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Issues Leading to the Recent Outbreaks of Hepatitis A

Jean M. O'Neil, DNP, RN, FNP-BC
Patricia A. Chin School of Nursing, California State University, Los Angeles, Los Angeles, CA, USA

Hepatitis A (HAV) is a topic that has been frequently discussed in the news due to the recent outbreaks in different parts of the world. It is a common viral illness that had seen a decline in incidence since l996, when the HAV vaccine was introduced.[1] The number of HAV cases between 1990 and 2009 decreased by 93.7%.[1] Over the same time period, hospitalization from HAV declined 68%. Although infections from HAV have not risen to the pre-vaccine numbers, these recent outbreaks of HAV are of concern to the medical community and the public.

Issues Related to the Outbreaks

Since 1996, children in the United States have been offered the vaccine as part of their immunization schedule. However, there are substantial number of adults born before 1996 who have never been immunized against HAV.[2] This makes them extremely susceptible to the infection, which in turn can lead them to also infect others.

Travel to HAV endemic countries by those who are unimmunized against HAV, poses a risk for contracting the infection. Between 2005-2007, 46% of HAV infections were potentially caused by travel outside of the US and Canada.[2] HAV is endemic is some areas of Central America and South America, the Middle East, Africa, Asia and the Western Pacific.[1] Travel is a popular form of recreation, and access to exotic locations has become easier. However, enhanced detailed HAV surveillance programs have proven to be a difficult undertaking due to either poor reporting or false-positive anti-HAV immunoglobulin M (IgM) findings in those with non-acute liver problems. Even with inconsistent HAV reporting, the Centers for Disease Control and Prevention (CDC) considers international travel to HAV endemic areas to be an important risk factor for HAV.

High-risk sexual behavior can also lead to the spread of HAV. In June 2017, 1,731 patients in 15 European countries were diagnosed with HAV, most of these diagnoses being in MSM.[3] In the United States, HAV has been reported in the MSM populations of urban cities across the country. In 2018, the CDC estimated that 10% of new HAV cases in the United States occur in the MSM population, an increase from 4.9% in 2010.[1,4]

From 2017 to early 2018, San Diego, California, had an outbreak of 587 reported cases of HAV, which resulted in 402 hospitalizations and 20 deaths.[5] Although there have been other reported HAV outbreaks, this was the largest HAV outbreak in the United States in 2 decades.[5] By April 2018, the CDC had received more than 2500 reports of HAV from multiple states.[5] The San Diego outbreak, as with most of these reported sites, have been mostly associated with the homeless population and illicit drug users in settings with limited sanitation. These outbreaks were a reminder that HAV, in certain populations, could result in increased morbidity and mortality.

Up until the development of the HAV vaccine, HAV was treated by stressing improved hygiene and sanitation, and by providing passive immunity by the administration of immune globulin (IG). However, since there is a decreased prevalence of previous HAV infections in plasma donors, the dosage for IG has recently been increased to provide enough HAV IgG antibodies for protection. Providers who are not updated on this information, may be providing insufficient dosing against HAV.

Transmission and Incubation

HAV is spread from person to person through the fecal-oral route. Hepatic replication of the virus is detectable in the blood and eventually excreted in the feces by days 10-12 post-exposure.[1] Feces from an infected person, which is then spread to food and water through poor handwashing or inadequate hygiene, is the main source of transmission of the virus.[6] Incubation of the virus in the human body can take anywhere from 15-50 days.[1]

Clinical presentation and diagnosis

70% of adolescents and adults will show some signs of clinical illness, such as jaundice.[1] The majority of children under 6 years of age are asymptomatic and can shed the virus 10 weeks longer than adults, which makes them a high risk for spreading the infection.[1,7]

Signs and symptoms of HAV can last as long as 2 months. Symptoms include jaundice, nausea, vomiting, fever, malaise, anorexia, abdominal pain, dark urine, pale stools and pruritus. Physical exam usually reveals hepatomegaly and jaundice. In the acute phase, laboratory testing will show elevated liver enzymes and a positive anti-HAV IgM. If the patient has already had the infection or had the HAV vaccine, then they will have a positive serum anti-HAV IgG. A positive anti-HAV IgG lets the provider know the patient has lifetime immunity.

