Hepatitis A vaccination: Need for universal immunization?

Jaydeep Choudhury

Journal of Pediatric Sciences 2010;5:e53

How to cite this article:
Choudhury J. Hepatitis A vaccination: Need for universal immunization?
Hepatitis A vaccination:
Need for universal immunization?
Jaydeep Choudhury

Abstract:
Hepatitis A is a common water-borne virus. Though it is an endemic disease but epidemics have occurred over the years. HAV infects more than 80% of the population of many developing countries by late adolescence. The difference in endemicity is related to the hygienic and sanitary conditions and also on other indicators of level of development. The outcome of hepatitis A may be extremely variable. Hepatitis A is a costly burden to society that could be countered by universal childhood immunization with hepatitis A vaccine. Considering other more pressing issues universal immunization may actually be a distant dream. Under prevailing conditions the disease can best be controlled by improving general living conditions.

Keywords: Hepatitis A virus, Hepatitis A vaccines
Received: 21/07/2010; Accepted: 22/07/2010

Introduction
Hepatitis as a clinical entity has been recognised for centuries. Evidences of large epidemics of jaundice are there in ancient and modern times. Epidemiologic and clinical studies have revealed the infective nature of the disease and subsequently the virus has been isolated just a few decades back. MacCallum proposed that the disease be known as hepatitis A and B. This suggestion was accepted by WHO in 1952. Feinstone and co-workers in 1973 identified hepatitis A virus in stool samples of experimentally infected human volunteers by immune electron microscopy. Since then different viruses are being identified and the array of viruses causing hepatitis are expanding. Among the hepatotropic viruses hepatitis A and E are the prominent water-borne viruses. These viruses mainly cause acute infection of the liver. The outcome of the infection is dependent not only on the cause but on the host immune response. Complete recovery depends on elimination of the infecting agent, resolution of the inflammatory changes and prevention of reinfection by effective antibody production (1).

The importance of the disease
Hepatitis A virus (HAV) infection is common throughout the developing world. It is frequently acquired during early childhood.

Though HAV commonly affects children but adolescent and adults are also at risk in many parts of the world. HAV infects more than 80% of the population of many developing countries by late adolescence (2). Countries in transition from developing to developed economies will be witnessing a shift in disease prevalence from high to intermediate endemicity, and HAV is likely to become a more serious problem in these areas. The aftermath of this changing endemicity pattern will
alter the incidence of the morbidity and mortality of
the disease and make the adolescent and adult
population more vulnerable (3).

The outcome of hepatitis A may be extremely
variable. Many children with inapparent or
subclinical hepatitis have neither symptoms nor jaundice. Patients may develop anicteric or icteric
hepatitis and have symptoms ranging from mild and transient form to severe and prolonged form. They
may recover completely or rarely develop fulminant hepatitis. The following are some of the atypical
manifestations of HAV.

**Relapsing hepatitis A**
Relapsing hepatitis is a relatively common
manifestation of hepatitis A that occurs in
approximately 10% patients (4). These patients have
a second episode 1-4 months after the initial episode
and they rarely have more than one relapses. The
illness usually lasts a total of 16-40 weeks and ends
in full recovery. The pathogenesis of relapsing hepatitis is unknown, most probably it is
immunologically mediated.

**Fulminant hepatitis A**
A small percent of fulminant hepatitis is caused by
HAV. Underlying chronic liver disease is a risk
factor. Fulminant hepatitis A has no distinctive
clinical features that distinguish it from fulminant hepatic failure of other causes. Complications include
cerebral edema, sepsis, gastrointestinal bleeding and hypoglycaemia.

**Cholestatic hepatitis A**
Cholestatic hepatitis occurs in a small percentage of
hepatitis A patients. These patients are deeply icteric,
may have pruritus, fatigue, fever, loose stools anorexia and weight loss. Patients recover completely
without therapy. A course of corticosteroids over 4
weeks with a gradual taper may hasten relief and
resolution of cholestasis.

