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EFFECTIVENESS AND SAFETY OF LOW-DOSE LITHIUM AUGMENTATION IN REDUCING SUICIDAL IDEATION AND SUICIDAL BEHAVIOUR AMONG PSYCHIATRIC PATIENTS: A 6-MONTH HOSPITAL-BASED FOLLOW-UP STUDY.

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Abstract

Background: Suicide is a major global public health concern and remains one of the leading causes of preventable mortality. Individuals with suicidal ideation and suicidal behaviour often have underlying psychiatric disorders and require interventions that specifically target suicidality. Although lithium has demonstrated anti-suicidal properties in mood disorders, evidence regarding its effectiveness as an adjunctive treatment among high-risk psychiatric patients in tertiary care settings remains limited. ***Objectives:*** To evaluate the effectiveness and safety of low-dose lithium augmentation in reducing suicidal ideation and suicidal behaviour among psychiatric patients receiving treatment as usual (TAU). ***Methods:*** A hospital-based prospective follow-up study was conducted in the Department of Psychiatry at Government Hospital for Mental Care and King George Hospital, Visakhapatnam, Andhra Pradesh, India, from February 2024 to January 2025. Ninety participants aged 18–60 years with suicidal ideation and/or suicidal behaviour and a Mini International Neuropsychiatric Interview–Suicidality (MINI-S) score >8 were enrolled and equally allocated to either the Lithium + TAU group (n = 45) or the TAU-only group (n = 45). Participants in the intervention arm received oral lithium 450 mg/day in addition to standard psychiatric treatment, with serum lithium levels maintained between 0.5 and 0.8 mEq/L. Assessments were performed at baseline, 1 month, 3 months, and 6 months using the MINI-S, Columbia-Suicide Severity Rating Scale (C-SSRS), and Clinical Global Impression–Severity (CGI-S) scale. Data were analysed using independent t-tests, Chi-square tests, Fisher's exact tests, and repeated measures analysis of variance. A p-value <0.05 was considered statistically significant. ***Results:*** All participants were classified as having high suicide risk (MINI-S score ≥17) at baseline, with comparable illness severity between groups (mean CGI-S score: 4.84 ± 0.95 vs 4.93 ± 0.78; p = 0.618). The Lithium + TAU group demonstrated a significant reduction in C-SSRS ideation scores from 3.11 ± 0.85 at baseline to 0.27 ± 0.58 at six months (p < 0.001), representing a 91.3% decrease. Compared with TAU alone, lithium augmentation produced significantly greater reductions in suicidal behaviour at 1 month (−1.84 vs −0.57; p < 0.001), 3 months (−2.06 vs −1.11; p < 0.001), and 6 months (−2.09 vs −1.86; p = 0.016). Greater reductions in overall suicidality, as measured by MINI-S scores, were observed in the Lithium + TAU group at all follow-up points, with a mean reduction of 35.31 points compared with 21.83 points in the TAU group at six months (p < 0.001). Clinical improvement was also significantly greater in the lithium group, with a mean CGI-S reduction of 3.40 points compared with 2.73 points in the TAU group at six months (p < 0.001). Lithium was generally well tolerated; tremor (26.7%) was the most common adverse effect, while serious adverse events were uncommon. ***Conclusion:*** Low-dose lithium augmentation, when added to treatment as usual, was significantly more effective than treatment as usual alone in reducing suicidal ideation, suicidal behaviour, overall suicidality, and illness severity among high-risk psychiatric patients. The anti-suicidal benefits were evident within the first month of treatment and were sustained over six months. With appropriate clinical and laboratory monitoring, low-dose lithium appears to be a safe and effective adjunctive strategy for suicide prevention in carefully selected patients.

Keywords: Suicide prevention; Lithium augmentation; Suicidal ideation; Suicidal behaviour; Mood stabilisers; Columbia-Suicide Severity Rating Scale.

