Diagnostic value of two reagent strips (Multistix® 8 SG and Combur® 2 LN) in cirrhotic patients with spontaneous bacterial peritonitis and symptomatic bacteraeasites

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SUMMARY

Objective — Spontaneous bacterial peritonitis is a life-threatening complication in patients with liver cirrhosis requiring a rapid diagnosis. We have tested two reagent strips, Multistix® 8 SG and Combur® 2 LN for bedside diagnosis of spontaneous bacterial peritonitis and symptomatic bacteraeasites, a variant of spontaneous bacterial peritonitis.

Methods — Responses of the two strips in colorimetric scale were compared with results given by cyto-bacteriological analysis of ascitic fluid. Results with positivity in grades 1 and 2 of colorimetric scale were analyzed.

Results — Four hundred and forty three paracentesis were performed in 116 patients including 46 samples of ascitic fluid with spontaneous bacterial peritonitis occurring in 25 patients and 20 samples of ascitic fluid with symptomatic bacteraeasites occurring in 17 patients. Forty two percent of spontaneous bacterial peritonitis were culture-negative neutrocytic ascites, gram-positive pathogens and enterobacteriaceae were responsible for 36% and 21% episodes of spontaneous bacterial peritonitis and 71% and 29% episodes of symptomatic bacteraeasites respectively. Fifty seven percent of spontaneous bacterial peritonitis had polymorphonuclear cell count < 1000/mm3. For spontaneous bacterial peritonitis diagnosis, grade 1 positive Multistix® and Combur® tests had an sensitivity of 69.6% and 80.4% respectively, and a negative predictive value of 96% and 97.3%. Grade 2 positivity increased specificity to 98% and 99.2% and positive predictive value to 75% and 91% for the two strips respectively. Grade 1 positive tests had a sensitivity of 100% and 90% and a negative predictive value of 100% and 99.4% respectively for diagnosis of spontaneous bacterial peritonitis with polymorphonuclear count > 1000/mm3. For symptomatic bacteraeasites diagnosis, grade 1 positive tests had a sensitivity of 22.4% and 44.4% respectively and a negative predictive value of 96% and 97%.

Conclusion — Although Combur® had a higher sensitivity than Multistix® for the diagnosis of spontaneous bacterial peritonitis, sensitivity of the two strips remains low with polymorphonuclear cell count < 1000/mm3. Grade 2 positive Combur® test had an acceptable positive predictive value. Sensitivity of both strips is insufficient for diagnosis of symptomatic bacteraeasites. Rapid cyto-bacteriological analysis of ascitic fluid remains necessary for diagnosis of these complications.

RéSUMÉ

Valeur diagnostique de deux bandelettes réactives (Multistix® 8 SG et Combur® 2 LN) dans l’infection spontanée du liquide d’ascite et la bacteraeasite symptomatique chez le malade cirrhotique

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Objectifs — L’infection spontanée du liquide d’ascite est une complication grave chez les malades atteints de cirrhose nécessitant un diagnostic en urgence. Nous avons testé deux bandelettes réactives, Multistix® 8 SG et Combur® 2 LN pour le diagnostic rapide, au lit du malade, de la péritonite spontanée et de la bacteraeasite symptomatique, variant de l’infection spontanée du liquide d’ascite.


