European Journal of Internal Medicine xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original Article

Bleeding after invasive procedures is rare and unpredicted by platelet counts in cirrhotic patients with thrombocytopenia☆

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ARTICLE INFO

Article history:
Received 14 June 2016
Received in revised form 21 October 2016
Accepted 8 November 2016
Available online xxxx

Keywords:
Cirrhosis
Liver cirrhosis
Bleeding
Hemorrhage
Platelets
Coagulation

ABSTRACT

Background: In cirrhotics with low circulating platelets (PLT), restoration of normal cell counts has been traditionally recommended before invasive procedures. However, there is neither consensus on the PLT transfusion threshold nor evidence of its clinical efficacy.
Patients: In order to fill this gap of knowledge, we prospectively collected and analyzed data on circulating PLT counts [and International Normalized Ratio (INR)] values in a case series of 363 cirrhotics scheduled to undergo invasive investigations. PLT and/or fresh-frozen plasma (FFP) units were infused at the discretion of the attending physician, and the occurrence of post-procedural bleeding was related to pre-and post-infusion results.
Results: 852 Procedures were carried out in 363 cirrhotics sub-grouped according to the Child-Pugh-Turcotte (CPT) classification (class A/B/C: 124/154/85). The infusion of PLT and/or FFP improved only marginally circulating PLT counts and INR values. Ten post-procedural bleeds occurred in the whole case series, i.e. 1 episode every 85 procedures or every 36 patients. Post-procedural bleeding was unrelated to the PLT counts, to the degree of INR abnormalities, nor to the CPT classes, but was more frequent in patients who underwent repeated investigations. In the 10 patients with the most profound alterations in PLT and/or INR values, no post-procedural bleeding occurred.
Conclusions: In cirrhotic patients with low PLT and/or abnormal INR values undergoing invasive investigations, post-procedural bleeding was rare and unpredicted by PLT counts or abnormal INR values. In particular, the recommendation to infuse platelets when counts are $<50 \times 10^3$/L is not substantiated by this case series of cirrhotic patients.

1. Introduction

Conventional coagulation tests, such as the prothrombin time and activated partial thromboplastin time, are frequently prolonged in patients with cirrhosis, and have been considered markers of a bleeding tendency [1–3]. Bleeding complications might be further explained by low platelet (PLT) counts. Thus, a frequent current practice is to correct thrombocytopenia with PLT transfusions prior to invasive procedures, in order to mitigate the risk of serious peri- or post-procedural bleeding [4,5]. The PLT count threshold that is recommended varies significantly. For example, in the UK the threshold is 50×10^3/L [6], in Belgium 30×10^3/L [7], in the United States 20×10^3/L [8], and in Germany 10×10^3/L [9], unless other risk factors for bleeding are in place. On the other hand, several observational studies demonstrated the safety of performing invasive procedures in patients with thrombocytopenia who had received no prophylactic PLT transfusions [10–16]. With these preambles and gaps of knowledge, we choose to investigate a case series of cirrhotic patients undergoing invasive diagnostic or therapeutic procedures, with the goal to correlate any post-procedural bleeding to alterations of the pre-procedural PLT count. Even though the main emphasis of our analysis was on the relationship between PLT count and bleeding, we also examined the same relationship with the prothrombin time, expressed as international normalized ratio (INR).

2. Material and methods

2.1. Patients

This case series was collected over a 38-month period (from January 2011 to March 2014), and enrolled all consecutive cirrhotic patients admitted to the Division of Gastroenterology, "Casa Sollievo della Sofferenza" Hospital in San Giovanni Rotondo, Italy, in order to undergo invasive procedures. Severe thrombocytopenia and significant coagulopathy were defined as a PLT count $\leq 50 \times 10^3$/L or a prothrombin time

☆ I certify that myself or any of the co-authors have no actual or potential conflict of interest in relation to this article.

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http://dx.doi.org/10.1016/j.ejim.2016.11.007
0953-6205/

value (INR) >1.3. The decision to transfuse PLT and/or fresh-frozen plasma (FFP), as well as that concerning the number of units to be transfused, was left to the discretion of the attending physician. The attained post-infusion PLT count and/or INR values were related to the occurrence or not of a bleeding event.

2.2. Collection of data

For each patient, the following baseline data were collected: age, gender, PLT count, prothrombin time values (INR), as well as the planned invasive procedure. Child-Pugh-Turcotte (CPT) score and the model for end-stage liver disease (MELD) were also calculated. Elective invasive procedures were categorized according to their potential bleeding risk: low risk (*category 1*) included endoscopic procedures, large volume paracentesis and dental extractions; intermediate risk (*category 2*), percutaneous needle biopsy of an organ, percutaneous HCC ablation and laparoscopic procedures; high risk (*category 3*) vascular catheterization and open incision of body cavity or tissue space. Patients underwent one or more invasive procedures during the same hospital admission. The risk of bleeding was related to the values of the aforementioned hemostasis parameters obtained close to the performance of the invasive procedure.

