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Content

NEUROFILAMENT AS A BIOMARKER OF RESPONSE TO GENETICALLY DESIGNED THERAPIES FOR SPINAL MUSCULAR ATROPHY

Miloš Brkušanin,[1] Vedrana Milić-Rašić,[2,4] Vesna Branković,[2] Zorica Stević,[3,4] Dimitrije Nikolić,[4,5] Ana Kosać,[2] Kristina Jovanović,[5] Jelena Karanović,[1] Jovan Pešović,[1] Goran Brajusković,[1] Dušanka Savić-Pavićević[1]

[1]Centre for Human Molecular Genetics, University of Belgrade-Faculty of Biology, Belgrade, Serbia;
[2]Clinic for Neurology and Psychiatry for Children and Youth, Belgrade, Serbia; [3] Neurology Clinic, Clinical Centre of Serbia, Belgrade, Serbia;
[4]University of Belgrade-School of Medicine, Belgrade, Serbia;
[5]University Children's Hospital Tirsova, Belgrade, Serbia

Considering the substantial impact of genetic therapies for spinal muscular atrophy (SMA), longitudinal follow-up of patients undergoing treatment is crucial to effectively monitor treatment response. While functional rating scales are commonly used as primary outcome measures, they may not fully capture all the therapeutic benefits. To address this limitation, the phosphorylated neurofilament heavy chain (pNF-H) protein has emerged as a promising biomarker for evaluating treatment response. pNF-H is a neuron-specific filament that exhibits increased levels in the cerebrospinal fluid (CSF) and plasma in the presence of neuronal degeneration. Our study includes individuals treated with Nusinersen (CSF and plasma samples) and Risdiplam (plasma), as well as age- and sex-matched control subjects (CSF and plasma). By examining the dynamics of pNF-H levels in these groups, we sought to identify significant differences indicative of treatment response. Before treatment, SMA individuals typically exhibit higher levels of pNF-H compared to non-SMA individuals. Elevated levels of pNF-H are associated with more severe clinical manifestations of the disease. During Nusinersen treatment, a notable decline in pNF-H levels during the first 2 months can be observed. Current findings suggest that genetic therapies have a notable impact on reducing pNF-H levels over time. By examining the changes in pNF-H levels, our study offers valuable insights into the underlying biochemical alterations associated with these therapies. Furthermore, it supports the use of pNF-H as a complementary measure to functional rating scales and as a potential biomarker for evaluating treatment effectiveness and monitoring disease progression in SMA.

Key words: Spinal muscular atrophy; Neurofilament; Nusinersen; Risdiplam

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