Hepatitis B Vaccination—A Singapore Experience

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A hepatitis B prevention and control programme has started in Singapore using B-Hepavac, an approved HB Vaccine manufactured for Singapore Biotech (Pte) by Merck Sharpe and Dohme (USA). 10 µg doses of the vaccine have been shown to be efficacious in populations under 40 years of age. In neonates, a smaller dose of 5 µg given three times at 0, 1, 2 months appears to be as effective as the 10 µg dose.

INTRODUCTION

Viral Hepatitis B is endemic in Singapore. The overall rate of HBsAg is 5%, with 120,000 carriers in the population.

HBV is a notifiable disease of major public health importance in Singapore, because of its association with Acute Viral Hepatitis (AVH), chronic active liver diseases, cirrhosis and primary hepatocellular carcinoma (HCC). AVHB accounts for 50% of acute viral hepatitis. Morbidity and mortality are due to related complications of HBV infections e. g. fulminant hepatic failure in progressing hepatitis, cirrhosis, HCC and patents on chemotherapy immunosuppressive therapy and irradiation therapies.

Seroepidemiological surveys show that transmission occurs vertically, perinatally and horizontally. 5% of babies born to HBeAg positive carrier mothers are carriers in-utero and 84% of neonatal infection are acquired by perinatal transmission. It has been calculated that 23% of carriers develop as perinatal infections but the larger amount of 77% is acquired horizontally. Prospective studies in acute VHB cases have shown that 33%
of infected persons remain as carriers. Confirmation of similar data were seen in retrospec-
tive analysis of transfusion recipients of HBsAg blood (prior to 1975), showing that 33% of
such HBsAg positive recipients remained as carriers (unpublished). The attack rate in
150 seronegative high-risk hospital staff over a three month period was 10%. Such staff
were screened for HBsAg, antiHBc and antiHBs prior to vaccine trials.

Horizontal transmission in susceptibles occur in homes of 'e' positive carriers who
share common items, such as shavers, toothpicks, handkerchiefs, towels, toothbrushes
and combs. High attack rates are also seen in spouses of 'e' positive carriers, prostitutes
and transvestites.

The majority of HBV infection is subclinical and infection occurs continually in all
age groups; about 50% of the population being infected by the age of 40–49 years and
100% by the age of 60 years.

STRATEGIES FOR PREVENTION AND CONTROL

Prevention and control strategies undertaken in Singapore are:
1. Phase introduction of Hepatitis B Vaccination and screening programmes.
2. Public health education for hospital staff, medical profession and public.
3. Long term plans for production of Hepatitis B Vaccine and reagents.

HEPATITIS B VACCINATIONS

The decision to use the MSD HB Vaccine was undertaken after extensive consulta-
tions as to the choice of a vaccine with the widest safety margin possible.

Cost calculations in 1981, had shown that a conservative cost for public health care
of diseases due to HBV (AVH, CH, cirrhosis, HCC) amounted to US $2M per annum.
Similarly, cost calculations showed that it was far cheaper to screen and vaccinate the
susceptibles than to vaccinate everyone at-risk. It was decided that the total cost of
funding the HB Vaccination and screening programme would be equivalent to the cost
of health care from the illness itself.

PILOT STUDIES

In January 1982, small pilot evaluation studies were undertaken in seronegative hos-
pital staff using 10 μg doses at 0, 1 and 2 months. AntiHBs conversions at six months
were 39/45 (87%) in those under the age of 40 years, 13/14 (90%) in those who over 40
years. The GMT one month after the third dose was 255 miU/ml and 305 miU/ml in
those below 40 years and in the over 40 years age group respectively. In a later study,
80 persons below the age of 40 years who received 10 μg doses at 0, 1, and 6 months
showed antiHBs conversions of 85% after the 3rd dose at six months, and 22/29 (76%)
in the over 40 year age group. The GMT for antiHBs, were 1261 and 1300 miU/ml res-
pectively. 5% of these non–responsive responded to a subsequent two doses of vaccines
but in lower titres (often below 30 miU/ml.). The rest were true non–responders.
ADULT VACCINATIONS

The baseline information provided the bases of a subsequent screening programme using HBsAg and antiHBs (because these two tests were cheaper than AntiHBc alone and infected carriers needed to be identified). 10 μg doses given intramuscularly at 0, 1, and 6 months were introduced for adults at-risk for cost reasons. Although a 10 μg dose (×3) was recommended for those over 40 years, it was also suggested that following vaccination, vaccines should be checked for AntiHBs conversion. Those who did not respond would then require two higher doses of 20 μg or 40 μg as may be indicated. A 5 μg dose used in young adults was found to be inadequate.

