EDITORIAL

Booster hepatitis B vaccination not necessary for long-term protection in children immunised with hexavalent vaccines

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In October 2000, two hexavalent vaccines (Hexavac, Sanofi Pasteur MSD and Infanrix Hexa, GlaxoSmith Kline) were licensed in the European Union for vaccinating children against diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and invasive infections caused by *Haemophilus influenzae b*. In September 2005, Hexavac was suspended by the European Medicines Agency (EMA) because of concerns over its ability to provide long-term protection against hepatitis B [1]. No action was taken over Infanrix Hexa since immunogenicity of its hepatitis B component did not raise equal concern. Until its suspension in 2005, approximately 10 million doses of Hexavac were distributed globally. Yet it is not known whether infants vaccinated with Hexavac have maintained protection or will require a booster vaccination to sustain immunity. This issue is crucial in Europe – especially in Italy, Germany, Austria and at lesser extend in France, Greece and Spain – where Hexavac was given to several cohorts of infants from 2000 until suspension in 2005.

An open-label, randomised, controlled, multicentre study was carried out in Italy in order to assess the duration of immunity from vaccination with Hexavac and Infanrix Hexa by testing whether concentrations of antibodies against hepatitis B (anti-HBs) were retained in 1543 children who had been vaccinated 5 years previously (833 with Hexavac and 710 with Infanrix Hexa), and whether a booster vaccination was needed [2].

At the start of the study, blood samples were taken from each child to measure levels of anti-HBs antibodies. Children with anti-HBs concentrations of 10 mIU/mL or higher were deemed immune. Children with levels of antibodies less than 10 mIU/mL were randomly assigned to a booster monovalent hepatitis B vaccine (either 5 μg of HBVaxPro, Sanofi Pasteur MSD or 10 μg of Engerix B, GlaxoSmithKline) and tested 2 weeks later.

Five years after primary immunisation, 38.4% of children who received Hexavac had protective concentrations of antibodies (≥ 10 mIU/mL) compared with 83.2% of children who received Infanrix Hexa ($p < 0.0001$). Geometric mean concentration (GMC) was lower among children primed with Hexavac than among those primed with Infanrix Hexa ($p < 0.0001$). In the multivariate analysis the type of hexavalent vaccine given was the only determinant of anti-HBs concentration after adjustment.

However, children in both groups who received a booster hepatitis B vaccination had a similar rapid anamnestic response, and the proportion of children who responded to the booster were similar between groups. 92.1% of children originally given Hexavac and 94.3% of children originally given Infanrix Hexa showed protective levels of antibodies after the booster vaccination, thus showing the presence of specific immune memory.

Side-effects were infrequent, mild, and did not differ between the two booster groups. No serious adverse events were reported.

These results suggest that infant immune systems are able to recall responding to hepatitis B more than 5 years after primary immunisation with hexavalent vaccines, thereby providing effective protection even in children showing low (< 10 mIU/ml) or undetectable levels of antibodies. Together, these findings suggest that in healthy children the immunological memory for hepatitis B surface antigen (HBsAg) may outlast the presence of antibody. In other words, children who have lost preventive antibody concentrations might still maintain T-cell memory that is able to trigger anti-HBs production by B cells when activated by revaccination or by natural exposure to hepatitis B virus (HBV) [3]. Therefore we can infer that if a vaccinated child is exposed to HBV, the immune memory rapidly induces a vigorous anamnestic response which prevent against acute disease and the development of a chronic carrier state.

In conclusion, the main message from this study is that Hexavac, although somewhat less immunogenic that Infanrix Hexa, induced immune memory. Thus at present routine booster doses of hepatitis B vaccine do not seem necessary to sustain immunity in children vaccinated with hexavalent vaccines. Whether the memory persists for life is questionable, and evidence suggests that its persistence is associated with time after primary vaccination and likely to the strength of the initial immune response [4, 5]. Additional follow-up is required to identify whether immunological memory persists during adolescence and adulthood – when risk of HBV exposure does significantly increase – or whether a booster might be needed later in life to maintain lifelong protection.

References

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