

Narcolepsy in children

Relationship to the H1N1 influenza vaccination, association with psychiatric and cognitive impairments and consequences in daily life

Akademisk avhandling

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- I. Szakács, A. Darin, N. Hallböök, T. **Increased childhood incidence of narcolepsy in western Sweden after H1N1 influenza vaccination.** *Neurology.* 2013 Apr 2;80(14):1315-21
- II. Szakács, A. Hallböök, T. Tideman, P. Darin, N.* Wentz E.* **Psychiatric comorbidity and cognitive profile in children with narcolepsy with or without association to the H1N1 influenza vaccination.** *Sleep.* 2015 Apr 1;38(4):615-21
- III. Chaplin, JE. Szakács, A. Hallböök, T. Darin, N. **The development of a health-related quality of life instrument for young people with narcolepsy: *NARQoL*.** *Submitted to Health and Quality of Life Outcome.* 2016 May
- IV. Szakács, A. Chaplin, JE. Tideman, P. Strömberg, U. Nilsson, J. Darin, N. Hallböök, T. **A population-based study of health-related quality of life, adaptive behavior and parenting stress in children with narcolepsy with or without association to the H1N1 influenza vaccination.** *Manuscript*

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ABSTRACT

Aims: The purpose of this thesis was to study a population-based cohort of children and adolescents with narcolepsy in western Sweden to determine the incidence and relationship with the H1N1 influenza vaccination, psychiatric comorbidity, cognitive profile, health-related quality of life, adaptive behavior and parenting stress.

Methods: We aimed to identify all individuals below 18 years of age who developed narcolepsy between January 1, 2000, and December 31, 2010. Post-H1N1 influenza vaccination (PHV) narcolepsy was considered in patients with clinical onset within 10 months of vaccination. Psychiatric comorbidity was investigated using a test battery of semi-structured interviews and screening tools. The cognitive assessments were made by a clinical psychologist using age specific Wechsler Scales. A narcolepsy-specific quality of life questionnaire, the NARQoL was generated based on statements from four focus groups comprising young people with narcolepsy and was used along with the generic KIDSCREEN questionnaire to assess the HrQoL in the study population. The Adaptive Behavior Assessment System was administered to measure adaptive skills in the children and the short form of the Parenting Stress Index questionnaire was used to measure parenting stress in their parents.

Results: The incidence of narcolepsy was 25 times higher in the period after the vaccination compared with the period before. The children in the PHV group had a lower age at onset and a more sudden onset than is generally seen. Psychiatric comorbidity was present in 43% of the patients in the PHV group; ADHD in 8/28, major depression in 6/30, general anxiety disorder in 3/30 and oppositional defiant disorder (ODD) in 2/30. In the non-post-H1N1 influenza vaccination (nPHV) narcolepsy group, 1/7 patients had ADHD in combination with ODD. The cognitive assessment showed decreased verbal comprehension and working memory in both groups. Parents in the PHV group rated significantly lower scores for adaptive behavior relating to conceptual and social skills. Parents also rated higher in “total stress”, “parent-child dysfunctional interaction” and “difficult child”, significantly so in the PHV group. The pilot NARQoL questionnaire consisted of two patient reported outcome modules: QoL and future perceptions. Test-retest reliability and convergent validity with the KIDSCREEN-10 was good. Children with narcolepsy had significantly diminished scores compared with controls on both the KIDSCREEN and NARQoL; the PHV children in all domains of the NARQoL. Furthermore, patients with psychiatric comorbidity had a significantly lower full-scale IQ, HrQoL and adaptive behavior compared with those without.

Conclusions: The H1N1 influenza vaccination with Pandemrix represents a precipitating factor for narcolepsy in children. The identified high prevalence of psychiatric comorbidity and cognitive difficulties highlights the importance of a careful psychiatric and neuropsychological follow-up. The NARQoL revealed a more globally affected QoL than previously reported. Impaired adaptive behavior and high levels of parenting stress indicate considerable impact on daily life.

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