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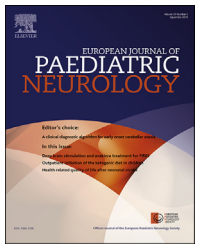

Editorial

Strategies for extinguishing FIRES

The role of inflammation in epilepsy in gaining an increasing interest and is thought to be a part of the epileptogenic mechanisms in several paediatric epileptic syndromes, e.g. antibody-mediated autoimmune encephalitis. A particularly troublesome form of acute epilepsy condition is the so called febrile infection-related epilepsy syndrome (FIRES), which affects previously healthy children with an explosive onset of super-refractory status epilepticus following a nonspecific febrile illness.[1] The poor outcome with a mortality rate up to 30% and refractory epilepsy and intellectual disability present in virtually all cases, warrants early, aggressive and effective treatments. However, finding such effective treatments has proven extremely difficult as FIRES is largely unresponsive both to antiepileptic drugs and immunotherapy.[2] The lack of knowledge concerning the pathophysiological mechanisms activated in FIRES further contributes to this troublesome picture.

One theory with increasing scientific support is that the pathogenesis of FIRES involves systemic inflammation and the release of pro-inflammatory cytokines with activation of innate immune mechanisms in certain brain areas.[3] Targeting such inflammatory pathways could thus offer alternative treatments, and several reports have focussed on the pro-inflammatory cytokine interleukin-1 beta and the possibility of blocking this pathway with the IL-1R1 antagonist Anakinra.

In the current issue of European Journal of Paediatric Neurology, Sa and colleagues describe two paediatric patients that were treated with Anakinra and also with deep brain stimulation targeting centromedian thalamic nuclei (CMN-DBS).[4] The latter has been used previously in refractory epilepsies, but has not been described in FIRES. Outcome varied between the two cases and whereas CMN-DBS abolished generalized seizures in both cases, Anakinra had a positive effect in one. Although only two patients, this is the first description of CMN-DBS for FIRES and it adds to the scarce literature on IL-1 blockade, rendering some support to both therapies that must be considered promising.

One obstacle in interpreting results in a complex and life-threatening medical condition like FIRES is the simultaneous use of multiple drugs along with a natural course due to mechanisms that we do not fully understand. Discriminating the effect of a specific drug or intervention from others will in this situation be very difficult. On the other hand, it will not be ethically possible to withhold or postpone treatments that may be lifesaving. Also, the rarity of the disease makes anything but multicentre studies impossible. So how do we proceed?

One possible strategy is to develop consensus treatment protocols defining standard treatments including doses and timing. If combined with a standardized protocol for data recording and biomarker sampling, we may achieve homogeneity among patients that will allow direct comparison and pooling. Such initiatives are on the way and will hopefully aid in larger scale evaluation of possible treatments within a near future.

A good thing, it is time to extinguish FIRES.

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Ronny Wickström
Neuropaediatric Unit, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden
E-mail address: Ronny.wickstrom@ki.se

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