

## Should We Use Lithium in Older People Mood Disorders?

Dr. Aziz VM

Consultant psychiatrist, Devon Partnership Trust, England.

*\*Corresponding Author: Dr. Aziz VM, Consultant psychiatrist, Devon Partnership Trust, England.*

### Abstract

*Lithium has been used in bipolar disorder both as monotherapy and in combination with other drugs. In this article, we outline the evidence for lithium use in the treatment of older people with mood disorders.*

**Keywords:** *Lithium, Older people, bipolar affective disorder, mood disorder*

Bipolar disorder (BD) is a heterogeneous disorder characterized by mood alterations. A United Nations report<sup>1</sup> showed that types I and II Bipolar Disorders affect 0.5–1.0% of older adults. Untreated bipolar affective disorder in older people is associated with morbidity and mortality and the diagnosis can be confounded by overlap with other clinical syndromes such as organic mood disorder, dementia, delirium and medical co-morbidities.<sup>2</sup>

Lithium has been used one of the major agents to treat mania, and prevent recurrent episodes in bipolar disorder. Concurrent use of lithium together with antidepressant is effective in the prophylaxis of recurrent depression.<sup>3</sup> Goodwin et al (2016) reported that lithium monotherapy is proved efficient against manic, depressive or mixed episodes and has better evidence for prevention of new episodes than other agents together with reduced risk of suicide in bipolar patients.<sup>4</sup> Additionally, lithium has been used for its anti-suicide effect.<sup>5,6</sup>

Also, the Canadian Network for Mood and Anxiety Treatments guidelines<sup>7</sup>, considered lithium as a first line treatment option in bipolar depression due to its mood stabilizer effect, its effectiveness in preventing mania and its anti-suicide effect.

In older people, the recommended lithium levels for the treatment of mania 0.4–0.8 mmol/L and for the maintenance therapy, serum concentrations are recommended to be 0.4–0.6 mmol/L.<sup>8</sup>

It is important to be cautious with patients with BD in older age as they are at a higher risk of developing adverse effects such as neurocognitive

and neurological symptoms, thyroid and renal side effects.<sup>9,10</sup> Increased age probably imports increased sensitivity to side-effects and toxicity of lithium may be both concentration and time dependent.<sup>11</sup>

Abrupt lithium discontinuation in patients stabilized on the medication can be associated with relapse and severe adverse effects.<sup>12</sup> It is therefore extremely important that clinicians discontinue lithium very slowly.

A systematic review and meta-analysis of clinical predictors of lithium response in bipolar disorder<sup>13</sup> reported that predictors of good response include: mania-depression-interval sequence, absence of rapid cycling, absence of psychotic symptoms, shorter pre-lithium illness duration, family history of bipolar disorder and later illness onset.

From a social, functioning and employment points of view, bipolar disorder is associated with significant functional deficits. Drakopoulos and colleagues<sup>14</sup> reported that executive functioning was a powerful predictor of occupational status in bipolar disorder patients than IQ and other clinical factors, including illness severity. Also, Lithium inhibits Glycogen synthase kinase 3 (GSK3) via Mg<sup>+</sup> competition and increased Ser21 (GSK3) or Ser9 (GSK3) phosphorylation, leading to enhanced myoblast fusion and myogenic differentiation which has implications for the treatment of several cognitive and myopathic conditions.<sup>15</sup> Also, lithium may be beneficial to neurocognitive functioning in patients with bipolar disorder.<sup>16</sup>

## Should We Use Lithium in Older People Mood Disorders?

Widespread fronto-limbic white matter abnormalities and altered White matter connectivity within the corpus callosum and the cingulum were demonstrated in BD.<sup>17</sup>

Neuroimaging techniques identified that long-term lithium treatment is associated with increased total grey matter<sup>18</sup>, increased hippocampal volume<sup>19</sup> and decreased white matter microstructural abnormalities.<sup>20</sup> Research is developing and genome-wide association studies have developed a polygenic risk score for lithium response<sup>21</sup> and biological markers<sup>22</sup>.

In conclusion, mood stabilizers especially lithium, continue to be pivotal in long term treatment of older people affective disorder and lithium remains beneficial and safe in older people. Early intervention and access to specialist services are important to reduce disease burden and improve outcomes. Future research should address outcomes beyond stabilization beyond mood.<sup>23</sup>

