

Liver and biliary

Ascitic fluid pH in alcoholic cirrhosis: a reevaluation of its use in the diagnosis of spontaneous bacterial peritonitis

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SUMMARY An ascitic fluid pH ≤ 7.31 has been advanced as being the best index in the early diagnosis of spontaneous bacterial peritonitis in cirrhotic patients. In order to test the validity of this criteria, 55 patients with alcoholic cirrhosis and ascites were studied. In each patient, arterial blood and ascitic fluid samples were analysed for pH, PCO₂, total CO₂ and PO₂, and the pH gradient between blood and ascites was calculated. White blood cell and polymorphonuclear cell counts were determined in ascitic fluid, and cultures of ascites were done under aerobic and anaerobic conditions. Twelve patients had a culture proven spontaneous bacterial peritonitis. Their mean ascitic fluid pH (\pm SD) was 7.38 ± 0.09 (range 7.21-7.49) and differed significantly ($p < 0.05$) from that found in patients without spontaneous bacterial peritonitis: 7.44 ± 0.06 (range 7.34-7.63). A marked overlap was observed, however, between the two groups, and only three out of the 12 patients with spontaneous bacterial peritonitis had an ascitic fluid pH ≤ 7.31 . The pH gradient was 0.10 ± 0.08 (range -0.01 to +0.28) in the spontaneous bacterial peritonitis group, as compared with 0.02 ± 0.04 (range -0.09 to +0.12) in the sterile group ($p < 0.01$), but a marked overlap was also noted between the two groups. In the spontaneous bacterial peritonitis group, the polymorphonuclear count was $3588 \pm 3849/\mu\text{l}$ (range 60-11 776) versus $41 \pm 138/\mu\text{l}$ (range 0-813) in the sterile group ($p < 0.0001$). All but one patient in the spontaneous bacterial peritonitis group and only two patients in the sterile group had over 250 polymorphonuclear/ μl . Thus, in our experience, neither the ascitic fluid pH nor the pH gradient values accurately discriminated the individual patients with and without spontaneous bacterial peritonitis. A polymorphonuclear count $> 250/\mu\text{l}$ remained the best criteria for the diagnosis of spontaneous bacterial peritonitis in cirrhotic patients, before having the results of ascitic fluid cultures.

Gitlin *et al* advocated the measurement of pH in ascitic fluid for the early diagnosis of spontaneous bacterial peritonitis in patients with alcoholic cirrhosis.¹ These authors showed that an ascitic fluid pH level of 7.31 perfectly separated the patients with spontaneous bacterial peritonitis from those without, and suggested that this index has a better diagnostic value for ascitic fluid infection than the cytologic criteria. These provocative results have recently been questioned,² and the aim of this study

was to reevaluate the ascitic fluid pH as an index for the diagnosis of spontaneous bacterial peritonitis.

Methods

PATIENTS

Fifty five patients (29 men, 26 women) with alcoholic cirrhosis and ascites were studied. Their mean age was 51.6 ± 12.5 years (range 31-79 years). Forty two of them were admitted to Henri Mondor Hospital (Créteil, France) and 13 to the CHU of Amiens (France), between February 1982 and November 1983. The diagnosis of cirrhosis was based on usual clinical, biological, and histological

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criteria. None of the patients had received an antibiotic treatment before the investigation. At the time of the study, none was in shock, had digestive haemorrhage, renal failure with acidosis, or a source of ascitic fluid infection such as abdominal surgery, intra-abdominal abscess or ruptured viscera. Eleven patients presented with hepatic encephalopathy and two had been under diuretic treatment, interrupted one week and one month before admission, respectively.

In each patient, an arterial blood sample was collected from the radial artery in an heparinised glass syringe. Immediately after the arterial puncture, ascitic fluid was collected anaerobically under aseptic conditions in a non-heparinised glass syringe. Blood and ascitic samples were analysed within five to 10 minutes for pH, PCO₂, total CO₂, and PO₂ on an Acid-Base Analyser (ABL 30 Radiometer, Copenhagen) for the patients admitted to Créteil and on a Corning Medical 178 (Corning Glass Works, Medfield, Massachusetts) for the patients admitted to Amiens. Another 50 ml of ascitic fluid was collected in a non-heparinised plastic syringe; 15 ml were injected at the bedside into two blood culture bottles for aerobic and anaerobic bacteriological cultures. The remaining 20 ml were used for determination of red blood cell count, white blood cell count, and differential count.

