Immunogenicity and reactogenicity of an inactivated hepatitis A vaccine in Indian adults

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ABSTRACT

Background. In India, a possible decrease in the prevalence of anti-HAV (hepatitis A virus) antibodies in adults has increased their susceptibility to HAV infection. We evaluated the immunogenicity and reactogenicity of an inactivated hepatitis A vaccine administered in a 3-injection protocol.

Methods. Thirty-five healthy adult volunteers, seronegative for anti-HAV IgG, were administered 720 ELISA units/ml of the inactivated hepatitis A vaccine intramuscularly at days 0, 30 and 180. Anti-HAV IgG was determined at days 30, 60, 90 and 180 to assess the efficacy of the vaccine and adverse reactions were noted to evaluate its reactogenicity.

Results. The mean (SD) age of the volunteers was 33.1 (12.3) years and the man:woman ratio was 19:16. An overall seroprotection of 37.2% (13/35) was obtained at day 30, 57.1% (20/35) at day 60 and 85.7% (30/35) at day 90. By day 180, all the vaccinees (35/35; 100%) achieved protective seroconversion. The vaccine in general was well tolerated and no serious side-effects were observed. Only 8.6% (3/35) of subjects developed minor self-resolving adverse reactions such as local pain, erythema and/or low-grade fever.

Conclusions. The inactivated hepatitis A vaccine in a three-injection protocol (0, 30 and 120 days) is safe, well tolerated and highly immunogenic in adult Indian subjects.


INTRODUCTION

India is endemic for enterically-transmitted diseases including hepatitis A virus (HAV) infection. In addition to a large number of inapparent or asymptomatic infections, about 60%-70% of clinical hepatitis in children below 15 years of age is due to HAV.1 Serological studies in the past have shown that most adults in India acquire anti-HAV IgG due to sub-clinical or clinical exposure early in life.2 Clinical hepatitis A is therefore believed to be relatively rare in the adult Indian population. A few decades ago, a similar situation was prevalent in many developed countries. However, due to improvement in environmental conditions, several European countries3 such as Spain,4 Greece,3 Italy4 and Portugal5 have witnessed a reduction in the incidence and prevalence of hepatitis A. Some recent preliminary Indian reports6,9 suggest that the prevalence of protective anti-HAV IgG has decreased. This decrease will expand the pool of susceptible adults and could result in an increase in the incidence of the infection.10 It is necessary to evolve strategies to counteract this possible increase of hepatitis A.

The inactivated hepatitis A vaccine has many advantages over immunoglobulins. It has been found to be highly immunogenic and extremely safe in several countries11,12. Unfortunately, it has not been evaluated adequately in Indian subjects and till date, only a single study4 has been reported. Therefore, we evaluated the immunogenicity and reactogenicity of the inactivated hepatitis A vaccine in a group of adult Indian volunteers.

SUBJECTS AND METHODS

Subjects

Between May 1996 and May 1997, 135 healthy volunteers of either sex, without any symptoms suggestive of hepatobiliary disease, were enrolled after written informed consent. The initial evaluation was done using a questionnaire followed by a complete clinical examination along with biochemical tests for liver function. Anti-HAV IgG was tested by an immunoenzymatic method (ELISA) using a commercially available kit (Hepavase A, General Biologicals, Taiwan). Only seronegative volunteers (35/135; 25.9%) were included in the study. The presence or absence of anti-HAV IgG was determined by comparing the absorbance values of the sample to the cut-off and the latter was calculated as per the manufacturer’s guidelines. Specimens with absorbance values less than or equal to the cut-off were considered reactive for anti-HAV IgG, while those with absorbance values greater than the cut-off were considered negative. Specimens with absorbance values within ±10% of the cut-off value were re-tested in duplicate.

Administration of vaccine

The 35 seronegative subjects received the inactivated hepatitis A vaccine with a potency of 720 ELISA units/ml (EU/ml) intramuscularly using a 3-injection protocol at days 0, 30 and 180.

Evaluation of immunogenicity

Blood samples were collected from all vaccinees at days 30, 60, 90 and 180 and the anti-HAV IgG was determined to assess the efficacy of the vaccine.

Evaluation of reactogenicity

All subjects were evaluated for 12 hours after each dose of the vaccine for any adverse reaction using a standard questionnaire. Side-effects such as fever, local pain, headache, nausea and vomiting were specifically enquired about and a complete examination was carried out for detection of erythema, induration or any other abnormal physical signs. All subjects were given vaccine cards to note any late adverse effects of the vaccine.

RESULTS

The mean (SD) age of the volunteers studied was 33.1 (12.3) years (range 18–60 years) and there were 19 men and 16 women. A seroconversion rate of 37.2% (13/35) was obtained at day 30, 57.1% (20/35) at day 60 and 85.7% (30/35) at day 90. By day 180 (even before the administration of the final dose of the vaccine), all the vaccinees had seroconverted. There was no difference in the seroconversion rates with respect to age or sex of the vaccinees at any time during the study.

The vaccine was well tolerated and there were no serious side-effects. Only three volunteers developed local pain, erythema and/or low-grade fever following administration of the first dose.
of the vaccine. These subsided spontaneously without any medication.

**DISCUSSION**

The epidemiology of HAV infection in India, at least in the urban population, seems to be changing. In 1982, Arankalle *et al.* had reported the prevalence of anti-HAV IgG in Pune to be 95%, reflecting an epidemiological pattern of high endemicity. In contrast to this, two recent studies from Mumbai and New Delhi confirmed, is likely to increase the disease burden, and may lead to community outbreaks and thus increase health care costs. Hence, active immunization using a hepatitis A vaccine assumes significance. Although information on the cost–benefit ratio of hepatitis A vaccination is lacking, the recently observed trend of decreasing seroprevalence suggests that such a strategy may be required, at least in the urban population.

The inactivated hepatitis A vaccine used by us has been evaluated extensively and found to be safe, well tolerated and highly immunogenic. However, it has not been evaluated in Indian adults.

We found that all the subjects seroconverted by day 180, even before the administration of the final dose of the vaccine. These results compare favourably with the seroconversion rate of 98%–100% reported in studies conducted elsewhere. However, seroconversion was low at day 30 (37.2%) and day 60 (57%) compared to the >95% rate achieved in trials carried out in other parts of the world. We did not find any difference in the seroconversion rates related to the age or sex of the vaccinees at any time during the study. This observation is consistent with the results reported in the literature. The slow seroconversion rate in our subjects during the initial stage of vaccination may be due to ethnic or geographical factors or due to other unknown reasons. Many workers have used a double dose (1440 EU/ml) and obtained 96% and 100% seroconversion at day 15 and day 30, respectively. It would be interesting to evaluate whether a higher dose of the vaccine results in faster seroconversion in Indian subjects.

In terms of reactogenicity, the vaccine was found to have a good tolerance profile and no major side-effects were observed. Only 3 out of 35 (8.6%) subjects developed local pain, erythema and/or low-grade fever after the first dose and these results compare favourably with the results of previous studies.

Thus, the inactivated hepatitis A vaccine in a 3-injection protocol (0, 30 and 180 days) is well tolerated and highly immunogenic in adult Indian subjects. However, a cost–benefit analysis of hepatitis A vaccination needs to be performed before a vaccination programme is recommended for a wider population in India.

**REFERENCES**