Safety of Ascitic Paracentesis in Patients with Budd-Chiari Syndrome on Oral Anticoagulation and Elevated International Normalized Ratio

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Background/Aims: **Anticoagulation is the standard of care in patients with Budd-Chiari Syndrome (BCS). Ascites is a common symptom in patients with BCS. Often such patients require paracentesis while taking oral anticoagulation concurrently. It is unclear whether paracentesis leads to increased bleeding in such patients or whether anticoagulation has to be temporarily suspended. We describe our experience with paracentesis in patients with BCS taking oral anticoagulation.** ***Methods:*** **Our study subjects included consecutive patients with BCS with ascites on oral anticoagulation admitted between 2007 and 2011. The dose of oral anticoagulation was titrated to achieve international normalized ratio (INR) between 2 and 3. Routine hematological tests included Factor VIII (FVIII) levels. Paracentesis was undertaken without the prior administration of fresh frozen plasma and without the aid of ultrasonography. We looked for occurrences of bleeding at the puncture site or hemoperitoneum during and after the procedure.** ***Results:*** **Thirty-two of the 60 patients with BCS patients taking oral anticoagulation concurrently developed ascites. Thirty among 32 patients required paracentesis on one or more occasions. A total of 51 paracentesis procedures were performed (Median 1.6, Range 1–7). The mean INR was 3.1 (Range 1.4–7.9). No patient developed bleeding or hemoperitoneum. The mean FVIII measured was 138.8% of laboratory control and mean platelet level was 2.2 $\times$ 10^5/ml.** ***Conclusions:*** **Ascitic paracentesis in patients with BCS on anticoagulation is safe without an increased risk of abdominal wall bleeding or hemoperitoneum. Normal or high FVIII and platelet levels likely mitigate against bleeding risks.** **(J Clin Exp Hepatol 2015;5:310–313)**

INTRODUCTION

Ascites is a common complication in patients with liver disease. It is the commonest symptom in patients with Budd-Chiari Syndrome (BCS), and occurs in 83% of patients at presentation.[1,2] Anticoagulation with or without diuretics is the first line treatment in such patients.[1,2] Ascitic paracentesis may often be needed in such patients for diagnostic as well as therapeutic purposes.[3] Complications such as bleeding following paracentesis are rare in patients who are not on anticoagulation.[3–8] The optimal strategy for paracentesis while on oral anticoagulation is unresolved. Should oral anticoagulation be stopped and international normalized ratio (INR) corrected with prophylactic fresh frozen plasma before embarking on paracentesis? Or should paracentesis be carried out within reasonable level of anticoagulation? In practice, physicians, gastroenterologists, and hepatologists often debate about the risks of bleeding or litigation or both.[9] This may often lead to non-performance of the procedure, referral to interventional radiologists for the procedure[10] or temporary cessation of oral anticoagulation with the potential risks of thrombosis. There are no formulated guidelines on the safety and the level of anticoagulation at which paracentesis can be performed. In addition, there are no data regarding the management of such patients. There is a need to evaluate the safety or risks of paracentesis in patients taking oral anticoagulation. We, therefore, undertook this study to investigate the incidence of bleeding complications following ascitic paracentesis in patients with BCS on oral anticoagulation.

METHODS

We examined consecutive patients with BCS admitted to the Department of Gastroenterology, St. John's Medical College Hospital, Bangalore, India from January 2007 to April 2011. The diagnosis of BCS was confirmed on imaging modality, which included ultrasonography, Doppler ultrasonography, computed tomography, or magnetic resonance imaging. All patients underwent routine hematological, and laboratory tests including prothrombotic work up. Patients underwent estimation of prothrombin time (PT)/INR and Factor VIII (FVIII) levels. Anticoagulation

Keywords: hemoperitoneum, hepatic vein, paracentesis, INR, anticoagulation

Received: 22.05.2015; *Accepted:* 24.08.2015; *Available online:* 1 September 2015

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Abbreviations: BCS: Budd Chiari Syndrome; INR: International Normalized Ratio; PT: Prothrombin Time

http://dx.doi.org/10.1016/j.jceh.2015.08.004

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was initiated with intravenous heparin and gradually transitioned to the oral anticoagulant warfarin, and the dose titrated to achieve a target INR between 2 and 3.

Ascitic paracentesis was carried out for diagnostic or therapeutic purposes. All procedures were carried out after admission in the inpatient ward with overnight monitoring. Ascitic paracentesis was carried out in a standard manner without the aid of ultrasonography. An 18-gauge needle was used for puncture, which was then connected to intravenous plastic tubing whose distal end was attached to a bottle. Albumin infusion was administered only when large volume paracentesis was undertaken. We defined bleeding as clinically overt sign of hemorrhage over the puncture site including abdominal wall hematoma or hemorrhage into ascitic fluid with a drop in hemoglobin of >1.5 g/dl following paracentesis. Because of the theoretical and potential risks of bleeding, patients were monitored very carefully and fresh frozen plasma was on standby if need arose. Patients were discharged at least a day after an overnight observation.

