

Investigation of the temporal association of Guillain-Barre' Syndrome with influenza vaccine and influenza-like illness

05 Mar 2009

Stowe J , Andrews N, Wise L, & Miller E. Investigation of the Temporal Association of Guillain-Barré Syndrome With Influenza Vaccine and Influenza-like Illness Using the United Kingdom General Practice Research Database. American Journal of Epidemiology Advance Access published on February 1, 2009, DOI 10.1093/aje/kwn310. Am. J. Epidemiol. 169: 382-388.

This article can be found [here](#).

DESCRIPTION

This paper details the use of the self-controlled case series method developed by this group and others to investigate the relation of Guillain-Barre syndrome (GBS) with influenza vaccination and influenza-like illness using data from the General Practice Research Database from 1990 to 2005, in the UK. This method automatically controls for individual-level confounders and requires only data on cases with their linked vaccination records.

The researchers found no evidence of an association between influenza vaccination and GBS (relative incidence: 0.76). In contrast an increased risk of GBS was seen during the month after influenza-like illness – ILI - (relative incidence: 16.64) whereas the risk averaged out over the three months after ILI was significantly lower (relative incidence: 7.35). The researchers comment that these results are consistent with observations that GBS is often preceded by a respiratory illness. These illnesses normally peak in the winter; for this reason this study cannot discern whether this association between GBS and influenza-like illness is only applicable to influenza virus infection or, on the other hand, could also be applied to other respiratory pathogens. The increased risk of GBS after influenza-like illness, if specific to infection with influenza virus, together with the absence of a causal association with influenza vaccine suggests that influenza vaccine should protect against GBS however such a protective relationship could not be demonstrated. The paper also describes limitations that could affect such calculations using the GPRD data set. That is the time lag between the onset of symptoms and the recorded diagnosis, the potential lack of accuracy on the coding of GBS in the GPRD and the lack of specificity of influenza like illness for actual influenza infection. To assess the first two factors, the authors used a vaccinated subset of cases on which these factors were accounted for. After the analysis, no significant differences in relative incidence were seen compared with the relative incidence found by using all GBS episodes. The authors particularly noted that this study has implications for the risk assessment process that will need to be put in place to evaluate the utility of pandemic influenza vaccines.

ECDC COMMENT (05/03/2009)

One of the more difficult areas of epidemiological study is investigating as rapidly as possible whether or not adverse events that seem to be associated in time with immunisation are actually bear some causal relationship.(1) The group publishing here are among the most innovative in Europe in this area of work and are internationally recognised.(1-4) Ever since the Swine Flu vaccine incident in the United States there has been the suspicion that influenza vaccination might occasionally be associated with Guillain-Barre syndrome (GBS).(5) Given this history and the persistent background incidence of GBS in the population it seems almost inevitable that when the next pandemic occurs and vaccines are mass deployed someone will report vaccine associated GBS. What then will be needed is pre-planned studies using techniques like this or data-linkage studies that can be deployed rapidly to test the hypothesis. It will not be possible to mount such studies in every country and a possible instance of European added value will be to test in one country (with say good data linkage systems) a hypothesis generated in another European country but where hypothesis testing is not feasible or at least cannot be done swiftly.

1. Taylor B, Lingam R, Simmons A, Stowe J, Miller E, Andrews N. Autism and MMR vaccination in North London; no causal relationship Mol Psychiatry. 2002;7 Suppl 2:S7-8.
2. Andrews N, Stowe J, Miller E, Taylor B. Post-licensure safety of the meningococcal group C conjugate vaccine Hum Vaccin. 2007 Mar-Apr;3(2):59-63. Epub 2007 Mar 17.
3. Miller E, Waight P, Farrington P. Safety assessment post-licensure. Dev Biol Stand. 1998;95: 235-43.
4. Verstraeten T, DeStefano F, Chen RT, Miller E. Vaccine safety surveillance using large linked databases: opportunities, hazards and proposed guidelines Expert Rev Vaccines. 2003 Feb;2(1):21-9.
5. Sencer DJ, Miller JD. Reflections on the 1976 Swine Flu Vaccination Programme. EID 2006; 12: 29-33.

