Transfusion Medicine Reviews 31 (2017) 51–55

Contents lists available at ScienceDirect

Transfusion Medicine Reviews

journal homepage: www.tmreviews.com

Clinical and Laboratory Consequences of Platelet Transfusion in Shiga Toxin–Mediated Hemolytic Uremic Syndrome☆

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ARTICLE INFO

Available online 21 June 2016

Keywords:
Platelet transfusions
Hus
Typical HUS
Thrombotic microangiopathy

ABSTRACT

Recent studies suggest that platelet transfusions are harmful in patients with thrombotic thrombocytopenic purpura, an entity of thrombotic microangiopathies. As the typical or Shiga toxin–producing *Escherichia coli*–induced hemolytic uremic syndrome (STEC-HUS) is also classified as thrombotic microangiopathy, we complement these data with an analysis of 250 patients from the German O104:H4 STEC-HUS outbreak. The effect of platelet transfusion in 44 patients who received platelet transfusions vs 206 control patients was investigated. Criteria for both groups were severe thrombocytopenia less than 50/nL, severe hemolysis with administration of packed red blood cells, and a complicated clinical course with admission to intensive care units. Readouts were clinical complications and changes in routine clinical chemistry and whole blood count. Chemistry values at admission and demographic parameters were comparable. Platelet transfusions were administered in 44 cases a median of 7 (interquartile range, 6-9) days after diarrhea onset. After platelet transfusion, we observed a transient and slight increase in inflammation parameters. No significant difference in major complications such as seizures, or requirement for ventilation or renal replacement therapy could be observed. Thrombotic events such as thrombosis or embolism were comparably rare in both groups (2.3% in platelet transfused vs 4.4% in controls, P = not significant). The mortality was not significantly different (0% vs 2.6%, P = not significant) in our study cohort, but overall in the outbreak, 6 of 711 STEC-HUS patients in Germany died of a procedural-related bleeding complications. In conclusion, platelet transfusions seem comparably safe in adult STEC-HUS patients, considering both the possible necessity for invasive procedures and potential risk for severe bleeding.

Contents

☆ Conflicts of interest: None.

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http://dx.doi.org/10.1016/j.tmrv.2016.06.004
0887-7963/

An ongoing controversy discusses the safety of platelet transfusions in patients with platelet consumptive disorders as thrombotic microangiopathy, which is characterized by hemolytic anemia, thrombocytopenia, and multiorgan impairment [1]. Restricted use of platelet transfusions is reasoned by clinical case series and the pathophysiologic rationale that transfusions could contribute to arterial microthrombi and tissue ischemia [2]. In 2015, 2 retrospective studies of large national cohorts suggested that platelet transfusion were harmful in patients with thrombotic thrombocytopenic purpura [3,4]. These studies prompted us to investigate this matter in Shiga toxin–producing *Escherichia coli*–induced hemolytic uremic syndrome (STEC-HUS), another form of thrombotic microangiopathy. Although restricted use of platelet transfusion is recommended for STEC-HUS patients [5,6], only one study has analyzed the effect of platelet transfusion on clinical outcome [7]. In that analysis, no clear disadvantage was found investigating 24 children.

In the following article, we describe the experience of the German STEC-HUS outbreak caused by ingestion of Egyptian fenugreek sprouts contaminated with Shiga toxin–producing *E. coli* serovar O104:H4 in May to July 2011 [8]. Our consortium gathered a detailed clinical data set of 711 patients with HUS from the German O104:H4 STEC-HUS outbreak. Sixty-one of these patients had received platelet transfusions during the hospitalization. Focus was set short-term effects and striking adverse effects such as complications in platelet transfusions, arterial or venous thrombotic events, in-hospital mortality, bleeding complications, or increase of inflammatory parameters. Extensive chemistry values and precise dates for interventions and complications allowed for the investigation of timewise relation between platelet transfusion and adverse effects.

Methods

Patients

Analyses were restricted to patients who had severe thrombocytopenia with platelet count of 50/nL or lower. To adjust the subgroups, further mandatory criteria were the admission to intensive care units (ICU) as indicator for severe clinical affliction and the transfusion of red blood cell (RBC) concentrates as a marker for extensive hemolysis. With these restrictions applied, 44 patients who received platelet transfusions within the first 14 days after onset of diarrhea were compared with 206 control patients without platelet transfusions. Some patients received platelets but were excluded from both groups because their data were incomplete (16 patients). In one case, the transfusion was related to secondary complications after the acute phase of STEC-HUS.