INTRODUCTION

Suicide is a major public health problem and one of the leading causes of preventable death worldwide. It represents a complex behavioural outcome influenced by biological, psychological, social, cultural and environmental factors. According to the World Health Organization, more than 720,000 people die due to suicide every year, and for every completed suicide, many more individuals attempt suicide. Suicide is particularly important among young adults, where it remains one of the major causes of mortality. A large proportion of global suicides occur in low- and middle-income countries, where access to mental health services, early identification and structured suicide-prevention interventions may be limited. [1] India contributes substantially to the global burden of suicide because of its large population, rapidly changing social structure, economic stressors, family-related problems, substance use, academic and occupational stress, and variable access to mental healthcare. Community-based data from India have shown that suicide mortality is high among young and middle-aged adults, and suicidal deaths impose a significant burden on families and society.[2] In the Indian setting, suicide prevention requires special attention because patients often present late to psychiatric services, and many individuals with suicidal ideation or behaviour may have underlying mood disorders, psychotic disorders, substance use disorders or adjustment-related problems.

Suicidal behaviour exists on a spectrum ranging from passive death wishes and suicidal ideation to suicide planning, suicide attempts and completed suicide. Suicidal ideation is clinically important because it may precede suicidal acts and provides an opportunity for early intervention. However, prediction of suicide remains difficult in clinical practice because suicidal behaviour is heterogeneous and may vary according to age, gender, psychiatric diagnosis, personality traits, impulsivity, family support, psychosocial stressors and previous suicide attempts. [3] Therefore, patients presenting with suicidal ideation or suicidal behaviour require systematic assessment, close follow-up and appropriate pharmacological and psychosocial interventions. Psychiatric disorders are among the strongest risk factors for suicide. Mood disorders, particularly bipolar disorder and major depressive disorder, are closely associated with suicidal ideation and suicidal attempts. Psychotic disorders, substance use disorders, personality disorders and severe anxiety-related conditions may also increase suicide risk. In many patients, suicidality is further aggravated by impulsivity, hopelessness, aggression, poor coping skills, interpersonal conflicts, financial problems, marital disharmony and adverse life events. Although treatment as usual, including antidepressants, antipsychotics, mood stabilisers, psychotherapy and crisis intervention, may reduce overall psychiatric morbidity, there remains a need for interventions that specifically reduce suicidal ideation and suicidal behaviour. [4]

Lithium has been used in psychiatry for more than seven decades and remains one of the most important mood stabilisers in clinical practice. Traditionally, lithium has been used in the treatment and prophylaxis of bipolar disorder, recurrent mood disorders and augmentation of antidepressant treatment. Beyond its mood-stabilising effect, lithium has attracted attention because of its possible specific anti-suicidal property. Several studies have suggested that lithium may reduce suicide attempts and completed suicide among patients with mood disorders, and this effect may be partly independent of its effect on mood stabilisation. [5] The anti-suicidal action of lithium is thought to be mediated through multiple mechanisms. Lithium may enhance serotonergic neurotransmission, reduce impulsivity and aggression, modulate intracellular signalling pathways, inhibit glycogen synthase kinase-3, reduce inflammatory mechanisms, and promote neuroprotective and neuroplastic changes. These biological effects may improve emotional regulation, reduce behavioural dyscontrol and decrease the likelihood of acting on suicidal thoughts. [6] Such mechanisms are clinically relevant because impulsivity, aggression and affective instability are important contributors to suicidal behaviour in high-risk psychiatric populations.

Evidence from systematic reviews and meta-analyses supports the role of lithium in suicide prevention, especially among patients with mood disorders. Cipriani et al. reported that lithium was associated with a reduced risk of suicide and all-cause mortality in individuals with mood disorders. [7] However, most available studies have focused on selected diagnostic groups such as bipolar disorder or recurrent depression, and many were conducted in outpatient or long-term maintenance settings. There is comparatively limited evidence from tertiary care hospital settings, where patients often present with severe symptoms, active suicidal ideation, recent suicidal behaviour, multiple comorbidities and psychosocial stressors. In this context, evaluating lithium augmentation among individuals presenting with suicidal ideation and suicidal behaviour in a tertiary care setting is clinically relevant. Low-dose lithium, when carefully prescribed and monitored, may be a useful adjunct to treatment as usual in reducing suicidality. However, because lithium has a narrow therapeutic index, assessment of tolerability, adverse effects, compliance and serum lithium levels is essential. Therefore, the present study was undertaken to assess the effectiveness and safety of low-dose lithium augmentation in reducing suicidal ideation and suicidal behaviour among psychiatric patients attending a tertiary care centre over a six-month follow-up period.

