ELSEVIER

Official Journal of the European Paediatric Neurology Society

Editorial

Beyond the annualized relapse rate: Assessment of cognitive outcome after treatment in paediatric multiple sclerosis

Paediatric multiple sclerosis (MS) is a devastating demyelinating and inflammatory disease of the central nervous system. Compared to adults, children with MS tend to have a higher relapse rate and more axonal damage.[1] Notably, they have a less than expected brain growth already in the very early phase of their disease.[2] A large proportion of children with MS face severe cognitive problems negatively impacting their educational trajectories.[1] For treatment in paediatric MS, traditionally an escalating model is applied, starting with first line injectables as interferon beta-1a, interferon beta-1b and glatiramer acetate. In case of failure of these first line regimes, therapy is escalated to more effective treatment modalities as fingolimod or natalizumab with potentially more serious side effects.[1,3] With an increasing availability of these highly effective treatment options we can now discuss if, instead of an escalating approach, we should apply an upfront approach with highly effective treatment already at the start of the disease.[4] Balancing the higher effectiveness of these newer treatment options against potential (long term) side effects remains a challenge in children. Therefore, more information on the outcome of these newer more effective modalities is necessary. Typically, treatment studies in paediatric MS report on annualized relapse rate as a primary outcome, but as cognition plays such an important role in paediatric MS more information about cognitive outcome of these newer treatment options is much needed.

In this issue Johnen et al. report on cognitive outcome after early effective treatment in children with paediatric MS.[5] They performed a single centre observational evaluation of a relatively small cohort of nineteen children with MS. The authors confirmed that children with MS experience cognitive impairment (CI) already in the very early phase of their disease. In their group comparison they found that the six patients treated with early highly effective treatments (fingolimod and natalizumab) had no signs of CI at last follow-up. Yet in the group of thirteen patients that did not receive received this highly effective treatment CI was observed in nine (69%). No baseline disease parameters appeared to attribute to these differences in CI at follow-up.

As the authors have stated themselves: These preliminary results based on an observational study in a very small number of children exposed to highly effective early treatment options cannot yet guide our treatment decisions and need validation. Importantly, this study emphasizes the need for multicentre and international standardized treatment evaluation in paediatric MS, including cognitive assessment.

REFERENCES

1. Neuteboom R, Wilbur C, Van Pelt D, Rodriguez M, Yeh A. The spectrum of inflammatory acquired demyelinating syndromes in children. *Semin Pediatr Neurol* 2017 Aug;**24**(3):189–200.
2. Kerbrat A, Aubert-Broche B, Fonov V, Narayanan S, Sled JG, Arnold DA, Banwell B, Collins DL. Reduced head and brain size for age and disproportionately smaller thalami in child-onset MS. *Neurol* 2012 Jan 17;**78**(3):194–201.
3. Chitnis T, Arnold DL, Banwell B, Brück W, Ghezzi A, Giovannoni G, et al., PARADIGMS Study Group. Trial of fingolimod versus interferon beta-1a in pediatric multiple sclerosis. *N Engl J Med* 2018 Sep 13;**379**(11):1017–27. https://doi.org/10.1056/NEJMoa1800149. PubMed PMID: 30207920.
4. McGinley M, Rossman IT. Bringing the HEET: the argument for high-efficacy early treatment for pediatric-onset multiple sclerosis. *Neurother* 2017 Oct;**14**(4):985–98.
5. Johnen A, Elpers C, Riepl E, Landmeyer NC, Krämer J, Polzer P, et al. Early effective treatment may protect from cognitive decline in paediatric multiple sclerosis. *Eur J Paediatr Neurol* 2019 Sep 5;**23**(6):783–91.

Rinze F. Neuteboom
Dep. of Neurology, Sophia Children's Hospital-Erasmus MC, the Netherlands
E-mail address: r.neuteboom@erasmusmc.nl

https://doi.org/10.1016/j.ejpn.2019.10.004