2.3. Grading of bleeding events

Bleeding events were recorded and graded from 0 to 4 according to the World Health Organization (WHO) classification [13]: grading 0 and 1 meant no or minor bleeding; grading 2 accounted for mild bleeding requiring medical intervention but no transfusion of red blood cells (RBC) concentrates; grading 3 accounted for gross blood loss responsible for the onset or deterioration of organ failures and/or requiring transfusion of up to two RBC concentrates within 24 h of onset, and grading 4 accounted for life-endangering blood loss including central nervous system or retinal hemorrhages, massive bleeding requiring transfusion of more than two RBC concentrates within 24 h of onset and fatal bleeding from any cause.

2.4. Statistical analysis

Baseline characteristics and measures of clinical and demographic variables were described as frequencies and percentages for categorical variables. Differences between these features were compared using a chi-square or Fisher Exact Test, as appropriate [17]. Continuous variables were expressed as median and range, and compared by the Mann–Whitney test. Risk factors potentially related to the occurrence of bleeding following the invasive procedures were explored by univariate analysis. A statistical significance level of 0.05 was used. All analyses were performed by using the SPSS 13.0.

3. Results

3.1. Study population

Patients included in the case series had a mean age of 67 ± 11 years, were predominantly males (67%) and homogeneously distributed among the several CPT classes: 124 (34%) class A, 154 (43%) class B, and 85 (23%) class C. Regarding the MELD stratification, 90 patients had a score ≥16.

Of the entire case series, 49 patients had very low PLT counts ($\leq 50 \times 10^3$/mL), 129 counts between >50 and <100, and the remaining 185 counts ≥100×10^3/mL. Abnormal INR values (>1.3) were registered in 126 patients. Concomitantly low PLT counts ($\leq 50 \times 10^3$/mL) and prolonged INR values (>1.3) were present in 20 patients.

During the 38 months study period, the 363 patients underwent a total of 852 invasive maneuvers. Following the procedures, 10 bleeding events were counted. The relationship between the occurrence of bleeding and the pre-procedural PLT and INR values is shown in Table 1. Bleeding was documented in one patient only in CTP class A, and in 5 and 4 patients in classes B and C. Five patients who bled had a MELD score <13, and the remaining 5 had a higher score. PLT units were transfused to 4 patients and produced a marginal augmentation of circulating counts (Table 1). FFP units were infused in 3 patients, but post-infusion INR values persisted to be abnormally high. The procedures were deemed at low risk (category 1) in 165 patients, and at intermediate or high risk (categories 2 to 4) in 198 patients.

The 10 patients with the most derangement in PLT and/or INR values are shown in Table 2: none of them experienced a post-procedural bleeding. Two of them were in CPT class A, 4 in class B and 4 in class C. As to the MELD score, 5 had a <16 value and the remaining 5 a ≥16 score. PLT units were given to 6 patients and post-infusion cell counts were barely affected (Table 1). FFP units were administered to 6 patients, but only one of them normalized the INR value (<1.2).

3.2. Post-procedural bleeding according to PLT counts and INR values (Table 3)

In the 89 patients with low PLT counts ($\leq 50 \times 10^3$/mL) (shown in the first two columns of Table 3), no bleeding occurred independently from a normal or abnormal INR, CPT classification and MELD score. In cirrhotics with PLT counts >50×10^3 mL, 5 bleeding episodes occurred in those with normal INR values, and 5 more in those with high INR values. In addition, bleeding was not more frequent in cirrhotics with more severe liver functional impairment, such as those in CPT class C or MELD score >16.

3.3. Evaluation of risk factors for a post-procedural bleeding (Table 4)

Potential risk factors related to the occurrence of bleeding following 852 invasive procedures were explored by univariate analysis of some patient features, altered hemostasis parameters and type of invasive

Table 1
Relationship between the bleeding event which occurred in 10 cirrhotic patients following an invasive procedure and hemostatic measurements (PLT count and INR values).

ID	Gender	Age years	CHILD classes	MELD score	PLT admission	PLT infusion	PLT following infusion	INR admission	PLASMA infusion	INR following infusion	Procedures
CS	F	77	B	13	55	Yes	48	1.21	Yes	1.20	Transarterial chemo-embolization
CF	M	59	B	17	166	No	-	1.47	No	-	Paracentesis + gastroscopy + biopsy
EP	F	55	B	17	58	Yes	55	1.54	Yes	1.47	Methrorragia
FT	M	63	C	21	134	Yes	115	1.70	Yes	1.80	Groin hematoma
GM	M	71	A	9	134	Yes	-	1.28	No	-	Endoscopic polypectomy
GF	M	81	C	19	76	No	-	1.85	No	-	Urethroscopy
LM	F	68	B	8	74	Yes	66	1.14	No	1.00	Endoscopic variceal ligation
LC	M	62	C	12	94	No	-	1.10	No	-	Endoscopic variceal ligation
MA	M	38	C	25	284	No	-	1.82	No	-	Paracentesis
MC	M	57	B	10	128	No	-	1.27	No	-	Central venous catheterization

Please cite this article as: Napolitano G, et al, Bleeding after invasive procedures is rare and unpredicted by platelet counts in cirrhotic patients with thrombocytopenia, Eur J Intern Med (2016), http://dx.doi.org/10.1016/j.ejim.2016.11.007