Résultats — Quatre cent quarante trois ponctions d’ascite ont été pratiquées chez 116 malades. Quarante six prélèvements ont montré une infection spontanée du liquide d’ascite chez 25 malades et 20 prélèvements une bacteraeasite symptomatique chez 17 malades. Quarante deux % des infections spontanées du liquide d’ascite étaient amicrobiennes, les germes pathogènes cocci gram + et les entérobactéries étaient responsables de 36 % et 21 % des épisodes d’infection spontanée du liquide d’ascite, 71 % et 29 % des épisodes de bacteraeasite symptomatique respectivement. Cinquante sept % des infections spontanées du liquide d’ascite avaient un nombre de leucocytes polynucléaires < 1000/mm3. Pour le diagnostic d’infection spontanée du liquide d’ascite, les bandelettes Multistix® et Combur® positives de grade 1 avaient une sensibilité de 69,6 % et 80,4 %, une valeur prédictive négative de 96 % et 97,3 %. La positivité de grade 2 augmentait la spécificité à 98 % et 99,2 % et la valeur prédictive positive à 75 % et 91 % pour les deux bandelettes respectivement. La positivité de grade 1 avait une sensibilité de 100 % et 90 % et une valeur prédictive négative de 100 % et 99,4 % pour les deux bandelettes respectivement pour le diagnostic d’infection spontanée du liquide d’ascite avec un nombre de leucocytes polynucléaires > 1000/mm3. Pour le diagnostic de bacteraeasite symptomatique, la positivité de grade 1 avait une sensibilité de 22,4 % et 44,4 % pour les deux bandelettes respectivement et une valeur prédictive négative de 96 % et 97 %.

Conclusion — Bien que Combur® ait une meilleure sensibilité que Multistix® pour le diagnostic d’infection spontanée du liquide d’ascite, la sensibilité des deux bandelettes reste médiocre avec un nombre de leucocytes polynucléaires < 1000/mm3. La positivité de grade 2 pour Combur® a une valeur prédictive positive acceptable. La sensibilité des deux bandelettes est insuffisante pour le diagnostic de bacteraeasite symptomatique. L’examen cyto-bactériologique en urgence du liquide d’ascite reste nécessaire pour le diagnostic de ces complications.
Reagent strips in spontaneous bacterial peritonitis

Introduction

Spontaneous bacterial peritonitis (SBP) is a severe complication in liver cirrhosis with a prevalence rate of 20-30% in hospitalized patients [1]. It requires rapid diagnosis which is based on cyto-bacteriological examination of ascitic fluid. A polymorphonuclear cell count above 250/mm³, irrespective of the ascitic fluid culture, is admitted as the standard criterion for diagnosis of SBP [2]. Result of the cyto-bacteriological examination of the ascitic fluid must be obtained without delay in order to carry out probabilist antibiotherapy based on third-generation cephalosporins. The mortality rate after an episode of SBP remains high, on average 10%, despite recent improvements in management of this complication [3]. However, regarding organization of hospital facilities, a bacteriological laboratory is not constantly available in all departments receiving ascitic cirrhotic patients. Therefore, alternative methods for rapid diagnosis of SBP are needed.

Reagent strips detecting leukocyte esterase activity in biological fluid have been validated for the diagnosis of urinary tract infection, peritonitis in patients on continuous ambulatory peritoneal dialysis, pleural infections and meningitis [4-9]. Previous studies have shown that reagent strips are reliable bedside methods for the diagnosis of SB in cirrhotic patients [10-14]. However, most of these studies have included few samples of ascitic fluid with SBP and only two studies have compared the diagnostic value of Multistix® 8 SG, Combur® 2 LN and Nephur® test, the tests most available in France [12, 14]. Moreover, the sensitivity of the strips with polymorphonuclear count close to the threshold of 250/mm³ is not well known and their diagnostic value in symptomatic bacteraemias (SB), a variant of SB, has not been established. On the other hand, patients with end-stage liver disease, hospitalized for a long time, some awaiting liver transplantation, are at high risk of this type of SBP [15]. The aim of this study was to compare the value of the two reagent strips, Multistix® 8 SG and Combur® 2 LN, in the diagnosis of SBP with a wide range of polymorphonuclear count in ascitic fluid and SB.

Patients and methods

Study population

All cirrhotic patients with ascites admitted to our department from December 2003 to February 2005 were included in the study. Our department receives patients from other hospitals in the Parisian region and is specifically devoted to the rehabilitation of patients with liver cirrhosis. Most patients included in the study were previously hospitalized in another institution for a complication of the disease (gastro-intestinal bleeding, ascites, hepato-renal syndrome, encephalopathy, acute alcoholic hepatitis, septic complication) before admission into our department. The diagnosis of cirrhosis was based on histological examination or usual clinical and biological manifestations of cirrhosis.

