Hepatitis A - Update and an Overview of Viral Hepatitis

Expires Wednesday, July 31, 2019 Nursing Patricia D. Hastings , RN, BSN, MSN, WHNP-C

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Objectives

1. Describe the differential for liver disorders seen in medicine and list some of the drugs and toxins that can produce liver dysfunction.
2. Discuss the impact of Hepatitis A infections on healthcare and the diagnostic work-up of the patient infected with this virus.
3. Describe the different ways in which the Hepatitis A virus can be transmitted between adults as well as children.
4. Discuss the potential treatment options for Hepatitis A, the effectiveness of immunoprophylaxis, and recommendations for immunoprophylaxis.

Article

Viral Hepatitis Overview and Update on Hepatitis A

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2. Discuss the impact of Hepatitis A infections on healthcare and the diagnostic work-up of the patient infected with this virus.
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4. Discuss the potential treatment options for Hepatitis A, the effectiveness of immunoprophylaxis, and recommendations for immunoprophylaxis.

General Overview

Disorders of the liver have a wide spectrum and are commonly seen in medicine. Table 1 gives a differential for liver disorders, one of which is hepatitis. By definition, hepatitis is an inflammation of the liver that is usually caused by a virus, drug, or toxin. When evaluating a patient with a diagnosis of possible hepatitis, obtaining a thorough history is imperative. This history should include any travel (outside and inside the United States), any use of drugs, medications, or herbs, any exposure to environmental toxins, and recent dietary intake. Drug and toxin induced causes for hepatitis are common. Table 2 lists some of the more common drugs and toxins that have been associated with a hepatitis-like reaction.

Viral induced hepatitis has always been a complex subject that has often resulted in confusion. At the present time, there are 5 distinct primary viruses that can cause hepatitis and possibly 2 others. In addition, many other viruses including cytomegalovirus (CMV), Epstein Barr virus (EBV), herpes virus, and coxsackieviruses can also produce a hepatitis-like appearance. The five main viruses have been designated with letters and are hepatitis A, B, C, D and E. The other 2 potential viruses are G and TT, but the full extent of these infections has not been completely determined.

Regardless of the viral type, most patients with viral hepatitis are asymptomatic. If symptoms do appear, they often are misdiagnosed as a viral flu syndrome. These symptoms include anorexia, nausea and vomiting, fatigue, myalgias and a low-grade fever. Only the more affected cases develop jaundice with light colored stools, dark urine and right upper quadrant pain consistent with a classic diagnosis of hepatitis. Though rare, severe cases of hepatitis can lead to acute liver failure resulting in

coagulopathy, delirium, and even death.

Table 1: Differential Diagnosis of Liver Disorders

A. Hepatitis

1. Drug or Toxin induced (see Table 2)
2. Viral induced (Hepatitis A, B, C, D, E, G, and TT; CMV; EBV; Herpes, Coxsackievirus, Mumps, etc.)

B. Hyperbilirubinemic States

1. Gilbert's syndrome
2. Dublin-Johnson syndrome
3. Rotor syndrome
4. Crigler-Najjar syndrome

C. Biliary Induced (cholecystitis, cholelithiasis, cholangitis, etc.)

D. Vascular

1. Budd-Chiari Syndrome (hepatic vein thrombosis)
2. Portal Vein Thrombosis

E. Cirrhosis and Chronic Liver Disorders

1. Induced by infection, alcohol, drug, or toxin
2. Disorders such as Wilson's disease, Hemochromatosis, etc.

F. Infiltration Disorders such as Fatty Liver

G. Tumors, Carcinoma, Metastatic CA, Granulomas, Cysts, etc.

H. Pregnancy Related

1. Acute Fatty Liver of Pregnancy
2. Liver Involvement with Pre-eclampsia (HELLP Syndrome)
3. Intrahepatic Cholestasis of Pregnancy
4. Hyperemesis Gravidarum

Table 2: Common Drugs / Toxins Associated with Liver Toxicity

1. Phenothiazines (chlorpromazine)
2. Phenytoin
3. Monoamine oxidase inhibitors
4. Isoniazid
5. Halogenated anesthetics
6. Tetracycline
7. Acetaminophen (overdose)
8. Methyldopa
9. Propylthiouracil (PTU)
10. Sulfonamides
11. Erythromycin Estolate
12. Zidovudine (AZT)
13. Excess Vitamin A

