DOI: 10.5152/alphapsychiatry.2023.27122022



## Commentary: Is Torasemide a Potential Agent in the Treatment of Autism?

Dear Editor,

Autism Spectrum Disorder (ASD) is a neurodevelopment disorder characterized for consistent deficits in communication and social interaction in multiple contexts, as well as by restricted and repetitive behaviors, interests or activities. According to Li et al. 1 showed that 1 in every 30 individuals aged between 3 and 17 years is on the ASD.

So far, there is no specific and effective drug for the treatment of autism symptoms, just to comorbidities associated with ASD.<sup>2</sup> A few years ago, some studies investigated the effects of a specific drug, called bumetanide on autism symptoms in children and adults.<sup>3-5</sup> Bumetanide is an inhibitor of the Na<sup>+</sup>–K<sup>+</sup>–2Cl<sup>-</sup> cotransporter 1 (NKCC1) that plays essential roles in GABA receptors.<sup>6</sup> Evidence has shown that dysfunction in the GABAergic signaling pathway is significantly associated with the main symptoms of ASD.<sup>7</sup>

Within this context, some years ago, Hampel et al.<sup>8</sup> demonstrated that bumetanide improved social reciprocity and behavioral symptoms in children and adolescents with ASD. Torasemide is another inhibitor of the NKCC1, however, there is neither clinical nor experimental study that investigated the effects of torasemide on ASD symptoms. Within this context, Doğan et al.<sup>9</sup> showed that Torasemide provided an improvement in sociability and passive avoidance learning in rats, as well as in histopathological and neurochemical measures, such as reduction in brain levels of malondialdehyde, tumor necrosis factor-alpha, interleukin-2, interleukin-17 and NF-KB. In addition, it had higher neuronal counts in the C1 and C2 areas of the hippocampus and Purkinje cells in the cerebellum, as well as lower GFAP immunostaining rates in C1 and cerebellum. Finally, lower levels of lactate were also observed. This is the first study to examine and show the effects of torasemide on autism symptoms. Its findings showed that Torasemide can increase GABA activity, and thus, can be considered another inhibitor of NKCC1 in the treatment of autism with a longer half-life and fewer side effects after additional studies. These findings are promising, despite being in animal models. Therefore, new studies must be conducted, but now with autistic individuals.

## References

- Li Q, Li Y, Liu B, et al. Prevalence of autism spectrum disorder among children and adolescents in the United States from 2019 to 2020. JAMA Pediatr. 2022;176(9):943-945. [CrossRef]
- Bird F, Harper JM, Luiselli JK, Shlesinger A, Gold J. Psychotropic medication monitoring in a human services organization for children with autism spectrum disorder: description and evaluation of interdisciplinary team review. Behav Anal Pract. 2022;15(4):1337-1347. [CrossRef]
- Crutel V, Lambert E, Penelaud PF, et al. Bumetanide oral liquid formulation for the treatment of children and adolescents with autism spectrum disorder: design of two Phase III studies (SIGN trials). J Autism Dev Disord. 2021;51(8):2959-2972. [CrossRef]
- Hadjikhani N, Zürcher NR, Rogier O, et al. Improving emotional face perception in autism with diuretic bumetanide: a proof-of-concept behavioral and functional brain imaging pilot study. Autism. 2015;19(2):149- 157. [CrossRef]
- Lemonnier E, Villeneuve N, Sonie S, et al. Effects of bumetanide on neurobehavioral function in children and adolescents with autism spectrum disorders. *Transl Psychiatry*. 2017;7(3):e1056.
   [CrossRef]
- Hampel P, Römermann K, Gramer M, Löscher W. The search for brain-permeant NKCC1 inhibitors for the treatment of seizures: Pharm acoki netic -phar macod ynami c modelling of NKCC1 inhibition by azosemide, torasemide, and bumetanide in mouse brain. *Epilepsy Behav*. 2021;114(A):107616.



Copyright@Author(s) - Available online at alpha-psychiatry.com.

Content of this journal is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.



Sergio Machado<sup>1</sup>

João Lucas Lima<sup>1</sup>

Claudio Imperatori<sup>2</sup>

Alberto Souza de Sá Filho<sup>3</sup>

<sup>1</sup>Laboratory of Physical Activity Neuroscience, Neurodiversity Institute, Queimados-RJ, Brazil <sup>2</sup>Cognitive and Clinical Psychology Laboratory, Department of Human Sciences, European University of Rome, Rome, Italy <sup>3</sup>Post Graduate Program of University Center of Anápolis (UniEVANGÉLICA), Anápolis, Brazil

Corresponding author: Sergio Machado ☑ secm80@gmail.com

Cite this article as: Machado S, Lima JL, Imperatori C, Souza de Sá Filho A. Commentary: Is torasemide a potential agent in the treatment of autism? *Alpha Psychiatry*. 2023;24(1):32-33.

- 7. Cellot G, Cherubini E. GABAergic signaling as therapeutic target for autism spectrum disorders. *Front Pediatr*. 2014;2:70. [CrossRef]
- 8. Hampel P, Römermann K, MacAulay N, Löscher W. Azosemide is more potent than bumetanide and various other loop diuretics to inhibit the
- sodium-potassium-chloride cotransporter human variants hNKCC1A and hNKCC1B. *Sci Rep.* 2018;8(1):9877. [CrossRef]
- 9. Doğan M, Albayrak Y, Erbaş O. Torasemide improves the propionic acidinduced autism in rats: A histopathological and imaging study. *Alpha Psychiatry*. 2022;19:1-2.