Eur J Clin Microbiol Infect Dis (2001) 20:185–187

Note

Control of a Community-Wide Outbreak of Hepatitis A by Mass Vaccination with Inactivated Hepatitis A Vaccine

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Abstract The epidemiology and control of hepatitis A virus was investigated during an outbreak of hepatitis A in a village in Israel. Postexposure administration of immune globulin to contacts was ineffective in controlling the outbreak. However, within 2 weeks of starting a mass immunization campaign with hepatitis A vaccine, the incidence of hepatitis A declined dramatically; the last case occurred 6 weeks after the immunization program began. The study demonstrated that while postexposure administration of immune globulin may diminish but not entirely arrest transmission of hepatitis A virus, active hepatitis A vaccination is a safe and effective intervention that can be used safely in hepatitis A virus antibody-positive children.

Introduction

Hepatitis A virus (HAV) infection is endemic in Israel and the surrounding region. Large hepatitis A outbreaks were common in Israel during the 1970s, and they still occur sporadically, particularly within defined communities. Such outbreaks are often difficult to arrest using various control measures. The use of active hepatitis A vaccination during outbreaks has been recently employed in some communities. In 1996, a community-wide outbreak of hepatitis A occurred in a village in Israel, and mass active vaccination was performed as a control measure.

Patients and Methods

In late 1996, a community-wide outbreak of hepatitis A occurred in an Arab village of a poor socioeconomic level in Israel. Epidemiologic investigations and hygiene improvement measures were initiated immediately, together with immune globulin immunization. Post-exposure immune globulin (0.02 ml/kg) was administered initially to household contacts aged 8 years and younger, and subsequently to children attending childcare facilities in which one or more hepatitis A cases had been observed. In all, 738 children received immune globulin as prophylaxis.

Despite these measures, the number of cases increased, and the Ministry of Health then approved mass active vaccination with hepatitis A vaccine. As most cases occurred in children, the target group for vaccination included children aged 1–6 years, excluding those who had already contracted clinical hepatitis A.

Within 5 days 1,133 children received a dose of hepatitis A vaccine (Havrix Pediatric, 360 Elisa Units [EU]; SmithKline Beecham, Belgium). Based on the results of serologic testing, anti-HAV-positive children received no further doses and anti-HAV-negative children received a second vaccine dose after 1 month and a booster 6–12 months later.

Results and Discussion

The epidemic curve (Figure 1) illustrates the weekly incidence of hepatitis A cases. The epidemiologic investigation did not reveal a common source of infection, nor did weekly microbiologic tests show any evidence of drinking water contamination. The irregular shape of the epidemic curve, as well as the occurrence of secondary hepatitis A cases within certain households, supported a pattern of person-to-person transmission. Most (83/96, 86.5%) of the hepatitis A clinical cases occurred in children aged 1–6 years. Six children were hospitalized, including a 4-year-old girl who sustained acute liver failure necessitating an emergency liver transplant.

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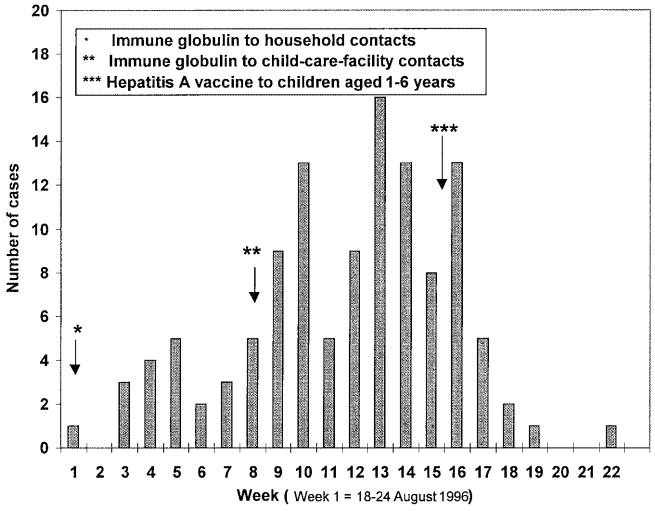

Figure 1 Number of cases of hepatitis per week of outbreak

The target population for the active hepatitis A virus (HAV) vaccination comprised those children aged 1–6 years who had not previously contracted HAV infection. The compliance rate was 90.4%: 1,133 of 1,254 children were vaccinated.