PERINATAL VACCINATIONS

In June 1983, a prospective clinical trial was conducted to evaluate the efficacy of a lower dose of HB vaccine given at 5 μg at birth, 1 and 2 months. This was compared with a 10μg dose given also at birth, 1 and 2 months. This schedule was planned to avoid other childhood vaccinations starting at 3 months. Six groups were involved in the study. All infants were healthy normal neonates born of birth weight between 2.5 to 4 kg b. w. and without any congenital defects. The groups consisted of babies of mothers who were HBsAg negative (controls), HBsAg pos/'e' neg, HBsAg pos/ HBeAg positive. 0.5 mls HBIG of antiHB titre greater than 200 IU/ml were given within 24 hours of birth together with HB Vaccine in the 'e' Ag positive groups. 406 neonates were studied.

For 5 μg evaluable neonates: At six months 31/34 (91%) of controls, 56/61 (92%), 18/21 (86%) of normal, 'e' negative, 'e' positive respectively showed antiHBs conversions.

For 10 μg: At six month 40/45 (89%), 54/57 (95%) and 19/25 (76%) of normal, 'e' negative and 'e' positive respectively showed conversions.

4/69 (5pg dose group), 4/71 (10pg) of HBeAg positive neonates were carriers from birth inspite of HBIG plus vaccine. They form the 5% infected in-utero.

IMMUNOPROPHYLAXIS FAILURES

Inspite adequate detectible antiHBs titres in neonates at 4 weeks in the 'e' Ag positive group, given HBIG and vaccine, there were 9 failures detected at 12 weeks; 4 out of 49 (5 μg) and 5 out of 56 (10 μg doses) respectively, giving an efficacy of 92% for the 5 μg doses and 91% for the 10 μg doses.

The GMT for antiHBs, was no different in all the groups studied nor between the 5 μg and 10 μg doses or sex of child.

STRATEGY OF HB VACCINATION

Selective vaccinations of at-risk persons were recommended for the following: (1)
Neonates born to HBsAg positive mothers, (2) hospital staff, including medical and dental students, (3) family contacts of acute and chronic carriers and (4) new military recruits and (5) contacts of prostitutes and transvestites.

Vaccination in the private and public sector have already begun since January 1983 and nearly 33,000 persons have received at least one dose of vaccine. Free vaccines were offered to groups 1, 2 and 4.

VACCINE-RELATED EVENTS

The vaccine is well accepted and adverse reactions occurring within six weeks of vaccination reported were seen in 49 persons (0.14%). These were: sore arm (27), transient fever (6), disorientation (4), muscular rash (4), superficial punctate keratitis (1). More serious events requiring termination of vaccination were: coexistent hepatitis A infection (2), pneumonia (1), aseptic meningitis (1), haematuria (1), urticarial rash (2).

EDUCATIONAL PROGRAMME

Both the public and medical profession have been kept constantly informed of the status of HBV, and the need for good hygienic practices and immunisation for those at risk. Although, it may appear necessary to expand the immunity of the population by a larger coverage as suggested by an advisor, cost and acceptance of new vaccines are limiting factors in implementation.

LONG TERM PROGRAMME

Since the programme is a long term one, facilities to produce the vaccine for the needs of the region are in hand. B-Hepavac, the licensed vaccine product of Singapore Biotech Pte Ltd, the manufacturing company is now available. It is available in 3 mls and 1 ml vials of 60 µg and 20 µg respectively. B-Hepavac is an FDA approved MSD vaccine produced for Singapore Biotech by Merck Sharpe and Dohme.

REFERENCE