

Introduction

- Factor XI (FXI) deficiency, aka Hemophilia C, is a rare autosomal recessive bleeding disorder with a variable bleeding phenotype. Heterozygotes (up to 8% in Ashkenazi Jewish) may also be bleeding phenotype.
- With fetal genetic screening now common, more parturients have diagnosis of FXI deficiency.
- Unlike Hemophilia A or B, most patients with FXI deficiency do not bleed spontaneously but occurs after tissue trauma, especially tissues with high fibrinolytic activity e.g. dental, reproductive tract.
- FXI activity levels do NOT correlate with bleeding risk. Unlike other factors, FXI levels do not increase during pregnancy. FXI level in the third trimester and anesthesia consult should occur. Routine hematologic testing does not correlate with FXI bleeding traditionally.
- The hematologic and anesthetic management of parturients with heterozygous mutations and intermediate levels of Factor XI activity has not been well defined, especially for neuraxial anesthesia. In neuraxial procedures, like neurosurgery, a small amount of bleeding can have catastrophic complications. Many choose to elevate FXI levels with FFP transfusion before neuraxial or use Tranexamic acid (TXA) or both.

Methods

We conducted an extensive literature review and present a novel anesthetic management strategy for FXI deficient parturients for neuraxial anesthesia.

Table 1: FXI Prophylaxis for Neuraxial Anesthesia

FXI classification			Prophylactic Treatment	
Genotype	Phenotype	FXI Level (%)	TXA	Factor Replacement*
Heterozygous	Bleeding	<15%		X
		16-39%		X
		40-49%	X	
		≥50%	N/A	N/A
	Non-bleeding	<15%		X
		16-39%	X	**
		40-49%	X	
		≥50%	N/A	N/A
Homozygous (FXI Level < 15%)	Bleeding	<15%		X
	Non-bleeding	<15%		X

*Factor replacement either: FFP 10-20 ml/kg, FXI concentrate 15U/kg or rFVIIa 15 mcg/kg

**If viscoelastic testing shows coagulation abnormalities, consider factor replacement

N/A: no prophylactic treatment recommended

Discuss all therapies with interdisciplinary team including hematologist at your local institution

Results

- Literature review revealed family history and bleeding scoring as predictive of bleeding while FXI was not.[1][2]
- Routine coagulation testing (PT, aPTT, FXI activity level, TEG) do NOT correlate with bleeding phenotype, in spite of FXI levels >40% or < 15%.

- Newer testing modalities correlate with bleeding phenotype and include thrombin generation assay, and perhaps ROTEM subtypes with specific reagents (recalcification instead of tissue factor) or use of platelet rich plasma.[3]
- Standard treatment for FXI replacement is fresh frozen plasma (FFP) 10-20ml/kg, which carries volume and transfusion risk. FXI concentrate has limited availability in Europe, dose 15U/kg. Recombinant Factor VIIa has also been described at low doses 15 mcg/kg for those refusing blood products.(see Table)
- Prophylactic TXA 10mg/kg for antifibrinolysis reduces risks from milder forms of FXI deficiency. Concurrent administration of both TXA and FXI concentrate or FVIIa increases the risk of thrombosis.

Conclusions

FXI deficiency (homozygous or heterozygous) has varying bleeding phenotypes. New testing modalities that correlate with bleeding are described, and a suggested hematologic prophylaxis for neuraxial anesthesia presented. Individualized interdisciplinary care should still be employed.

References

1. Blood 1985;65:719
2. Br J Haematol 2012;156:245
3. Hamostaseologie 2020;40:491