RESULTS

Sixty consecutive patients with BCS were admitted from 2007 to 2011; of which, 32 patients (53.3%) developed ascites. The other frequent symptoms were abdominal pain in 30 (50%), jaundice in 26 (43%), and encephalopathy in 10 (16.6%) patients. The laboratory characteristics of the 30 patients who underwent paracentesis while on anticoagulation are shown in Table 1.

Table 1 Laboratory Characteristics of Patients with Budd-Chiari Syndrome who Underwent Paracentesis while on Anticoagulation (*N* = 30).

Variable	Mean ± SD
Hemoglobin (g/dl)	11.07 ± 0.39
WBC count (10^3/ml)	9.1 ± 5.2
Platelet count (10^5/ml)	2.2 ± 1.9
Total protein (mg/dl)	5.93 ± 0.18
Serum albumin (mg/dl)	2.6 ± 0.12
Total bilirubin (mg/dl)	4.18 ± 2.25
AST (U/L)	77.1 ± 16.26
ALT (U/L)	61.91 ± 13.1
GGT (U/L)	70.47 ± 8.86
Serum creatinine (mg/dl)	0.91 ± 0.06
Serum sodium (mEq/L)	132.64 ± 0.87
Serum potassium (mEq/L)	4.44 ± 0.13
INR (on anticoagulation)	3.02 ± 0.29
Factor VIII levels (%)	138.8 ± 6.02

SD, Standard deviation; WBC, white blood cell count; AST, aspartate amino transaminases; ALT, alanine amino transaminases; GGT, gamma glutamyl transaminase.

Fifty-one abdominal paracentesis were undertaken in 30 patients on anticoagulation (Range 1–7 paracentesis). Two patients with BCS and minimal ascites, without indication for paracentesis were not included in the analysis. Four patients underwent diagnostic paracentesis and the remaining 26 underwent therapeutic paracentesis. The amount of fluid removed varied from 3 to 5 L. The mean INR at the time of paracentesis while on anticoagulation was 3.1 (Range 1.4–7.9). Causes could be identified in 32 of the 60 patients: myeloproliferative disease (*n* = 11), JAK 2 V617F mutation (*n* = 6), of whom 2 had no clinical evidence of myeloproliferative disease, post-pregnancy state (*n* = 7) (pregnancy within 3–6 months before diagnosis), protein C deficiency (*n* = 4), protein S deficiency (*n* = 3), factor V Leiden mutation (*n* = 2), anti-thrombin deficiency (*n* = 1), homocysteinemia (*n* = 2), and paroxysmal nocturnal hemoglobinuria (*n* = 2). Three patients had 2 concomitant factors causing BCS.

Among the 51 abdominal paracentesis that was carried out, none developed clinically significant bleeding as defined earlier. However, in the ascitic fluid analysis, 5 patient's fluid demonstrated few RBCs (<10 red blood cells/HPF(high power field)), although none appeared hemorrhagic.

The mean FVIII level was 138.8% (Range 90–190%) (Normal level: 50–150%).

DISCUSSION

Our experience with paracentesis in patients with BCS on oral anticoagulation suggests that the procedure has no clinically significant risk of bleeding. Abdominal wall hematoma or hemoperitoneum did not occur despite a mean INR of 3.1. The presence of higher than normal levels of FVIII and a normal or high platelet likely had a mitigating effect on bleeding.

Ascitic paracentesis has been shown to be a relatively safe procedure in patients not on anticoagulation. Pache and Bilodeau, in a series of 4729 abdominal paracentesis, observed a 0.2% incidence of severe hemorrhage and a death rate of 0.02%.[4] In a more recent prospective study, Gottardi and colleagues observed a 2.3% incidence of local bleeding and 1% incidence of major bleeding including 3 patients with intra-peritoneal bleeding and one death.[5] On the contrary, Grabau et al. in a retrospective analysis of 1100 paracentesis in 628 patients did not find any major complication including bleeding.[6] In their series, no hemorrhage occurred despite the INR ranging from 0.9 to 8.7 and the platelet count ranging from 19,000 to 341,000 cells/mm^3.[6] Likewise, there are other reports of lack of bleeding after paracentesis.[7,8]

Elevated INR is a useful test to prognosticate severity of liver disease and is a critical component of models prioritizing the need for liver transplantation.[11] There is little evidence that it signifies an increased risk of bleeding.[12]