

On the possible relationship between narcolepsy and vaccines: the analysis of AEFI reports from the VAERS database

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Narcolepsy is a rare chronic sleep disorder severely debilitating presenting with excessive daytime sleepiness and manifestations of disrupted rapid eye movement sleep stage (Dauvilliers et al., 2001). Mechanisms underlying narcolepsy are not fully understood, however experimental data indicate that the dysregulation of the sleep-wake cycle is caused by the destruction of hypocretin forming neurons in the hypothalamus, which is thought to result from an auto-immune process triggered by environmental factors in susceptible individuals (Zawilska et al., 2012). A correlation with vaccination was also supposed; available data are mainly related to a possible involvement of influenza vaccination (Nohynek et al., 2012; Carnovale et al., 2017; Lee et al., 2016). Since millions of vaccines are given each year the possibility that vaccination might be somehow involved in this serious chronic sleep disorder requires being addressed.

In order to explore a potential causal correlation between vaccines and narcolepsy, we performed an extensive analysis of the adverse event following immunization (AEFI) reports (from 1990 to 2017) contained in the VAERS database which represents a real-world source of data.

For each report of narcolepsy/cataplexy following immunization, we applied the established criteria for AEFI causality assessment; the quality of the reports was determined by the level of evidence using the Automated Brighton Collaboration case definition tool (ABC-tool) for narcolepsy. For the top three vaccines mostly involved we calculated the 95% confidence interval around the proportional reporting ratio (PRR).

182 AEFI reports were initially identified. Duplicated reports (17) and literature cases (25) were excluded, resulting in 140 reports included in the analysis of the causality assessment. 88% (123) of these were indeterminate, 12% (17, all excluded from the analysis) not related or not classified. According to BC criteria, we identified 10 cases defined as not a case (level 5 of evidence) and excluded them from the analysis. The vaccines mostly involved in the remaining 113 validated cases of narcolepsy were vaccines against influenza virus (70 reports, 62%; PRR: 6.9%, CI:6.9±0.16), followed by Human Papilloma Virus (HPV) vaccine (41 reports, 36.2%; PRR: 7.2, CI:7.2±0.14) and Hepatitis B vaccine (4 reports, 3.5%; PRR: 0.3). There was a female predominance (67% vs 37%) and an increasing trend starting from 2010. Overall, 61 reports (54%) were serious, 52 (46%) were classified as not serious.

Although further studies are still needed to confirm a correlation between vaccines and narcolepsy, our analysis suggests that this occurrence is likely to occur and the need to monitor this issue above all for Influenza virus vaccine and HPV vaccination is recommended for a prompt diagnosis.

Dauvilliers et al. (2001). *Neurology*. 57, 2029-33.

Zawilska et al. (2012). Postepy Hig Med Dosw. 66,771-86.

Nohynek et al. (2012). PLoS One. 7, p. e33536.

Carnovale et al. (2017). J Neurol Sci. 373,179-181.

Lee et al. (2016). J Neurol Sci. 356, 29-34.