Management of myoclonic epilepsy in MERRF patients

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Objectives: To summarise and discuss previous and recent findings concerning antiepileptic drug (AED) treatment of myoclonic epilepsy in patients with myoclonic epilepsy with ragged-red fibers (MERRF)-syndrome. Results: MERRF syndrome (OMIM #545000) is a maternally inherited, multisystem mitochondrial disorder (MID) caused by pathogenic variants predominantly in the mitochondrial DNA (mtDNA). Canonical clinical features of MERRF include myoclonus, generalized epilepsy, ataxia, and a ragged-red fiber myopathy. Additionally, a plethora of other manifestations in the central nervous system (CNS), peripheral nerves, eyes, ears, heart, gastrointestinal tract, and endocrine organs, may occur. Genotypically, MERRF is due to mutations in 13 mtDNA located gene and 1 nDNA located gene. The strongest genotype phenotype correlation exists for the genes MT-TK, MT-TL1, and POILG1. Epilepsy is the second most frequent phenotypic feature of MERRF. Seizure types associated with MERRF include generalised or focal myoclonic seizures, focal atonic, generalised tonic-clonic, generalised atonic, generalised myoclonic-atonic, tonic-clonic seizures, or typical absences. Treatment of epilepsy in MERRF relies on expert opinions. According to their recommendations, AEDs of choice for epilepsy in MERRF include levetiracetam, topiramate, zonisamide, piracetam, and benzodiazepines. Perampanel is promising but has been applied only in non-mitochondrial myoclonic epilepsy. Mitochondrion-toxic AEDs (valproate, carbamazepine, phenytoin, barbiturates), should be avoided as well as AEDs potentially enhancing the frequency of myocloni (phenytoin, carbamazepine, lamotrigine, vigabatrin, tiagabine, gabapentin, pregabalin, oxcarbazepine). Conclusions: Epilepsy in MERRF favourably responds to levetiracetam, topiramate, zonisamide, piracetam, and benzodiazepines. Mitochondrion-toxic AEDs should not be given as first-line AEDs and AEDs enhancing frequency and intensity of myocloni should be avoided.