Paracentesis

Paracentesis was performed at admission and during hospital stay for treatment of ascites or in the presence of clinical signs of SBP. Immediately after the paracentesis, the ascitic fluid was tested by use of the two reagent strips: the Multistix® 8 SG (Bayer Diagnostics Corporation, Puteaux, France) and the Combur® 2 test LN (Roche Diagnostics, Meulan, France). Fresh ascitic fluid was collected in a clean dry container and the strip was immediately immersed in ascitic fluid. Excess ascitic fluid was removed and after 2 minutes, the colour of the leukocyte reagent area was compared with the colour chart on the bottle. The strips were read by the physician who carried out the paracentesis and an assisting nurse. These two strips had a colorimetric 5-grade scale (from 0 to 4) and 4-grade scale (from 0 to 3) for the Multistix™ test and the Combur® 2 test LN, respectively. A correlation between leukocytes (Leu) and the 5-grade scale was suggested by the manufacturer as follows for Multistix® 8 SG, grade 0: 0 Leu/mm³; grade 1: 15 Leu/mm³; grade 2: 75 Leu/mm³; grade 3: 125 Leu/mm³ and grade 4: 500 Leu/mm³. For the Combur® 2 test LN, the correlation was grade 0: 0 Leu/mm³, grade 1: 25 Leu/mm³, grade 2: 75 Leu/mm³, grade 3: 200 Leu/mm³. Laboratory analysis of the ascitic fluid was performed without delay in all patients and used a standard sterile technique and including the following: total and differential cell counts, gram stain and total protein levels. Cultures of ascitic fluid were performed at the bedside in all patients using blood culture bottles, including both aerobic and anaerobic media (Bact/Alert FN FA, Becton Dickinson Inc. DURHAM UK). A minimum of 10 ml of ascitic fluid was inoculated in each bottle.

Diagnostic criteria

The diagnosis of SBP was based on a polymorphonuclear leukocyte cell count > 250/mm³ in ascitic fluid irrespective of a positive ascitic fluid culture and clinical signs of SBP and an absence of intra-abdominal sources of infection, inflammation or tuberculosis. The diagnosis of symptomatic bacteraeemias was based on a positive ascitic fluid culture, associated with a PMN cell count < 250/mm³ in ascitic fluid and clinical signs of SBP (abdominal pain, fever or hypothermia, diarrhea, acute episode of encephalopathy, collapsus) [15].

Treatment regimen

Empiric antibiotic therapy was initiated immediately after paracentesis when the diagnosis of infection was suspected or after the results of cyto-bacteriological analysis of ascitic fluid when clinical signs of infection were lacking. The antibiotics used were a third-generation cephalosporin (ceftriaxone) which has the same efficacy as cefotaxin but with a lower dose (1 g/d) and cost. Paracentesis was performed 2 days after initiation of antibiotic therapy to determine leukocyte and polymorphonuclear cell counts in ascitic fluid and to ascertain a negative culture if initially positive. Antibiotic therapy was adapted to the individual patient, on the basis of the results of the culture sensitivity of the isolate from that patient or empirically in case of negative ascitic fluid culture and lack of efficacy of initial treatment.

Statistical analysis

Quantitative variables are given as the mean ± SD, and as frequencies for qualitative variables. We determined the sensitivity, the specificity, the positive predictive value and the negative predictive value of the two reagent strips. Comparisons of quantitative variables between two groups were performed using Student’s t test or Mann and Whitney test as appropriate. Comparisons of qualitative variables between several groups were performed using non parametric Kruskall-Wallis test.