**Hepatitis A triggering autoimmune hepatitis**
A genetic predisposition suggested by T-cell defect
triggered by HAV is usually the underlying cause.
These patients may require prolonged corticosteroid
therapy.

There may be some extrahepatic manifestations of
HAV like transient rash or arthralgia, papular
acrodematitis of childhood, cutaneous vasculitis,
Guillain-Barre acute syndrome, neurologic
syndromes like myeloradiculopathy, mononeuritis,
vertigo, meningoencephalitis, renal syndromes like
acute renal failure, nephritic syndrome, acute
glomerulonephritis, pancreatitis, aplastic anemia and
thrombocytopenia.

**Epidemiology**
Though hepatitis A occurs worldwide but the
epidemiologic pattern is not uniform. The difference
is endemicity is related to the hygienic and sanitary
conditions and also on other indicators of level of
development.

It is quite obvious that HAV is more common in
developing countries. Most children in the
developing countries in the prevaccination era
suffered from hepatitis A by 5 years age. Though
HAV most commonly gives rise to an asymptomatic
infection, but due to its high prevalence worldwide,
HAV alone accounts for 20-25% of clinically
apparent hepatitis (1, 5).

Depending on the endemicity the countries are
classified as low, medium or highly endemic for
Hepatitis A. In countries with high endemicity like
India, most individuals acquire natural infection in
childhood and burden of disease including incidence
of outbreaks is low. As a shift occurs towards
medium endemicity due to improvements in hygiene
and sanitation a certain proportion of children remain
susceptible till adulthood. Thus burden of
symptomatic disease and incidence of outbreaks
paradoxically increase. In India seropositivity ranged
from 32% to 80% in children younger than 10 years
age in different demographic profile (6-8).

**Pathogenesis and its relation to prevention**
Feco-oral is the usual route of transmission of HAV.
The primary site of replication is liver. Viremic stage
begins up to 2 weeks before the onset of clinical
symptoms. Virus is shed from the infected liver cells
and passes into the intestine. It is then excreted in the
feces.
It is difficult to judge the effect of mucosal immunity because antibody in saliva and feces either is not detected or is present at very low levels (9).

Need for prevention
Isolation of patients and contacts do not significantly influence the spread of hepatitis (10). The virus is disseminated before the diagnosis is made as it is excreted in the feces 2 weeks before the appearance of jaundice.

From the economic perspective, hepatitis A is a costly burden to society that could be countered by universal childhood immunization with hepatitis A vaccine. The cost of HAV infection was calculated to be $332 million to $580 million annually in the United States (11). The medical costs for hepatitis A cases requiring hospitalization are estimated to be $1,070 to $2,460 each (12). One economic analysis indicated that either universal vaccination or screening and vaccination of 2-year-old children should be considered cost-effective in developed countries (13). In another analysis, neither universal vaccination nor screening and vaccination of adults who were >50 years old were cost-effective (14). These data support the most recent recommendation of universal vaccination of children in US areas of high endemicity as a method of disease control.

Experiences from high income countries may not necessarily be directly applicable to low income countries, and such should not be extrapolated without consideration of other factors. The vaccines most needed may be different, immune responses may vary and monetary resources and infrastructure are substantial obstacles for the implementation of the vaccine programs (15).

