LETTER TO THE EDITOR

Assessing the anesthetic effectiveness of remimazolam in MELAS patients requires careful investigations

Josef Finsterer*

Keywords: COVID-19, SARS-CoV-2, Neuroimmunology, Anxiety, Depression

Letter to the Editor

We read with interest the article by Kitaura et al. about a 47-year-old male with mitochondrial encephalopathy, lactic acidosis, and stroke-like episode (MELAS) syndrome, who underwent elective transcatheter mitral valve repair because of mitral insufficiency [1]. MELAS was due to the common variant m.3243A>G and manifested phenotypically with short stature, cerebral and cerebellar atrophy, deafness, hypertrophic cardiomyopathy, Wolff-Parkinson-White syndrome, heart failure, renal insufficiency requiring hemodialysis, myopathy, and lactic acidosis [1]. General anesthesia for the procedure was successfully induced and maintained with remimazolam and remifentanil, without circulatory compromise or metabolic acidosis [1]. It was concluded that remimazolam may be a new anesthetic option for MELAS [1].

The study is attractive but raises concerns that should be discussed.

We do not agree with the statement in the discussion that serum lactate is elevated in MELAS because of metabolic acidosis [1]. It is the other way around. Metabolic acidosis develops because of lactic acidosis, and lactate is produced in tissues with impaired oxidative phosphorylation [2].

The two statements “propofol can be safely used in patients with MELAS” and “it is safer to avoid the continuous administration of propofol in patients with mitochondrial disorders” are contradictory [1]. This discrepancy should be solved. The topic is conflicting as there are reports describing the safe use of propofol but also reports that describe propofol infusion syndrome after propofol administration in mitochondrial disorders [3].

A shortcoming of the study is that the heteroplasmy rate (relation of mutated mtDNA to wild-type mtDNA in a single mitochondrion or single cell) of the m.3243A>G variant was not provided [1]. Knowing heteroplasmy rates in various tissues is crucial as they determine the clinical course and outcome of MELAS patients [4]. It would be also interesting to know the mtDNA copy number (absolute number of mtDNA copies within a mitochondrion or single cell) as it is a further factor determining the phenotype.

We do not agree with the conclusions that remimazolam can be a new option for anesthetizing MELAS patients [1]. Findings in a single patient cannot be generalized. To assess if remimazolam is truly a novel option for anesthetizing MELAS patients, further, appropriately designed studies are warranted.

We should be told what the authors mean with “bilateral pathologic reflex positive” [1]. Do they mean that the tendon reflexes were exaggerated? If this is the case, it would contradict with the statement that there was “weakness of tendon reflexes” [1]. We should be told if there was a mixture of exaggerated and reduced tendon reflexes. Obviously, the index patient had myopathy, implying that tendon reflexes are reduced. However, the patient also had cerebral atrophy, which does not exclude that there was affection of the pyramidal tract.

*Correspondence: fifigs1@yahoo.de
Neurology & Neurophysiology Center, Postfach 20, 1180 Vienna, Austria

© The Author(s) 2022. Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article’s Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article’s Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.
Missing are the reference limits in the text and Table 1, which makes it impossible to interpret the provided results. Missing is the current medication the patient was regularly taking prior to MitraClip® implantation. Missing is also the previous history, particularly if the patient had generalized anesthesia before and if any complications had occurred.

Overall, the interesting study has some limitations that call the results and their interpretation into question. Clarifying these weaknesses would strengthen the conclusions and could improve the study. Whether remimazolam is beneficial for MELAS in general remains unsupported.

Authors’ contributions
JF: design, literature search, discussion, first draft, critical comments, and final approval. The author read and approved the final manuscript.

Funding
No funding was received.

Declarations

Ethics approval and consent to participate
This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Competing interests
The author declares no competing interests.

Received: 7 June 2022 Revised: 13 June 2022 Accepted: 15 June 2022 Published online: 21 June 2022

References
1. Kitaura A, Kosumi R, Iwamoto T, Nakao S. Remimazolam anesthesia for transcatheter mitral valve repair in a patient with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome: a case report. JA Clin Rep. 2022;8(1):38. https://doi.org/10.1186/s40981-022-00528-1.
2. Foucher CD, Tubben RE. Lactic acidosis. In: StatPearls. Treasure Island: StatPearls Publishing; 2022.
3. Shimizu J, Tabata T, Tsujita Y, Yamane T, Yamamoto Y, Tsukamoto T, et al. Propofol infusion syndrome complicated with mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes: a case report. Acute Med Surg. 2019;7(1):473. https://doi.org/10.1002/ams2.473.
4. Shi Y, Chen G, Sun D, Hu C, Liu Z, Shen D, et al. Phenotypes and genotypes of mitochondrial diseases with mtDNA variations in Chinese children: a multi-center study. Mitochondrion. 2022;62:139–50. https://doi.org/10.1016/j.mito.2021.11.006.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.