Anesthetic Considerations in Patients with Inherited Coagulation Defects

Essay

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List of Abbreviations

ADP	Adenosine diphosphates
APC	Activated partial thromboplastin time
AT	Antithrombin
ATP	Adenosine triphosphates
Ca	Clacium
CFC	Clotting factor concentrates
DDAVP	desmopressin
DIC	Disseminated Intravascular coagulopathy
FDA	Us food and drug administration
FDPs	Fibrin degradation products
FVIII:c	factor VIII pro coagulant activity
GPIb	Glycoprotein Ib
HMWK	High-molecular- weight-kininogen
NSADs	Non steroidal anti inflammatory drugs
PAIS	Plasminogen- activation inhibitors
PCA	Patient controlled analgesia
PCR	Polymerase chain reaction
PFA-loo	Platelet function analysis
PGI2	Prostacycline
PPH	Post partum hemorrhage
PT	Prothrombin time
Rcof	Ristocetin cofactor

RFLP	Restriction fragment length polymorphism
SNP	Single nucleotide polymorphism
TAFI	Thrombin activatable fibirnolysis inhibitor
TAX_2	Thromboxane A2
TCT	Thrombin clotting time
TF	Tissue factor
TFPI	Tissue factor pathway inhibitor
TGF- α	Tumor growth factor-α
TPA	Tissue plasminogen activator
TT	Thrombin time
TXA	Tranexamic acid
U-PA	Urokinase plasminogen activator
VNTR	Microsatellite variable number tandem repeat
VWD	Von willibrand disease
VWF	Von willibrand factor
VWF:Ag	Concentration of von willibrand factor antigen

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Introduction

Hereditary bleeding disorders are a diverse group of diseases that include abnormalities of primary and secondary hemostasis. The most common congenital bleeding disorders include:- Von Willebrand disease, Hemophilia A (factor VIII deficiency), Hemophilia B (factor IX deficiency) Less common congenital bleeding disorders include:- Factor I (fibrinogen) deficiency, Factor II (prothrombin) deficiency, Factor V deficiency, Factor VII deficiency, Factor X deficiency, Factor XI deficiency, Factor XIII deficiency, Platelet disorders. ***(Kendall Crookston et al., 2010)***

Primary hemostasis involves formation of the platelet plug which involves platelets, the blood vessel wall and von Willebrand factor abnormalities can include problems in platelet number, adhesion or aggregation.

Secondary hemostasis involves the formation of fibrin through the humoral coagulation cascade; abnormalities include deficiencies of coagulation factors or contact factors, deficiencies or abnormalities of fibrinogen or connective tissue diseases. Mutations can be inherited in an autosomal dominant, recessive or X-linked pattern. ***(Kendall Crookston et al., 2010)***

Hemophilia A and B are the most frequent inherited bleeding disorders. Together with Von Will brand disease these X- linked disorders include 95% to 97% of all the inherited deficiencies of coagulation factors. ***(Mannucci and Tuddenham, 2003)***

The remaining defects, generally transmitted as autosomal recessive traits in both sexes, are rare, with prevalences of the presumably homozygous forms in the general population ranging from approximately 1 in 2 million for factor II (prothrombin) and factor XIII (FXIII) deficiency to 1 in500 000 for factor VII (FVII) deficiency. Exceptions to these low prevalences are countries with large Jewish communities (where FXI deficiency is much more prevalent), Middle Eastern countries, and Southern India. In the last 2 regions, consanguineous marriages are relatively common, so that autosomal recessive traits occur more frequently in homozygosity. ***(Peyvandi et al., 2002)***

Preoperative assessment ideally must be done by a team of hematologist, surgeon, and anesthetist, so that a tailored individual plan is formulated and discussed with the patient. Detailed history about the type of hemophilia and VWD (von will brand disease) and its severity must be obtained. Prior information about response to DDAVP

(desmopressin), use of recombinant factors VIII and IX, and previous transfusion of blood will be useful. A complete blood count, coagulation profile and fibrinogen level, and specific factor assays must be done if indicated.

