

The Therapeutic Effects of Lithium in Affective Disorders

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Summary

Objective The main objective of this research was to explore the psychopathological aspects of affective disorder and the clinical effects of pharmacological treatment with lithium.

Materials and Methods: The study involved 40 patients (26 females, 14 males) with an average age 45,5 years, hospitalized in the Psychiatric Hospital in Skopje and the Department of Psychiatry of Clinical Hospital in Tetovo, with a clinical diagnosis of affective disorder. The diagnosis of affective disorder is set against the classification DSM-IV (Diagnostic and Statistical Manual of Mental Disorder). All subjects were under pharmacological treatment with lithium carbonates whose dose depends of the clinical subentity, the beginning and duration of the disorder. Clinical-laboratory examinations included: history and clinical status, determination of serum lithium concentration. The serum lithium concentrations were measured by Ion-Selective Electrode (ISE) with the COBAS/INTEGRA 700 analyzer.

Results: The results of the research show us that patient with acute phase of mania had higher concentration of lithium in serum compared with patients with bipolar affective psychosis. Also the patients who received combination therapy (lithium/neuroleptic or antidepressant) mean values of lithium in serum range 1,89 mmol/L compared to patients who only used lithium whose mean values are 0,82 mmol/L. Pearson correlation between two groups was significantly significant at the level of 0,01.

Conclusions: With the regular and continued use of lithium in affective disorders and good co-operation with the patient during the therapy could be reduced the relapses of the disease and improved the quality of life of the person.

Key words: affective disorder, lithium therapy, quality of life

Introduction

Bipolar disorders, also called maniac-depressive psychosis, are a group of disorders that cause mood fluctuations characterized by phases of depression and phases of mania. Manic episodes are characterized by a predominantly elevated, expansive or irritable mood that presents as a prominent or persistent part of the illness. Manic patients classically have abundant resources of energy and engage in multiple activities and ventures. At baseline and between episodes, the bipolar manic patient may indeed function at a high level of productivity, particularly in areas requiring creative talent. The mood is often accompanied by a sense of absolute conviction or certitude, usually involving a self-perceived talent or perception, but occasionally centering around more metaphysical and cosmic matters.

On the other hand a variety of studies have distinguished depressed individuals with prominent psychomotor retardation and anhedonia from those who evidence psychomotor activation, guilt, anxiety, depressive thinking and depressive affect. Patients with bipolar disorder, mixed type, may likewise exhibit features of severe depression, but will also present manic symptoms.

Mood changes are a normal part of life. However, with bipolar disorders, the swings are more extreme. They become so intense, that the person does not realize that he/she is not behaving normally or the person suffers as much from depression that he/she is paralyzed and overwhelmed by suicidal thoughts. These states may cause problem at work, with the family, with finances and sometimes with legal authorities.

The etiology of affective psychosis is very complex (Lenox, 2003; Paunovic, 1999). Today generally is accepted hypothesis for multifactorial genesis for this group of psychosis. Among most important etiologic factors include: genetic, biochemical, neuropsychological and psychological, as well as a great number of socio-cultural and psychosocial factors.

Treatment of bipolar disorder depends upon the specific form of behavioral disorder. Several definitions for mood stabilizer have been proposed. In the most definition, three models of clinical action for bipolar disorder are required: antimanic, antidepressive and prophylactic effects. Lithium is the first and only mood stabilizer in which these three reactions were confirmed and thus it is the first drug of choice in the treatment for bipolar disorder in spite of availability of alternative mood stabilizers, in less stringent criteria. However, a significant percentage of bipolar patients show no or a partial response to lithium treatment. Selecting an appropriate mood stabilizer is still a matter of great concern for many clinicians.

Ever since Cade (1949) observed the antimanic effect of lithium and Schow et al. (1954) conducted extensive clinical studies to elucidate its application in the treatment of affective disorders, reports continue to appear in the world literature.

Hartigan (1963) for the first time reported on the prophylactic effects of lithium on manic as well as depressive episodes. This property, of lithium was later on confirmed by studies comparing frequency and intensity of episodes of mania and depression before and after administration of lithium (Dodan, 2003; Kalicanin, 2004). Bertelson (2007) confirmed that treatment with lithium reduced the number of relapses and hospital admissions. However, experience over the following 30 years indicated that lithium carbonate is the best mood stabilizer for this kind of psychosis.