Hepatitis A vaccines

i- Inactivated vaccines
The inactivated vaccines are derived from HM 175/GBM strains and grown on MRC5 human diploid cell lines. The virus is formalin inactivated and adjuvanted with aluminium hydroxide. The vaccine is stored at 2-8°C. The vaccines are given in a two dose schedule, 6 months apart intramuscularly. The pediatric dosage of Havrix (GlaxoSmithKline Biologicals) is 720 EL U (0.5 mL) and that of Avaxim (Sanofi Pasteur) is 80 antigen units (0.5 mL0. The adult formulation is double that of the above mentioned doses and should be used after the recommended cut-off age of 15 years according to one manufacturer and 18 years according to the other. Protective antibodies are seen in 95-100% 1 month after the first dose and almost 100% after the second dose. The protective efficacy is around 90-100% and onset of protection is 2 weeks – 1 month after the first dose of the vaccine. The vaccine efficacy is lower in the elderly, immunocompromised, those with chronic liver disease, in transplant recipients and those with pre existing maternal antibodies (16). The vaccine may be safely given with other childhood vaccines. Immunity is lifelong due to anamnestic response and no boosters are recommended at present in the immunocompetent. Adverse reactions are minor and usually include local pain and swelling.

A liposomal adjuvanted hepatitis A vaccine derived from the RG-SB strain, harvested from disrupted MRC-5 cells and inactivated by formalin is now available. The liposome adjuvant is immunopotentiating reconstituted influenza virosome (IRIV) composed of phosphatidylethanolamine, phosphatidylethanolamine and hemagglutinin from an H1N1 strain of influenza virus. The efficacy and safety profile is nearly similar to the other inactivated vaccines.

ii- Live attenuated vaccine
This vaccine is derived from the H2 strain of the virus attenuated after serial passage in Human Diploid Cell (KMB 17 cell line). It has been in use in China since the 1990’s in mass vaccination programs. The vaccine meets requirements of the Chinese drug authority and the WHO. It is also now licensed and available in India. The recommended dose in 1 ml SC (10 (6.5) CCID50/ml) in children aged 1-15 years. Immunogenicity studies with single dose show seroconversion rates of more than 98% two months after vaccination and persistence of protective antibodies in more than 80% of vaccines at 10 year follow up.

Uncontrolled studies show an efficacy of almost 100% sustained over 10 years despite decline in seroprotection rates and antibody titers. No horizontal transmission or serious adverse effects have been noted. The vaccine is not effective as post exposure prophylaxis (17, 18).
Recommendations in India

The Indian Academy of Pediatrics Committee on Immunization recommends offering the vaccine to healthy children of parents who can afford the vaccine after explaining the pros and cons to the parents on a one-to-one “named child” basis (Category 3) (19).

The vaccine is recommended for use in all individuals who can afford the vaccine in certain risk groups as enumerated below:

(i) Patients with chronic liver disease.
(ii) Carriers of Hepatitis B and Hepatitis C.
(iii) Congenital or acquired immunodeficiency.
(iv) Transplant recipients.
(v) Adolescents seronegative for HAV who are leaving home for residential schools.
(vi) Travelers to countries with high endemicity for Hepatitis A

Vaccination with inactivated vaccines may also be offered to household contacts of patients with acute Hepatitis A virus infection within 10 days of onset of illness in the index case. It may not always be effective under such circumstances when the contact has had the same source of infection as the index patient.

If a decision to administer the vaccine is taken any of the licensed vaccines may be used as all have nearly similar efficacy and safety (exception post exposure prophylaxis, immunocompromised patients where only inactivated vaccines may be used) (19).

Conclusion

It is known that second to clean drinking water, vaccination is the most effective public health measure for control of infectious diseases. There are 3 million people, mostly children below 5 years of age living in developing countries that die each year from various vaccine preventable diseases.

WHO through Expanded Programme on Immunization (EPI) has targeted 6 diseases – tuberculosis, diphtheria, tetanus, pertussis, polio and measles for prevention. Initiatives are also taken to control Hemophilus influenzae B and Pneumococcal infections as these are also important causes of under 5 children mortality. Prevention of hepatitis B infection comes in between. Hepatitis A is water borne disease which can be prevented to a great extent by good hygiene and safe drinking water use. Though it is quite prevalent in many developing countries but universal immunization may actually be a distant dream considering other more pressing issues. Under prevailing conditions the disease can best be controlled by improving general living conditions in the developing countries.

REFERENCES


