

### LETTER TO THE EDITOR

# Inositol supplementation in patients taking lithium or valproic acid: strengthening the multidisciplinary approach

Francesca Pacitti

Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy

Corresponding Author: Francesca Pacitti, MD; e-mail: francesca.pacitti@univaq.it

## Dear Editor,

I've read with great interest the review recently published by Kamenov et al<sup>1</sup> about the importance of inositol supplementation in recovering side effects induced by mood stabilizers and anticonvulsant drugs. The authors gathered scientific publications, demonstrating the efficacy of inositol supplementation in counteracting the side effects of lithium or valproic acid, focusing on the importance of a multidisciplinary approach.

Although pharmacological therapies, such as lithium and valproic acid, succeed to stabilize mood in patients with bipolar disorder (BD), they may induce severe side effects, worsening quality of life and compliance<sup>2</sup>. Patients feel like hanging in a critical balance between the positive effects of the pharmacological therapies and the difficulties of the adverse effects, including weight gain, polyuria/polydipsia, cardiac and thyroid alterations, psoriatic plaques, and polycystic ovary syndrome<sup>3,4</sup>. Recent works pointed out that all these adverse conditions share the depletion of inositol in the related peripheral tissue<sup>4</sup>. Indeed, both lithium and valproic acid include the depletion of inositol in the central nervous system (CNS) among their mechanisms of action, but they also influence inositol levels in peripheral tissues. This latter – inositol – represents a family of molecules, among which myo-inositol and D-chiro-inositol are the two main ones, with positive effects on metabolic, endocrine and reproductive

In their clinical practice psychiatrists are starting to consider the complexity of patients with BD under lithium or valproic acid, considering side effects and the related low compliance and poorer prognosis<sup>6</sup>. In this

perspective, the review by Kamenov et al<sup>1</sup> brings the attention to scientific evidence clearly demonstrating that inositol supplementation may improve such side effects without reducing the therapeutic activity on mood<sup>7,8</sup>. However, using a controlled dosage of inositol in patients under lithium or valproic acid without interfering with the mechanism of the drugs, is a crucial aspect to bear in mind<sup>7,8</sup>. In this regard, a subsequently published clinical study by Cantelmi et al<sup>9</sup>, bridged this missing piece strengthening the evidence reported by Kamenov and colleagues. In such a pilot study, they demonstrated the safety and the beneficial effects of 4 grams per day of inositol in patients with BD, using myo- and D-chiro-inositol in the combined 80:1 ratio, respectively. All patients with borderline blood values of thyroid and metabolic markers, exhibited improved levels after 6 months of the inositol supplementation, without interfering with mood and drugs' effectiveness. The novelty of this approach is that for the first time psychiatrists dispose of a useful and safe tool for counteracting side effects in patients taking lithium or valproic acid without the risk of dampening the central therapeutic action. So far, they only considered side effects as a consequence of the therapy, testing new dosages and drug combinations without any significant results. To this end, the review by Kamenov et al<sup>1</sup>, along with the following study by Cantelmi and colleagues<sup>9</sup>, stimulates a new perspective in psychiatric clinical practice aiming to focus on the importance of a multidisciplinary approach in such patients.

**Conflicts of Interest.** The author declare that she has no conflicts of interest or competing financial interests.

# NUTRIMENTUM ET CURAE

Nutrimentum et Curae is an Indicon S.r.l. project





### References

- 1. Kamenov Z, Lepore E, Montanino Oliva M, Unfer VR, Unfer V. Why inositol supplementation may help to recover side effects induced by mood stabilizers and anticonvulsant drugs. Nutr Cur. 2022; 01: e112. Doi: 10.57625/nec.2022.17.
- 2. Gitlin M. Lithium side effects and toxicity: prevalence and management strategies. Int J Bipolar Disord. 2016; 4(1): 27. Doi: 10.1186/s40345-016-0068-y.
- 3. Janiri L, D'Ambrosio F, Di Lorenzo C. Combined treatment of myo-inositol and d-chiro-inositol (80:1) as a therapeutic approach to restore inositol eumetabolism in patients with bipolar disorder taking lithium and valproic acid. Eur Rev Med Pharmacol Sci. 2021; 25(17): 5483-5489. Doi: 10.26355/eurrev 202109 26657.
- 4. Lepore E, Lauretta R, Bianchini M, Mormando M, Di Lorenzo C, Unfer V. Inositols Depletion and Resistance: Principal Mechanisms and Therapeutic Strategies. Int J Mol Sci. 2021; 22(13): 6796. Doi: 10.3390/ijms22136796.
- 5. Dinicola S, Unfer V, Facchinetti F, Soulage CO, Greene ND, Bizzarri M, Laganà AS, Chan SY, Bevilacqua A, Pkhaladze L, Benvenga S, Stringaro A, Barbaro D, Appetecchia M, Aragona C, Bezerra Espinola MS, Cantelmi T, Cavalli P, Chiu TT, Copp AJ, D'Anna R, Dewailly D, Di Lorenzo C, Diamanti-Kandarakis E, Hernández Marín I, Hod M, Kamenov

- Z, Kandaraki E, Monastra G, Montanino Oliva M, Nestler JE, Nordio M, Ozay AC, Papalou O, Porcaro G, Prapas N, Roseff S, Vazquez-Levin M, Vucenik I, Wdowiak A. Inositols: From Established Knowledge to Novel Approaches. Int J Mol Sci. 2021; 22(19): 10575. Doi: 10.3390/ijms221910575.
- 6. Bonnín CDM, Reinares M, Martínez-Arán A, Jiménez E, Sánchez-Moreno J, Solé B, Montejo L, Vieta E. Improving Functioning, Quality of Life, and Well-being in Patients with Bipolar Disorder. Int J Neuropsychopharmacol. 2019; 22(8): 467-477. Doi: 10.1093/ijnp/pyz018.
- 7. Bersudsky Y, Grisaru N, Yaroslavsky U, Gheorghiu S, Ivgi D, Kofman O, Belmaker RH. The effect of inositol on lithium-induced polyuria/polydipsia in rats and humans. Human Psychopharmacology: Clinical and Experimental 1992; 7(6): 403-407. Doi: 10.1002/hup.470070606.
- 8. Kontoangelos K, Vaidakis N, Zervas I, Thomadaki O, Christaki S, Stavrianeas NG, Papadimitriou GN. Administration of inositol to a patient with bipolar disorder and psoriasis: a case report. Cases J. 2010; 3: 69. Doi: 10.1186/1757-1626-3-69.
- 9. Cantelmi T, Lepore E, Unfer VR, Unfer V. Safety of inositol supplementation in patients taking lithium or valproic acid: a pilot clinical study. Eur Rev Med Pharmacol Sci 2022; 26(19): 7269-7276. Doi: 10.26355/eurrev 202210 29920.