Lithium is a metallic element widespread in nature. In psychiatry, lithium is used in the form of easily dissociating salts and the most common preparations are lithium carbonates and citrates. The therapeutic action is displayed by lithium cations, which are easily absorbed in the gastrointestinal tract after oral intake and are not bind by plasma proteins. The maximum blood concentrations appear 2-4 hours after the intake (Carno et al., 2001).

Jope (1999) showed that lithium salts were more effective in the concentration of 0,8-1,2 mmol/L in the plasma than at the level of 0,4-0,6 mmol/L. However, higher lithium concentrations caused the occurrence and intensification of side effects of lithium therapy. So monitoring serum lithium concentrations is accepted as a necessary feature of lithium therapy, because the consequences of lithium toxicity can be quite serious.

So the aim of the present study is to examine the effect of treatment with lithium in patients with affective disorder and relationship between the clinical picture and serum lithium concentration.

Materials and methods

Sample collection

The study included 40 patients (26 females, 14 males) with a mean age of 45,5 years and with a clinical diagnosis of affective disorder (unipolar mania, unipolar depression and bipolar disorder). The diagnosis of affective disorder is set

against the classification DSM-IV (Diagnostic and Statistical Manula of Mental Disorder) published by the American Psychiatric Association (APA, 2004).

All the subjects were treated hospitality in the Psychiatric Hospital in Skopje and the Department of Psychiatry of Clinical Hospital in Tetovo. The patients had not clinical evidence of a medical or neurological illness that could be responsible for psychiatric symptoms, not any history of alcohol or drug abuse, head trauma, neurologic or somatic disorder. The patients have been treated with lithium carbonats, neuroleptic medication and antidepressants.

Before patient was started on lithium therapy in each patient these following biochemical measures have been conducted:

- * Electrocardiogram
- * Complete haemogram and urianalysis.
- * Determination of blood urea, blood sugar, serum creatinine, serum cholesterol, serum electrolytes (Na^+ , K^+).
- * Liver function.
- * Weight charting.

We divided the sample in the two groups: 20 patients with acute symptoms of affective disorder and 20 patients with chronic form of the same disorder. In the first group daily dose of lithium was from 900-1800 mgr. in combination with neuroleptic or antidepressant, while in the second group the daily dose of lithium was 600-1200 mgr. After 48 to 72 hours of commencement of lithium blood samples were drawn twelve hours after the last oral dose of lithium. For the first six months the patients were reviwed once in 2-3 weeks and later in longer intervals. During each review serum lithium was estimated, besides recording clinical assessment, side-effects, weight charting and use of other concomitant medication. Every patients was informed about possible side effects and an instruction sheet for the same provided.

Lithium determination by Ion – Selective Electrode

The serum lithium was estimated by the Ion-Selective Electrode (ISE module) with the COBAS/INTEGRA 700 chemical analyzer from Roche Diagnostics (Switzerland). All the analyses were done at the Department of Clinical Biochemistry in Skopje.

Lithium is measured in the COBAS/INTEGRA 700 Na/K/Li analyzer by the interaction of lithium with ionophore contained in a polyvinyl chloride membrane. We measured sodium by a sodium-sensitive glass capillary and potassium by use of a polyvinyl chloride/valinomycin electrode enbrane.

The instrument aspirated 120 μL of serum into sequential chambers that housed the sodium, potassium, lithium and reference electrodes. The instrument automatically performed a one-point calibration after each sample and initiated a three-point calibration every 3 hours. Daily and weekly maintaince was performed as specified in the operation manual. Serum specimens analyzed in the ISE instrument required no pre-treatment. The reference values for lithium were 0,5-1,5 mmol/L.

Results

As shown in table 1 the majority of patients had bipolar psychosis (60%) followed by unipolar-manic episode (40%).

Table1. Distribution of patients according to the type of affective disorder

Diagnosis	N	%
Manic phase	16	40
Bipolar disorder	24	60
Total	40	100

Also we found that most of patients 25 (62,5%) used lithium together with neuroleptic or antidepressant, while 15 (37,5%) patients were treated only with therapy of lithium carbonats (Table 2).

Table2. Distribution of patients according to the form of therapy

Therapy	N	%
Lithium	15	37.5
Lithium/neuroleptic/antidepressant	25	62.5
Total	40	100,00

Manic patients showed significantly higher mean lithium serum levels as compared with the group of subjects with bipolar psychosis (Table 3). The correlation of statistical significance by Pearson between the two groups is at the level of 0,01.