Results

Study population

Four hundred and forty three paracentesis were performed in 116 patients. Characteristics of patients are shown in table I. Thirty three episodes of SBP occurred in 25 patients. One episode was observed in an ambulatory patient, other episodes occurred in inpatients. Among these 33 episodes, 13 paracentesis performed 48 hours after initial diagnosis showed persistence of cytological signs of infection with increase or lack of decrease in polymorphonuclear count. Culture of ascitic fluid remained positive in four cases of multisistant isolates (methicillin resistant Staphylococcus aureus N = 2, E.coli N = 1, Enterobacter aerogenes N = 1). A total of 46 episodes with cytological signs of SBP were taken into account. Twenty paracentesis were performed in 17 episodes of SB occurring in 17 patients. The nature of bacteria isolated from culture of ascitic fluid in patients with SBP and SB is shown in table II. Forty two percent of SB were culture negative neutrocytic ascites, 36% were caused by gram positive pathogens, 21% by enterobacteriaceae. Seventy one percent and 29% of SB were respectively caused by gram positive pathogens and enterobacteriaceae. Four patients had both episodes of SBP and SB. Ten patients had hepatocellular carcinoma, among these patients two paracentesis performed in one patient showed symptomatic bacteraeemias.
Among the 25 patients with SBP, 11 died during hospital stay (44%). The 4 patients with both SBP and SB died. Among the 13 patients with SB only 5 patients died (38.5%).

Polymorphonuclear counts according to the nature of pathogens isolated in ascitic fluid are shown in table III. Polymorphonuclear count was lower in culture negative neutrocytic ascites when compared with SBP caused by enterobacteriaceae and gram positive pathogens. Regarding the total group of SBP, mean polymorphonuclear count was $1863 \pm 2812/\text{mm}^3$.

### Comparison between the 2 reagent strips

Polymorphonuclear counts in ascitic fluid according to the colorimetric response of the two reagents strips are shown in table IV. Reagent strips could not be read in 15 cases because of the haemorrhagic aspect of ascitic fluid. Polymorphonuclear cell count shown by grade 1 Multistix® strip was higher than that shown by grade 1 Combur® 2 LN strip ($P = 0.03$). It tended to be higher for the highest grades but the difference was not statistically significant.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients N = 116</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>57.0 ± 11.6</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>76/40</td>
</tr>
<tr>
<td>Prothrombin Index (%)</td>
<td>53.3 ± 17.7</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>27.5 ± 5.6</td>
</tr>
<tr>
<td>Bilirubin (µmol/L)</td>
<td>108 ± 115</td>
</tr>
<tr>
<td>Pugh score</td>
<td>10.7 ± 1.8</td>
</tr>
<tr>
<td>Child classification (A/B/C)</td>
<td>0/38/78</td>
</tr>
<tr>
<td>Protein in ascitic fluid (g/L)</td>
<td>14.4 ± 9.2</td>
</tr>
<tr>
<td>% patients with protein in ascitic fluid &lt; 15 g/L</td>
<td>61.2 %</td>
</tr>
</tbody>
</table>

### Table I. – Characteristics of patients.

Caractéristiques des malades.

### Table II. – Types of bacteria isolated from cultures of ascitic fluid obtained from patients with spontaneous bacterial peritonitis and symptomatic bacterascites.

<table>
<thead>
<tr>
<th>Nature des bactéries isolées lors des épisodes d’infections spontanées du liquide d’ascite et de bacterascites.</th>
</tr>
</thead>
<tbody>
<tr>
<td>表</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Escherichia coli</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
</tr>
<tr>
<td>Klebsiella oxytoca</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
</tr>
<tr>
<td>Enterobacter aerogenes</td>
</tr>
<tr>
<td>Streptococci</td>
</tr>
<tr>
<td>Streptococcus bovis</td>
</tr>
<tr>
<td>Streptococcus species</td>
</tr>
<tr>
<td>Streptococcus oralis</td>
</tr>
<tr>
<td>Streptococcus mitis</td>
</tr>
<tr>
<td>Enterococci</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
</tr>
<tr>
<td>Enterococcus faecium</td>
</tr>
<tr>
<td>Staphylococci</td>
</tr>
<tr>
<td>Methicillin resistant Staphylococcus aureus</td>
</tr>
<tr>
<td>Methicillin susceptible Staphylococcus aureus</td>
</tr>
<tr>
<td>Coagulase negative staphylococcus</td>
</tr>
<tr>
<td>Culture negative neutrocytic ascites</td>
</tr>
</tbody>
</table>

