to have lacked control groups (Charatan, 1954; Garmany et al., 1954; Labhardt, 1954 and many others).

The assessment of improvement by individual interview is also apt to lack objectivity; though with a well controlled experiment (e.g. Elkes et al., 1954), this criticism cannot be sustained.

The present experiment, recording numerically as it does, the occurrences of one particular easily detected symptom, can claim to be objective. It is also controlled in that one group had inert identical-appearing tablets and that the selection of groups was clinically random. Also, the identity of the control group was unknown, but unfortunately side-effects such as dryness of the mouth, gave the nurse-observers a clue as to which were the active tablets.

The most serious source of error in this experiment seems to be in the definition of "aggressive" behaviour. The degree of affective involvement in the noisy or motor outbursts of schizophrenic patients may vary a great deal, so an apparently simple symptom such as a shout, may be an expression of differing psychopathological states. Objection, too, might be taken to the different "degrees" of aggressiveness, as defined above, but these were of no importance in the final result.

The finding that, in this controlled experiment, chlorpromazine, even in a dosage of 300 mgm. daily, made no significant difference in the aggressive psychomotor behaviour of chronic schizophrenic patients, is interesting in that it is not supported by the findings of other observers who, however, often found that the schizophrenic group was the least responsive to the drug (Lehmann, 1954; Elkes et al., 1954) and that the more chronic schizophrenics showed a worse response than the more recent ones (Labhardt, 1954). On the other hand Labhardt (1954) also showed that the paranoid schizophrenic group gave a far better response than any other schizophrenic group, the improvement rate being as high as 60 per cent. in an uncontrolled experiment.

Finally, the writer makes no apology for the apparent crudity of this experiment. The patients are grouped together as disturbed schizophrenics, a crude symptom is recorded and untrained observers are used to record it. But to have attempted to separate the patients into different categories or record groups of elaborate symptoms, would have been to have destroyed the whole object of the experiment, which was to record the effects of the drug in a group of patients in which all other factors remained unchanged.

**Conclusion**

The findings in the present experiment suggest that environmental factors may play a bigger part in the apparent effectiveness of chlorpromazine than is realized and stress that care should be taken in prescribing a drug that is by no means a panacea, lest its reputation should suffer unnecessarily.

There would also appear to be need for more experiments similar to this to be carried out on a larger scale and more carefully controlled than has been possible here.
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Summary

An experimental method of assessing the effect of chlorpromazine on symptoms of aggression in male chronic schizophrenic patients is described and it is concluded that statistically there is no change in the symptoms following a dosage of chlorpromazine of up to 300 mg. daily by mouth.

Acknowledgments

I wish to thank Dr. R. Gordon McLaren, Medical Superintendent, Oakwood Hospital, Maidstone, Kent, for permission to publish these results. I should particularly like to thank the nursing staff of Ward M.7 of that hospital, without whose enthusiastic co-operation this experiment could not have been completed. My thanks are also due to Dr. W. R. Thrower of May and Baker Ltd. for his advice and encouragement and to that firm for making supplies of tablets freely available.

References