Table3. Mean serum lithium levels and the type of affective disorder

Li mmol/l	Manic phase	Bipolar disorder
N	16	24
Mean	1.767	1.312
Std. Deviation	0.581	0.640
Pearson Correlation	1	0.784**

** . Correlation is significant at the 0.01 level

From the Figure 1 it is clear that patients in the manic phase of affective disorder had higher values of lithium in blood, because they had been treated with higher doses of lithium carbonats. It is very important, because if patients in this phase take the lowest doses of lithium, the risk of relapse of illness is very high.

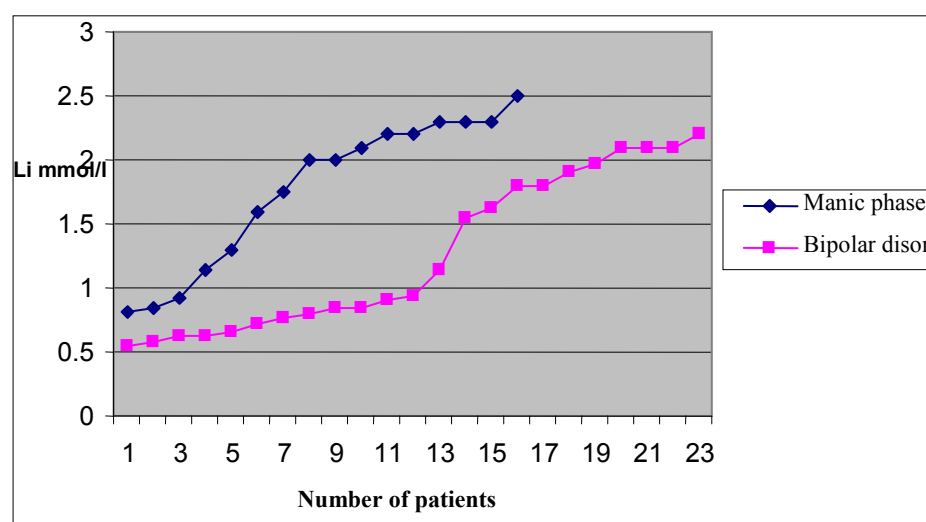


Figure1. Mean serum lithium levels and the type of affective disorder

Table 4 shows the mean serum lithium levels and relationship between the duration of psychoses and serum levels in the two lithium intake groups. There were significant differences in mean serum levels of lithium in comparisons among two subgroups of patients with affective disorders.

Table4. Mean serum lithium levels according to the duration of psychosis

Li mmol/l	Mean	Std. Deviation	N	Pearson Correlation
6 months to 1 year	2.078	0.238	20	1
1 to 5 years	0.911	0.308	20	0.903**

** . Correlation is significant at the 0.01 level

In our study we observed that patients in acute phase of affective disorder had higher concentration of lithium in serum compared with chronic group ($p < 0,01$) (Figure 2). There is an interesting trend, which warrants further investigation for lithium to rise with duration of hospitalization

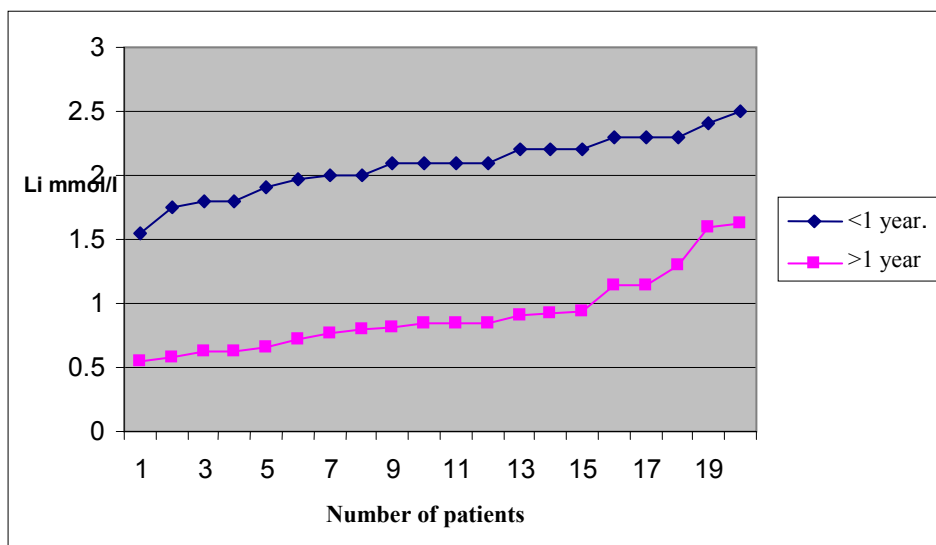


Figure2. Mean serum lithium levels according to the duration of psychosis

Antipsychotic or antidepressant drugs are used extensively in the maintenance treatment of patients with bipolar disorder. For rapid-cycling bipolar, the combination therapy (lithium/neuroleptic or antidepressant) stabilize mood swings. So in our studied population we observed that in patients who received lithium together with the other psychopharmacological drugs mean values of serum lithium range 1,895 mmol/L compared to patients who used only lithium where the mean values of serum lithium was only 0,827 mmol/L (Table 5).

