Management of Myoclonic Epilepsy in Tofana Syndrome

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Letter to the Editor:

In a recent article, Lamperti and Zeviani discussed the management of epilepsy in patients with myoclonic epilepsy with ragged-red fibers (MERRF) syndrome and Alpers-Huttenlocher disease (AHS) [Lamperti & Zeviani 2016]. We have the following comments and concerns.

Mitochondrial epilepsy is not only prevalent in MERRF syndrome and AHS but also in MELAS and particularly non-syndromic mitochondrial disorders (MIDs) [Lee et al. 2016, Whittaker et al. 2015]. Myoclonic epilepsy in MIDs may not only occur in MERRF and AHS but also in coenzyme-Q deficiency, and non-syndromic MIDs [Mancuso et al. 2014]. In MELAS, epilepsy particularly occurs in the context of stroke-like episodes [Whittaker et al. 2015]. There are indications that seizures even trigger a stroke-like episode [Finsterer & Wakil, 2016]. This is why it is recommended to achieve maximal seizure control in patients with stroke-like episodes, particularly in MELAS.

Because of the association between structural abnormalities in MIDs and seizures, we should be informed about the frequency of stroke-like episodes or other cerebral morphological abnormalities in MERRF patients. Structural cerebral lesion in MERRF in addition to stroke-like lesions, include atrophy or white matter lesions [Zsurka et al. 2013].

Though the authors recommend clonazepam or zonisamide for myoclonus in MERRF syndrome, these antiepileptic drugs (AEDs) have been only rarely applied in clinical practice. On a PubMed search clonazepam was mentioned only 3 times in association with MERRF syndrome and zonisamide was mentioned only once.

We do not agree with the recommendation of lamotrigine for myoclonic epilepsy [Lamperti & Zeviani 2016]. There are indications that lamotrigine may even aggravate myoclonus [Michelucci et al. 2016]. Other AEDs which may aggravate myoclonus include phenytoin, carbamazepine, oxcarbazepine, vigabatrin, tiagabine, gabapentin, and pregabalin [Michelucci et al. 2016]. AEDs which are commonly used for myoclonic epilepsy include valproate, clonazepam, phenobarbital, or primidone [Michelucci et al. 2016]. Among the novel AEDs piracetam, levetiracetam, topiramate, zonisamide, and possibly perampanel are the ones recommendable for the treatment of myoclonic epilepsy [Michelucci et al. 2016]. It should be also mentioned that coenzyme-Q exhibited a beneficial effect on mitochondrial epilepsy in mice [Scalais et al. 2013]. Coenzyme-Q was also effective in myoclonic epilepsy due to primary coenzyme-Q-deficiency [Scalais et al. 2013].

Concerning the mitochondrion-toxicity of AEDs, it has to be taken in mind, that some of the AEDs recommended for myoclonic epilepsy have been proven severely mitochondrion-toxic, why they should be avoided, if possible, as AEDs in mitochondrial epilepsy in general. AEDs with the strongest mitochondrion-
toxic effect include valproate, carbamazepine, phenytoin, and phenobarbital [Finsterer & Zarrouk-Mahjoub, 2012]. Accordingly, myoclonic epilepsy in MIDs should be treated with levetiracetame, zonisamide, topiramate, or possibly perampanel.

Occasionally, myoclonic epilepsy may be refractory to conventional AEDs [Lii et al. 1991]. In this case, alternative therapeutic options should be considered, such as the ketogenic diet, L-tryptophan, N-acetyl-cysteine, vagal nerve stimulation, or deep brain stimulation [Michelucci et al. 2016].

We do not agree with the statement that lactic acidosis can be controlled by bicarbonate [Lamperti & Zeviani 2016]. Though bicarbonate can exhibit a short-term effect on lactic acidosis in MIDs, the long-term results are poor [Kraut & Madias, 2016]. Alternative buffers for lactic acidosis could be tris-hydroxymethyl aminomethane (THAM) or carbicarb [Kraut & Madias, 2016]. Side effects associated with bicarbonate therapy include hypercapnia, hypokalemia, hypocalcemia, or QTc prolongation [Adeva-Andany et al. 2014].

Overall, this interesting review could profit from discussion of alternative agents for myoclonic epilepsy in case of contraindications or refractoriness to conventional AED treatment. AED treatment in MIDs in general should rely on the avoidance of any mitochondrion-toxic agents including mitochondrion-toxic AEDs. AEDs potentially enhancing the frequency of myoclonic seizures should be avoided not to unnecessarily jeopardise any patient.

References:


