LITHIUM IN THE PROPHYLACTIC TREATMENT OF RECURRENT AFFECTIVE DISORDERS

E H Kua
S L Lee
K T Chee

SYNOPSIS

A one-group longitudinal trial of lithium on 40 patients with recurrent affective disorders showed improvement in 75 per cent of cases. There was a highly significant reduction ($p < 0.001$) in total hospital admissions after commencement of lithium treatment — it was more evident in manic-depressive and schizo-affective psychoses than in recurrent depressive illness. Patients on lithium therapy do relapse but these episodes tend to be less severe and infrequent.

INTRODUCTION

After the clinical trial by Baastrup and Schou (1) in 1967, lithium was given cautious approval as a prophylactic agent in cases of recurrent affective disorders. This term encompasses recurrent manic-depressive psychosis, endogenous depression and schizo-affective psychosis, which designates a mixture of manic-depressive and schizophrenic symptoms. In a model of international collaborative study, Angst and his colleagues (2) confirmed that treatment with lithium reduced the number of relapses and hospital admissions. Misgiving was assuaged when double-blind studies (3, 4, 5) conclusively demonstrated the effectiveness of lithium over placebo.

This study conducted in Woodbridge Hospital, Singapore, was a longitudinal trial which retrospectively compared the course of recurrent affective disorders without and with lithium treatment.

METHODOLOGY

The data were derived from patients with affective disorders on lithium therapy in Woodbridge Hospital. Out of a total of 68 cases, only 40 were selected as fulfilling both the following criteria:

(1) Before lithium treatment they had at least two relapses requiring admissions within the last two years.
(2) Lithium had been given continuously for at least two years.

This study was carried out as a one-group design; the procedure to evaluate the efficacy of the treatment was by intra-indivdual comparison of the illness course during lithium treatment and a period of similar length before treatment.

For each patient hospital admissions were counted in the two years of lithium therapy and a preceding period of two years.

Department of Psychological Medicine
National University of Singapore
Faculty of Medicine
Sepoy Lines
Singapore 0316

E H Kua, MBBS, MRC Psych (UK)
Lecturer

Woodbridge Hospital
Singapore

S L Lee, MBBS
Medical Officer

K T Chee, MBBS, DPM, MRC Psych (UK)
Consultant Psychiatrist

Table I
DISTRIBUTION OF PATIENTS ACCORDING TO SEX AND TYPE OF AFFECTIVE DISORDER

Type of Disorder	Female	Male	Total
Manic depressive	17	4	21
Endogenous depressive	4	3	7
Schizo-affective	10	2	12
Total	31	9	40

Table II
NUMBER OF ADMISSIONS BEFORE AND DURING LITHIUM TREATMENT AND TYPE OF AFFECTIVE DISORDER

Type of Disorder	Before Lithium	After Lithium
Manic depressive	92	18
Endogenous depressive	22	6
Schizo-affective	41	9
Total	155	33

Manic depressive psychosis : $P < 0.005$
Endogenous depression : $P < 0.01$
Schizo-affective psychosis : $P < 0.005$

Table III
OUTCOME OF PATIENTS ON LITHIUM TREATMENT AND TYPE OF AFFECTIVE DISORDERS

Change	Manic Depressive	Endogenous Depressive	Schizo-affective	Total
Improvement	16	5	9	30
No change	5	2	3	10
Total	21	7	12	40

As shown in Table III, 30 patients (75 per cent) out of a total of 40, improved during lithium treatment — this is statistically significant ($p < 0.005$).

Manic depressive psychosis : $P < 0.005$
Endogenous depression : $P < 0.01$
Schizo-affective psychosis : $P < 0.005$

With this method the following null hypothesis was tested: if lithium was without prophylactic action, there would be no difference between the number of hospital admissions during the periods with and without lithium. The numbers observed were tested for this hypothesis with Wilcoxon's matched-pairs signed-ranks test; for each patient the number of hospital admissions during the period without lithium and the period with lithium constituted a 'pair'.

RESULTS

There were 31 female and 9 male patients with a preponderance of manic-depressive psychosis as seen in Table I.

The effect of lithium shows a highly significant decrease ($p < 0.001$) in the total number of hospital admissions. Prior to lithium treatment there were 155 admissions compared to 33 during treatment (Table II).

In all the three types of affective disorder there is a reduction in admissions after commencement of lithium therapy. This is more evident in manic-depressive and schizo-affective psychoses than in recurrent depression but the differences are all significant.

DISCUSSION

The longitudinal study is based on the assumption that the

course of the illness during the years preceding lithium treatment could be used as an estimate of the course to be expected during treatment if lithium were inactive (2). As in most drug trials, more cogent evidence can only be obtained from double-blind design.

A problem in the investigation is the definition of relapses which should include not only hospital admissions but also manic or depressive episodes that necessitate supplementary therapy. Unfortunately on examining the case records it was difficult to ascertain these episodes.

In this study the periods with lithium always followed periods without lithium, and the conditions, therefore, did differ in addition to the lithium administration: the patients had become older and the illness histories longer when lithium was given. But the tendency in recurrent affective disorders is towards more frequent relapses with increasing age and duration of illness. The passage of time would tend to raise rather than lower relapse frequencies.

It could be argued that lithium was likely to be instituted at a time when relapses were unusually frequent and a decrease in relapse frequency might be due to spontaneous variations with no relation to lithium administration. This hypothesis was tested and found to be untrue (1).

The results concur with other studies that lithium prophylaxis is efficacious in recurrent affective disorders — the null hypothesis is rejected. The sample size is small for recurrent depressive illness and schizo-affective psychosis to draw convincing conclusion. The prevailing opinion supports the view that it ameliorates recurrence of schizo-affective psychosis but is effective only on the affective component (6).

Angst et al (2) found the response to lithium prophylaxis was independent of sex, age and number of previous relapses. They confirmed that during treatment, patients might relapse but these episodes tended to be less severe and infrequent.

Some of our patients obtained full prophylactic effect from the commencement of lithium therapy, they suffered no further recurrences of mania or depression. There were other patients in whom the prophylactic action seemed to set in gradually so that they had relapses during the early months of treatment. However in spite of lithium therapy, 25 per cent of cases made no improvement.

Lithium does not cure recurrent affective disorders; it must be given continuously to prevent relapses. It is essential that the patients understand that further attacks may occur — these episodes may be safely treated by other methods but lithium treatment should continue.

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