Complications from HAV

Acute liver injury by HAV can lead to *fulminant hepatic failure*. This is a rare complication and mostly seen in patients older than age 50 or in those with pre-existing liver problems. Mortality rate from fulminant hepatic failure can be as high as 80%.[1] *Cholestatic hepatitis* from HAV can last for longer than 3 months and cause serum bilirubin levels, alkaline phosphatase, liver function tests and lipids to become abnormally elevated. This usually resolves spontaneously.[8] *Relapsing hepatitis A* can occur in up to 10% of patients, occurring 6 months AFTER the onset of the acute illness. These patients need to be watched for the possible development of acute liver failure.[9] *Autoimmune HAV* is a rare complication leading to a prolonged illness and findings of hyperglobulinemia and circulating autoantibodies. These patients may require a liver biopsy to determine further treatment.[10]

Occasionally, an anti-HAV IgM can be a false positive. A false-positive result should be suspected if the patient is asymptomatic, has no known HAV exposure or any risk factors for HAV. For example, a high titer of rheumatoid factor, or other cross-reacting antibodies, can interfere with anti-HAV IgM testing, causing a false-positive result.[11] The CDC does not recommend anti-HAV IgM testing as a screening tool for HAV in asymptomatic patients or those with nonacute liver abnormalities.[12]

Pre- and post-exposure immunization

Active immunization starts in children between 12-23 months of age as they receive 2 doses of the inactivated HAV vaccine at 0 and 6 months.[1] It is highly recommended in all adults as pre-exposure immunization for those who have not been previously immunized, in MSM, illegal drug users, have blood-clotting disorders, have chronic liver disease or are immunocompromised.

Passive immunization is with **i**mmune globulin (IG) and is recommended for those who are unimmunized and will be traveling to an HAV endemic area within the next 2 weeks. This will provide immediate protection. They can additionally, unless contraindicated, receive the first dose of the HAV vaccine and get the second dose when they return from their travels. Pre-exposure dosing is 0.1 mL/kg if traveling for 1 month or 0.2ml/kg if traveling for 2 months. IG may be repeated if traveling for longer than 2 months.[7]

Post-exposure treatment of HAV can be with either active or passive immunization. To be of maximum benefit, immunization should be given within 2-weeks post-exposure. Those who have been exposed to HAV and are pregnant, may be allergic to the HAV vaccine, are under the age of 1 year, are immunocompromised and/or are adults over the age of 40, should be given immune globulin (IG). IG only

gives temporary protection, so active immunization with the HAV vaccine may be eventually required.[13,14] Post-exposure dosing of IG is 0.1 mL/kg.[8] Patients between the ages of 1-40 years, who are not pregnant or have no contraindications, may receive the HAV vaccine as their post-exposure treatment. Administration of either the HAV vaccine or the IG may actually prevent or attenuate symptoms, even though it does not always prevent the infection.[15]

Implications for practice

Providers should educate their patients on ways to prevent HAV transmission. They also need to offer the correct pre- and post-exposure immunizations, report infections to public health, design a supportive treatment plan for the patient infected by HAV, as well as recognize complications that require more interventions to avoid liver failure.

Title:

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Abstract Summary:

Since the use of the hepatitis A (HAV) vaccine in 1996, this infection had been rapidly decreasing. However, in 2016, recent outbreaks of hepatitis A have been reported globally. The provider needs to be aware of those issues leading to these outbreaks and the changes in immunization procedures and dosing.

Content Outline:

Introduction:

Hepatitis A (HAV) had been on the decline since the introduction of the vaccine in 1996. However, in 2016 there have been frequent reports of outbreaks in the US and Western Europe. In 2017-2018, San Diego, California had one of the biggest outbreaks in the last two decades. This outbreak had 587 reported cases, 402 hospitalizations and 20 deaths. Since then the Center for Disease Control (CDC) has had approximately 2500 reported cases, but believes there are many more incidents that are not reported.

Issues Related to Recent Outbreaks:

1. Lack of immunization of current adult population, or those born before 1996, which was the year the vaccine became part of the pediatric immunization schedule.

2. Increased travel to hepatitis A endemic areas due to the fact that travel has become a popular hobby and there is more access to areas not normally visited than ever before.