Ascitic fluid and blood gas analyses were undertaken on the first day of admission and repeated during hospitalisation in presence of clinical suspicion of spontaneous bacterial peritonitis – that is, a temperature exceeding 37.5°C or lower than 36.5°C, diarrhoea, abdominal pain or tenderness, hepatic encephalopathy.^{3 4}

Among the 55 patients, 12 had spontaneous bacterial peritonitis as defined by a positive ascitic fluid culture (Table 1). *Escherichia coli* was isolated in six cases, *Streptococci* in three cases (one *bovis*, one β -haemolytic and one species undetermined), *Klebsiella pneumoniae* in two cases, and *Escherichia coli* associated with *Streptococcus faecalis* in the remaining patient. All of these patients had one or several symptoms compatible with spontaneous bacterial peritonitis, as defined above.

Statistical analysis used the Mann and Whitney test and the standard linear regression method. Results are expressed as mean \pm 1 SD.

Results

The individual values for ascitic fluid pH in patients with spontaneous bacterial peritonitis are shown in Table 1. The mean ascitic fluid pH in this group was 7.38 \pm 0.09 (range 7.21 to 7.49). In the non-infected

Table 1 Blood and ascitic fluid evaluation in cirrhotic patients with spontaneous bacterial peritonitis

Patient (no)	Blood pH	Ascites			Germs
		pH	WBC/ μ l	PMN/ μ l	
1	7.54	7.49	7 400	5 772	<i>Escherichia coli</i>
2	7.52	7.39	12 100	8 712	<i>Escherichia coli</i>
3	7.52	7.42	610	451	<i>Escherichia coli</i>
4	7.50	7.38	4 800	4 368	<i>Escherichia coli</i>
5	7.44	7.33	2 800	2 632	<i>Escherichia coli</i>
6	7.47	7.48	80	60	<i>Escherichia coli</i>
7	7.54	7.48	490	368	<i>E. coli</i> + <i>Streptococcus faecalis</i>
8	7.49	7.21	340	275	<i>Klebsiella pneumoniae</i>
9	7.47	7.39	1 710	1 642	<i>Klebsiella pneumoniae</i>
10	7.44	7.26	12 800	11 776	<i>Streptococcus bovis</i>
11	7.40	7.31	8 000	6 320	β -haemolytic <i>Streptococcus</i>
12	7.40	7.39	870	679	<i>Streptococcus*</i>

* species undetermined

group, the mean pH was 7.44 \pm 0.06 (range 7.34 to 7.63) (Table 2). Although the difference in the pH values was significant ($p < 0.05$), a marked overlap was noted between the two groups (Figure). Among the 12 patients with spontaneous bacterial peritonitis, only three had ascitic fluid pH values \leq 7.31, the cut off level proposed by Gitlin *et al.*¹ It is interesting to note that one of the patients with a low ascitic fluid pH (case 8) was investigated one month before the occurrence of spontaneous bacterial peritonitis and presented with a marked systemic respiratory alkalosis at this moment (arterial blood pH: 7.55, Pa CO₂: 28.5 Torr). This shows that systemic alkalosis does not prevent any acidification of the ascitic fluid if spontaneous bacterial peritonitis occurs.

The mean arterial blood pH did not significantly differ in the two groups of patients: 7.48 \pm 0.05 (range 7.40 to 7.54) in the spontaneous bacterial peritonitis group as compared with 7.45 \pm 0.04 (range 7.37 to 7.55) in the non-infected group. A

Table 2 Mean values (\pm SD) of the parameters determined in cirrhotic patients with and without spontaneous bacterial peritonitis (SBP)

