Reliability and validity of leukocyte Esterase Reagent Strips in Diagnosis of Spontaneous Bacterial Peritonitis

Thesis

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Abstract :

- **Spontaneous bacterial peritonitis** is one of the most serious complications of ascites in cirrhotic patients. The condition should be suspected in any cirrhotic patient with ascites with evidence of clinical deterioration, regression in hepatic or renal function, worsening malaise, encephalopathy or unexplained persistent leucocytosis.

Diagnostic aspiration should be performed and neutrophil count>250 cells/mm^3 is indicative of underlying SBP.

- **Leukocyte esterase** (LE) is a urine test for the presence of white blood cells and other abnormalities associated with infection by detecting esterase which is an enzyme released by white blood cells and this test was tried for diagnosis of SBP using the ascetic fluid as the substrate.
- Our study aims to assess the reliability and validity of leukocyte esterase reagent strips in diagnosis of SBP in cirrhotic patient with ascites and compare this method with other conventional methods used in diagnosis.

key words : ascites, cirrhosis, portal hypertension, spontaneous bacterial peritonitis, leukocyte esterase.

introduction

Introduction

Spontaneous bacterial peritonitis is a frequent and severe complication in patients with cirrhosis and ascites.

(Rimola et al., 2001).

Approximately half the episodes of SBP are present at the time of hospital admission and the remainder are acquired during hospitalization. **(Navasa et al., 1996).**

Without early antibiotic treatment, this complication is associated with a 30-50% mortality rate, and death can occur in a matter of hours. With effective antibiotic treatment, effective elimination of the offending bacteria can be achieved within 48h. **(Runyon et al., 1990).**

SBP is considered ar indication for liver transplantation because the prognosis after the first episode of SBP is extremely poor. **(Van Thiel et al., 1996).**

The prevalence and mortality rates in SBP increase in end-stage liver disease patients such as those awaiting liver transplantation because these patients often present with impaired immune response and have developed resistance to prophylactic regimens **(Runyon et al., 1988).**

Early diagnosis and treatment of SBP are therefore essential for survival. Symptoms of SBP, however, are non-specific and are not sensitive. Those include fever, abdominal pain, nausea and vomiting. However, in this setting ascitic fluid cultures can be negative in up to 60% of cases.

(Fernandez et al., 2002).

Culture results are delayed for several days; thus, diagnosis of SBP must be based on the polymorph nuclear [PMN] cell count. The criterion for making the diagnosis of spontaneous bacterial peritonitis is (an absolute neutrophil count in the ascetic fluid $\geq 250/mm^3$ in the absence of surgically treatable intra-abdominal source of infection.

(Runyon et al.,2002).

Sometimes only hepatic encephalopathy or a precipitating event such as an upper gastrointestinal hemorrhage from ruptured esophageal varices will herald SBP. The absence of any sympotom is not rare. For these reasons, diagnostic paracentesis is considered a standard procedure in medical practice for any patient with newly diagnosed ascites due to cirrhosis, or in a known patient with ascites who develops signs or risk factors suspecting SBP. In patients requiring repeated large-volume paracentesis due to diuretic resistance (most often seen in an outpatient setting), it is still not clear whether it is

cost-effective to perform systematic ascitic fluid analyses. **(Thierry et al., 2005).**

The laboratory standard point for the diagnosis of SBP is an ascetic fluid polymorphonuclear (PMN) count of more than 250 cells/ul, irrespective of the ascitic fluid culture, which is variably positive (40-90% of cases).**(Siersema et al., 1992)**.

Once this cut-off is reached, the antibiotic therapy must be started without waiting for a culture from ascetic fluid. The improved survival might, in part, be explained by a more rapid diagnosis and treatment by avoiding occurrence of a septic shock, a condition well known for its frequently fatal outcome. **(Moreau et al., 1992).**

However, the ascitic fluid total leukocyte and PMN count are not always available , thereby delaying time to diagnosis. Therefore, searching for a rapid, simple screening tool for diagnosis of SBP could be useful in this context.

(Casstello et al., 2003).

Reagent strip testing for leukocyte esterase activity could be such a tool. The test is based on the esterase activity of granulocytes. 3-Hydroxy-5-phenyl-pyrrole esterified with an amino acid used as the substrate. Hydrolysis of this ester by the esterase releases 3-hydroxy-5phenyl-pyrrole, which in turn reacts with a suitable diazonium salt, yielding a violet azo dye,

the intensity of which correlates to the leukocyte count. **(kutter et al., 1987).**

Use of reagent strip testing for leukocyte esterases has been proposed for the rapid diagnosis of meningitis, **(Moosa et al., 1995)** urinary tract infections **(Levy et al., 1989)** and peritonitis in chronic renal failure patients on peritoneal dialysis.**(Sam et al., 2002).**

