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Letter to the Editor

The Delphi-Method is Unsuitable for Eliminating the Uncertainty Regarding the Nature and Management of Stroke-Like Episodes in MELAS

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Letter to the Editor

The article by Mancuso *et al*. on a consensus paper regarding the diagnosis and treatment of stroke-like episodes (SLEs) in patients with mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome using the Delphi-method [1] has several limitations.

The first point is that the Delphi-method has some drawbacks that can render the results unreliable. The Delphi-method is often used when there is no existing answer to a question and opinions are the most valuable resource available [2]. Even if the group of respondents has sufficient experience and expertise, it is difficult to reach clear conclusions and recommendations when there is a lack of evidence and when sound basic and clinical knowledge regarding diagnosis and treatment is limited. The Delphi-method also uses controlled feedback, which means that ideas are not openly discussed by participants (questionnaire responses) and they may not be able to articulate their views as thoroughly as with other research methods. The Delphi-method also reaches its limits when opinions are highly polarized and more in-depth investigations are required beforehand. This cannot be prevented by excluding experts from the Delphi panel who are expected to hold opposing views. Since the consensus-building process using the Delphi-method may sometimes require several rounds of questionnaires, this can lead to a decline in engagement or a lack of responses, thereby compromising the quality of the results.

The second point is that the term MELAS encompasses not only SLEs but also lactic acidosis and encephalopathy. Therefore, diagnosing MELAS based solely on the presence of SLEs and pathogenic mtDNA is not appropriate. MELAS cannot be reduced to SLEs, as these patients exhibit symptoms and signs that go beyond SLEs. In particular, MELAS patients suffer from lactic acidosis and exhibit symptoms of encephalopathy, including cognitive decline, hemiparesis, hemianopia, cortical blindness, aphasia, migraine-like headaches, seizures, and psychiatric disorders.

The third point is that SLEs and MELAS are not only attributable to mtDNA mutations but also to variants in cDNA genes such as POLG1, VARS2, MRM2, and FASTKD2 [3]. Furthermore, SLEs occur not only in MELAS but also frequently in other syndromic and non-syndromic mitochondrial disorders.

The fourth point is that there is currently no solid evidence that glucocorticoids are beneficial in SLEs. On the contrary, there are isolated reports showing that glucocorticoids may even be harmful in MELAS [4]. Only isolated case reports have shown a positive effect of glucocorticoids [5].

The fifth point is that the treatment of seizures should follow ILAE guidelines, as these provide the highest level of expertise regarding their management. Seizures should not be treated based on suspicion alone, but only when they have been observed, clinical signs are present, or an abnormal EEG is detected; SLEs are not necessarily associated with seizures.

Overall, clarifying the diagnostic criteria for MELAS, as well as the nature and optimal treatment of SLEs, cannot be achieved through expert opinion alone but requires basic research using appropriate scientific methods. Currently, there is no evidence that steroids are beneficial in SLEs, and seizures in MELAS should be treated in accordance with ILAE guidelines.

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