Recent Updates in Anesthetic Management of Coagulation Disorders in Obstetric Patients

Essay

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Contents

List of Abbreviations

A	**:**	Current amplitude
A5 A10, and A15	**:**	Amplitude at specific minute interval; ten and fifteen minutes
AA	**:**	Arachidonic acid
ACC/AHA	**:**	American College of Cardiology/American Heart Association
ACS	**:**	Acute coronary syndromes
ADAMTS13	**:**	A Disintegrin And Metalloproteinase with Thrombospondin type 1 motif, member 13
ADP	**:**	Adenosine diphosphate
AFLP	**:**	Acute fatty liver of pregnancy
Alpha	**:**	α-angle
AMR	**:**	Ashwell- Morrell receptor
APC	**:**	Activated protein C
aPTT	**:**	Activated partial thromboplastin time
ASRA	**:**	American Society of Regional Anesthesia and Pain Medicine
ATP	**:**	Adenosine triphosphate
cAMP	**:**	Cyclic adenosine monophosphate
CFT	**:**	Clot formation time
CI	**:**	Coagulation index
CT	**:**	Clotting time

cTTP	**:**	Congenital Thrombocytopenic Purpura
DDAVP	**:**	Desmopressin
Deg	**:**	Degree
DIC	**:**	Disseminated intravascular coagulopathy
EPCR	**:**	Endothelial protrein c receptor
EPL	**:**	Estimated per cent lysis
ESA	**:**	European Society of Anesthesiologists
ESC	**:**	European Society of Cardiology.
EVs	**:**	Extracellular vesicles
FAO	**:**	Fatty acid oxidation
FAOD	**:**	Fetal fatty acid oxidation defects
FDA	**:**	Food and drug adminstration
fdp	**:**	Fibrin-degradation products
FEIBA	**:**	Factor Eight Inhibitor Bypassing Activity
FFP	**:**	Fresh frozen plasma
G	**:**	Clot strength
GPIb	**:**	Glycoprotein 1 beta
GPVI	**:**	Glycoprotein VI
HDL	**:**	High-density lipoprotein
HELLP	**:**	Hemolysis elevated liver enzymes and low platelet count
HIT	**:**	Heparin-induced thrombocytopenia
HMWK	**:**	High-molecular-weight kininogen

Humate-P	**:**	Antihemophilic factor–von Willebrand factor complex
HUVEC	**:**	Human umbilical vein endothelial cells
IL-1b	**:**	Interlukin 1 beta
INR	**:**	International normalized ratio
ITP	**:**	Idiopathic thrombocytopenic purpura
K	**:**	Kinetics time
LCHAD	**:**	Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency
LMWH	**:**	Low-molecular-weight heparin
LY30	**:**	Clot lysis at 30 minutes
LY60	**:**	Clot lysis at 60 minutes
MA	**:**	Maximal amplitude
MCAD	**:**	Medium chain acyl-CoA dehydrogenase
MCF	**:**	Maximum clot firmness
MTP	**:**	Mitochondrial trifunctional protein
NLRP3	**:**	Nuclitide binding domain and lucine rich repeat containing proteins
PAF	**:**	Platelet-activating factor
PAI	**:**	Plasminogen activator inhibitor
PCC	**:**	Prothrombin complex concentrate
PE	**:**	Phosphatidylethanolamine
PF4	**:**	Platelet factor 4
Pg	**:**	Plasminogen

PGI2	**:**	Prostacyclin
PIVKAs	**:**	Proteins formed in vitamin K absence
PLA2	**:**	Phospholipase A2
Pm	**:**	Plasmin
PMA	**:**	Projected maximal amplitude
PPH	**:**	Post partum hemorrhage
PS	**:**	Phosphatidylserine
PT	**:**	Prothrombin time
R	**:**	Reaction time
RCoA	**:**	Ristocetinco factor
rFVIIa	**:**	Recombinant activated factor VII
RIPA	**:**	Ristocentin-induced platelet aggregation
ROS	**:**	Reactive oxygen species
ROTEM	**:**	Thromboelastometry
SCAD	**:**	Short chain acyl-CoA dehydrogenase
sFlt-1	**:**	Soluble fms tyrosine kinase-1
TAFI	**:**	Thrombin-activatable fibrinolysis inhibitor
TEC	**:**	Thromboembolic complications
TEG	**:**	Thromboelastography
TF	**:**	Tissue factor
TFPI	**:**	Tissue factor pathway inhibitor
TM	**:**	Thrombomodulin
t-PA	**:**	Tissue plasminogen activator
TPO	**:**	Thrombopoeitin receptors

TTP	**:**	Thrombocytopenic purpura
TXA	**:**	Tranexamic acid
TXA2	**:**	Thromboxane A2
UFH	**:**	Unfractionated heparin
VKAs	**:**	Vitamin K antagonist
VKORC	**:**	Vitamin K epoxide reductase
VLCAD	**:**	Very long chain acyl-CoA dehydrogenase
VLDL	**:**	Very low-density lipoprotein
VTE	**:**	Venous thrombo embolism
vWF	**:**	Von Willebrand factor
VII	**:**	Stable factor
IX	**:**	Christmas factor
XI	**:**	Plasma thromboplastin
XII	**:**	Hagman factor
XIII	**:**	Fibrin stabllizing factor

List of Tables

List of Figures

Introduction

The process of hemostasis is complex and is further complicated in the parturient because of the physiological changes of pregnancy. Understanding these changes and the impact that they have on the safety profile of the anesthetic options for labour and delivery is crucial to any anesthetist caring for the parturient ***(Abbassi et al., 2009).***

These changes include physiological anemia and fluctuating coagulation factor concentrations alter the balance between bleeding and clot formation in preparation for peripartum blood loss ***(Prisco et al., 2005).***

Coagulopathy may be caused by reduced levels or absence of blood-clotting proteins, known as clotting factors or coagulation factors. Genetic disorders, such as hemophilia and Von Willebrand's disease, can cause a reduction in clotting factors. Anticoagulants such as warfarin will also prevent clots from forming properly. Coagulopathy may also occur as a result of dysfunction or reduced levels of platelets (small disk-shaped bodies in the bloodstream that aid in the clotting process) ***(Spahn et al., 2013).***

Thromboelastography and rotational thromboelastometry are point of-care tests used to measure whole blood coagulation, including fibrinolysis. Thromboelastography is useful because it encompasses, and is sensitive to, all the cellular and plasma factors in whole blood involved in clot formation and degradation. It is widely used within a number of hospital settings including intensive care and among patients undergoing liver and cardiac surgery ***(Figueroa et al., 2014).***

Although attempts at establishing peripartum reference ranges for rotational thromboelastometry have been made, these ranges have not yet been widely accepted or validated. There are few longitudinal data demonstrating how the normal hemostatic changes that occur throughout pregnancy and the puerperium affect thromboelastography parameters ***(Antony et al., 2015).***

It has long been postulated that women become hypercoaguable as pregnancy progresses, but how these changes directly affect clot mechanics is poorly understood. It has been confirmed the hypercoaguable status of women at term through thromboelastography analysis. Similarly, a shift toward hypercoagulability as measured by thromboelastography and rotational thromboelastometry

has been reported in uncomplicated pregnancies as pregnancy advances ***(Sharma et al., 2013).***

Globally, postpartum hemorrhage (PPH) is the leading cause of maternal morbidity and mortality. In the UK, PPH with blood loss of more than 500 mL occurs in approximately 18% of births, with approximately 4% of births being associated with significant PPH, defined as blood loss of more than 1000 mL. Although there is a growing a focus on thromboelastography/rotational thromboelastometry in guiding PPH management, uptake of this technology for clinical use in obstetric units has been slow ***(Allard et al., 2014).***

The overall estimated risk of epidural or spinal hematoma after neuraxial anesthesia in the obstetric population is 1:168000 ***(Ruppen et al., 2005).***

The instances of anesthesia-related spinal hematoma in pregnant and non-pregnant patients and found that it most often occurred in patients with coagulopathies (68%) ***(Hoffman et al., 2007).***

The anesthetic management of the obstetric patient with hematologic disease requires establishing a plan for anesthesia that incorporates the patient's specific hematologic problem, comorbidities, and the obstetric situation ***(O Riordan et al., 2005).***

Physiology of Coagulation Process

Coagulation is the process by which blood changes from liquid to a gel, forming a blood clot. It begins almost instantly after an injury to the blood vessel has damaged the endothelium lining the vessel. Leaking the blood through the endothelium initiates two processes: changes in platelets, exposure of subendothelial tissue factor to plasma factor VII, which ultimately leads to fibrin formation.

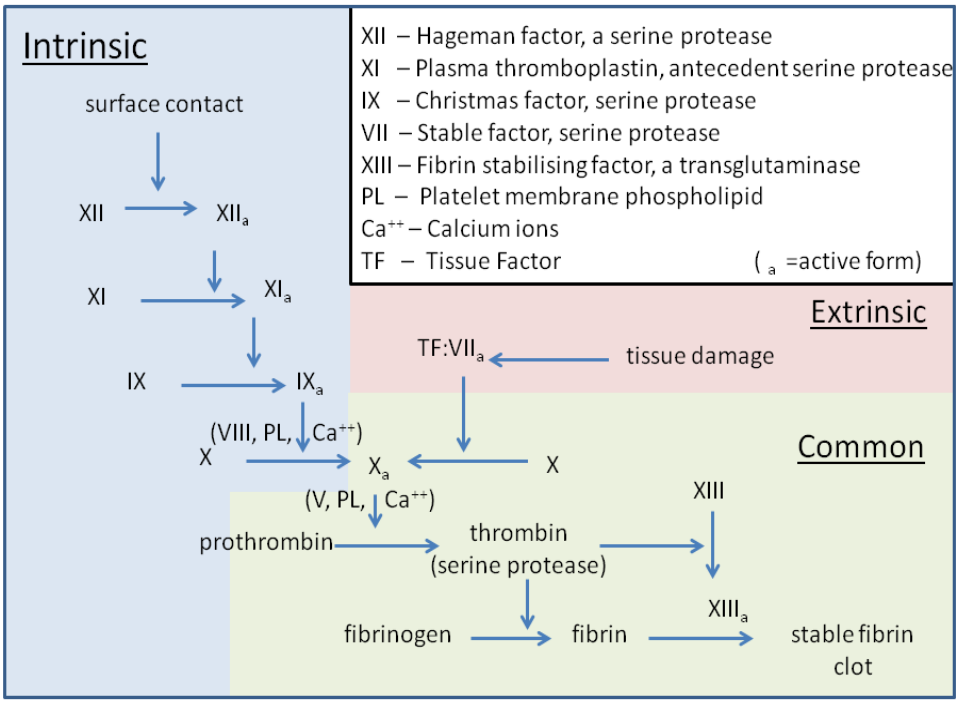

Figure (1): Classical blood coagulation pathway ***(Pallister and Watson, 2010).***