These reagent strips are best known for their ability to diagnose pyuria in routine general practice with a high sensitivity (96%) and specificity (98%).**(Hiscoke et al., 1990).**

Many types of these strips are available on the market. Current strips could detect as few as 20 leukocytes/uL or 5-15 cells per high-power field. Most of these test strips can also detect other substrates (e.g. glucose, protein, nitrites), all at a minimal cost. **(Thierry et al., 2005).**

Spontaneous bacterial peritonitis

Spontaneous Bacterial Peritonitis : Pathogenesis, Diagnosis, Treatment

Introduction :

According to recent statistical data, hepatic cirrhosis represents the tenth major cause of death in USA **(Amadon et al., 2003).**

Among the major complications of cirrhosis, ascites seems to be the most frequent one, along with hepatic encephalopathy and upper GIT hemorrhage caused by ruptured esophageal varices **(Runyon et al., 2004).**

Patients with cirrhosis and ascites show a higher susceptibility to bacterial infections- mainly because of the inadequate defence mechanisms. In those patients, the most severe and frequent infectious complication that occurs (about 25% of cases), is spontaneous bacterial peritonitis (SBP), followed by urinary infections (about 20%), pneumonia (about 15%) and bacteremia (about 12%) **(Garcia-Tsao., 2005).**

Since 1970, when SBP was first described and up to the present time, the mortality rate has been decreased from 80% to 30% due to the prompt diagnosis and early initiation of adequate treatment **(Genuit et al., 2004).**

Although SBP has been described in different clinical settings, such as nephrotic syndrome and heart failure, most SBP episodes develop in patients with advanced cirrhosis as a manifestation of severe derangement of hepatic function. Therefore, an episode of ascitic fluid (AF) infection has been proposed as an indication for liver transplantation, in the absence of contraindications. **(Bunyon et al., 1998).**

Definitions :

Several variants of ascetic fluid (AF) infection have been described (table 1).

SBP is the infection of the ascitic fluid that occurs in the absence of a visceral perforation and in the absence of an intraabdominal inflammatory focus such as abscess, acute pancreatitis or cholecystitis. For SBP diagnosis, the number of polymorphonuclear leucocytes (PMN) from the ascitic fluid obtained by paracentesis must exceed 250 cells/mm^3 and from bacteriological cultures only one microorganism must be isolated **(Guarner et al., 2005).**

Because SBP is almost a monomicrobial infection, the presence of more than one microorganism in the culture , should raise the suspicion of secondary peritonitis **(Levison et al., 2005).**

Another type of ascitic fluid infection is ***culture negative neutrocytic ascites (CNNA)***, the diagnosis criteria being the same as those for SBP but the cultures are negative; and other causes of neutrocytic ascites (pancreatitis, peritonitis, tuberculosis and peritoneal carcinomatosis) must be excluded . Because CNNA has the same clinical and prognostic characteristics of SBP, the treatment is also the same. **(Such et al., 1998).**

Monomicrobial non neutrocytic bacterascites is a form in which the cultures from the ascetic fluid are positive but the number of PMN is <250/mm^3. The clinical evolution depends on the presence or absence of the signs or symptoms suggestive of infection. Patients with infection signs have morbidity and mortality rates similar with those with SBP or CNNA **(Such et al., 1998).**

The secondary bacterial peritonitis is ascetic fluid infection, diagnosed when the number of PMN exceeds 250 cells/mm^3 and there is a source of infection that can be surgically treated; the cultures are positive (frequently polymicrobial). The ascetic fluid must present two of the following characteristics :

- The glucose concentration <50mg/dl.
- A total protein content of >1g/dl

- Or LDH>225u/ ml (or higher than the upper normal limit). The diagnosis of secondary bacterial peritonitis must be made early in the course of illness, because without the adequate surgical treatment, the evolution is very severe. Another type of ascetic fluid infection is the ***polymicrobial bacterascites*** – in which the number of PMN is <250/mm^3 and cultures of ascetic fluid (or Gram staining) demonstrate multiple organisms. **(Such et al., 1998).**

This variant usually occurs as a result of inadvertent puncture of the intestine during paracentesis, being stimulated by the presence of multiple surgical scars and post-operative adhesions or by the presence of ileus. If protein concentration exceeds 1 g/dl in the ascetic fluid and the fluid activity is adequate, the colonization resolves spontaneously **(Quenzer et al., 2001).**

Table 1. Classification of ascetic fluid infections.

Type of infection	***PMN cell count (/mm^3)**	**Bacterial culture result**
Spontaneous bacterial peritonitis	≥250	Positive (usually one organism)
Culture-negative neutrocytic ascites	≥250	Negative
Monomicrobial nonneutrocytic bacterascites	<250	Positive (one organism)
Secondary bacterial peritonitis	≥250	Positive (polymicrobial)
Polymicrobial bacterascites	<250	Positive (polymicrobial)

* PMN = polymorphonuclear: