Diagnostic Value of Leukocyte Esterase Test Strip Reagents for Rapid Clinical Diagnosis of Spontaneous Bacterial Peritonitis in Patients Admitted to Hospital Emergency Departments in Iran

Amir Masoud Hashemian, Koorosh Ahmadi, Hamid Zamani Moghaddam, Hosein Zakeri, Seyed Akbar Davoodi Navakh, Mohammad Davood Sharifi, Abdollah Bahrami

1Department of Emergency Medicine, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran
2Department of Emergency Medicine, Alborz University of Medical Sciences, Karaj, IR Iran
3Department of Emergency Medicine, Hasheminejad Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran
4Emergency Medicine Specialist, Help Hospital of Sabzevar, Sabzevar, IR Iran
5Department of Internal Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran

*Corresponding Author: Mohammad Davood Sharifi, Department of Emergency Medicine, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran. Tel: +98-9151156758, Fax: +98-5138525312, E-mail: sharifimd@mums.ac.ir

Received 2014 June 30; Revised 2014 December 1; Accepted 2015 February 21.

Abstract

Background: Spontaneous bacterial peritonitis (SBP) is a common and important clinical problem and is life-threatening in decompensated liver disease. Ascites fluid test by leukocyte esterase test strip has been recently proposed as an effective and rapid method to diagnose SBP in patients with cirrhosis.

Objectives: This study aimed to evaluate sensitivity and specificity of leukocyte esterase test strip in the diagnosis of SBP.

Patients and Methods: The population of this research was all patients with cirrhosis and ascites admitted to the emergency room at Imam Reza (AS) hospital, Mashhad. A written consent was taken for inclusion in the study. 50 mL ascites sample was taken from all patients for use in a urine test strip (LER) (Urine Test Strips Convergys®Urine Matrix 11). The patient’s ascites samples were evaluated for cell counting. Positive dipstick test for LER in this study considered as grade 3+. The values of WBC > 500 cell/mm3 or PMN > 250 cell/mm3 considered as positive result of the gold standard method for the diagnosis of SBP.

Results: In this study, 100 patients with ascites due to cirrhosis, with an average age of 38.9 ± 6.54 years were evaluated. Twenty cases had positive results, of whom 17 cases were also detected based on the standard diagnostic criteria and other three cases were healthy individuals. Thus, sensitivity, specificity, positive and negative predictive values, and accuracy of the method were 95%, 96.3%, 85%, 97.5% and 95%, respectively.

Conclusions: The use of leukocyte esterase urine dipstick test can be a quick and easy method in early diagnosis of SBP to start the treatment until preparation of SBP-cell count results.

Keywords: Liver Cirrhosis, Spontaneous Bacterial Peritonitis, Leukocyte Esterase Reagent Strip

1. Background

Spontaneous bacterial peritonitis (SBP) is a common and important clinical problem in decompensated liver disease (1). Over the past three decades, increasing use of paracentesis of ascites fluid led to an increased diagnosis of this life-threatening condition (2). In the early years after 1800, Laennec and cirrhosis names fused together, spontaneous bacterial peritonitis (SBP) was introduced as a separate diagnosis. Kerr et al. (3) and Conn (4) articles published within a year of each other, described injection of ascites fluid without a source of contagious infection or an intra-abdominal inflammatory source. Despite reports published from France since 1893 on the subject, Conn finally presented the term SBP in his 1964 paper (4).

Subsequent researches redefined the disease that seemed daunting at first (with a mortality rate of 90% in the initial report (4)) to a treatable problem of decompensated cirrhosis (5); however, the prevalence of SBP is monotonous and the recurrence rate is high (6, 7).