Blood samples were drawn from 1,126 (99.5%) of the children. The children were divided into three groups, based on their HAV antibody status (Table 1): group 1 comprised those who had no past or recent exposure to HAV (nonimmune group); group 2 comprised those recently infected in the current epidemic; and group 3 comprised those with evidence of past infection.

The prevalence of HAV antibodies was significantly associated with age (chi square = 404.7, $P < 0.001$) (Table 1). Furthermore, the older the child, the more likely the infection was to manifest clinically. In children aged 12–35 months, 16% had overt clinical infection, whereas 31% of children aged 36–72 months had clinical infection. (chi-square = 25.3, $P < 0.001$).

Adverse reactions to the hepatitis A vaccine were uncommon and consisted of pain and tenderness at the injection site; none required medical attention. The 336 children who were anti-HAV IgM positive at the time of vaccination were followed up closely. Thirty-one (9.2%) of these children attended the local clinic during the 4-week follow-up period. Most visits ($n = 25$) were due to mild respiratory and nonspecific febrile illnesses.

Hepatitis A outbreaks in communities are often difficult to control, despite the introduction of simple hygienic and sanitary control measures and postexposure immunoglobulin prophylaxis. The outbreak reported here occurred in a village of a very low socioeconomic level. The high rate of anti-HAV antibodies in young children is typical of communities in which hepatitis A is endemic and of those of a low socioeconomic level [1–3].

Passive immunization with human immunoglobulin has been the mainstay of prophylaxis since the 1970s, and there are several reports of its efficacy in outbreaks in childcare facilities [4, 5]. However, while immune globulin is of value in preventing secondary cases of hepatitis among household contacts, it has not proved efficacious in controlling large community-wide outbreaks [6–8]. Our study reinforced this concept: the outbreak was neither arrested nor decelerated by the widespread use of immune globulin.

Before embarking upon mass immunization with active hepatitis A vaccine, we were faced with several questions. Obviously, active immunization does not provide immediate protection, so we were uncertain as to how effective it would be in curtailing the spread of disease. Moreover, the question of possible adverse effects of active vaccination, especially in recently infected children (group 2), has not been determined unequivocally.

Previous reports have demonstrated high immunogenicity and protective efficacy of active hepatitis A vaccine [9, 10]. Protective anti-HAV levels are attained in 95% of children aged 1–17 years 1 month after the first dose of 360 EU inactivated HAV vaccine [11–14]. The current outbreak persisted for 8 weeks and was entirely arrested 3 weeks after the initiation of active vaccination (Figure 1). This suggests that the immuni-

Table 1 Antibody status of vaccinated children

Group no.	Description	HAV serologic status		No. (%) of children		
		IgM	IgG	12–35 mos. of age	36–72 mos. of age	Total
1	nonimmune	neg.	neg.	190 (43.4)	122 (17.7)	312 (27.7)
2	recent infection	pos.	pos.	203 (46.4)	133 (19.3)	336 (29.8)
3	past infection	neg.	pos.	44 (10.1)	434 (62.9)	478 (42.5)
Total				437	689	1,126

HAV, hepatitis A virus; neg., negative; pos., positive

zation campaign played a major role in the abrupt termination of the outbreak, presumably by rapid induction of herd immunity.

There were no significant adverse reactions to the vaccine, which is consistent with other reports [9, 13, 14]. Since we extensively documented the serologic status of our patients, we were able to confirm that, even when administered to patients during the HAV incubation period or to those with asymptomatic infection, the immunization was effective and there were no untoward effects.

The outbreak was typical for a community with a high rate of hepatitis A [15]. It is notable that we were able to achieve a remarkable vaccination coverage within 5 days, immunizing 1,133 children, i.e. over 90% of the pediatric population. We also had the noteworthy opportunity of evaluating the serologic status of over 99% of the vaccinees. As a result of these impressive epidemiologic data, we can now conclude that mass active hepatitis A vaccination appears to be a safe and effective intervention for control of community-wide outbreaks. The future routine use of the vaccine in children in high-risk communities, as well as in other susceptible groups, may result in benefits such as decreased morbidity, lower rates of fulminant hepatitis, and reduced need for liver transplantation.

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