	SBP group	Sterile group	Significance
Ascitic pH	7.38 \pm 0.09	7.44 \pm 0.06	$p < 0.05$
Δ pH*	0.10 \pm 0.08	0.02 \pm 0.04	$p < 0.01$
Ascitic WBC/ μ l	4333 \pm 4661	168 \pm 236	$p < 0.0001$
Ascitic PMN/ μ l	3588 \pm 3849	41 \pm 138	$p < 0.0001$
Ascitic PCO ₂	40.90 \pm 5.55	45.37 \pm 53.26	$p < 0.05$
Blood PCO ₂	30.45 \pm 4.20	30.66 \pm 5.24	NS

* Δ pH = arterial blood pH – ascitic fluid pH

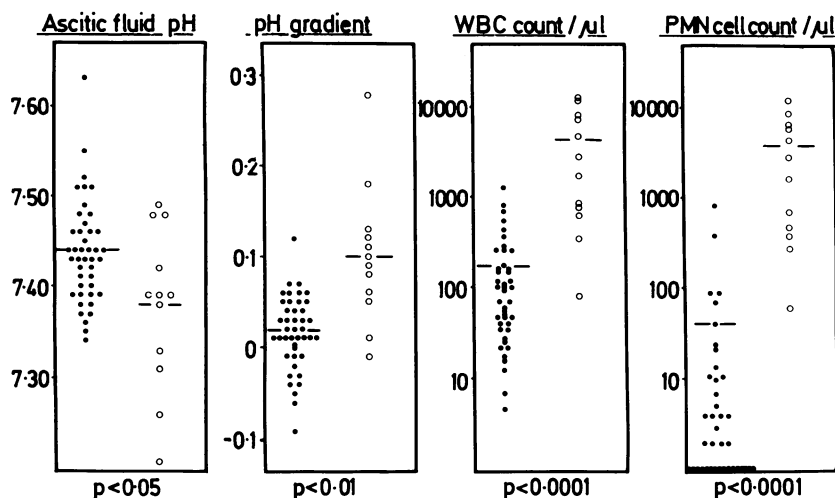


Figure Ascitic pH, pH gradient, white blood cell (WBC) count and polymorphonuclear (PMN) cell count in ascitic fluid in cirrhotic patients without (●) and with (○) spontaneous bacterial peritonitis.

good correlation was found between ascitic fluid and blood pH values in the non-infected group ($r=0.725$; $p<0.01$). On the other hand, no correlation was found in the spontaneous bacterial peritonitis group ($r=0.544$; NS).

The mean pH gradient between blood and ascites (arterial blood pH – ascitic fluid pH) was 0.10 ± 0.08 (range -0.01 to $+0.28$) in the spontaneous bacterial peritonitis patients and differed significantly ($p<0.01$) from the values in the sterile group: 0.02 ± 0.04 (range -0.09 to $+0.12$) (Table 2). A marked overlap still existed, however, for the individual values between the two groups of patients (Figure).

The mean ascitic white blood cell and polymorphonuclear cell counts were $4333 \pm 4661/\mu$ l (range 80–12 800) and $3588 \pm 3849/\mu$ l (range 60–11 776) respectively in the spontaneous bacterial peritonitis group (Tables 1 and 2). In the sterile group, they were respectively 168 ± 236 (range 5–1270) and 41 ± 138 (range 0–813) (Table 2). For these two parameters, the difference between the infected and sterile groups was highly significant ($p<0.0001$). In the patients with sterile ascitic fluid cultures, four had more than 500 white blood cell/ μ l in their ascites; their ascitic fluid pH ranged from 7.40–7.51. Two patients with clinical symptoms of spontaneous bacterial peritonitis had more than 250 polymorphonuclear/ μ l (357 and 813, respectively). Their ascitic fluid pH and pH gradient values were 7.46 and 7.44, and $+0.02$ and $+0.04$, respectively. In the spontaneous bacterial peritonitis group, three out of the 12 patients had less than 500 white blood

cell/ μ l and one had less than 250 polymorphonuclear/ μ l. None of these patients had an ascitic fluid pH ≤ 7.31 and a pH gradient >0.1 . In the spontaneous bacterial peritonitis group as well as in the sterile group, neither the white blood cell nor the polymorphonuclear cell counts were correlated with the ascitic fluid pH or the pH gradient.

