ADVANCES IN HEPATOLOGY

Current Developments in the Treatment of Hepatitis and Hepatobiliary Disease

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Spontaneous Bacterial Peritonitis



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G&H What is spontaneous bacterial peritonitis?

KK Spontaneous bacterial peritonitis is an infection that occurs in ascites, fluid in the abdomen that may develop in patients with cirrhosis. The colon contains a large number of bacteria, more than the number of cells in the entire human body. In patients with liver disease, the immune system is often damaged to some extent, impairing the body's ability to remove bacterial antigens. As a result, fluid in the abdominal cavity acts as a sort of Petri dish where bacteria can colonize, potentially leading to clinical infection. The bacteria with which this occurs are usually derived from the gut. Spontaneous bacterial peritonitis can be a major complication in patients who have liver disease.

G&H What are the mechanisms by which bacterial peritonitis occurs?

KK The buildup of fluid in the abdomen occurs through a series of events that are not well understood. A cirrhotic liver results in increased pressure in the portal vein, which drains blood into the liver. This condition is called portal hypertension and may result in shunting of blood from the portal to systemic circulation. Portal hypertension may also result in accumulation of fluid in the peritoneal cavity (ascites).

Several hemodynamic changes occur as a result of portal hypertension. The systemic arteries become dilated, the blood pressure typically decreases, and the renal arteries become vasoconstricted. One result of this conglomeration of events is that salt and water are retained in the body, leading to the accumulation of fluid in the abdomen that is essentially waiting to become infected. Ascitic fluid, especially in patients whose liver function starts to decompensate, leads to bacterial migration through the walls of the intestine, resulting in bacterial peritonitis.

G&H Are some patients with cirrhosis more likely than others to develop spontaneous bacterial peritonitis?

KK The risk of spontaneous bacterial peritonitis is related to the level of liver function. The more decompensated the liver function, the greater the risk for peritonitis. In some patients with compensated cirrhosis, ascites may develop transiently due to an acute illness and usually resolves when the illness does. By contrast, ascites that remains persistent and does not resolve is usually a sign or consequence of decompensated liver disease. This can then become infected, resulting in spontaneous bacterial peritonitis.

Another risk factor is immune function. In particular, patients with alcoholic cirrhosis with extremely low levels of certain immunoglobulins may have reduced opsonic activity. Normally, immune cells clean up bacteria when the population rises above a certain level. However, that ability can become impaired when the body does not have enough protein to make antibodies and immunoglobulins. As a result of reduced immunologic function and reduced gut barrier function, the colonic wall that would normally prevent bacteria from getting into the ascites becomes leaky, and once the bacteria enter the ascites, an effective immune response to clear these bacteria cannot be mounted.

G&H Does proton pump inhibitor intake increase the risk of spontaneous bacterial peritonitis?

KK Yes, proton pump inhibitor use has been associated with this condition and with increased mortality rates as a result of this condition.

G&H How dangerous is spontaneous bacterial peritonitis?

KK If left untreated, this condition can be fatal. Thus, it is crucial that spontaneous bacterial peritonitis be diagnosed early. Patients with this condition have some level of immunosuppression due to cirrhosis and thus may not manifest all of the obvious signs of infection, such as fever, chills, and abdominal pain. Therefore, clinicians have to be on the lookout for spontaneous bacterial peritonitis, particularly because it is associated with decreased survival. Even a single episode puts a patient with cirrhosis and ascites into a high-risk category. In addition, patients who experience 1 episode of spontaneous bacterial peritonitis are likely to have subsequent episodes.

G&H Are there any visible signs of spontaneous bacterial peritonitis?

KK Specific symptoms would include severe abdominal pain, fever, chills, and a high white blood cell count. There are also several nonspecific symptoms. If a patient with cirrhosis develops confusion, low blood pressure, or worsening renal function, these symptoms may be signs of decompensation. Spontaneous bacterial peritonitis could be the underlying cause of the decompensation.

However, it is important to emphasize that patients may have no symptoms or obvious signs, so a high level of clinical suspicion is required to consider spontaneous bacterial peritonitis in any patient with cirrhosis and ascites with any form of acute clinical illness or deterioration.

G&H Why do patients with cirrhosis decompensate?

KK This question is the focus of current research. We have known for a long time that patients with cirrhosis have a very good survival rate if no complications develop. However, once ascites occurs and is complicated by an infection, survival time may be drastically reduced.

A growing body of research suggests that low-grade bacterial products could be entering the liver and ascitic fluid via the portal vein, and could be producing a variety of toxins. These toxins may be the tipping point that transforms a patient from having compensated liver disease to decompensated liver disease.

G&H Can the use of endoscopic ultrasound improve the diagnosis of spontaneous bacterial peritonitis?

KK Yes, but this approach is not better than paracentesis with standard transcutaneous ultrasound.

G&H Is this condition treatable?

KK Spontaneous bacterial peritonitis is easy to treat because most patients are infected with gram-negative or enteric bacteria. These bacteria are very sensitive to antibiotics. Patients with this condition are generally treated with cephalosporins. For patients who respond to this therapy, it is important to continue suppressive antibiotics to prevent recurrence.

Following the acute infection, low-dose suppressive antibiotics should be given. This treatment keeps the concentration of the bacteria down and has been used as a prophylactic therapy for quite some time.

G&H What new treatments are being investigated?

KK Several antibiotics are being examined. There is a great deal of interest in altering the microbiome as a way of preventing the infection. Probiotics or nonabsorbable oral antibiotics may have a cleansing effect in the gut. This area of research is very active as we try to understand how the microbiome can be manipulated to prevent recurrent episodes. With this new approach, we are looking at the possibility of changing the bacterial composition of the colon, rather than suppressing bacterial concentrations. The aim is to allow more favorable bacteria to have an advantage over less favorable bacteria by using probiotics or nonabsorbable antibiotics that do not get into the system.

G&H How can nonabsorbable antibiotics be used?

KK Antibiotics that are nonabsorbable may allow certain unfavorable bacteria to be cleansed. Bacteria in the colon produce toxins and vasoactive substances, which might be a tipping point in the transformation from compensated cirrhosis to decompensated cirrhosis.

Several ongoing studies are investigating whether nonabsorbable antibiotics can be used to cleanse the colon of toxic bacteria and allow more favorable bacteria to grow. In one study, a nonabsorbable antibiotic is being given to patients with ascites to determine whether the subsequent risk of decompensation is reduced.

G&H How could probiotics be used in these patients?

KK It may be possible to use probiotics to allow certain favorable bacteria to accumulate. The concept is very similar to that behind the research of nonabsorbable antibiotics.

Experimental data with animals and humans are providing us with a better understanding of the microbiome in patients with spontaneous bacterial peritonitis compared with patients without peritonitis. Some animal data show that probiotics may reduce the rate of bacteria translocating across the gut.

G&H When are results expected from any of the ongoing studies?

KK A clinical trial investigating the nonabsorbable antibiotic rifaximin (Xifaxan, Salix) is fully enrolled, and the results are expected in the next 6 to 12 months. Some observational, single-center studies of probiotics are also expected to yield results in the next year or two.

G&H Is there any concern about overuse of antibiotics with regard to their use for the prevention of this condition?

KK Yes. Antibiotic resistance is a major concern, and multidrug resistance has been observed. This concern is the rationale for using probiotics or nonabsorbable antibiotics that will not result in drug resistance. However, clinicians are awaiting additional data on whether the use of these nonabsorbable antibiotics increases the risk of resistance.

Dr Kowdley has no relevant conflicts of interest to disclose.

Suggested Reading

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