We also analysed mononuclear leukocyte count in ascitic fluid in patients without SBP or SB. Mean values ± SD/mm$^3$ were respectively $45 \pm 64/mm^3$, for grade 0 (N = 338); $93 \pm 102$ for grade 1 (N = 11); $49 \pm 69$ for grade 2 (N = 4) and $394 \pm 646$, for grade 3 (N = 3) of colorimetric response of Multistix® 8 SG and $67 \pm 67$, for grade 0 (N = 322); $53 \pm 50$, for grade 1 (N = 31) and $409 \pm 633$, for grade 2 (N = 3) of colorimetric response of Combur® 2 LN.

Sensitivity, specificity, positive and negative predictive values of the two reagent strips in the diagnosis of SBP and SB with the grade 1 of colorimetric scale and in the diagnosis of SBP with the grade 2 of colorimetric scale are shown in table VI. With regards to the diagnosis of SBP, Combur® 2 LN had higher sensitivity that Multistix® 8 SG. The highest sensitivity was observed with grade 1 of the colorimetric scale of one of the two strips. The highest positive predictive value was observed with Combur® 2 LN with grade 2 of the colorimetric scale. With regards to the diagnosis of SBP, sensitivity and positive predictive value of the two strips were lower in comparison with the diagnosis of SBP. Combur® 2 LN had a higher sensitivity than Multistix® 8 SG.

Among the 46 samples of ascitic fluid with SBP, 20 samples had polymorphonuclear count > 1000/mm$^3$. In this group of 20 samples, sensitivity of Multistix® 8 SG and Combur® 2 LN were 100% and 90% respectively and negative predictive values were 100% and 90% respectively and negative predictive values
were 100% and 99.4% respectively with grade 1 of the colorimetric scale.

**Discussion**

Patients included in this study were at high risk of SBP because most had advanced disease and were hospitalized for a long time for severe complications of their disease. Moreover, patients exhibited high serum bilirubin level and 61% of them had protein level in ascitic fluid below 15 g/L, these two factors are associated with an increased risk of SBP [16-17]. Symptomatic bacterascites is a variant of SBP. In a previous study we have shown that SB and SBP share the same severity since mortality rate was in the same range in the two types of complications [15, 18]. Our present study confirm these previous findings. Taking together SBP and SB the prevalence was 33% which was somewhat higher than in previous studies [1]. Regarding the nature of isolates responsible for these septic complications, a culture positive ascitic fluid was found in 58% of SBP which was higher than previously reported [19]. Cocci gram positive pathogens were predominant as well as in SBP and in SB, confirming the change in nature of organisms responsible for septic complications in hospitalized cirrhotic patients [15, 19]. This change may influence the neutrocytic reaction in ascitic fluid since we have demonstrated that cocci gram positive pathogens are associated with a lower polymorphonuclear count in ascitic fluid than enterobacteriaceae [15]. In the present study, mean polymorphonuclear cell count in ascitic fluid according to the nature of infection and pathogens.

<table>
<thead>
<tr>
<th>Spontaneous bacterial peritonitis</th>
<th>Symptomatic bacterascites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae</td>
<td>Gram positive pathogens</td>
</tr>
<tr>
<td>N</td>
<td>10</td>
</tr>
<tr>
<td>PMN count</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Median</td>
<td>1375</td>
</tr>
</tbody>
</table>

* P = 0.0045. Comparison between the three groups was performed using Kruskall-Wallis test.

**Table IV.** – Polymorphonuclear cell count in ascitic fluid according to the colorimetric response of Multistix® 8 SG (A) and Combur® 2 LN (B) strips.

<table>
<thead>
<tr>
<th>A</th>
<th>Grades</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>369</td>
</tr>
<tr>
<td>PMN count</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Median</td>
<td>14</td>
</tr>
<tr>
<td>Leukocyte count indicated by the manufacturer</td>
<td>0</td>
</tr>
</tbody>
</table>

* P < 10-4. Comparison between the five groups was performed using Kruskall-Wallis test.

