

International Research Journal of Ophthalmology

Letter to the Editor

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Monoamines, pterines, or tetrahydrofolate are not useful as biomarkers for diagnosing mitochondrial disorders

Josef Finsterer^{1*} and Sinda Zarrouk-Mahjoub²

¹Krankenanstalt Rudolfstiftung, Vienna, Austria, Europe

²University of Tunis El Manar and Genomics Platform, Pasteur Institute of Tunis, Tunisia

***Corresponding Author:** Finsterer J, MD, PhD, Krankenanstalt Rudolfstiftung, Vienna, Austria, Postfach 20, 1180 Vienna, Austria, Europe, Tel: +43-1-71165-72085; Fax: +43-1-4781711; Email: fifigs1@yahoo.de

Received Date: Jan 23, 2019 / **Accepted Date:** Feb 21, 2019 / **Published Date:** Feb 22, 2019

Cite this article as: Josef Finsterer, Sinda Zarrouk-Mahjoub. 2019 Monoamines, pterines, or tetrahydrofolate are not useful as biomarkers for diagnosing mitochondrial disorders. *Int Res J Optha.* 1: 13-14.

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Keywords: Mitochondrial; mtDNA; Phenotype; Genotype; Myopathy; Muscle biopsy

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In a recent article Batllori et al. reported about a retrospective study of cerebrospinal fluid (CSF) concentrations of monoamines (homovanillic acid (HVA), 5-hydroxyindolacetic acid (5HIAA)), pterines (neopterin, biopterin), and 5-methyl-tetrahydrofolate (5MTHF) in 29 patients with a genetically confirmed mitochondrial disorder (MID) [1]. The study showed that high HVA is associated with low folate levels in KSS but was otherwise in-conclusive [1]. We have the following comments and concerns.

Parkinson syndrome (PS) was an exclusion criterion as mentioned in the method section [1], but at least two patients with PS were nonetheless included. Which was the rationale for this contradictory approach? Data were retrospectively collected over a period of 12y.

Were the methods applied for determining monoamines, pterines, and 5MTHF truly the same in all 29 patients over this period of time? Which were the reference limits of the 5 assessed parameters? Heteroplasmy rates in primary mtDNA mutations strongly determine the phenotype [2]. Did CSF levels of monoamines, pterines, and 5MTHF correlate with heteroplasmy rates of the mtDNA variants in patients with a primary mtDNA mutation? According to table 1, CSF lactate was measured by MRS in only 3 patients [1]. Thus, a correlation between imaging studies or monoamines and CSF lactate cannot be established, as indicated in the results section. Was CSF lactate also measured directly in the CSF? CSF monoamines, pterines, and 5MTHF may depend on the redox status of the individuals. Was the anti-oxidative capacity ever measured in the included patients? Was there a relation between the anti-oxidative capacity and CSF monoamines, pterines, and

5MTHF levels? Was there a difference in the levels of CSF monoamines, pterines, and 5MTHF levels between patients carrying a mtDNA variant and those carrying a nDNA mutation? Since MIDs may secondarily induce immunological reactions [3], and since neopterin is a non-specific marker of inflammatory/immunological processes [4], it may be elevated in case such an immunologic reaction is induced by a MID. Thus, elevated CSF monoamines may be a secondary, non-specific finding and thus not helpful as a biomarker of MIDs. The monoamine profile may be abnormal also in extrapyramidal syndromes (EPS) or depression. According to table 1, at least 10 patients had EPS (dystonia (n=8), PS (n=2)). In how many of the patients with EPS was a dopamin transporter SPECT (DAT scan) carried out? According to table 1 monoamines were normal, elevated, or decreased in the 10 patients with EPS. Since MIDs frequently go along with EPS [5] and since monoamine levels in the 10 EPS patients were conflicting, CSF monoamines have to be regarded as a non-specific finding and are thus not helpful as a biomarker of MIDs.

In case the choroidal plexus is truly malfunctioning in MIDs, why is there hardly ever hydrocephalus in MID patients? Chromosomal defects are usually not regarded as responsible for MIDs. Why was a patient with a chromosomal defect included as a patient with genetically confirmed MID?. In conclusion, we do not regard CSF levels of monoamines, pterines, or 5MTHF CSF as useful biomarkers for MIDs, since deflections of these parameters are multifactorial and thus non-specific. Inclusion and exclusion criteria of the presented study need to be revised and reference limits of the evaluated parameters need to be provided.

Author contribution: JF: design, literature search, discussion, first draft, SZ-M: literature search, discussion, critical comments

References

1. Batllori M, Molero-Luis M, Ormazabal A, et al. 2018. Cerebrospinal fluid monoamines, pterins, and folate in patients with mitochondrial diseases: systematic review and hospital experience. *J Inher Metab Dis*. Ref.: <https://bit.ly/2SfMzLG>
2. Uimonen S, Moilanen JS, Sorri M, et al. 2001. Hearing impairment in patients with 3243A-->G mtDNA mutation: phenotype and rate of progression. *Hum Genet*. 108: 284-289. Ref.: <https://bit.ly/2V8pIDv>
3. Holmøy T, Beiske AG, Zarnovicky S, et al. 2016. Severe inflammatory disease activity 14 months after cessation of Natalizumab in a patient with Leber's optic neuropathy and multiple sclerosis - a case report. *BMC Neurol*. 16: 197. Ref.: <https://bit.ly/2T2uUvc>
4. Alanbay I, Mutlu Ercan C, Coksuer H, et al. 2012. Neopterin: a promising marker for the inflammation in polycystic ovary syndrome. *Gynecol Endocrinol*. 28: 879-883. Ref.: <https://bit.ly/2TWUejm>
5. Andalib S, Vafae MS, Gjedde A. 2014. Parkinson's disease and mitochondrial gene variations: a review. *J Neurol Sci*. 346: 11-19. Ref.: <https://bit.ly/2TW5c95>