Discussion

Putting on a parallel the low pH found in infected pleural, cerebrospinal or synovial fluids,⁵⁻⁷ Gitlin *et al* studied the advantages of measuring the pH in ascitic fluid in patients with alcoholic cirrhosis in the early diagnosis of spontaneous bacterial peritonitis.¹ In their study, an ascitic fluid pH level of 7.31 or less appeared to be the most accurate criteria for spontaneous bacterial peritonitis before obtaining the results of ascitic fluid cultures. Our results differ from those reported by these authors. Although the ascitic fluid pH was significantly different in the spontaneous bacterial peritonitis and sterile groups, a marked overlap existed between the individual values (Figure) and no cut off level could be defined to separate the two groups of patients. In addition, although none of our non-infected patients had an ascitic fluid pH of 7.31 or less, the use of this index would have enabled the diagnosis of spontaneous bacterial peritonitis in only three out of the 12 patients with bacteriologically proven infection. Two recent studies concord with our results and corroborate the poor sensitivity of this test: an ascitic fluid pH ≤ 7.31 was found in none of the five

patients with spontaneous bacterial peritonitis studied by Kao and Reynolds,² and in only five out of 10 episodes of spontaneous bacterial peritonitis reported in abstract form by Garcia-Tsao and Conn.⁸ In the Gitlin *et al* study, the patients with a low ascitic fluid pH were infected mainly by Gram-negative germs (*Escherichia coli*). Among our three patients with an ascitic fluid pH ≤ 7.31 , two were infected by Gram-positive cocci (*Streptococcus bovis* and β -haemolytic *Streptococcus*) and one by a Gram-negative bacteria (*Klebsiella pneumoniae*). Our findings tend to indicate that the decrease in ascitic fluid pH is independent of the Gram-staining type of the germ.

The pH gradient between blood and ascites provided a somewhat better discrimination between the patients with and without spontaneous bacterial peritonitis than the ascitic fluid pH did. This could probably be explained by the fact that, in the spontaneous bacterial peritonitis group, lower values for ascitic fluid pH as compared with the sterile group, were associated with slightly higher values for arterial blood pH. Nevertheless, even when using this index, a marked overlap persisted between the individual values of the two groups (Figure): a pH gradient of +0.1 or less was found in seven out of the 12 infected patients. One of our patients (case 6) presented with clinical symptoms of spontaneous bacterial peritonitis and a positive ascitic fluid culture but had only 60 polymorphonuclear/ μl in his ascites; in this patient, neither the ascitic fluid pH value (7.48) nor the pH gradient (-0.01) were of any use in establishing the right diagnosis.

In our study, the cytologic criteria – that is, >500 white blood cell/ μl and >250 polymorphonuclear/ μl ^{3 9-11} was the most valuable method for separating infected and non-infected patients, before the results of ascitic fluid cultures. Two patients in this series presented with clinical symptoms of spontaneous bacterial peritonitis and had over 250 polymorphonuclear/ μl in their ascites; however, the cultures remained sterile. These cases could represent false-negative results of the ascitic fluid cultures. It is worth noting that in these two patients, neither the ascitic fluid pH value (which was over 7.31), nor the pH gradient value (which was below +0.1) would have valuably supported the diagnosis of spontaneous bacterial peritonitis.

In conclusion, the results of the present study do not confirm those of Gitlin *et al*.¹ In our experience, the value of pH in ascitic fluid does not enable the separation between patients with and without spontaneous bacterial peritonitis, and the determination of the pH gradient between blood and ascites is of no more indication than the

common cytologic criteria. At the present time, those criteria remain the best indexes for the diagnosis of spontaneous bacterial peritonitis, before the obtention of the results of ascitic fluid cultures.

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Addendum

Since the submission of this paper, Attali *et al* (*Gastroenterol Clin Biol* 1984; **8**: 518–22) found an ascitic fluid pH value ≤ 7.31 in only two out of six patients with culture proven spontaneous bacterial peritonitis, but also in two out of 83 patients with a sterile ascitic fluid. This confirms the poor value of the index proposed by Gitlin *et al* for the diagnosis of spontaneous bacterial peritonitis.

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