<table>
<thead>
<tr>
<th>B</th>
<th>Grades</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>342</td>
</tr>
<tr>
<td>PMN count</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Median</td>
<td>14</td>
</tr>
<tr>
<td>Leukocyte count indicated by the manufacturer</td>
<td>0</td>
</tr>
</tbody>
</table>

* P < 10-4. Comparison between the four groups was performed using Kruskall-Wallis test.
nuclear count was in the same range in the two types of isolates although median value was lower with cocci gram positive pathogens. On the other hand, polymorphonuclear count was lower in culture negative neutrocytic ascites, suggesting that most of these episodes of SBP were likely related to cocci gram positive pathogens, which may account for the lack of efficacy of empiric antibiotic therapy in some of these SBP episodes.

Reagent strips may be an alternative for rapid diagnosis of SBP in cirrhotic patients. These tests detect esterase activity of granulocytes which are mostly polymorphonuclear cells. Therefore, it is admitted that leukocytes indicated by the manufacturer are mainly polymorphonuclear cells. Several studies have evaluated the diagnostic value of reagent strips in this setting [10-14]. Most of them have shown high sensitivity and specificity and disagree with our own results. However, in four of these studies, the number of ascitic fluid samples with SBP was lower than in our study while polymorphonuclear count was higher as shown in table VI. Castellote et al. [11] reported 52 SBP samples with high polymorphonuclear count (> 1000/mm³) in most

Table V. – Colorimetric response of Multistix® 8 SG (A) and Combur® 2 LN (B) in spontaneous bacterial peritonitis, symptomatic bacterascites and lack of infection.

<table>
<thead>
<tr>
<th>A</th>
<th>Grades</th>
<th>SBP</th>
<th>SB</th>
<th>Lack of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>14</td>
<td>11</td>
<td>5</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>14</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>338</td>
<td>11</td>
<td>4</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

Table VI. – Diagnostic values of the two reagent strips for spontaneous bacterial peritonitis and symptomatic bacterascites with grade 1 of colorimetric scale (A) and for spontaneous bacterial peritonitis with grade 2 of colorimetric scale (B).

<table>
<thead>
<tr>
<th>A</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multistix® 8 SG</td>
<td>SBP</td>
<td>69.6%</td>
<td>94.9%</td>
<td>64%</td>
</tr>
<tr>
<td></td>
<td>SB</td>
<td>22.2%</td>
<td>94.9%</td>
<td>18.2%</td>
</tr>
<tr>
<td>Combur® 2 LN</td>
<td>SBP</td>
<td>80.4%</td>
<td>90.4%</td>
<td>52%</td>
</tr>
<tr>
<td></td>
<td>SB</td>
<td>44.4%</td>
<td>90.4%</td>
<td>19%</td>
</tr>
<tr>
<td></td>
<td>SBP</td>
<td>84.5%</td>
<td>89.3%</td>
<td>50.6%</td>
</tr>
<tr>
<td>Positivity of Multistix® 8 SG or Combur® 2 LN</td>
<td>SB</td>
<td>44.4%</td>
<td>89.3%</td>
<td>17.4%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multistix® 8 SG</td>
<td></td>
<td>45.7%</td>
<td>98%</td>
<td>75%</td>
</tr>
<tr>
<td>Combur® 2 LN</td>
<td></td>
<td>63.0%</td>
<td>99.2%</td>
<td>91%</td>
</tr>
<tr>
<td>Positivity of Multistix® 8 SG or Combur® 2 LN</td>
<td></td>
<td>67.4%</td>
<td>98.3%</td>
<td>83.8%</td>
</tr>
</tbody>
</table>
Table VII. – Polymorphonuclear cells count in ascitic fluid and performance of different reagent strips for diagnosis of spontaneous bacterial peritonitis reported in previous studies.

 entrevist [10] | 9 | 4700 ± 5104 | 2150 | 100 | 100 | 100 | 100 | Multistix® 8 SG