AIMS AND OBJECTIVES

Primary Objective

To evaluate the effectiveness of low-dose lithium augmentation in reducing suicidal ideation and suicidal behaviour among psychiatric patients receiving treatment as usual.

Secondary Objectives

1. To compare changes in suicidality scores between the Lithium + Treatment as Usual (TAU) group and the TAU-only group over six months.
2. To assess clinical improvement using the Clinical Global Impression (CGI) scale.
3. To evaluate treatment adherence and tolerability of lithium augmentation.
4. To assess the safety profile of low-dose lithium therapy.

MATERIALS AND METHODS

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Secondary Objectives

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2. To assess clinical improvement using the Clinical Global Impression (CGI) scale.
3. To evaluate treatment adherence and tolerability of lithium augmentation.
4. To assess the safety profile of low-dose lithium therapy.

MATERIALS AND METHODS

Study Design

Hospital-based prospective follow-up study.

Study Setting

Department of Psychiatry, Government Hospital for Mental Care and King George Hospital, Visakhapatnam, Andhra Pradesh, India.

Study Duration

February 2024 to January 2025.

Study Participants

A total of 90 participants with suicidal ideation and suicidal behaviour were enrolled and allocated equally into two groups:

* Lithium + TAU group (n = 45)
* TAU-only group (n = 45)

Eligibility Criteria

Inclusion criteria:

* Age between 18 and 60 years.
* Presence of suicidal ideation and/or suicidal behaviour.
* MINI-S score greater than 8.
* Provision of informed consent by participants and caregivers.

Exclusion criteria:

* Significant cardiac, renal, endocrine, or neurological disorders.
* Pregnancy or lactation.
* Current use of medications contraindicated with lithium.
* Previous lithium therapy within the last six months.
* Acute alcohol intoxication or withdrawal requiring emergency intervention.

Intervention

Participants in the intervention arm received oral lithium 450 mg/day in addition to treatment as usual. Serum lithium levels were assessed after one week and dosage was adjusted to maintain therapeutic concentrations between 0.5 and 0.8 mEq/L.

Follow-up Assessments

Participants were assessed at baseline, 1 month, 3 months, and 6 months.

Statistical Analysis

Data were analysed using SPSS version 22.0. Continuous variables were summarised as mean ± standard deviation or median (interquartile range). Categorical variables were expressed as frequencies and percentages. Independent t-test or Mann-Whitney U test was used to compare continuous variables, while Chi-square test or Fisher's exact test was used for categorical variables. Repeated measures analysis of variance or mixed-effects models should be used to assess changes in suicidality scores across follow-up visits. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 90 participants with suicidal ideation and/or suicidal behaviour were enrolled and followed for six months. Participants were equally allocated to the Lithium plus Treatment as Usual (TAU) group (n = 45) and the TAU-only group (n = 45). All participants completed baseline assessments and follow-up evaluations at 1 month, 3 months, and 6 months using the Mini International Neuropsychiatric Interview–Suicidality (MINI-S), Columbia-Suicide Severity Rating Scale (C-SSRS), and Clinical Global Impression (CGI) scale.

Table 1. Baseline MINI-S Risk Categories in Both Groups

MINI-S Risk Category	Lithium + TAU (n = 45)	TAU (n = 45)	Total (n = 90)	P value
Low (1–8)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.000
Moderate (9–16)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1.000
High (≥17)	45 (100.0%)	45 (100.0%)	90 (100.0%)	1.000

Interpretation: All participants in both study groups were classified as having high suicide risk (MINI-S score ≥17) at baseline, confirming that the study population represented a clinically severe, high-risk cohort with no significant difference between groups at enrolment.

