The ratio of calprotectin to total protein as a diagnostic marker for spontaneous bacterial peritonitis in patients with liver cirrhosis and ascites

Thesis

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Amr Ahmed Abd Elkader

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ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC	Area under the curve
BT	Bacterial translocation
CNNA	Culture negative neutorcytic ascites
CT	Computed Tomography
Dl	Deci litre
DNA	Deoxy ribonucleic acid
ELISA	Enzyme linked Immuno sorbent assay
F-Calprotectin	Faecal calprotectin
HB	Haemoglobin
HFL	Hepatic focal lesion
HRS	Hepatorenal syndrome
IBD	Inflammatory bowel disease
IL	Inter leukin
INR	International normalized ratio
IV	Intravenous
Kg	Kilogram
LC	Liver cirrhosis
LDH	Lactate dehydrogenase
LERS	Leukocyte Esterase Reagent Strips
LF	Lactoferrin
LVP	Large volume paracentesis
MCP-1	Monocyte chemotactic protein-1
Mg	Milli gram
ML	Milli liter
MMOL	Milli mol
MNB	Monomicrobial non-neutrocyticbacterascites
MRSA	Methicillin resistant staphylococcus aureus
NASH	Nonalcoholic steatohepatitis

NO	Nitric oxide
NOD	Nucleotide-binding oligomerization domain
NPV	Negative predictive value
PCR	Polymerase chain reaction
PCT	Procalcitonin
PLT	Platelet
PMN	Polymorph nuclear
PNB	Polymicrobial non-neutrocyticbacterascites
PPI	Proton pump inhibitor
PPV	Positive predictive value
PVS's	Peritoneovenous shunts
ROC curve	Receiving operating characteristic curve
SAAG	Serum ascitic albumin gradient
SBP	Spontaneous bacterial peritonitis
SLE	Systemic lupus erythematosus
TIPS	Transjugular intrahepatic portosystemic shunt
TLC	Total leucocytic count
TNF	Tumor necrosis factor
WBC	White blood cell
Mg	Micro gram
Ml	Micro liter

Abstract

Background: Spontaneous bacterial peritonitis (SBP) is a potentially fatal condition, characterized by infection of ascitic fluid in absence of any intra-abdominal surgically treatable source of infection.Diagnosis of SBP is based on a differential ascites leucocytic count. **Aim of the Work:** to assess the role of ascitic fluid calprotectin in diagnosis of SBP. **Patients and Methods:** A cross sectional study was conducted on 60 patients with decompensated liver disease were selected. They were divided into: 1) Non SBP Group: included 30 patients with cirrhotic ascites without clinical or laboratory evidence of spontaneous bacterial peritonitis. 2) SBP Group: included 30 patients with cirrhotic ascites and spontaneous bacterial peritonitis. **Results:**. Ascitic fluid calprotectin level and the ratio of calprotectin to total protein was statistically significant higher in SBP group than non SBP group. There was a significant decrease in total protein and albumin in ascitic fluid in SBP group compared to non SBP group .A significant positive correlation was detected between ascitic fluid calprotectin and ascitic fluid TLC and PNLs among SBP group, A significant positive correlation between the ratio of calprotectin to total protein and ascitic fluid TLC and PNLs among SBP group. Asitic fluid calprotectin at cut-off value 96 ng/ml, had a sensitivity 86.67 % and a specificity 76.67 % in diagnosis of SBP with positive predictive value 85.2 % and negative predictive value 78.8%. - The ratio of calprotectin to total protein at cut-off value 9.6, had a sensitivity 96.67 % and a specificity 90 % in diagnosis of SBP with positive predictive value 96.4 % and negative predictive value 90.6%. **Conclusion:** The ratio of calprotectin to total protein had high sensitivity and specificity in diagnosis of SBP and better than calprotectin alone. The ratio of calprotectin to total protein could be a useful diagnostic test for SBP.

Key words : calprotectin, total protein, spontaneous bacterial peritonitis, cirrhosis, ascites

Introduction

Spontaneous bacterial peritonitis (SBP) is a distinct form of infectious peritonitis occurring in patients with advanced liver cirrhosis and ascites **(Wiest et al.,2012)**.

SBP is associated with a high one year mortality after the first episode of about 30% (**Ariza et al.,2012).** While SBP has a low incidence in outpatients **(Evans L,2003)**, approximately 50% of SBP episodes in hospitalized patients are diagnosed at the time of admission **(Rimola, et al., 2000).**

Symptoms of SBP include fever, chills, nausea, vomiting, abdominal pain and general malaise.Patients may complain of worsening of ascites**(Lata et al., 2009).**

Thirteen percent of patients have no symtoms and signs **(Koulaouzidis et al., 2009).**Clinical diagnosis and systemic laboratory parameters are unreliable for diagnosis of SBP **(Su et al.,2012).**

SBP is thought to result from a combination of factors inherent in cirrhosis and ascites, such as prolonged bacteremia secondary to compromised host defenses, intrahepatic shunting of colonized blood , and defective bactericidal activity within the ascitic fluid **(Runyon et al., 1984).**

According to international guidelines, diagnosis of SBP is based on a polymorphonuclear (PMN) cell count of > 250/ μL in the ascites in the absence of a surgically treatable intra-abdominal infection **(Arroyo et al., 2000).** However, a differential cell count is not readily available in all clinical settings **(Mendler et al.,2010).** Nevertheless, a delay in establishing the diagnosis is associated with a poor prognosis **(Kim et al.,2014).**

Attempts to establish alternative diagnostic tests are of limited success. In addition, no test provides prognostic information.A urinary test strip that detect leukocytes by their esterase activity performed well with a sensitivity of 100% and a specificity of 58% .A drawback is that this test cannot be applied to bloody or chylous ascites samples, so that 16% of the tests could not be interpreted.First results of a urinary test strip were promising but have to be confirmed **(Mendler et al.,2010)**.

An alternative approach is to detect proteins secreted by inflammatory cells into ascites. Lactoferrin, which is produced mainly by neutrophilic granulocytes, showed good test results**(Parsi et al.,2008),** but has not been introduced into clinical practice due to the lack of commercially available diagnostic test kits. Recently, a study evaluated calprotectin levels in ascites due to different etiologies of liver cirrhosis and found a strong correlation to ascites polymorphonuclear(PMN) number **(Burri et al.,2013)**

Calprotectin is an acute phase inflammatory reaction protein originating mainly from polymorphonuclear(PMN) which exerts regulatory, antimicrobial and antiproliferative functions **(Yui et al.,2003)**

Fecal calprotectin has been established as diagnostic tool in inflammatory bowel disease.Calprotectin can be measured also in bloody and chylous ascites, so that all samples could be analyzed **(Sherwood,2012).**

The ascitic fluid total protein concentration is lower in "spontaneously" infected ascitic fluid compared to sterile fluid obtained from different patients **(Llach J et al.,1992).**

The opsonic activity (endogenous antimicrobial activity) of ascitic fluid has been shown to correlate closely with the fluid's protein concentration; fluids with < 1.0 g/dl of protein have been reported to have essentially no opsonic activity and therefore no protection from bacterial infection **(Feldman et al., 2007**).

The protein concentration of ascitic fluid does not change with the development of spontaneous bacterial peritonitis **(Runyon and Hoefs et al.,1985).**

Aim of the work

Assessment of ratio of calprotectin to total protein in ascites as an alternative diagnostic marker of SBP.