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Medical Update Memo

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Small study suggests MS development may be linked to hepatitis B

SUMMARY

A new study has found a threefold increase in the likelihood of individuals developing MS if they had had a hepatitis B vaccination within the prior three years compared to individuals who had no hepatitis B vaccination in that time frame. The study findings are in the September 14 issue of *Neurology*. Major points of note from the study are:

- The study included 163 people with MS (11 of whom had had hepatitis B vaccinations within 3 years prior to developing symptoms of the disease) and 1,604 controls without MS.
- The vast majority of individuals with MS in the study had not had hepatitis vaccination, indicating that hepatitis vaccination might be only one factor contributing to the development of MS.
- An accompanying editorial notes that while the methods used in this study are sound, the data presented related to MS do not provide sufficient evidence to change immunization policies, especially given the serious and at times fatal nature of hepatitis B.

DETAILS

A new study has found a threefold increase in the likelihood of individuals developing MS if they had had a hepatitis B vaccination within the prior three years compared to individuals who had no hepatitis B vaccination in that time frame. The study, supported by the National MS Society (USA), included 163 people with MS (11 of whom had had hepatitis B vaccinations within 3 years prior to developing symptoms of the disease) and 1,604 controls without MS. Miguel A. Hernan, MD, DrPH (Harvard School of Public Health, Boston) and colleagues report their findings in the September 14 issue of *Neurology* (2004;63:838-842). While noting the association between vaccination and development of MS, the authors also stress that 93% of the people in their sample who

had MS had not been vaccinated, and developed MS anyway. An accompanying editorial notes that while the methods used in this study are sound, the data presented related to MS do not provide sufficient evidence to change immunization policies, especially given the serious and at times fatal consequences of hepatitis B.

Background

Hepatitis B virus causes some 4 million acute infections worldwide annually. More than 350 million individuals are chronic carriers of the virus after infection, and some 25% of those will die as a consequence of cirrhosis of the liver or liver cancer brought on by the viral infection. Vaccination against hepatitis B has been established to be safe and effective in helping to prevent infection and subsequent liver disease.

However, in recent years, concerns have been raised that vaccination against hepatitis B virus might increase risk for developing a variety of diseases, including MS. The concerns related to MS were due in part to a report from France in the mid-1990s of a possible increase in autoimmune diseases, including MS, after hepatitis B vaccination. However, efforts to confirm this report had been unsuccessful and two separate reports concluded that there was no evidence of an association between vaccination and the risk either of developing MS or having MS relapses (*The New England Journal of Medicine*, February 1, 2001). The World Health Organization and, separately, the Institute of Medicine reviewed all available data and concluded that there was no association between hepatitis B and MS.

In spite of considerable evidence to the contrary, some public concern has remained about a possible link between hepatitis B vaccine and MS. Dr. Hernan and colleagues examined this possibility using the General Practice Research Database (GPRD), which includes more than three million people in the United Kingdom health care system.

Study background

From the entire GPRD database, Dr. Hernan and colleagues identified 713 people who had been diagnosed with MS between January 1993 and December 2000. Of these cases, the researchers identified 163 (23%) in whom the diagnosis of MS could be confirmed via examination of medical records - an essential step to be certain of the diagnosis, and who had records in the GPRD for at least 3 years prior to the onset of MS symptoms. A total of 1,604 control cases without MS but with at least three years of GPRD records (approximately 10 for each case of MS) were chosen for comparison.

The results show that 11 (6.7%) of the 163 people with MS received at least one hepatitis B immunization during the 3 years before MS symptom onset, compared with 39 (2.4%) of controls who did not develop MS. To address the specificity of hepatitis B vaccination the authors also extracted data on influenza and tetanus vaccinations, two common immunizations. But, compared to controls, there was no difference in the frequency of these immunizations in people who developed MS compared with those who did not.

The study does not evaluate whether hepatitis B vaccination increased MS relapses or disease activity in those already diagnosed with MS. And, the authors provide no biological explanation as to why there might be an association between hepatitis B vaccination and development of MS.

While demonstrating in this study a threefold increase in the likelihood of developing MS after hepatitis vaccination, the authors note that the vast majority of individuals in the GPRD with MS - 93% of the sample of 163 people with MS - had not been vaccinated within three years of symptom onset. Thus, hepatitis B vaccination may be only one contributor - and perhaps a minor one - to the likelihood of developing of MS.

Conclusion

This study found a threefold increase in the likelihood of individuals developing MS if they had had a hepatitis vaccination within the prior three years compared to individuals who had no vaccination. But the vast majority of individuals with MS in the study had not had hepatitis vaccination, indicating that hepatitis vaccination might be only one factor contributing to the development of MS.

In an accompanying editorial, Robert T. Naismith, MD, and Anne H. Cross, MD (Washington University in St. Louis) commented that although the methods used by Dr. Hernan and colleagues are sound, the data are derived from only 11 cases of MS and are at variance with the findings of most prior studies. At the time the data were collected, hepatitis B vaccination was targeted primarily to individuals at high risk for developing the disease, such as health-care workers. These individuals may have been more aware of neurologic symptoms and more likely to report them earlier than people in other professions. The editorial adds: "Thus, this article should be viewed as another piece of the puzzle of MS causation, but the data presented do not provide proof of an association sufficient to implement policy changes with regard to immunization programs."

Hepatitis B vaccination is commonly recommended for all children under the age of 18. The vaccination is considered to safe and effective in preventing the development of hepatitis B.

(Adapted from Research Programs Department, National MS Society [USA])

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