Table 2. Baseline Clinical Global Impression–Severity (CGI-S) Scores

Variable	Lithium + TAU (n = 45)	TAU (n = 45)	P value
Mean CGI-S score (Mean ± SD)	4.84 ± 0.95	4.93 ± 0.78	0.618
Mildly ill, n (%)	5 (11.1%)	3 (6.7%)	0.887
Moderately ill, n (%)	10 (22.2%)	14 (31.1%)	
Markedly ill, n (%)	17 (37.8%)	14 (31.1%)	
Severely ill, n (%)	13 (28.9%)	14 (31.1%)	

Interpretation: Baseline illness severity was comparable between the two groups. Most participants were classified as markedly ill or severely ill, indicating a substantial burden of psychiatric symptoms at study entry.

Table 3. Changes in C-SSRS Ideation Scores in the Lithium + TAU Group

Time Point	Mean Score ± SD	Mean Change from Baseline	P value
Baseline	3.11 ± 0.85	–	–
Month 1	1.16 ± 0.80	−1.95	<0.001
Month 3	0.33 ± 0.56	−2.78	<0.001
Month 6	0.27 ± 0.58	−2.84	<0.001

Interpretation: Participants receiving lithium augmentation demonstrated a rapid and sustained reduction in suicidal ideation. The mean C-SSRS ideation score decreased by 91.3% from baseline to six months, with statistically significant improvement observed as early as the first month.

Table 4. Comparison of Changes in C-SSRS Behaviour Scores Between Study Groups

Time Period	Mean Change: Lithium + TAU	Mean Change: TAU	Between-Group Difference	P value
Baseline to Month 1	−1.84	−0.57	−1.27	<0.001
Baseline to Month 3	−2.06	−1.11	−0.95	<0.001
Baseline to Month 6	−2.09	−1.86	−0.23	0.016

Interpretation: Both groups showed reductions in suicidal behaviour over time; however, the Lithium + TAU group exhibited significantly greater improvements at all follow-up points. The largest between-group difference was observed during the first month of treatment, suggesting an early anti-suicidal effect of lithium augmentation.

Table 5. Comparison of Changes in MINI-S Scores Between Study Groups

Time Period	Mean Change: Lithium + TAU	Mean Change: TAU	Between-Group Difference	P value
Baseline to Month 1	−30.51	−17.91	−12.60	<0.001
Baseline to Month 3	−32.98	−20.00	−12.98	<0.001
Baseline to Month 6	−35.31	−21.83	−13.48	<0.001

Interpretation: The Lithium + TAU group demonstrated significantly greater reductions in overall suicidality compared with TAU alone at every follow-up assessment. By six months, the reduction in MINI-S score was 61.8% greater in the lithium group, indicating superior efficacy of lithium augmentation in reducing suicide risk.

Table 6. Comparison of Changes in CGI-S Scores Between Study Groups

Time Period	CGI-S Change: Lithium + TAU	CGI-S Change: TAU	Between-Group Difference	P value
Baseline to Month 1	−1.97	−1.82	−0.15	0.042
Baseline to Month 3	−2.64	−2.26	−0.38	0.018
Baseline to Month 6	−3.40	−2.73	−0.67	<0.001

Interpretation: Clinical improvement was observed in both groups; however, participants receiving lithium augmentation showed significantly greater reductions in overall illness severity. The magnitude of improvement increased progressively over time, suggesting sustained therapeutic benefits with continued lithium use.

Table 7. Adverse Effects Reported in the Lithium + TAU Group

Adverse Effect	**Frequency (n = 45)**	**Percentage (%)**
No adverse effects	18	40.0
Tremor	12	26.7
Polyuria/Polydipsia	5	11.1
Sedation	4	8.9
Multiple adverse effects	4	8.9
Nausea/Vomiting	2	4.4
Weight gain	2	4.4
Gastrointestinal disturbances	1	2.2
Hypothyroidism	1	2.2

Interpretation: Lithium augmentation was generally well tolerated. Forty percent of participants reported no adverse effects. Tremor was the most common side effect, followed by polyuria/polydipsia and sedation. Serious adverse events were uncommon, and only one participant developed hypothyroidism during the follow-up period.

Summary of Findings

The present study demonstrated that low-dose lithium augmentation, when added to treatment as usual, resulted in significantly greater reductions in suicidal ideation, suicidal behaviour, overall suicidality, and clinical illness severity compared with treatment as usual alone. Improvements were evident from the first month of treatment and were sustained throughout the six-month follow-up period. Lithium was generally well tolerated, with predominantly mild and manageable adverse effects.