The HUS diagnosis was established by the treating physician. For the present analysis, we retrospectively collected demographic, clinical, laboratory, and information on hospital course and medication on a standardized case-history form by a dedicated study team. The extracted data were imported into a database. Data were checked for correctness, consistency, and plausibility by a second investigator.

Statistical Evaluation

Data are presented as total (n [%]) or median and interquartile range. Comparisons were calculated by Student *t* test as numeric value, “not

Table
Baseline parameters, clinical complications, and interventions for 711 STEC-HUS patients

	Platelet transfusion (n = 44)	Controls (n = 206)	*P*	All nonincluded patients (n = 667)	*P*
Baseline characteristics					
Age (y)	37.5 (5-78)	44 (9-83)	n.s.	41 (27.3-58)	n.s.
Sex female, n (%)	36 (81.8)	153 (74.3)	n.s.	470 (70.5)	n.s.
BMI admission (kg/m^2)	22.6 (20.3-24.8)	23.4 (20.8-26.4)	n.s.	23.7 (21.3-26.4)	n.s.
Platelet count at admission (/nL)	81 (43.3-222.1)	89 (37.4-218)	n.s.	99.7 (41.4-222.3)	n.s.
Hemoglobin at admission (g/dL)	12.3 (10.2-13.9)	12.8 (10.2-14.3)	n.s.	12.2 (10.4-14)	n.s.
LDH at admission (U/L)	680 (221.8-1244)	596 (196.9-1295.8)	n.s.	548.2 (205-1182.3)	n.s.
Creatinine at admission (μmol/L)	113.8 (66.5-217)	119 (71-306.5)	n.s.	119 (71-252)	n.s.
Therapy					
Platelet transfusion, n (%)	44 (100)	0 (0)	n.a.	17 (2.5)	<.001
Platelets on day of transfusion (/nL)	23.5 (14-32.3)		n.a.	23 (17-45)	n.s.
Day of first platelet transfusion	7 (5-9)		n.a.	7.5 (7-9)	n.s.
Count of platelet transfusions	2.1 ± 1.3		n.a.	2 (1-2.3)	n.s.
Clinical course					
Day of lowest platelet count	7 (6-8.3)	7 (5-9)	n.s.	8 (6-10)	n.s.
First day of platelets <50/nL	6 (4-6.5)	6 (4-7.5)	n.s.	6 (5-8)	n.s.
Minimal platelet count (/nL)	23.5 (14-32.3)	24 (18-34)	n.s.	33 (21-54)	<.001
Minimal hemoglobin (g/dL)	6.2 (5.6-6.7)	6.1 (5.6-6.7)	n.s.	6.7 (6-7.8)	<.001
Maximal LDH (U/L)	1759 (1401.8-2185)	1521 (1154-1990)	n.s.	1242 (747-1858.5)	.003
Maximal creatinine (μmol/L)	392.5 (257.3-602.5)	469 (273.5-652.5)	n.s.	318 (155-566)	n.s.
Maximal leukocyte count	19.6 (15.6-28.9)	20 (14.7-26)	n.s.	16.5 (5.7-111)	<.001
ICU, n (%)	44 (100)	206 (100)	n.a.	331 (53)	<.001
Day of ICU admission	6 (5-8)	8 (5-11)	.022	8 (5-11)	.013
Duration for ICU (d)	12 (7-21)	11 (5-20)	n.s.	10 (4-18)	n.s.
Dialysis, n (%)	38 (86.4)	165 (80.1)	n.s.	391 (58.6)	<.001
Blood transfusion, n (%)	44 (100)	206 (100)	n.a.	423 (64.7)	<.001
No. of RBC transfused	8 (6-10)	4 (2-8)	<.001	4 (2-6)	<.001
Ventilation, n (%)	21 (48.8)	86 (42.6)	n.s.	132 (21.5)	<.001
Seizures, n (%)	15 (35.7)	70 (34.8)	n.s.	114 (17.6)	.003
Death, n (%)	0 (0)	6 (2.9)	n.s.	18 (2.7)	n.s.
Day of decease		16 (15-18)	n.a.	16 (10-27)	n.a.
Eculizumab, n (%)	28 (63.6)	115 (56.1)	n.s.	251 (38)	<.001
Plasma exchange, n (%)	42 (95.5)	196 (95.1)	n.s.	510 (76.5)	.004

Platelet-transfused patients meeting the inclusion criteria (n = 44) are compared both to the control group (n = 206) and all other patients (n = 667, including the control group). Seventeen patients with platelet tranfusion were excluded from both intervention and control groups because they either provided insufficient data or, in some cases, received transfusion long after the acute phase of STEC-HUS. n.a., not available; n.s., not significant

Abbreviations: BMI, body mass index; n.a., not available; n.s., not significant.