Haemostatic Problems In Liver Surgery And New Trends In Management

Essay

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ADP	adenosine diphosphate.
AHTRs	Acute hemolytic transfusion reactions.
ALI	acute lung injury.
APC	Activated protein C.
aPTT	activated partial thromboplastin time.
AT	Antithrombin.
CPB	cardio pulmonary bypass.
DIC	disseminated intravascular coagulation.
DVT	deep vein thrombosis.
ELISA	Enzyme Linked Immuno Sorbent assay.
ESLD	endstage liver disease.
FDA	Food and Drug Administration.
FDPs	fibrin degradation products.
FFP	fresh frozen plasma.
FFP	fresh frozen plasma.
FIO2	arterial/fraction of inspired oxygen.
FNHTRs	Febrile nonhemolytic transfusion reactions.
FVIIa	activated factor VII.
FXII	factor XII.
Gla	glutamic acid.
HBOCs	obin-based oxygen carriers.

IgM	immunoglobulin (Ig) M.
IL-6	interleukin 6.
INR	international normalized ratio.
ISI	International Sensitivity Index.
ITP	Idiopathic immune thrombocytopenia.
LA	lupus anticoagulant.
LMWH	Low Molecular Weight Heparin.
MPs	Microparticles.
PAIgG	platelet associated immunoglobulins.
PaO2	partial pressure of oxygen.
PC	protien c.
PE	phosphatidyl ethanolamine.
PFA	platelet function analyser.
PFCEs	Perfluorocarbon emulsions.
PR	prothrombin ratio.
PS	Phosphatidyl serine.
PT	prothrombin time.
RAMs	risk assessment models.
rfVIIa	recombinant factor VIIa.
ROTEM	rotational Thromboelastometry.
SIRS	systemic inflammatory response syndrome.
SpO2	oxygen saturation as measured by pulse oximetry.
TA	tranexamic acid.

TACO	transfusion-associated circulatory overload.
TAFI	thrombin-activatable fibrinolytic inhibitor.
TAT	thrombin–antithrombin.
TEG	Thrombelastograph.
TF	tissue factor.
TFPI	tissue factor pathway inhibitor.
TFPI	Tissue Factor pathway inhibitor.
TNFá	tumour necrosis factor-alpha.
tPA	tissue-type plasminogen activator.
TPO	thrombopoietin.
TRALI	transfusion-related acute lung injury.
TRIM	transfusion-related immunomodulation.
UFH	unfractionated heparin.
uPA	urokinase-type plasminogen activator.

INTRODUCTION

INTRODUCTION

Understanding of blood coagulation has evolved significantly in recent years. Both new coagulation proteins and inhibitors have been found and new interactions among previously known components of the coagulation system have been discovered. This increased knowledge has led to the development of various new diagnostic coagulation tests and promising antithrombotic and haemostatic drugs. **(Bombeli and Spahn.,2004)**.

Massive blood loss requiring allogenic blood product transfusion has been a major problem during liver resection and transplantation surgery. The transfusion of red blood cell units (RBCs) and plasma has been adversely linked to 1-year survival rates. Improved surgical and anaesthetic techniques have resulted in a dramatic reduction of blood product requirements during orthotopic liver transplantation (OLT) and liver resection surgery compared to historical controls.**(Gordon and Patty.,2009)**.

Recent publications report that between 17.5% and 81% of OLT operations and > 90% of hepatic resections can now be performed without red blood cell transfusions. In both groups, reduction in blood transfusions has led to improved outcome.Severe bleeding still occurs in a minority of cases and efforts to define clinical and blood test predictors for major bleeding during liver surgery remain elusive.Excessive bleeding during liver surgery can be due to surgical factors, haemostatic problems due to liver disease and poor anaesthetic technique. **(Gordon and Patty.,2009)**.

AIM OF WORK:

The aim of the work is to have rapid updated review in perioperative coagulation physiology and mangment of thromboembolism and haemostatic problems in liver surgery.

Chapter 1

Coagulation system and new aspects

The hemostatic system is a vital protective mechanism that is responsible for preventing blood loss by sealing sites of injury in the vascular system. However, hemostasis must be controlled so that blood does not coagulate within the vasculature and restrict normal blood flow. Understanding of hemostatic mechanisms has progressed substantially over the last century, with the majority of investigations occurring in static, cell-free in vitro systems. Recent advancement in the ability to study coagulation have dramatically expanded information regarding coagulation mechanisms. New models that include the contributions of cells in vitro and systems that involve real-time in vivo imaging of coagulation have significantly modified current understanding of how hemostasis occurs in vivo. **(Furie and Furie.,2007)**.

coagulation models:

1-The cascade model:

