RESEARCH NOTE

ANTI-HEPATITIS A ANTIBODY TITERS AFTER PASSIVE IMMUNIZATION WITH HEPATITIS A HYPERIMMUNE GLOBULIN

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Hepatitis A virus (HAV) is a non enveloped, icosahedral virion, 27 nm heparna virus, belonging to the picorna virus family. It composed of an outer protein shell with structural proteins (VP1-4), enclosing a single stranded RNA genome. The virus is stable in an acid environment and can, therefore, survive transit through the stomach. There are many genotypes of human hepatitis A virus; however, they appear to immunologically indistinguishable and belong to one serotype.

Hepatitis A has been a major problem in many countries, especially in areas where the infection pattern is changing from hyperendemic to hypoendemic. Improvement in living standards has postponed childhood infection into adolescence or adulthood. HAV infection in early childhood is usually subclinical, while symptomatic hepatitis A infections occur with increasing age. (Hadler *et al,* 1980; Benenson *et al,* 1980). The increasing numbers of susceptible individuals has resulted outbreaks and has become a problem particularly in schools, communities and among high risk groups. (Sinlaparatsamee *et al,* 1995; Chidon *et al,* 1992; Halliday *et al,* 1991; Hayashi *et al,* 1988).

There is no specific treatment for hepatitis A infection. Pre-or post-exposure prophylaxis with immune globulin is 40-90% effective. (Provost, 1991; Winokur and Stapleton 1992; Conrad and Lemon, 1987) However, immune serum globulin (ISG) produced from plasma collected in developed countries has very low anti-HAV antibody titers. A hyperimmune globulin or specific globulin from screened plasma is recommended for use in prophylaxis. In this report, we studied the anti-HAV antibody titers after passive hepatitis A hyperimmune globulin prophylaxis.

In late 1991 to early in 1992, there was an outbreak of hepatitis A infection at a University campus in Bangkok. More than 10 cases of acute viral hepatitis A occurred. After obtaining informed consent for passive prophylaxis in contact cases, hepatitis A hyperimmune globulin (Globuman Berna Hepatitis A, Lot : 115900214) was administered to healthy non immune contact. (2 milliliter, 0.035-0.05 ml/kg). The immunoglobulin was injected intramuscularly. One milliliter contained 100 international units. Fifteen healthy subjects, age 14 to 24 years (average age 21 ± 2.2 yr.) participated. There were 2 males and 13 females. The average body weight was 45 kgs (41-58 kgs). Blood was taken before and 3-5 days after passive immunization and kept at -20°C. Anti-hepatitis A antibody titer was determined by using an automated microparticle enzyme immunoassay test kit (IMX HAVAB; Abbott Laboratories, North Chicago, Ill) with antibody levels expressed as mIU/ml. A reference serum (World Health Organization, Geneva, Switzerland) was run in parallel with the samples. The geometric mean titer (GMT) of anti-HAV pre- and post-injection are shown in Fig 1. After passive immunization, all subjects had protective levels of anti-HAV antibody 20 mIU/ml (GMT = 68.7 mIU/ml). None developed symptoms of hepatitis A infection.

Human immune serum globulin (ISG) is effective in the prevention of HAV infection. It is administered at a dose of 0.02 ml/kg of body weight and protection is estimate to last for up to 4 months. (Provost, 1991; Winokur and Stapletan 1992; Conrad and Demon, 1987). However, ISG produced from the Western countries has very low anti-HAV titers. In normal immunoglobulin preparations the hepatitis A antibody titer varies from batch to batch. Therefore the hyperimmune hepatitis A globulin obtained from screened plasma with high hepatitis A antibody titers was developed and tested. Ambrosch *et al,* (1991) found that when normal ISG was injected into

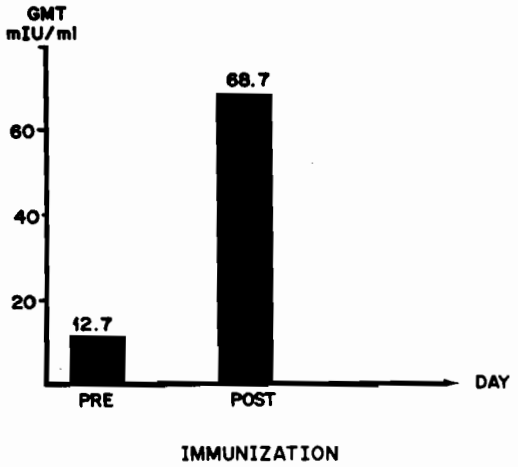

Fig 1- GMT of anti-HAV after hyperimmune globulin (2 ml) administration in healthy subjects n = 15.

seronegative subjects, a mean titer of 21 mIU/ml was observed. This is approximately one third the titer obtained with the hyperimmune globulin. These data can be used as a reference for the immunogenicity of hepatitis A vaccine as relate to protective level of antibodies.

Although the hyperimmune hepatitis A globulin can prevent hepatitis A infection, it is not feasible for developing countries to use hyperimmune globulin due its expensive and short term protection. Long lasting antibody from hepatitis A vaccine should be considered after or together with immune globulin prophylaxis.

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