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IS IT TIME TO HAVE ANOTHER LOOK AT LITHIUM MAINTENANCE THERAPY IN BIPOLAR DISORDER?

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Abstract

Akhondzadeh Shahin, Effat-Sadat Emamian, Ali Ahamadi-Abhari, Omid Shabestari and Manoucher Dadgarnejad: Is it time to have another look at lithium maintenance therapy in bipolar disorder? Prog. Neuropsychopharmacol. & Biol. Psychiat. 1999, 23, pp. 1011–1017. ©1999 Elsevier Science Inc.

1. Bipolar disorder is typically a chronic disease entailing an episodes course, whereby psychiatric status alternates between periods of normal functioning and periods of illness. Lithium is well established and approved for the treatment of bipolar disorder. However, its efficacy in practice is not as great as expected. This retrospective record study was undertaken to determine the efficacy of lithium in bipolar disorders.
2. 48 patients who met DSM-III-R diagnostic criteria for bipolar I disorder and had been admitted once before lithium therapy and twice or more after that, were included in this study.
3. No significant difference in length between episode (frequency) was observed before and after lithium maintenance therapy. In addition, the percentages of manic episode after lithium therapy were much greater than before that.
4. The results indicate that it is worth re-examining the efficacy of lithium in bipolar disorders.

Keywords: bipolar disorder, lithium efficacy, mania

Abbreviation: diagnostic and statistical manual of mental disorders, 3rd ed., revised (DSM-III-R).

Introduction

Although over 40 years have elapsed since the effects of lithium

on mania were first described (Cade, 1949), lithium is still the treatment of choice in the acute treatment of mood disorders and in the prevention of recurrent manic and depressive episodes (O'Connel et al., 1991; American Psychiatric Association, 1994). The response rate is about 70 to 80%, with a delay of one to two weeks before the therapeutic effects occur (Schou, 1993a). A response, in this context, refers to a decrease in the frequency, severity or duration of episodes. It is also reported that lithium itself is ideal for the initial treatment of bipolar depression in untreated patients (Jan et al., 1982), since it eliminates the risk of antidepressants-induced mania (Lewis and Winokur, 1982). Indeed, lithium remains the standard against which new mood stabilizing or thymoleptic drugs are measured (American Psychiatric Association, 1994).

In spite of a great deal of research, it is still not known how lithium works. There are different, sometimes speculative hypotheses concerning the whole field of biological psychiatry (Wood and Goodwin, 1987). Most of the findings are based on preclinical studies, many of them performed in vitro, with some effects occurring more rapidly than clinical responses in human or at higher lithium concentrations than those that are therapeutic in humans.

Despite all reports about the clinical efficacy of lithium, we face the fact that the rate of response to lithium for maintenance treatment of bipolar disorder in practice, is not as much as is claimed in text books (70 to 80%) (Kaplan and Sadock, 1995). Moreover, abrupt lithium discontinuation markedly increases the risk of an early recurrence of bipolar disorder (Schou, 1993b). It has been reported that mania occurs in 25% of patients within three months and in 54% within one year (Klein et al., 1992).

The authors believe that one should never be afraid to re-evaluate the evidence on which the clinical use of lithium has been based. In this study, we tried to have an look at the clinical efficacy of lithium once more through a retrospective record study.

Methods

Subjects

Medical records were examined from Roozbeh Psychiatric Hospital for patients who met the DSM-III-R diagnostic criteria for bipolar I disorder (American psychiatric Association 1987)) between 21 March 1987 and 21 March 1997. The records were reviewed by Emamian E. S. using a structured data sheet. Patients' records were included if the patients had had one admission to Roozbeh psychiatric Hospital before lithium maintenance therapy (episode -2) and two or more admissions after lithium therapy (episodes 0,1,2), did not systematically refuse treatment and were not experiencing a mixed episode. In another words, patients started lithium therapy from episode -1.

Only 48 patients met clearcut criteria for our study. There were 32 women and 16 men; their mean ± SD age was 35.866 ± 10.431 years. There are several methodological limitations to the design of this study which should be noted. The study is a retrospective record work, it is naturalistic and depends upon observations made by clinicians and not by researchers. An important complication of this study was that it was impossible to know exactly whether a patient's episode was due to lithium discontinuation (lithium withdrawal) or not. We sought to determine only the length between episodes (frequency) and type of episode before and after lithium maintenance therapy.

Data Analysis

One-way Analysis of variance (ANOVA) and Fisher's exact test were used to compare the length between episodes and type of episode before and after lithium therapy. Results are presented as mean ± SD.

Results

48 patients who met the DSM-III-R diagnostic criteria for bipolar I disorder and had been admitted to Roozbeh Psychiatric Hospital once before lithium therapy and twice or more after that, were

eligible for inclusion in the outcome study.

Length Between Episodes Before and After Lithium Therapy.

A one-way ANOVA showed no significant difference in length between episodes, before and after lithium maintenance therapy (F=0.8036; P=0.4939) (Table. 1). In another words, lithium did not decrease the frequency of episodes.

Type of Episode.

Comparison of percentage of type of episode that occurred before and after lithium maintenance therapy showed a significant difference (Table. 2).

Fisher's exact test with a two-tailed P value revealed a significant difference between episode -1 (before lithium therapy) and episode 0 (after lithium therapy) (P<0.0001). Moreover, the difference between episode -1 and episode 1 (the second episode after lithium therapy) was even greater than the first episode after lithium therapy (P<0.0001). In another words, after lithium maintenance therapy, patients had more manic episodes than depression.

Table 1

Length Between Episodes Before and After Lithium Maintenance Therapy (Months)

Length Between Episodes	Length Between Episodes	Length Between Episodes	Length Between Episodes
(-2) & (-1)	(-1) & (0)	(0) & (1)	(1) & (2)
mean ± SD	mean ± SD	mean ± SD	mean ± SD
25.8±16.788	26.659±22.378	30.562±25.993	22.28±20.184

Table 2

Type of Episode Before and After Lithium Maintenance Therapy

	Episode (-1)	Episode (0)	Episode (1)
Mania	58%	90%	98%
Depression	42%	10%	2%

Discussion

Lithium is a generally accepted therapy in manic states and in the prophylaxis of bipolar disorder (Peselow et al 1994). It has been reported that lithium is effective in both the short-term treatment and prophylaxis of bipolar I disorder in about 70 to 80 percent of patients (American Psychiatric Association 1994). However, in practice it is difficult to achieve this percentage. Several points should be considered before discussing these results. Most important, this was a retrospective record study with its own limitations. Nevertheless, the authors could compare exactly the frequency of episodes (length between episodes). Lithium would be expected to decrease the frequency, severity or duration of episodes. However, the results indicate that lithium failed to decrease the frequency of episodes. Due to limitations of this study, we could not determine the effects of lithium on the severity of episodes. On the other hand, it has been reported that one of advantages of lithium therapy in bipolar disorder is that lithium might protect against tricyclic antidepressants-induced mania (Lewis and Winokur 1982). However, this study showed that lithium may not be effective in preventing manic episodes. In addition, the proportion of manic episodes was greater after lithium therapy compared to before. This result is in agreement with the report of Solomon et al (1990). Nevertheless, the authors could not determine whether these manic episodes were due to lithium discontinuation or not. On the other hand, the risk of discontinuation always should be considered in our evaluations.

Conclusions

Overall, although lithium is still the most commonly used short-term and prophylactic treatment for bipolar I disorder, one should not be afraid to re-examine the efficacy of lithium in bipolar disorder and this suggestion is in line with Moncrieff's report (1995).

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