The cascade model consists of a sequence of steps where enzymes cleave zymogen substrates (also known as proenzymes) to generate the next enzyme in the cascade. The majority of the steps in the cascade occur on phospholipid membrane surfaces and require calcium. The cleavage of fibrinogen by thrombin is the most notable exception to the membrane requirement.Some enzymes cleave their substrates poorly without binding to their required cofactor. The model was divided into the familiar extrinsic and intrinsic pathways.The extrinsic system was

localized outside (or extrinsic from) the blood, and consisted of tissue factor (TF) and activated factor VII(FVIIa). The intrinsic system was localized within the blood (or intrinsic to) and was initiated through the contact activation of factor XII (FXII) on negatively charged surfaces, which subsequently activated other contact components. Either pathway could activate FX to FXa, which in turn (with its cofactor FVa) could activate prothrombin to thrombin, which then cleaved fibrinogen to form fibrin. This latter portion was generally referred to as the common pathway (Figure 1) **(Colman et al.,2006)**.

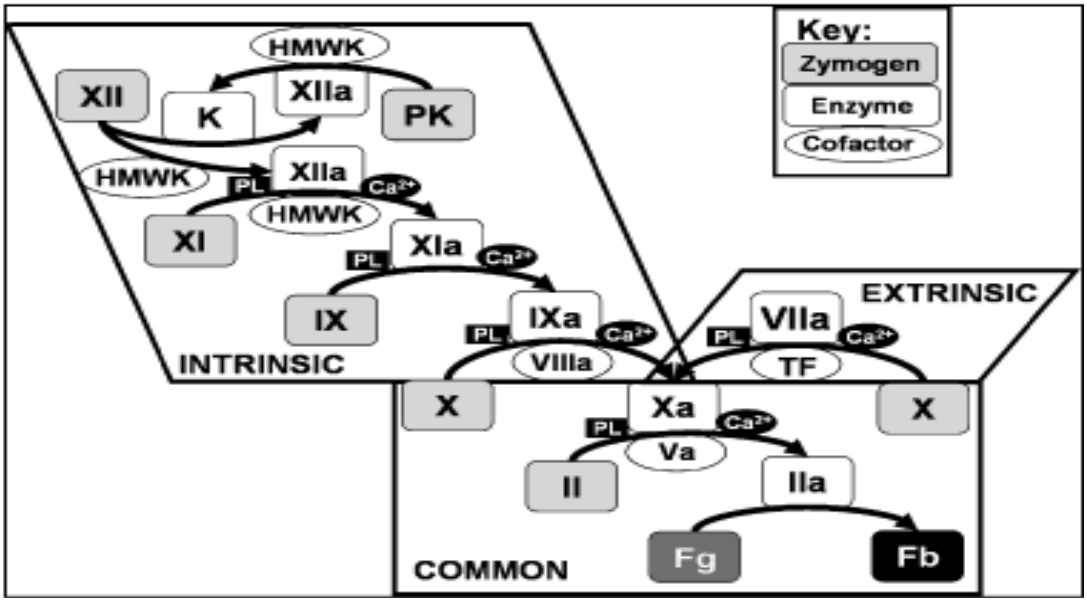

Figure 1: The cascade model of fibrin formation. This model divides the coagulation system into separate redundant pathways(extrinsic and intrinsic) either of which can result in generation of FXa. The common pathway results in generation of thrombin and subsequent cleavage of fibrinogen to fibrin. Many of the enzymes and enzymatic complexes require calcium(Ca21) and binding to active membrane surfaces (PL) for full activity. For simplicity, feedback activation of procofactors to cofactors and the many inhibitors of the various enzymes have been omitted. **(Colman et al.,2006)** .

Utility of the cascade model

The cascade model was extremely useful in advancing the understanding of how coagulation enzymatic steps occur in plasma-based in vitro coagulation. The understanding of the calcium dependence of coagulation allowed for prevention of coagulation in blood collection using calcium chelators. The description of the cascade model has also allowed for clinically useful interpretation of laboratory tests for plasma coagulation abnormalities. Specifically, deficiencies in the extrinsic or common pathways are identified using the prothrombin time, while deficiencies in the intrinsic or common pathways are reflected with prolongation of the activated partial thromboplastin time (aPTT) **(Mann et al.,2003)**.
Additional less commonly used tests such as the Russell's viper venom time, the thrombin time, and assays for function of specific factors, have allowed for further isolation of the exact site of coagulation defects. The description of the cascade model has also allowed for isolation and study of specific steps in protein-dependent coagulation processes, leading to better understanding of the properties of individual enzyme complexes. Continued experimentation based on the cascade model has led to the discovery of previously unidentified cross-interactions between different components, and to identification of and understanding of the roles of the more recently discovered specific inhibitors of coagulation.

The cascade model, as modified over the last few decades to include these new