A series of papers in the recent years led to national and international guidelines (8-11). According to studies, the prevalence of SBP in patients with cirrhosis varies from 7% to 30% per year (1). This complication accounts for about 25% of hospital mortality rate, but a rapid detection and treatment leads to significant reduction in the mortality rate of disease to less than 10% (12-14). SBP has non-specific signs and symptoms including abdominal pain, fever, nausea, vomiting, unexplained encephalopathy, unstable hemodynamic state and renal failure (1). This situation is typically accompanied with fever and
generalized abdominal tenderness, but may be clinically asymptomatic or appears with the development of hepatic encephalopathy and renal failure (2, 13).

The most common organisms causing this complication extracted from ascites fluid contain *Escherichia coli* (about 70%), *Klebsiella* (10%), *Proteus mirabilis* and *Enterococcus faecalis* (each about 4%), *Pseudomonas aeruginosa* (approximately 2%) and other agents (approximately 6%) (15, 16). Endotoxemia caused by these infections can lead to the release of proinflammatory cytokines such as TNF-α, IL-6, IL-1, which ultimately leads to the activation of polymorphonuclear cells (PMN) (17).

The ascitic fluid PMN count over 250/mm³ objectively confirms the diagnosis of SBP and individual immediately needs treatment with antibiotics (9). According to the American Association for the Study of Liver Diseases, patients with more than 250 mm³ PMN are classified as at risk for SBP (10). PMN count typically is performed by conventional hematological with an optical microscope and manually. This method, which is still the gold standard evaluation of PMN count in ascites, is difficult and time consuming (1). We have evidence showing that automated cell counting device offers the same results by manually counting; therefore, these modalities are reliable tools for a faster diagnosis of SBP (18). Nevertheless, these methods are still not available in many places. Given the high prevalence and mortality rate of disease and necessity for a prompt treatment, a rapid, cheap test, available at all times of day, with a high sensitivity and specificity is required. Leukocyte esterase dipstick test is used to diagnose the infection in some cases such as urine (19), bronchoalveolar lavage fluid (20), pleural fluid (21) and cerebrospinal fluid (22). This test is based on esterase activity of granulocytes (neutrophils). Only an active PMN can release leukocyte esterase into extracellular environment (1).

Ascites fluid test by leukocyte esterase dipstick test has been recently proposed as an effective and rapid method to diagnose SBP in patients with cirrhosis.

2. Objectives

This study aimed to evaluate sensitivity and specificity of leukocyte esterase dipstick test in the diagnosis of SBP. Using this test in peritoneal fluid, a color change on the strip that shows a certain amount of neutrophils (PMN) is compared with the amount of standard PMN (gold standard) measured by manual counting under a microscope, and then the sensitivity and specificity are calculated.

3. Patients and Methods

Study population included patients with cirrhosis and ascites admitted to the emergency room at Imam Reza (AS), Mashhad. In this study, a non-probability convenient sampling method was used. Since the positive likelihood ratio (PLR) is valuable about 4, the lower limit of CI for likelihood was 4.

A written consent was initially obtained from patients prior to entry into the study. No change or delay occurred in the treatment. In addition to routine sampling from all patients based on the patients’ requirements, 50 ml ascites sample was taken to use in the urine dipstick test (LER). The samples were examined and interpreted according to the manufacturer’s protocol of LER and sent to the laboratory for other required tests. Patients’ ascites samples were evaluated for cell count, smear and culture (as a standard test).

To perform dipstick test for leukocyte esterase, ascites sample was poured into a clean test tube and then a urine dipstick test (Urine Test Strips Convergys®Urine Matrix II brand) was floated in the tube recommended by the manufacturer for 1 to 2 seconds, and then laid out on a clean sheet, following adding the sample. After 2 minutes, the developed color was compared with the standard sample provided.

Positive Dipstick test for LER in this study considered as grade 3+ (purple). Cases of WBC > 500 cell/mm³ or PMN > 250 cell/mm³ considered as positive result of the gold standard method for the diagnosis of SBP. Data collection for SBP test for each patient containing data on age, gender, history of disease, previous diagnosis of disease, color change results, laboratory results and other required parameters.