3. There is an increase of hepatitis A reports in those who practice high-risk sexual behaviors, especially in men who have sex with men (MSM). The CDC estimated that 10% of new HAV cases in the U.S are from MSM, an increase from 4.9% in 2010.

4. Increased homeless encampments and illicit drug uses with limited access to sanitary conditions are were a lot of hepatitis A outbreaks have been occurring.

5. 70% of unvaccinated children less than age 6 years can carry the infection without being symptomatic, and therefore can be a big source of this infection.

6. Many providers are not reporting hepatitis A because this infection is usually self-limting and usually requires only symptomatic treatment. However, this infection can cause increased morbidity and mortality in the frail, elderly and immunocompromised.

7. Providers may not be doing adult HAV vaccines or they may be giving the wrong dosing for passive immunization with immune globulin, since dosages have changed.

Virus, Transmission, Incubation:

1. Hepatitis A is a viral infection that replicates in the liver and can cause hepatic injury. It is endemic in some areas of Central and South America, the Middle East, Africa, Asia and the Western Pacific. In severe cases, it can cause fulminant liver failure.

2. Hepatitis A is transmitted via the fecal-oral route and has an incubation period of 15-50 days. 70% of adults will show some type of symptom, which is usually jaundice. By day 14, the virus is usually present in the stool.

Clinical Presentation and Diagnosis:

1. The patient usually complains of nausea, vomiting, fever, malaise, anorexia, jaundice and abdominal pain.

2. Physical exam may reveal jaundice, hepatomegaly and liver enzymes (LFT) are usually elevated and their anti-HAV IgM is positive. Full clinical recovery is usually seen in 3 months.

3. If the anti-HAV IgG is positive, then they now have lifetime immunity from either having the infection, or through immunization with the HAV vaccine.

Complications:

1. Fulminant hepatic failure has a mortality rate that can be as high as 80%. Patient may need a liver transplant.

2. Cholestatic hepatitis results in jaundice, off and on fevers, malaise, pruritus, weight loss lasting more than 3 months. This usually resolves spontaneously.

3. Relapsing HAV can occur in up to 10% of patients with HAV, when symptoms occur again during the resolution phase and cause a prolonged finding of anti-HAV being IgM positive.

4. Autoimmune HAV is a rare complication, and may occur with the same symptoms as HAV infection.

5. Other HAV-related extra hepatic complications can be: arthritis, glomerulonephritis, optic neuritis, myocarditis and changes in the patients immune system.

Active Immunization vs. passive immunization:

1. Active immunization is with the HAV vaccine, which is offered to children as part of their immunization schedule after 1 year of age. It can also be offered to adults who need catch-up vaccination

2. Passive immunization is with Immune globulin (IG). IG provides HAV antibodies from donated plasma.

3. Pre-exposure treatment consists of offering the HAV vaccine or IG if traveling within the next 2 weeks. Dosing for IG is 0.1mL/kg if traveling for a month, 0.2mL/kg if traveling for 2 months.

4. Post-exposure treatment consists of either offering the HAV vaccine or IG if you need immediate protection of the patient depending of the health status and age of the patient. Dosing for IG is 0.1mL/kg. IG must be given within 2 weeks post-exposure to be effective.

5. If the patient is already symptomatic, then treatment of symptoms and watching for signs of hepatic failure are the interventions of choice

Implications for Practice:

1. Providers need to be aware that HAV in the frail, elderly and immunocompromised could be catastrophic.

2. It is important to offer the HAV vaccine in those who are not immunized. Pre-and post-exposure immunization management is also beneficial to prevent or attenuate symptoms from HAV.

First Primary Presenting Author

Primary Presenting Author

Jean M. O'Neil, DNP, RN, FNP-BC
California State University, Los Angeles
Patricia A. Chin School of Nursing
Assistant Professor of Nursing
Los Angeles CA
USA

Author Summary: Dr. O'Neil specializes in family medicine in both primary care and an emergency department in Los Angeles. As a FNP, she has diagnosed and treated numerous infections, including hepatitis A. In 2017-2018, providers, especially in California, were on high alert for hepatitis A due to a very large outbreak in San Diego, California. She has recently published an article related to the recent outbreaks of hepatitis A in the United States and globally.