Estimation of Drug Rejection by Schizophrenic In-Patients, with Analysis of Clinical Factors

By J. D. WILSON and M. D. ENOCH

Biochemical studies on the urine of schizophrenic in-patients and out-patients have shown the drug rejection rate to vary from 5 per cent. to 32 per cent. in the U.K., U.S.A., and U.S.S.R. (3, 4, 8, 9, 11, 12). Even higher rejection rates (70 per cent.) were found with depressed out-patients (12), and high rejection rates have been found in antenatal patients prescribed ferrous sulphate, out-patients supposedly taking P.A.S. for their tuberculosis, and patients on drugs for rheumatoid arthritis (1, 2, 5, 6, 7).

SUBJECTS AND METHODS

Twenty-five unequivocally schizophrenic male, and 25 similar female in-patients, who were not prescribed imipramine or any phenothiazines other than chlorpromazine thrice daily, were chosen for this study. Urine specimens were collected after the morning dose, a code number being used for each specimen, and extra totally random specimens were included. All specimens were tested by the F.P.N. (ferric chloride perchloric acid, nitric acid, general test) method (3), within five hours of collection. The few patients unable to produce specimens that day were similarly tested within twenty-four hours.

These patients were then given chlorpromazine in the form of syrup at the same dosage, and the test repeated after five or six days. Two female patients did not complete the trial because they left the hospital.

Eight patients’ urine tests changed from negative to positive on the syrup, but none from positive to negative, while three patients gave negative urines on both occasions. The eight that changed, together with a control group of eight randomly selected from the original total patients, were examined clinically by the second author. In addition, the nursing staff completed a short questionnaire.

RESULTS

Statistical analysis showed two items to be reasonably significant. The first was in the change of results of urine tests when change occurred from tablets to syrup, cf. Table I. This demonstrates that it is extremely likely that drug rejection does occur, and that with a change of mode of prescribing, i.e., from tablets to syrup, the problem appears to be overcome. The three patients whose tests remained negative were receiving only 25 mg. t.d.s. of the drug.

Secondly, patients with paranoid delusions rejected tablets more frequently than any other group, cf. Table II.

The Fisher-Yates test of significance in a 2 x 2 contingency table (10) showed no
Table II

Significance of Paranoid Delusions: the hypothesis being that such patients will reject tablets more frequently

<table>
<thead>
<tr>
<th>Paranoid delusions</th>
<th>Real</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>No paranoid delusions</td>
<td>7</td>
<td>2</td>
</tr>
</tbody>
</table>

Fishers exact p, in a one-tailed test, was calculated for this plus the more extreme case.

\[ p = 0.02028 \]

-significance in a number of other items, which included:

(a) whether or not the patients were active in attending industrial or occupational therapy or any kind of work
(b) onset acute or insidious
(c) whether patient approved of drugs or not
(d) orientation in place (name of ward)
(e) orientation in time
(f) insight regarding the presence of mental illness in themselves
(g) dose of chlorpromazine
(h) thought disorder
(i) disturbed ward behaviour
(j) doubts of nursing staff as to patient's drug rejection
(k) auditory hallucinations
(l) affective flattening or incongruity
(m) history of E.C.T.
(n) history of insulin coma therapy
(o) history of both E.C.T. and insulin coma therapy
(p) sex

In addition a Median test on the two groups, by the Fisher-Yates test, and using an assumed median, showed no significant difference for:

(1) Present age
(2) Duration of illness
(3) Age of onset

Discussion

This study shows up the hazard in the prescribing of drugs without verifying whether they are ingested, and conforms with the findings of workers in medicine in general. The results of all drug trials therefore, controlled or otherwise, are made questionable.

Even on close questioning of patients, haphazard ingestion may be suggested by nebulous replies as to what colour tablets they take and when the tablets are taken.

This poses the question of how drug rejection can be reduced or eliminated. Laboratory testing is time-consuming, and doses of chlorpromazine of 25 mg. three times a day are at the lower limit of detection, except by chromatography (12).

This study does, however, indicate that drug rejection occurs to a high level of probability, mainly in patients with clinically detectable paranoid delusions, and that the drug rejection problem appears to be overcome by prescribing the drug in syrup form.

As it is usually imperative to be sure of ingestion of chlorpromazine and related drugs in the disturbed patients for whom it is most highly indicated, it would appear advisable to administer the drugs in syrup form in such patients, especially if they have paranoid delusions.

In view of these findings, when patients do not respond to drug therapy as expected, it might well be more useful to test their urine than merely increase the dose prescribed (3).

Summary

Testing was performed on the urines of 48 schizophrenic in-patients, using the F.P.N. reagent. The results of the administration of tablets and syrup were compared, and clinical assessment was made on those apparently rejecting the tablets, and a control group.

The results indicate that

(a) significant drug rejection occurred on tablets
(b) patients with clinical paranoid delusions were mostly implicated and
(c) administration of chlorpromazine in syrup form was very useful in overcoming this difficulty.

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REFERENCES

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