14. Alcohol
15. Carbon tetrahydrochloride
16. Hydrocarbons
17. Industrial solvents and phosphorus
18. Poison Mushrooms

Diagnostic Workup and General Management:

The preliminary evaluation of a patient with possible hepatitis is relatively simple and involves obtaining liver enzymes (alanine amniotransferase-ALT and aspartate amniotransferase-AST) along with a bilirubin count. Most patients with acute hepatitis will have elevated liver enzymes and elevated bilirubin levels. Once the patient is found to have elevated liver enzymes suggestive of hepatitis, the confusion sets in when trying to identify the cause. The patient's blood should then be screened for the presence of acute hepatitis A, B, and C. A drug screen might also be obtained, especially if the history is suggestive of drug or toxin exposure. If all of these are negative, the patient can then be evaluated for atypical viruses such as CMV, EBV, herpes, Hepatitis E, etc.

The management of acute hepatitis is primarily supportive. No treatment currently exists that can be given to reverse the disease process unless it is a specific medication that counteracts a specific drug or toxin. A few patients are at risk for becoming severely dehydrated from intractable nausea and vomiting and may require admission for hydration and treatment of the nausea and vomiting. In addition, fulminant cases of hepatitis with evidence of liver failure will obviously require admission in order to treat the severe problems that can occur with this disorder (coagulopathy, delirium, etc.). However, the overall treatment is supportive care along with expectant management as the disease runs its course. In addition, appropriate immunization of family members and offspring should occur if the cause is viral induced. Furthermore, drugs that are metabolized by the liver should be avoided if at all possible.

Hepatitis A – Background and Healthcare Impact:

Hepatitis A (HAV) is a single-stranded RNA (ribonucleic acid) virus that is 27 nm (nanometers) in size. It has no viral envelope and is in the enterovirus subgroup of the picornavirus family. The picornavirus family is commonly associated with human disease. It has two main subgroups, which are the rhinoviruses and enteroviruses. The rhinoviruses are the main group of viruses responsible for the common cold and well over 150 different strains have been identified to date (one of the reasons why a cure for the common cold is hard to develop). The enteroviruses include poliovirus (3 serotypes), coxsackievirus A (23 to 24 serotypes), coxsackievirus B (6 serotypes), and echovirus (31 serotypes). The various coxsackievirus and echovirus serotypes can cause respiratory illnesses, meningitis, pericarditis, myocarditis, herpangina, and hand-foot-and-mouth disease. There are a few other enteroviruses that do not fit into these three subcategories and are by themselves individually. They have been numbered 67 to 72. Enterovirus 72 is hepatitis A.

The initial reports on this viral infection occurred in the 1940's when it was determined that the hepatitis responsible for the epidemic in soldiers in World War II was caused by contaminated drinking water. These publications reported that treatment with gamma globulin and superchlorination of the drinking water could minimize the risk of developing this infection. The actual virus was discovered in 1973 by electron microscopy in fecal samples of patients with acute hepatitis.

The virus has a relatively short incubation period of approximately 2-7 weeks. The onset of the illness is usually abrupt and clinical resolution usually occurs within 2-3 weeks. The likelihood of being symptomatic is related to the person's age. Most adults and older children do have symptoms, whereas, children under the age of 6 are usually asymptomatic. Some symptomatic individuals (usually < 10%) may have prolonged or relapsing symptoms that last for up to 6 months. There is no known chronic carrier state for hepatitis A, and once the disease has completely resolved, the patient is then immune, usually for life.

Despite the fact that no chronic form of the disease exists, the impact on healthcare is still significant. The Centers for Disease Control estimates that about 150,000 to 180,000 cases occur annually in the United States of which only 50% have symptoms. It is estimated that 100 deaths occur each year from liver failure due to hepatitis A. Of those individuals with symptoms, approximately 15% are hospitalized. Adults who become ill will miss an average of 27 workdays. The estimated cost (direct and indirect) in 1997 was $300 million.