Table5. The form of therapy and mean serum lithium levels

Li mmol/l	Lithium	Li/neuroleptic/antidepressant
N	15	25
Mean	0.827	1.895
Std. Deviation	0.226	0.460
Pearson Correlation	1	0.819**

** . Correlation is significant at the 0.01 level

This investigation suggest that longterm treatment with antipsychotic drugs enables a proportion of patients with bipolar disorder to experience periods of greater stability. The mechanisms involved may be primarily antimanic, but result in less subseguement depression, as a argued for lithium.

Discussion

Our emotional goal is to be happy. Unfortunately some people can not reach their goal of happiness. This disorder is called depression. Not only to those who suffer depression try to find ways to become happy again, but also others who want to help are in a constant search to find a means to offset depression. One way to offset depression is through medication and one of the many medications is lithium.

Lithium has been found to be effective in manic-depressive disorder. Manic-depressive disorder (also called bipolar or affective disorder) is a mood disorder in which a person alternates between depression and mania. Mania (or a manic episode) is a mood disorder in which a person tends to be hyperactive and wildly optimistic. A person suffering from a manic phase is overtalkative, overactive, elated, loud and hard to understand. He or she has little need for sleep, shows fewer sexual inhibitions and has grandiose optimism. Lithium aids to control

manic episodes, but is not as effective at controlling depressive episodes. This is why patients who respond to lithium most effectively are those with bipolar psychosis and a predominant behavior of mania. Patient whose behavior alternates between manic and depressive often, do less well with lithium treatment (Bohacek, 1986; Compton, Nemeroff, 2000; Siever, 1987; Solomon et al., 1996).

A large number of clinical research studies on psychopathological predictors of lithium response has been reported. As predictors of positive lithium response, the following have been reported: euphoric mood, small number of episodes, maniac-depression-free interval pattern in the illness course and positive family history (Chand, Marroo and Sharan, 2004; Maj, Pirozzi and Magliano, 1996). In contrast, the following have been confirmed as predictors of poor lithium response: mixed states, psychotic features, depression-mania-free interval pattern, rapid cycling and comorbid alcohol and/or drug abuse (Carrol, 1999; Maj, Pirozzi and Starace, 1989).

During our research we followed serum levels of lithium in blood during initial treatment (acute episode of the disease) and maintenance treatment (patients with chronic disease). We found that during continuously and long-term use of lithium response is positive in all subjects, but lithium especially shows its activity in the early stages of acute mania states. In all the two groups of lithium intake, a dose range of 300 mg to 1800 mg was sufficient to bring about the desired clinical response and an increase in dosage of lithium is accompanied by a corresponding increase in the values of level which always remained within the recommended therapeutic range, through mostly on the lower side. The clinic research suggest that the levels from 0,4 to 0,8 mg would suffice for prophylaxis, thought recognizing the need for higher levels of 0,6 – 1,2 mg for controlling acute manic episodes. Also patients who received combination therapy (lithium with the other psychopharmacological drugs) had higher concentration of lithium in serum. At the same time determining the concentration of lithium in serum serves as a valid indicator for monitoring the dose. We would expect that patients treated with a combination of lithium and neuroleptic/antidepressant drugs would respond significantly better than patients treated with either drug alone.

Mood disorders can be chronic and recurrent and they are associated with high preterm mortality due to a high risk of suicidal attempts and increased exposure to somatic illnesses compared o rhe general population (Swann, Bowden and Morris, 1997). Mode disorders have serious consequences, like the deteriorated quality of family and professional life, among patients and their families.

Also lithium does not cure recurrent affective disorder, it must be given continuously to prevent relapses (Angst and Wels, 1970). 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.

Conclusions

Although has been used in psychiatry for many years, during which new medications producing similar effects have been introduces, it remarks a medicine of the first choice long-term stabilizing therapy, in the light of current research, lithium monotherapy in acute manic conditions or severe and moderate depressive episodes is not ecommended. It is known that psychiatrist can prevent complications related to lithium therapy if they continually monitoring of its plasma level and observing the patient to detecting side effects.

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