All patients must be evaluated for the presence of transfusion-related infections such as HIV and hepatitis B and C. Examination for the presence of joint deformities, contractures, and a thorough airway assessment. ***(Martlew, 2000)***

There are case series and reports of central neuraxial blocks with catheters in hemophiliac patients undergoing lower limb orthopedic surgeries after correction of factor levels, but there are no randomized controlled trials. Therefore, the risk–benefit ratio must be assessed individually on a case-to-case basis. ***(Choi and Brull, 2009)***

Aim of the Essay

Is to present the significant challenges in the perioperative period in patients with inherited coagulation defects and the different anesthetic management in such cases.

Physiology of Coagulation System and Hemostasis

The concept of blood coagulation dates back to the 1960's when Davie, Rat off and Macfarlane described the "waterfall" and "cascade" theories showing the fundamental principle of a cascade of proenzymes leading to the activation of some enzymes. Usually, the process of coagulation is controlled by several inhibitors that limit the clot formation and prevents more propagation of the thrombus. This thrombo-hemorhagic balance is maintained in the body by some complicated interactions between the coagulation and the fibrinolytic system as well as the platelets and the blood vessel wall. ***(Achneck et al., 2010)***

Hemostasis is defined as the arrest of bleeding. It comes from Greek, where, haeme means blood and stasis means to stop. When a vessel is injured or ruptured, hemostasis occurs by several mechanisms:- (1) vascular constriction, (2) formation of a platelet plug, (3) formation of a blood clot as a result of blood coagulation, and (4) the growth of fibrous tissue into the blood clot which closes the hole in the vessel permanently. ***(Anderson et al., 2006)***

Steps of coagulation:-

1. Vascular Constriction:-

After a blood vessel has been cut or ruptured, the trauma to the vessel wall itself causes the smooth muscle in the wall to contract immediately; this causes instant reduction of the flow of blood from the ruptured vessel.

The contraction results from (1) local myogenic spasm, (2) local autacoid factors released from the traumatized tissues and platelets, and (3) nervous reflexes. Initiation of the nervous reflexes is by pain nerve impulses or sensory impulses that originate from the traumatized blood vessel or the tissues nearby***. (Anderson et al., 2006)***

In the resting state, blood is actively maintained in a liquid form by endothelial cells and circulating plasma protein inhibitors. When the vascular integrity is disrupted or the endothelium becomes inflamed, the thrombotic activity of the endothelial cells is triggered. This occurs through secreting platelet-activating factor, a substance that induces platelet aggregation and formation of Von Willebrand factor (VWF), which is a cofactor for adherence of platelets to the subendothelium. The endothelium is also able to secrete plasminogen activator inhibitor which inhibits the fibrinolytic system. ***(Dittman and Majerus, 2001)***

Damage to the endothelium exposes blood to a highly thrombogenic subendothelial connective tissue which initiates the clot formation. This connective tissue consists of various types of compounds including fibrillar collagen, which is a potent stimulus for the activation and adhesion of platelets. Simultaneously, subendothelial components convert inactive coagulation factors into powerful enzymes, initiating an intrinsic stimulation of the plasma coagulation system. ***(Edward and Juan, 2000)***

2. Formation of the platelet plug:-

Platelets have an over-expanding role in hemostasis. Beside their role when vascular integrity is disturbed, they also maintain the integrity of normal endothelium. This is why patients with platelet deficiencies have a tendency to develop purpuric bleeding. ***(Edward and Juan, 2000)***

Platelets respond through three steps:-

1. Adhesion:-

When platelets become in contact with a damaged blood vessel, along with the collagen fibres present in the vascular wall, the platelets begin to swell, forming irregular shapes with multiple radiating pseudopods protruding from their surfaces, following that their contractile proteins contract forcefully and release granules that contain