Combination Hepatitis A-Hepatitis B Vaccine

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Summary

▲ The adult formulation of this combination hepatitis A-hepatitis B vaccine contains 720 enzyme-linked immunosorbent assay units (EU) of formalin-inactivated hepatitis A virus strain HM175 and 20 μg of recombinant DNA yeast-derived hepatitis B surface antigen adsorbed onto aluminium salts in 1ml for injection. The paediatric formulation contains half this dosage in 0.5ml for injection.

▲ The combination vaccine has been shown to be highly immunogenic in healthy young adults after the full dosage schedule of 3 doses at 0, 1 and 6 months. Trials in older adults and children indicate that immunogenicity is adequate in these groups also.

▲ The immunogenicity of the combination vaccine appears to be similar to that of hepatitis A vaccine and hepatitis B vaccine administered separately. Possible advantages for the combination vaccine recipient include fewer injections and lower costs.

▲ Local adverse reactions such as soreness at the injection site, redness and swelling occur often with the first dose of the series, but the incidence falls with subsequent doses. Local reactions are usually mild and transient, and reported systemic reactions (fatigue, headache) are thought not to have a causal link with the vaccine.
A combination hepatitis A-hepatitis B vaccine has been formulated for adults using 720 enzyme-linked immunosorbent assay (ELISA) units (EU) of formalin-inactivated hepatitis A virus strain HM175 and 20 μg of recombinant DNA yeast-derived hepatitis B surface antigen. The antigenic components are adsorbed onto aluminium salts in a 1 ml injection for intramuscular administration into the deltoid region. The paediatric formulation for children aged ≤15 years contains half this dosage in 0.5 ml.

Hepatitis B and hepatitis A are common viral diseases worldwide. The WHO Expanded Programme on Immunization has recommended that programmes for hepatitis B immunisation of infants be in place in all countries by the end of 1997. Vaccines are also available using similar doses of hepatitis A antigen or hepatitis B surface antigen alone.\(^1\),\(^2\) A combination vaccine, however, would be useful for individuals (both adults and children) at risk for both infections, such as healthcare workers, travellers to areas where both types of hepatitis are endemic, institutional residents, military personnel and patients with certain underlying medical conditions (e.g. chronic liver disease, haemophilia). Administering the 2 vaccines in the same formulation means that fewer injections (3 compared with 5 or 6 if the single formulations are used) are required, which may improve vaccine acceptability (and possibly compliance) and lower administration costs.

### 1. Immunogenicity Profile

The immunogenicity of the combination hepatitis A-hepatitis B vaccine has been investigated in healthy volunteers. Seroconversion, measured by an ELISA, was assumed at antibody titres of ≥20 or ≥33 IU/L for anti-hepatitis A antigen and ≥1 IU/L for anti-hepatitis B surface antigen. Titres of hepatitis B antibodies ≥10 IU/L were considered to be seroprotective.

- Several studies investigated the immunogenicity of pilot formulations (with the same antigen components and doses as the present commercial formulation) while the vaccine was under development.\(^3\)-\(^5\) After intramuscular administration at months 0, 1 and 6 to healthy individuals aged 18 to 49 years, seroconversion to anti-hepatitis A had occurred in 90 to 96% of recipients [geometric mean titres (GMT) 162 to 471 IU/L], 98 to 100% (GMT 538 to 625 IU/L) and 100% (GMT 4438 to 5368 IU/L), respectively, at months 1, 2 and 7. Hepatitis B antibodies were detected in 26 to 73% (GMT 4 to 8 IU/L), 85 to 98% (GMT 16 to 42 IU/L) and 99 to 100% (GMT 1305 to 21360 IU/L) of recipients at months 1, 2 and 7.\(^4\),\(^5\) and titres indicative of seroprotection were seen in 28%, 50% and 94% of recipients.\(^3\)

- Two double-blind randomised studies compared the immunogenicity of 3 batches of the commercial formulation.\(^6\),\(^7\) In these studies, 276 healthy adults aged 18 to 43 years received 1 ml of the vaccine at 0, 1 and 6 months. Since there were no significant differences among the batches in immunogenicity results in either study, immunogenicity data were pooled. Seroconversion rates (and GMT values) for hepatitis A antibody at 1, 2 and 7 months were 95 to 99% (307 to 394 IU/L), 100% (764 to 1311 IU/L) and 100% (4578 to 8895 IU/L), respectively. Seroconversion rates (and GMT values) for hepatitis B antibody at 1, 2 and 7 months were 69 to 80% (10 to 16 IU/L), 95 to 98% (73 to 104 IU/L) and 100% (2678 to 7097 IU/L), respectively. Seroprotection rates against hepatitis B were 34%, 84% and 99 to 100%, respectively. Immunogenicity results from one of the trials\(^6\) are shown in figure 1.

- Four other double-blind randomised clinical studies of different batches of the combination vaccine have been carried out by the manufacturers.\(^8\) There were no significant differences among the batch lots, and the data from each trial were amalgamated as above. A combined analysis of the results from all 6 studies (n = 784 eligible vaccinees)\(^8\) showed essentially similar immunogenicity for the combination vaccine to that reported above.\(^6\),\(^7\)

Comparative Immunogenicity

- In a comparative nonblinded study, the immu-