DISCUSSION

The present hospital-based follow-up study evaluated the effectiveness and safety of low-dose lithium augmentation in reducing suicidal ideation and suicidal behaviour among psychiatric patients receiving treatment as usual. The study included 90 participants, with 45 patients in the Lithium + TAU group and 45 patients in the TAU-only group. At baseline, all participants in both groups belonged to the high-risk MINI-S category, indicating that the study population consisted of clinically severe suicidal patients. The baseline CGI-S scores were also comparable between groups, with mean scores of 4.84 ± 0.95 in the Lithium + TAU group and 4.93 ± 0.78 in the TAU group, showing that both groups had similar illness severity before intervention. In the present study, lithium augmentation produced marked improvement in suicidal ideation. The mean C-SSRS ideation score in the Lithium + TAU group decreased from 3.11 ± 0.85 at baseline to 1.16 ± 0.80 at 1 month, 0.33 ± 0.56 at 3 months and 0.27 ± 0.58 at 6 months. The overall mean reduction from baseline to 6 months was 2.84 points, which was statistically significant ($p<0.001$). This indicates that lithium had a rapid and sustained effect on suicidal ideation. This finding is supported by Tondo et al., who reported that long-term lithium treatment was associated

with a lower risk of suicide in patients with major affective illness. [8] Similarly, Goodwin et al. observed that patients with bipolar disorder treated with lithium had a lower risk of suicidal behaviour compared with those receiving divalproex.[9]

The reduction in suicidal behaviour was also greater in the Lithium + TAU group compared with the TAU group. The mean C-SSRS behaviour score in the Lithium + TAU group reduced by 1.84 points at 1 month, 2.06 points at 3 months and 2.09 points at 6 months, while the TAU group showed reductions of 0.57, 1.11 and 1.86 points at the same time points. The between-group differences were statistically significant at all follow-up points, with $p<0.001$ at 1 month and 3 months and $p=0.016$ at 6 months. These findings suggest that lithium augmentation was more effective than TAU alone in reducing suicidal behaviour, particularly during the early phase of treatment. Gonzalez-Pinto et al. similarly reported that good adherence to long-term lithium treatment was associated with lower suicidal risk among patients with bipolar I disorder. [10] The MINI-S score showed substantial improvement in both groups, but the improvement was significantly greater in the Lithium + TAU group. In the Lithium + TAU group, the mean MINI-S score decreased from 40.09 ± 12.62 at baseline to 9.58 ± 7.39 at 1 month, 7.11 ± 5.54 at 3 months and 4.78 ± 4.36 at 6 months. The corresponding mean reductions were 30.51, 32.98 and 35.31 points, respectively, all of which were statistically significant ($p<0.001$). In comparison, the TAU group showed a reduction from 35.27 ± 8.37 at baseline to 17.36 ± 8.27 at 1 month, 15.27 ± 7.38 at 3 months and 13.44 ± 6.96 at 6 months. The between-group difference in MINI-S score reduction was also significant at all time points, with differences of 12.60 at 1 month, 12.98 at 3 months and 13.48 at 6 months ($p<0.001$). This indicates that lithium augmentation had a broader effect on overall suicidality, including suicidal thoughts, intent, plans and behaviour. Guzzetta et al. reported similar anti-suicidal benefits of lithium in recurrent major depressive disorder, suggesting that lithium's protective effect is not limited only to bipolar disorder. [11]

The present findings are clinically important because improvement was seen as early as the first month of treatment. The early reduction in C-SSRS ideation, C-SSRS behaviour and MINI-S scores suggests that lithium may have a relatively rapid anti-suicidal effect when added to standard psychiatric treatment. This is consistent with the review by Lewitzka et al., who described lithium as one of the most consistently supported pharmacological agents for suicide prevention over more than two decades of research. [12] However, the rapid response observed in the present study may also be partly due to close monitoring, family involvement, crisis intervention and structured follow-up in addition to lithium therapy. Clinical improvement assessed using the CGI-S scale also favoured the Lithium + TAU group. The CGI-S score reduced by 1.97 points at 1 month, 2.64 points at 3 months and 3.40 points at 6 months in the Lithium + TAU group. In comparison, the TAU group showed reductions of 1.82, 2.26 and 2.73 points at the same time points. The between-group differences were statistically significant at 1 month ($p=0.042$), 3 months ($p=0.018$) and 6 months ($p<0.001$). These findings indicate that lithium augmentation not only reduced suicidality but also improved overall clinical status. Müller-Oerlinghausen et al. also highlighted that lithium prophylaxis may reduce both suicidality and excess mortality in affective disorders, supporting the broader clinical benefit of lithium treatment. [13]