Diagnosis of Hepatitis A:

The best diagnostic procedure for identifying acute hepatitis A is the presence of an IgM antibody. A positive IgG antibody only implies past infection. The IgM antibody usually becomes detectable about 3 to4 weeks after exposure and disappears 3 to 4 months later, but can last up to 6 to 10 months. No hepatitis A antigen blood tests exist. In addition, HAV RNA can be detected in the blood and stool during the acute phase of the disease, but again these tests are primarily limited to research laboratories. The presence of the hepatitis A virus in blood and stool usually develops within 2 to 3 weeks of becoming infected and is often detected about 2 weeks before clinical symptoms. Viremia on average lasts about 60 to 90 days, which is short in duration when compared to other hepatitis viruses. However, in a few cases, it can be detected up to a year in patients who have a relapsing illness.

Transmission of Hepatitis A:

The transmission of hepatitis A is mainly through the oral-fecal route. Therefore, a hepatitis A infection may occur by either person-to-person contact or when a person ingests food, water, or shellfish that has been contaminated with stool containing the virus. This promotes spread in areas of close contact, for example in families, the military, and institutionalized individuals. In addition, HAV spread is seen in the homosexual male population as well as in day care centers. This virus has also been transmitted through blood products though only a few reports exist. The parenteral transmission of HAV is extremely rare and can only occur during the short window of viremia, because a chronic carrier state for hepatitis A does not exist.

In the United States, the reported incidence is highest among children between the ages of 5 and 14 with one-third of all cases occurring in children under age 15. Approximately 50% of persons with hepatitis A do not have an identifiable source for their infection. The most common identifiable source, seen in about 25% of cases, is person-to-person contact, either household or sexual contact with a person infected with hepatitis A. About 15% of reported cases occur in children or employees of daycare centers. Another 5% of reported cases occur in international travelers. The remaining cases occur from small food-borne epidemics; occur within the homosexual male population; or occur in the IV and non-IV drug using populations.

Hepatitis A is a reportable disease in all states. The goal of hepatitis A surveillance is to identify contacts of the patient who might require post-exposure prophylaxis; to detect outbreaks; to monitor disease incidence and characteristics; and to determine the effectiveness of vaccine therapy and or missed opportunities for vaccination.

Vertical Transmission of Hepatitis A:

As an overview, the incidence of viral hepatitis in the pregnant population in the United States is no different than the non-pregnant population. In addition, the severity of the illness in this country also does not appear to be affected by the fact that a woman could be pregnant. There is one virus (Hepatitis E) that does seem to be more severe in the pregnant population, but this is discussed in a different article.

Hepatitis in pregnancy is the number one cause of jaundice in pregnancy accounting for about 40% of cases. The main risk to the mother is the potential for developing acute liver failure as well as transmission of the virus to other family members. The fetal risks are primarily related to an increased risk of premature delivery in addition to becoming infected with the virus. In the United States, the spontaneous abortion rate and stillbirth rate do not appear to be increased in pregnant women with hepatitis when compared to the general pregnant population. In addition, there have been no confirmed fetal anomalies related to any of the hepatitis viruses.

In utero transmission of the hepatitis A virus from the mother to the neonate essentially does not occur. There has been one case report of a documented transmission in a woman who developed acute hepatitis A at 20 weeks gestation. The fetus developed ascites and HAV-IgM antibody was detected in the fetal blood obtained by cordocentesis. The pregnancy was ultimately delivered at 35 weeks gestation and the overall outcome was good.

A second case of possible vertical transmission has also been reported. A mother developed acute hepatitis A shortly after delivery. Her husband and 2 other children also developed hepatitis A. The newborn infant received immunoglobulin on day 5. The infant's blood and serum were HAV-RNA positive by PCR on day 17 and day 32, but were negative on day 101. The infants IgG was positive at 6 months. The IgM was negative and the infant never had any symptoms. The immunoglobulin did not appear to prevent the infection in this case but may have decreased its severity.

In summary many cases of acute hepatitis A in pregnancy have occurred and the newborns for the most part have been unaffected. However, treatment of the newborn is indicated in a mother who has active disease near delivery (just like other

family members).

