Abstract: PB3360

Title: TREATMENT OF CRITICAL BLEEDS IN PATIENTS WITH IMMUNE THROMBOCYTOPENIA: A SYSTEMATIC REVIEW

Abstract Type: Publication Only

Topic: Platelet disorders

Background:

Intracranial hemorrhage and other critical bleeds in adults and children with immune thrombocytopenia (ITP) represent a medical emergency. However, evidence-based treatment protocols are lacking.

Aims:

To inform a clinical practice guideline addressing the issue, we undertook a systematic review of treatments for critical bleeding in patients with ITP.

Methods:

We conducted literature searches in four electronic databases from inception to October 2023: Ovid MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), and PubMed. An ITP Critical Bleed was defined as (i) a bleed in a critical anatomical site including intracranial, intraspinal, intraocular, retroperitoneal, pericardial, or intramuscular with compartment syndrome; or (ii) an ongoing bleed that results in hemodynamic instability or respiratory compromise (Sirotich et al, 2021). We included randomized controlled trials, observational studies, case series, and single case reports that enrolled patients with ITP who received one or more interventions for the management of critical bleeding. Eligible studies reported any of the following outcomes: death, platelet count response, bleeding, and disability of patients and included any of the following interventions aimed to raise the platelet count: corticosteroids, intravenous immunoglobulin (IVIG), platelet transfusions, splenectomy, thrombopoietin receptor agonists (TPO-RAs) used alone or in combination. We used the GRADE approach to evaluate the certainty of the evidence.

Results:

We identified 47 eligible studies that reported on 94 ITP patients with critical bleeds, including 51 children (median age = 9.5 years), 32 adults (median age = 44 years), and 11 (11.7%) age unreported. The majority of critical bleeds were ICH (n=71). Others were gastrointestinal bleeds (n=5), ocular bleed (n= 1), and intraperitoneal bleed (n=1). Either alone or in combination with other treatments, patients received IVIG (n=49), corticosteroids (n=48), platelet transfusions (n=19), TPO-RAs (n=19), and splenectomy (n=7). Studies reported 38 unique treatment strategies, the most common of which were IVIG alone (n=18), corticosteroids + IVIG (n=11), corticosteroids + IVIG + TPO-RA (n=8), TPO-RAs alone (n=5), corticosteroids + platelet transfusion (n=4), and corticosteroids alone (n=4). Of patients with outcomes reported, 21.3% died and 24.3% developed disability; 71.4% achieved a platelet count >30 x109/L, 57.1% achieved a platelet count >50 x109/L, and 88.5% had bleeding resolution.

Of the outcomes reported in Figure 1, the text below highlights the platelet count responses (>30 x109/L).

Corticosteroids vs. no corticosteroids

16/20 (80.0%) patients who received corticosteroids achieved a platelet count >30 x109/L compared to 14/22 (63.6%) who did not receive corticosteroids.

IVIG vs. no IVIG

18/22 (81.8%) patients who received IVIG achieved a platelet count >30 x109/L compared to 12/20 (60.0%) who did not receive IVIG.

Platelet transfusion vs. no platelet transfusion

7/8 (87.5%) patients treated with platelet transfusion achieved a platelet count >30 x109/L compared to 23/34 (67.6%) patients not treated with platelet transfusion.

Splenectomy vs. no splenectomy

3/4 (75.0%) patients treated with splenectomy achieved a platelet count >30 x109/L compared to 27/38 (71.1%) patients without splenectomy.

TPO-RA vs. no TPO-RA

10/11 (90.9%) patients who received TPO-RAs achieved a platelet count >30 x109/L compared to 20/31 (64.5%) who did not receive TPO-RAs.

Inferences on mortality, platelet count responses, bleeding resolution, and disability were highly uncertain due to the very low quality of evidence.

Summary/Conclusion:

Treatments for the management of critical bleeds in ITP patients are variable and the quality of evidence in support of specific treatments was very low. The most common treatments for ITP critical bleeds were IVIG, corticosteroids, TPO-RAs, and platelet transfusions alone or in combination. Given the rarity of ITP and the further rarity of critical bleeds among ITP patients, treatment decisions will rely on a weak evidence base.