### REFERENCES

- [1] Population Division. Department of Economic and Social Affairs; United Nations: World Population Ageing: 1950-2050
- [2] McDonald WM. Epidemiology, aetiology and treatment of geriatric mania. *J Clin Psychiatry* 2000; 61 (13): 3-11
- [3] Souza FGM & Goodwin GM. Lithium treatment and prophylaxis in unipolar depression: a meta-analysis. *British Journal of psychiatry*, 1991; 158: 666-675
- [4] Goodwin GM, Haddad PM, Ferrier IN, et al. Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for Psychopharmacology. *J Psychopharmacol.* 2016; 30(6): 495–553
- [5] Cipriani A, Hawton K, Stockton S, and Geddes JR. Lithium in the prevention of suicide in mood disorders: updated systematic review and meta-analysis. *BMJ*, 2013; 346:f3646. doi: 10.1136/bmj.f3646
- [6] Yatham LN, Kennedy SH, Parikh SV, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. *Bipolar Disord.* 2018; 20(2):97–170.
- [7] Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. *Bipolar Disord* (2018) 20 (2):97–170. doi: 10.1111/bdi.12609
- [8] Shulman KI, Almeida OP, Herrmann N, Schaffer A, Strejilevich SA, Paternoster C, et al. Delphi survey of maintenance lithium treatment in older adults with bipolar disorder: An ISBD task force report. *Bipolar Disord* (2019) 21(2):117–23. doi: 10.1111/bdi.12714
- [9] Forester BP, Streeter CC, Berlow YA, Tian H, Wardrop M, Finn CT, et al. Brain lithium levels and effects on cognition and mood in geriatric bipolar disorder: a lithium-7 magnetic resonance spectroscopy study. *Am J Geriatr Psychiatry* (2009) 17(1):13–23. doi: 0.1097/JGP.0b013e318172b3d0
- [10] Shine B, McKnight RF, Leaver L, Geddes JR. Long-term effects of lithium on renal, thyroid, and parathyroid function: a retrospective analysis of laboratory data. *Lancet* (2015) 386(9992):461–8. doi: 10.1016/S0140-6736(14)61842-0
- [11] Mirchandani Ic & Young RC. Management of mania in elderly: an up-date. *Ann Clin Psychiatry*, 1993; 5: 67-77
- [12] Faedda GL, Tondo L, Baldessarini RJ, Suppes T, Tohen M. Outcome after rapid vs gradual discontinuation of lithium treatment in bipolar disorders. *Arch Gen Psychiatry* (1993) 50(6): 448–55. doi: 10.1001/archpsyc.1993.01820180046005
- [13] Hui TP, Kandola A, Shen L, et al. A systematic review and meta-analysis of clinical predictors of lithium response in bipolar disorder. *Acta Psychiatr Scand.* 2019;140(2):94-115. doi:10.1111/acps.13062
- [14] Drakopoulos J, Sparding T, Clements C, Pålsson E, Landén M. Executive functioning but not IQ or illness severity predicts occupational status in bipolar disorder. *Int J Bipolar Disord.* 2020;8(1):7. Published 2020 Feb 7. doi:10.1186/s40345-019-0168-6

## Should We Use Lithium in Older People Mood Disorders?

- [15] Kurgan N, Whitley KC, Maddalena LA, et al. A Low-Therapeutic Dose of Lithium Inhibits GSK3 and Enhances Myoblast Fusion in C2C12 Cells. *Cells*. 2019; 8(11):1340. Published 2019 Oct 29. doi: 10.3390/cells8111340
- [16] Burdick KE, Millett CE, Russo M, et al (2020). The association between lithium use and neurocognitive performance in patients with bipolar disorder. *Neuropsychopharmacology*. <https://doi.org/10.1038/s41386-020-0683-2>
- [17] Favre P, Pauling M, Stout J, et al. Widespread white matter microstructural abnormalities in bipolar disorder: evidence from mega- and meta-analyses across 3033 individuals [published correction appears in *Neuropsychopharmacology*. 2019 Sep 16;]. *Neuropsychopharmacology*. 2019; 44(13): 2285-2293. doi:10.1038/s41386-019-0485-6
- [18] Moore GJ, Bebchuk JM, Wilds IB, Chen G, Manji HK. Lithium-induced increase in human brain grey matter. *Lancet*. 2000; 356:1241–1242
- [19] Hajek T, Kopecek M, Hoschl C, Alda M. Smaller hippocampal volumes in patients with bipolar disorder are masked by exposure to lithium: a meta-analysis. *J Psychiatry Neurosci*. 2012; 37: 333–343
- [20] Macritchie KA, Lloyd AJ, Bastin ME, et al. White matter microstructural abnormalities in euthymic bipolar disorder. *Br J Psychiatry*. 2010; 196:52–58
- [21] Hou L, Heilbronner U, Degenhardt F et al. Genetic variants associated with response to lithium treatment in bipolar disorder: a genome-wide association study. *Lancet* 2016; 387: 1085–1093.
- [22] Scott J, Etain B, Bellivier F. Can an integrated science approach to precision medicine research improve lithium treatment in bipolar disorders? *Front Psychiatry* 2018; 9: 360
- [23] Simonetti A, Koukopoulos AE, Kotzalidis GD, et al. Stabilization Beyond Mood: Stabilizing Patients With Bipolar Disorder in the Various Phases of Life. *Front Psychiatry*. 2020; 11:247. Published 2020 Apr 27. doi: 10.3389/fpsy.2020.00247

**Citation:** Dr. Aziz VM. *Should We Use Lithium in Older People Mood Disorders?. Archives of Psychiatry and Behavioral Sciences*. 2020; 3(2): 01-03.

**Copyright:** © 2020 Dr. Aziz VM. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.