Treatment for Hepatitis A:

For hepatitis A (and all other hepatitis viruses) once a person is infected, there is no treatment for cure. Fortunately, with hepatitis A, if the disease course is not fulminant, it is usually self-limited with no known long-term sequela (unlike hepatitis B and C). The best treatment for hepatitis A is prevention of the infection. For pre-exposure and acute post-exposure prophylaxis, the treatment is serum immune globulin and the dosages are seen in Table 3 below. It is important to remember that most fecal excretion of the virus occurs before jaundice develops and that infectivity rapidly declines once the jaundice is clinically apparent. Therefore, immunoprophylaxis must occur rapidly for household contacts once the index case has been diagnosed. If the exposure to hepatitis A has been greater than 2 weeks, immune globulin is not indicated since it probably would not be effective.

The overall incidence of hepatitis A has decreased in the United States during the past 20 years (mostly due to better hygienic and sanitary conditions); however, it is still one of the most frequently reported vaccine preventable diseases. The majority of studies show that immunity following vaccination is long-lasting. In addition, because children constitute about one third of the cases, immunization practices have begun to focus on this group. Immunizing children would decrease the child-to-child transmissions and would decrease future adult transmissions (as these children become of adults). Theoretically, this could result in the potential eradication of hepatitis A (similar to what is occurring with polio).

Immune globulin in the United States goes through a purification process so that there is essentially no risk of transmitting HIV or hepatitis B and C. It comes in an intramuscular (IGIM) form and an intravenous (IGIV) form. The IGIM form is the product that should be used for preventing an HAV infection. IGIM is provided in preparations with a preservative called thimerosal and it also is available without a preservative. If the use of IGIM is indicated in pregnant women and or in infants, the preparation without thimerosal should be administered. Immune globulin does not interfere with the effectiveness of inactivated vaccines nor does it appear to affect the polio or yellow fever vaccines. However, it can decrease the effectiveness of the MMR and varicella vaccines. Therefore, if possible, it should not be administered within 3 weeks of receiving these vaccinations. Likewise, the administration of the MMR vaccine should be delayed for at least 3 months and the varicella vaccine delayed for 5 months after giving immune globulin.

Regarding vaccine therapy, studies in children have revealed good results in preventing the illness. Werzberger et al prospectively randomized 1037 children to receive either the hepatitis A vaccine versus a placebo. The incidence of hepatitis A in the children in the vaccine group was 0 out of 519 cases compared to 25 cases of acute hepatitis A in 518 placebo cases. In their evaluation, 99.7% of the children studied developed antibody by one month following the vaccination. A second study administered over 109,000 doses of HAV vaccine and no serious adverse reactions were reported. The development of antibody after the initial dose with a repeat at one month was 94%, which increased to 99% following a third dose at 12 months. Currently, two formalin inactivated hepatitis A vaccines have been produced and are licensed in the United States (which are Havrix and VAQTA). For both, different dosages are used depending on the person's age, which is shown in Table 3 below.

One potential problem regarding immunity is seen in children under the age of 2. If a pregnant woman has had hepatitis A in the past, her IgG antibodies will cross the placenta and can remain in the child's circulation for up to 18 months. Vaccination in these cases may result in a decrease in effectiveness. However, immunity following vaccination (in children under the age of 2) is good if the mother has not had hepatitis A in the past.

Table 3: Recommendations for Immuno-prophylaxis for Hepatitis A

A. Pre-exposure prophylaxis – travel to an endemic area

1. 0.02 cc/kg single injection IGIM if less than a 2 months stay
2. 0.06 cc/kg injection of IGIM every 5 months for prolonged stay

B. Post-exposure prophylaxis

1. 0.02 cc/kg single injection IGIM (especially for sexual and household contacts) – use the deltoid or gluteal muscle; for infants under the age of 2, use the anterolateral thigh.

C. Perinatal exposure

1. 0.02 cc/kg of IGIM at birth for the infant and possibly repeat at one month of age

D. Havrix dosages

1. Age 2 to 18 administer 0.5 cc in two doses – initial with repeat in 6 to 12 months
2. Age over 18 administer 1 cc in two doses – initial with repeat in 6 to 12 months

E. VAQTA dosages

1. Age 2 to 17 administer 0.5 cc in two doses – initial with repeat in 6 to 18 months
2. Age over 17 administer 1 cc in two doses – initial with repeat in 6 months

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