Outcome	Impact		Plain language summary
	Corticosteroids	**No Corticosteroids**	
Mortality Data from 94 participants in 47 studies	11 of 48 patients died	9 of 46 patients died	We are uncertain whether corticosteroids decrease mortality
	Mortality: 22.9% vs. 19.6%		
Platelet count response Data from 42 participants in 25 studies	13 of 20 had platelet count >50 x10^9/L; 16 of 20 had platelet count >30 x10^9/L	11 of 22 had platelet count >50 x10^9/L; 14 of 22 had platelet count >30 x10^9/L	We are uncertain whether corticosteroids improve platelet count
	Platelet count >30 x10^9/L: 80.0% vs. 63.6%		
Bleeding resolution Data from 26 participants in 21 studies	11 of 13 had bleeding resolution	12 of 13 had bleeding resolution	We are uncertain whether corticosteroids improve bleeding resolution
	Bleeding resolution: 84.6% vs. 92.3%		
Disability Data from 37 participants in 18 studies	6 of 25 had disability	3 of 12 had disability	We are uncertain whether corticosteroids decrease disability
	Disability: 24.0% vs. 25.0%		
	IVIG	**No IVIG**	
Mortality Data from 94 participants in 47 studies	7 of 48 patients died	13 of 46 patients died	We are uncertain whether IVIG decreases mortality
	Mortality: 14.6% vs. 28.3%		
Platelet count response Data from 42 participants in 25 studies	12 of 22 had platelet count >50 x10^9/L; 18 of 22 had platelet count >30 x10^9/L	12 of 20 had platelet count >50 x10^9/L; 12 of 20 had platelet count >30 x10^9/L	We are uncertain whether IVIG improves platelet count
	Platelet count >30 x10^9/L: 81.8% vs. 60.0%		
Bleeding resolution Data from 26 participants in 21 studies	7 of 9 had bleeding resolution	16 of 17 had bleeding resolution	We are uncertain whether IVIG improves bleeding resolution
	Bleeding resolution: 77.8% vs. 94.1%		
Disability Data from 37 participants in 18 studies	6 of 22 had disability	3 of 15 had disability	We are uncertain whether IVIG decreases disability
	Disability: 27.3% vs. 20.0%		
	Platelet Transfusion	**No Platelet Transfusion**	
Mortality Data from 94 participants in 47 studies	6 of 19 patients died	14 of 75 patients died	We are uncertain whether platelet transfusion decreases mortality
	Mortality: 31.6% vs. 18.7%		
Platelet count response Data from 42 participants in 25 studies	7 of 8 had platelet count >50 x10^9/L; 7 of 8 had platelet count >30 x10^9/L	17 of 34 had platelet count >50 x10^9/L; 23 of 34 had platelet count >30 x10^9/L	We are uncertain whether platelet transfusion improves platelet count
	Platelet count >30 x10^9/L: 87.5% vs. 67.6%		
Bleeding resolution Data from 26 participants in 21 studies	8 of 8 had bleeding resolution	15 of 18 had bleeding resolution	We are uncertain whether platelet transfusion improves bleeding resolution
	Bleeding resolution: 100% vs. 83.3%		
Disability Data from 37 participants in 18 studies	4 of 12 had disability	5 of 25 had disability	We are uncertain whether platelet transfusion decreases disability
	Disability: 33.3% vs. 20.0%		
	Splenectomy	**No Splenectomy**	
Mortality Data from 94 participants in 47 studies	2 of 6 patients died	18 of 88 patients died	We are uncertain whether splenectomy decreases mortality
	Mortality: 33.3% vs. 20.5%		
Platelet count response Data from 42 participants in 25 studies	3 of 4 had platelet count >50 x10^9/L; 3 of 4 had platelet count >30 x10^9/L	21 of 38 had platelet count >50 x10^9/L; 27 of 38 had platelet count >30 x10^9/L	We are uncertain whether splenectomy improves platelet count
	Platelet count >30 x10^9/L: 75.0% vs. 71.1%		
Bleeding resolution Data from 26 participants in 21 studies	3 of 3 had bleeding resolution	20 of 23 had bleeding resolution	We are uncertain whether splenectomy improves bleeding resolution
	Bleeding resolution: 100% vs. 87.0%		
Disability Data from 37 participants in 18 studies	1 of 3 had disability	8 of 34 had disability	We are uncertain whether splenectomy decreases disability
	Disability: 33.3% vs. 23.5%		
	TPO-RA	**No TPO-RA**	
Mortality Data from 94 participants in 47 studies	3 of 20 patients died	17 of 74 patients died	We are uncertain whether TPO-RA decreases mortality
	Mortality: 15.0% vs. 23.0%		
Platelet count response Data from 42 participants in 25 studies	7 of 11 had platelet count >50 x10^9/L; 10 of 11 had platelet count >30 x10^9/L	17 of 31 had platelet count >50 x10^9/L; 20 of 31 had platelet count >30 x10^9/L	We are uncertain whether TPO-RA improves platelet count
	Platelet count >30 x10^9/L: 90.9% vs. 64.5%		
Bleeding resolution Data from 26 participants in 21 studies	5 of 6 had bleeding resolution	18 of 20 had bleeding resolution	We are uncertain whether TPO-RA improves bleeding resolution
	Bleeding resolution: 83.3% vs. 90.0%		
Disability Data from 37 participants in 18 studies	0 of 6 had disability	9 of 31 had disability	We are uncertain whether TPO-RA decreases disability
	Disability: 0% vs. 29.0%		
GRADE (Grading of Recommendations Assessment, Development and Evaluation) Certainty of the evidence: VERY LOW due to very serious Risk of Bias (Data did not include concomitant comparators and we collected relevant patient data in the form of observational study designs from randomized, non-randomized studies, case reports, and case series. Thus, data began as low-quality evidence and were rated down further for risk of bias)			
Platelet count response: achievement of any platelet count >50 x10^9/L; **Minimal platelet count response**: achievement of any platelet count >30 x10^9/L; **Disability**: neurological sequelae or declining mental state; IVIG: intravenous immunoglobulin, TPO-RA: thrombopoietin receptor agonist.			

Figure 1. Outcomes per intervention after critical bleeding events in immune thrombocytopenia patients

Keywords: Bleeding, Immune thrombocytopenia (ITP), Thrombocytopenia, Treatment