

Bleeding and Thrombosis in Patients Treated with Danaparoid for Suspected HIT: A Retrospective Single-Center Study

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Abstract

Introduction. Suspicion of heparin-induced thrombocytopenia (HIT) requires immediate discontinuation of heparin and initiation of an alternative anticoagulant. Danaparoid is a synthetic heparinoid with anti-Factor Xa (anti-Xa) activity and anti-thrombin activities. Despite decades of use in France, real-world data on outcomes and anti-Xa monitoring during danaparoid treatment for suspected HIT remain limited.

Objective. This study aimed evaluate the risk of bleeding, thrombosis and death in patients treated with danaparoid for HIT suspicion.

Methods. This monocentric retrospective study included all consecutive patients with HIT suspicion referred to our hospital and treated with danaparoid between 2017 and 2022. HIT diagnosis was supported by clinical and laboratory data including anti-platelet factor 4/heparin antibody testing and platelet functional assay. Study outcome was major bleeding or non-major but clinically relevant bleeding (CRNMB), thrombotic events occurring during danaparoid treatment and mortality 30 days after danaparoid initiation.

Results. Between 2017 and 2022, 425 patients with suspected HIT were evaluated, of whom 68 (17%) were treated with danaparoid; HIT was confirmed in 42 (62%). Among them, we observed 8 (12%) patients with thrombosis, 7 (10%) with major bleeding or CRNMB, and 8 (12%) patients died during the study period. No difference in the occurrence of any outcome was noticed according to HIT confirmation or not. A higher duration of danaparoid treatment and a lower first anti-Xa activity (0.3 U/mL IQR 0.3–0.5 vs 0.5 IQR 0.4–0.7) were risk factors for thrombosis. Furthermore, male sex, higher duration of danaparoid treatment, longer time to normalize platelet count, and a higher leucocyte count were risk factors for major bleeding or CRNMB.

Conclusion. HIT remains a prothrombotic disorder with substantial morbidity despite anticoagulation. Our findings support danaparoid use in acute HIT and underscore the need for therapeutic dosing until diagnosis is confirmed, along with anti-Xa monitoring to mitigate thrombotic risk

Keywords: danaparoid, heparin-induced thrombocytopenia, bleeding, thrombosis, mortality

Table 1. Outcomes during danaparoid treatment in patients with HIT suspicion and time spent within the target range

IQR: interquartile range; HIT: heparin induced thrombocytopenia; DVT: deep vein thrombosis; PE: pulmonary embolism; CRNMB: critical non major bleeding; NA for non-availed; SmPC: summary of product characteristics

Bleeding events we classified during the period of treatment by danaparoid, according to the ISTH classification. For the purpose of group comparison, each patient was evaluated based on the first occurrence of their most severe bleeding, categorizing the data into two primary groups: "no bleeding or minor bleeding" and "major or clinically relevant non-major bleeding (CRNMB)". For categorical attributes like the severity of complications, the maximum severity noted for any event was considered for each patient.

*One patient had a stroke, and one had both an infrarenal aortic thrombosis and a stroke.

	Total patients with HIT suspicion N=68	Non-HIT patients n=26	HIT patients n=42	p-value
Thrombotic event – n (%)	8 (12)	3 (12)	5 (12)	1.0
Thrombosis localization – n (%)				
Venous thrombosis	4 (6)	3 (12)	1 (2)	
PE	1 (2)	1 (4)	0 (0)	
DVT	2 (6)	1 (12)	1 (2)	
Extension of previous VTE	1 (2)	0 (0)	1 (2)	
Arterial thrombosis*	2 (3)	0 (0)	2 (5)	
Dialysis filter thrombosis	2 (3)	0 (0)	2 (5)	
Time between thrombosis and danaparoid initiation (d) – median [IQR]	11 [5–15]	14 [11–17]	5 [5–15]	0.5
Bleeding event – n (%)	7 (10)	1 (4)	6 (14)	0.2
Bleeding severity – n (%)				
Major	5 (71)	1 (100)	4 (6)	
CRNMB	2 (29)	0 (0)	2 (33)	
Minor	0 (0)	0 (0)	0 (0)	
Death at 30 days since danaparoid initiation – n (%)	8 (12)	5 (19)	3 (7)	0.2
During hospitalization, number of days with anti-Xa – median [IQR]:				
Target locally defined				
Above target	1 [0–2]	1 [0–2]	1 [0–2]	0.5
In target	6 [2–14]	3 [2–10]	7 [2–18]	0.4
Under target	1 [0–4]	1 [0–4]	1 [0–3]	0.3
Target according to the SmPC				
Above target	0 [0–1]	0 [0–0]	0 [0–1]	0.8
In target	2 [1–10]	2 [1–7]	4 [1–10]	0.5
Under target	2 [1–10]	2 [1–7]	4 [1–10]	0.5