IMPLICATIONS OF BLOOD URIC ACID LEVELS ON MOOD DISORDERS – AN UNSYSTEMATIC REVIEW

Teixeira, D.⁽¹⁾, Costa, L.⁽¹⁾, Marques, A.⁽¹⁾ Melo, B.⁽¹⁾; Alves Pereira, C. ⁽¹⁾; Sousa, R. ⁽¹⁾; Brás, J. ⁽¹⁾; Borges, S.⁽¹⁾;
¹ Serviço de Psiquiatria do Centro Hospitalar Tondela-Viseu

BACKGROUND AND AIMS: Bipolar Disease Spectrum (BDS) affects around 2-4% of the world’s population. Despite its great prevalence, few new therapeutic approaches have come along, as the etiology and pathofisiology of this disease remains largely unknow. The differentiation between unipolar depression (UD) and bipolar depression (BD) remains a clinical challenge. Uric Acid is the final product of the purines metabolism; purines seem to modulate dopamine and glutamine cerebral expression, and are thought to be involved in sleep regulation, motor activity, cognition, memory, appetite, aggressive behaviour and social interaction. The authors decided to conduct an unsystematic review on articles linking BDS and Uric Acid Serum Levels (UASL).

OBJECTIVES AND METHODS To present a scientific poster with an unsystematic review about the implications of the UASL on Mood Disorders (MD). A bibliographic research was conducted using the search engine Pubmed® and the keywords: “Blood Uric Acid Levels and Bipolar Disease Spectrum”.

RESULTS

High UASL have been correlated with greater drive and energy, desinhibition, hyperthymia, irritable temperament, impulsivity and excitement seeking. Lesch-Nyhan syndrom is caused by a purine metabolism dysregulation, leading to high UASL; these patients have impulsive and aggressive behaviours (including desinhibited sexual behaviours)

The relationship between the purines metabolism and mania was described by Kraeplin wich, in 1921, mentioned the association between maniac episodes, UASL and gout. Lithium was used for dissolving urine uric acid crystals before Cade discovered it’s anti-maniac properties in 1949.

One of the main functions of the adenosine receptors in the central nervous system (CNS) is to work as a endogenous anticonvulsionant. A dysregulation of this system might contribute to both psychotic and manic symptoms. Some authors have speculated if the the BDS-CNS is more vulnerable because of this dysregulation, (wich, in that case, would give UASL a role as a trait marker), or if after a maniac phase the following purinergic dysregulation would contribute to the maintenance of the manic symptoms (wich, in that case, would give UASL a role as a state marker)

Allopurinol reduces UASL and has shown mild-modest effects in the reduction of manic symptoms, raising the hypothesis if it can be used as an adjuvant therapeutic in severe/treatment-resistant manic cases.

Some evidence suggests UD patients have lower UASL than controls and BDS patients. BDS patients (in the depressive, mixed and maniac state) have higher UASL than UD patients, but especially higher during first-untreated maniac phases; from all the BDS phases, evidence suggests that it is during the manic phases that the UASL is especially raised. Recently, a pioneer portuguese study has shown some potential in the UASL as a biomarker between UD and BD.

CONCLUSIONS The clinical differentiation between UD and BD remains a challenging diagnosis, and perhaps there is a role for UASL as a future biomarker. However, no study to date proved that high UASL is either a trace or a state marker of BDS. New studies with greater samples and different methodologies are needed.

BIBLIOGRAPHY

Albert, U., De Cori, D., Aguglia, A., Barbaro, F., Bogetto, F., Maina, G., 2015. Increased Uric Acid Levels In Bipolar Disorder Subjects During Different Phases Of Illness. *J. Affect. Disord.* 173, 170e175.

Bartoli, F, Et Al. “Uric Acid Levels In Subjects With Bipolar Disorder: A Comparative Meta-analysis.” *Journal Of Psychiatric Research.*, U.S. National Library Of Medicine, Oct. 2016

Bartoli, F, Et Al. “Allopurinol As Add-on Treatment For Mania Symptoms In Bipolar Disorder: Systematic Review And Meta-analysis Of Randomised Controlled Trials.” *The British Journal Of Psychiatry : The Journal Of Mental Science.*, U.S. National Library Of Medicine, Jan. 2017,

Bowman, G.L., Shannon, J., Frei, B., Et Al., 2010. Uric Acid As A CNS Antioxidant. *J. Alzheimers Dis.* 19, 1331–1336.

Burnstock, G., 2006. Historical Review: ATP As A Neurotransmitter. *Trends In Pharmacological Sciences* 27 (3), 166–176.

Burnstock, G., 2007. Physiology And Pathophysiology Of Purinergic Neurotransmission. *Physiological Reviews* 87 (2), 659–797.

Cade, J. F. “Lithium Salts In The Treatment Of Psychotic Excitement.” *Bulletin Of The World Health Organization*, World Health Organization, 2000

Dossantos Oliveira PM, Santos V, Coroa M, Ibeiro J, Madeira N. Erum Uric Acid As A Predictor Of Bipolarity In Individuals With A Major Depressive Episode. *Bipolar Disord.* 2018;00:1–9.

Kesebir, S, Et Al. “Uric Acid Levels May Be A Biological Marker For The Differentiation Of Unipolar And Bipolar Disorder: The Role Of Affective Temperament.” *Journal Of Affective Disorders.*, U.S. National Library Of Medicine, Aug. 2014

Kesebir, S, Et Al. “Increased Uric Acid Levels In Bipolar Disorder: Is It Trait Or State?” *Journal Of Biological Regulators And Homeostatic Agents.*, U.S. National Library Of Medicine

Lorenzi, T.M., Borba, D.L., Dutra, G., Lara, D.R., 2010. Association Of Serum Uric Acid Levels With Emotional And Affective Temperaments. *Journal Of Affective Disorders* 121 (1–2), 161–164.

Machado-vieira, R, Et Al. “Purinergic Dysfunction In Mania: An Integrative Model.” *Medical Hypotheses.*, U.S. National Library Of Medicine, Apr. 2002

Mcquillain, A, Et Al. “Case-control Studies Show That A Non-conservative Amino-acid Change From A Glutamine To Arginine In The P2RX7 Purinergic Receptor Protein Is Associated With Both Bipolar- And Unipolar-affective Disorders.” *Molecular Psychiatry.*, U.S. National Library Of Medicine, June 2009

Muti, M, Et Al. “Serum Uric Acid Levels And Different Phases Of Illness In Bipolar I Patients Treated With Lithium.” *Psychiatry Research.*, U.S. National Library Of Medicine, 28 Feb. 2015

Salvadore, G., Viale, C.L., Luckenbaugh, D.A., Zanatto, V.C., Portela, L.V., Souza, D.O., Zarate Jr., C.A., Machado-vieira, R., 2010. Increased Uric Acid Levels In Drug-naïve Subjects With Bipolar Disorder During A First Manic Episode. *Progress In Neuropsychopharmacology & Biological Psychiatry* 34 (6), 819–821.

Sutin, A.R., Cutler, R.G., Camandola, S., Uda, M., Feldman, N.H., Cucca, F., Zonderman, A.B., Mattson, M.P., Ferrucci, L., Schlessinger, D., Terracciano, A., 2014. Impulsivity Is Associated With Uric Acid: Evidence From Humans And Mice. *Biological Psychiatry* 75 (1), 31–37.