Thévenot [12] | 9 | 2800 ± 3750 | 1650 | 89 | 100 | 100 | 99 | Multistix® 8 SG

Sapey [13] | 13 | 2724 ± 2009 | 3392 | Center 1 = 86 | Center 2 = 100 | 100 | 92.5 | 75 | Nephur® Test

Sapey [14] | 17 | 4093±5047 | 1350 | 64.7 | 99.6 | 91.7 | 97.4 | Multistix® 10 SG

*PPV: positive predictive value; NPV: negative predictive value.*

of them. However the strip used in this study was different from those used in our study, which hampers the comparison. However, a recent study has reported a greater number of episodes of SBP with a low sensitivity of the Multistix® 8 SG strip (62.4%) which was very close to our own results [20]. Moreover, Sapey et al. [14] have recently shown in accordance with our results that another reagent strip, Nephur® test, has also higher performance than Multistix® (see table VII). The main results of our study is the lack of sensitivity of the strips, polymorphonuclear counts measured at the different grades of colorimetric scale were far from those announced by the manufacturer, especially for Multistix® 8 SG. Combur® 2 LN seemed more sensitive than Multistix® 8 SG, with lower polymorphonuclear counts at the different grades. Therefore, sensitivities of Combur® 2 LN and Multistix® 8 SG strips were respectively 80.4% and 69.6% at grade 1 in colorimetric scale while increase in this scale parallels increase in specificity. Positive predictive value was higher for Combur® 2 LN than for Multistix® 8 SG at grade 2 in colorimetric scale, respectively 91% vs 75%. The weak activity of leukocyte esterase activity in the absence of leukocyte lysis may contribute to this low sensitivity [21]. Almost all of the patients included in our study were inpatients and many of them had refractory ascites and had repeated paracentesis. As a consequence, the diagnosis of SBP was performed at a very early phase of the septic complication in most patients. This fact may participate to the higher prevalence of symptomatic bacterascites. Therefore, it is possible that paracentesis were performed before leukocyte lysis at time of diagnosis of SBP. On the other hand, we report false positive results with the two reagent strips suggesting other sources of esterase activity than polymorphonuclear leukocytes in ascitic fluid. Hepatocellular carcinoma does not seem to be involved in false positive results since among patients with hepatocellular carcinoma, only one sample and two samples of ascitic fluid showed false positive results with Multistix® and Combur® respectively. Mononuclear leukocytes are a potential source of esterase activity and may contribute to false positive results at the highest grades in colorimetric scale as shown by mean mononuclear cell count in non infected patients with positive grade 3 Multistix® and grade 2 Combur® strips. These reagent strips have been validated for diagnosis of urine infection but the composition of urine and ascites are very different and it may be hypothesized that other factor interfere with the reaction of strips in ascitic fluid. Regarding diagnostic value of the two strips in the diagnosis of SB, sensitivity was very low mainly with Multistix®. This result is in accordance with the low polymorphonuclear counts in ascitic fluid in SB, which was close to that observed when infection is lacking. However, negative predictive value was in the same range in SB and SBP.

Our results show that Combur® 2 LN has a higher sensitivity than Multistix® 8 SG in the detection of SBP. Combination of the two strips slightly increases the sensitivity. However, this sensitivity remains insufficient and seems dependent on the clinical setting. Reagent strips are reliable bedside tools to detect SBP with high polymorphonuclear count (> 1000/mm³) in ascitic fluid, however their sensitivity is insufficient in SBP with lower polymorphonuclear count. Such infections, including SBP related to cocci gram positive pathogens and symptomatic bacterascites, are preferentially observed in patients with end-stage liver disease characterized by long hospital stay, a high risk of recurrence of septic complications and repeated antibiotic treatments. Nevertheless, reagent strips, preferentially Combur® 2 LN, can be used in this setting, because a positive grade 2 result in colorimetric scale has a high positive predictive value. However a negative result cannot exclude the diagnostic of SBP or SB. Finally, requirement of a laboratory for rapid cyto-bacteriological examination of ascitic fluid remains necessary in management of these patients.

REFERENCES