The safety profile of lithium in the present study was acceptable. Among 45 participants in the Lithium + TAU group, 18 patients (40.0%) reported no adverse effects. The most common adverse effect was tremor, observed in 12 patients (26.7%), followed by polyuria/polydipsia in 5 patients (11.1%), sedation in 4 patients (8.9%), nausea/vomiting in 2 patients (4.4%), weight gain in 2 patients (4.4%), gastrointestinal disturbance in 1 patient (2.2%) and hypothyroidism in 1 patient (2.2%). Multiple side effects were reported by 4 patients (8.9%). These findings suggest that low-dose lithium was generally tolerable when prescribed with proper monitoring. Lauterbach et al., in a randomized placebo-controlled trial, also studied adjunctive lithium in suicidal patients with depressive disorders and emphasized the importance of careful monitoring while using lithium for suicide prevention. [14] Although the present study showed significant benefit with lithium augmentation, findings should be interpreted with some caution. Katz et al., in a randomized clinical trial among veterans with major depression or bipolar disorder and recent suicide-related events, did not find a significant reduction in repeat suicide-related outcomes with lithium added to usual care.[15] This difference may be due to variations in study population, comorbidities, treatment adherence, serum lithium levels, follow-up structure and outcome definitions. The present study had close follow-up at 1, 3 and 6 months, which may have improved adherence and early recognition of worsening suicidality.

Overall, the present study supports the role of low-dose lithium augmentation as an effective adjunctive treatment for reducing suicidal ideation, suicidal behaviour and overall suicidality in high-risk psychiatric patients. The significant reduction in MINI-S, C-SSRS ideation, C-SSRS behaviour and CGI-S scores indicates that lithium produced both symptom-specific and global clinical improvement. The findings are also consistent with Rombold et al., who evaluated adjunctive lithium in suicidal patients with depression and comorbid personality disorder and emphasized the need to identify patient groups who may benefit most from lithium-based suicide-prevention strategies.[16] Therefore, lithium may be considered as a useful adjunct in carefully selected suicidal patients, provided that clinical monitoring, laboratory assessment, patient education and follow-up are ensured.

CONCLUSION

The present hospital-based follow-up study demonstrated that low-dose lithium augmentation, when added to treatment as usual, was significantly more effective than treatment as usual alone in reducing suicidal ideation, suicidal behaviour, and overall suicidality among high-risk psychiatric patients. Participants receiving Lithium + TAU showed substantially greater reductions in C-SSRS ideation scores, C-SSRS behaviour scores, MINI-S scores, and CGI-Severity scores across all follow-up assessments at 1 month, 3 months, and 6 months. The beneficial effects of lithium were evident as early as the first month of treatment and were sustained throughout the six-month follow-up period, indicating both rapid and durable anti-suicidal effects. The Lithium + TAU group demonstrated a mean reduction of 35.31 points in MINI-S scores compared with 21.83 points in the TAU group. Similarly, greater improvements were observed in C-SSRS behaviour scores and overall clinical status, highlighting lithium's efficacy across multiple dimensions of suicidality. Low-dose lithium was generally well tolerated, with tremor, polyuria/polydipsia, and sedation being the most commonly reported adverse effects. Most side effects were mild and manageable with regular clinical and laboratory monitoring, and serious adverse events were uncommon. These findings support the use of low-dose lithium augmentation as an effective and safe adjunctive strategy for suicide prevention in carefully selected psychiatric patients presenting with suicidal ideation and suicidal behaviour. Routine monitoring of serum lithium levels, renal function, thyroid function, and treatment adherence remains essential to optimise therapeutic benefits and minimise adverse effects.

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