3.1. Methods of Data Analysis and Statistical Evaluation

The collected data entered SPSS v.17 software (IBM Corp, New York) and then descriptive analysis was performed using appropriate tables and sensitivity, specificity, and positive and negative predictive values were calculated by related formula.

4. Results

Sixty-four patients (64%) were males and 36 (36%) females. The mean age of patients was 38.9 ± 6.54 years (average 6.54, SD 38.9), ranging from 25 to 70 years.

In our evaluation, the most frequent cause of cirrhosis was viral hepatitis (HBV) with 61% of cases. Other causes were autoimmune hepatitis (11%) and alcoholic liver disease (7%). In 9% of cases, the cause of cirrhosis was unknown.

Based on the experiments of cell count of ascites fluid and diagnostic standard criteria of spontaneous bacterial peritonitis (SBP), 19 SBP cases were diagnosed.

Considering grade 3+ on urine dipstick test, 20 cases had positive results. Among them, 17 cases were confirmed on standard diagnostic criteria and the other three cases were healthy individuals. Table 1 shows the details of results.

Based on standard calculation, sensitivity, specificity, positive and negative predictive values, and accuracy based on the results were 95%, 96.30%, 85.0%, 97.5% and 95.0%, respectively.
5. Discussion

In this study, we evaluated diagnostic value of leukocyte esterase test strip reagents for rapid clinical diagnosis of SBP. Our results are largely consistent with studies in other parts of the world.

DY and colleagues in their study calculated sensitivity of 50% - 67%, specificity and PPV of 100% - 100% and NVP of 87% - 89% using two UriScan test strip and Multistix test strip 10SG (23).

Our findings revealed higher sensitivity and NVP and lower PPV than this study. The results were almost identical for specificity. In another study conducted by Sarwar et al. in Lahore, using a combur 10 test strips, sensitivity of 97.7%, specificity of 89.4%, PPV of 97.7%, NPV of 97.7% and accuracy of 96.2% were calculated (24). The findings of NVP and accuracy in that study were consistent with our study; however, our findings revealed higher specificity and lower sensitivity.

The differences observed in our study and the studies mentioned above can be attributed to two things. Primarily, differences in the type of test strips used in the studies leading to a slight difference, secondly, differences in the rate of color change created as a positive sample; in studies that less color changes (lower grades the test strip) were considered as positive result, the calculated sensitivity was higher and proportionally specificity was lower.

Leukocyte esterase test strips are not specific for neutrophils, and not designed primarily to detect SBP. Most of them are designed to detect ~125 leukocytes (mostly PMN) per mm3 of 100 leukocytes per mm3.

Considering lower PPV generally leads to higher sensitivity and lower specificity, while higher cut-offs lead to inverse results. Thus we can say that in the clinical case with SBP, lower cut-offs should be preferred to increase sensitivity (even with a reduced specificity); because in these cases, the diagnosis should not be delayed, patients are at risk of death. These patients need a rapid treatment. This means that some patients with a false-negative result may be given an unnecessary dose of antibiotics; therefore, it has great advantages in contrast to losing patients.

Finally we can say that despite differences in sensitivity and positive predictive values reported in other studies, proper calculated NVP in most studies confirms that the use of leukocyte esterase urine test strip in clinical settings can be used beneficially for patients with ascites caused by cirrhosis with SBP due to the high decision rate, ease of use and low cost.

It is suggested to perform further studies with a larger sample size to assess advantages and disadvantages of leukocytes esterase test strips in the diagnosis of SBP.

Footnote

Authors’ Contributions: Amir Masoud Hashemian, Koorosh Ahmadi and Seyed Zamani Moghaddam contributed to the design and data collection. Hosein Zakeri and Seyed Khodadadi Navakham contributed to data analysis. Mohammad Davood Sharifi and Abdollah Bahrami contributed to paper writing and revising.

References


