Updated Trends in Diagnosis and Management of Trauma-Induced Coagulopathy in Injured Patients

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التوجهات المحدثة فى طرق تشخيص و علاج الاعتلال الخثرى الناتج عن الإصابات المتعددة

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Summary

Bleeding is one of the leading causes of preventable death after traumatic injury. Trauma-associated coagulopathy complicates the control of bleeding.

Coagulation defects related to severe trauma have a number of causal factors including: major blood loss with consumption of clotting factors and platelets, and dilutional coagulopathy after administration of crystalloids and colloids to maintain blood pressure. In addition, activation of the fibrinolytic system or hyperfibrinolysis, hypothermia and acidosis can also affect the coagulation system.

Coagulopathy in trauma patients is currently defined by the results of RCoT such as PT and aPTT. These results offer little in the haemostatic resuscitation.

VHA such as TEG and ROTEM is a technique that can offer rapid, near-patient testing of coagulation status.

New insights into the pathophysiology of trauma-induced coagulopathy, the increasing availability of point-of-care devices have encouraged new concepts for managing trauma-induced coagulopathy.

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List of Abbreviations

ACT	Activated clotting time
ADP	Adenosine diphosphate
ADPase	Adenosine diphosphatase
AMP	Adenosine monophosphate
APC	Activated protein C
APTT	Activated partial thromboplastin time
ARDS	Acute respiratory distress syndrome
Arg	Arginine
Asn	Asparagine
ATIII	Antithrombin III
ATC	Acute traumatic coagulopathy
ATP	Adenosine triphosphate
BT	Bleeding time
Ca	Calcium
CFT	Clot formation time
cGMP	Cyclic 3', 5'-guanosine monophosphate
CPB	Cardiopulmonary bypass
CPD	Citrate phosphate dextrose
CPDA	Citrate phosphate dextrose adenine
CT	Clotting time
Da	Dalton
DCO	Damage control operation
DCR	Damage control resuscitation
DCS	Damage control surgery
DDAVP	1-Deamino-8-D-arginine vasopressin (Desmopressin)
DIC	Disseminated intravascular coagulopathy
EXTEM	Extrinsic thromboelastometry
FFP	Fresh frozen plasma
FIBTEM	Fibrinogen thromboelastometry
GP	Glycoprotein
Gs	Stimulatory G-protein
Gu	Glutamine

List of Abbreviations (Cont.)

Hb	Haemoglobin
HMWK	High molecular weight kininogen
5-HT_2	5-hydroxytryptamine subtype 2
INR	International normalized ration
INTEM	Intrinsic thromboelastometry
ISI	International sensitivity index
MA	Maximum amplitude
MCE	Maximum clot elasticity
MCF	Maximum clot firmness
ML	Maximum lysis
MW	Molecular weight
NO	Nitric oxide
PAI	Plasminogen activator inhibitor
PCC	Prothrombin complex concentrate
PGD_2	Prostaglandin D_2
PGE_2	Prostaglandin E_2
PGI_2	Prostaglandin I_2
PL	Phospholipids
PRBCs	Packed red blood cells
PT	Prothrombin time
PTT	Partial thromboplastin time
RCoT	Routine coagulation tests
ROTEM	Rotational thromboelastometry
SID	Strong ion difference
SIRS	Systemic inflammatory response syndrome
STRs	Seven-transmembrane receptors
TAFI	Thrombin - activatable fibrinolysis inhibitor
TEG	Thromboelastography
TEM	Thromboelastometry
TF	Tissue factor
TFPI	Tissue factor pathway inhibitor
TM	Thrombomodulin

List of Abbreviations (Cont.)

tPA	Tissue plasminogen activator
TT	Thrombin time
TXA_2	Thromboxane A_2
uPA	Urokinase plasminogen activator
Val	Valine
VHA	Viscoelastic haemostatic assays
vWf	Von Willebrand factor

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Introduction

Coagulopathy in trauma patients is common and interest in this subject has risen exponentially over the past decade. The incidence of coagulopathy present at admission has been shown to be between 25% and 34% in civilian patients and between 31% and 38% in military patients. This incidence is associated with a fivefold increase in mortality ***(Doran et al., 2010).***

Coagulopathy associated with severe injury complicates the control of bleeding and is associated with increased mortality in trauma patients ***(Hess et al., 2008).***

Coagulopathy associated with traumatic injury is the result of multiple independent but interacting mechanisms. Early coagulopathy is driven by shock and requires thrombin generation from tissue injury as an initiator. Initiation of coagulation occurs with activation of anticoagulant and fibrinolytic pathways. This acute coaguloapthy of Trauma-Shock is altered by subsequent events and medical therapies, in particular acidaemia, hypothermia and dilution. There is significant interplay between all mechanisms ***(Hess et al., 2008).***

Coagulopathy in trauma patients is currently defined by the results of standard laboratory tests (prothrombin time and activated partial prothrombin time). These tests do not fully characterize the coaguloathy and have significant limitations, which reduce their clinical utility. Thrombo-elastometry is a technique that can offer rapid near-patient testing of coagulation status ***(Doran et al., 2010).***

Thromboelastometry provides a timely and convenient method that measures a number of aspects of the coagulation profile including initial clotting, platelet interaction, and fibrinolysis in a sample of whole blood ***(Doran et al., 2010).***

Because of the clinical significance of trauma-induced coagulopathy, management strategies to reduce the morbidity and mortality have recently become of interest. New insights into the pathophysiology of trauma-induced coagulopathy, the increasing availability of point-of-care devices and awareness of side effects of intravenous fluids and traditional fresh frozen plasma therapy has encouraged new concepts for managing massive blood loss in trauma-induced coagulopathy ***(D'Angelo and Dutton, 2010).***

The wide variety of coagulation abnormalities are detected by recent point-of-care devices which allows for accurate, goal-directed resuscitation instead of previously blind therapies ***(Schöchl et al., 2010).***

Finally, progressive postinjury coagulopathy continues to consume enormous hospital resources, and result in high mortality in the injured patient. Current progress in early diagnosis, monitoring and resuscitation is hindered by a lack of scientific understanding of the underlying pathophysiology driving the complex process of hemostasis. Point-of-care thromboelastography could provide important insights into the fundamental mechanisms of the cell-based model of coagulation, and may ultimately optimize our management of the critically injured patient at risk of coagulopathy ***(Kashuk et al., 2010).***

Physiology of Blood Coagulation

Haemostasis is the process of forming clots in the walls of damaged blood vessels and preventing blood loss while maintaining blood in a fluid state within the vascular system. A collection of complex interrelated systemic mechanisms operates to maintain a balance between coagulation and anticoagulation ***(Barrett et al., 2009).***

Normal endothelium maintains blood fluidity by producing inhibitors of blood coagulation and platelet aggregation, modulating vascular tone and permeability, and providing a protective envelope, thereby separating haemostatic blood components from reactive subendothelial structures. Endothelial cells synthesize and secrete basement membrane and extracellular matrix, which contain adhesive proteins, collagen, fibronectin, laminin, vitronectin, and Von Willebrand factor (vWF). The endothelium inhibits blood coagulation by synthesizing and secreting thrombomodulin (TM) and heparan sulfate onto its surface; modulates fibrinolysis by synthesizing and secreting tissue plasminogen activator (tPA), urokinase plasminogen activator (uPA), and plasminogen activator inhibitors; inhibits platelet aggregation by releasing prostaglandin I_2 (PGI_2) and nitric oxide (NO); and regulates

vessel wall tone by synthesizing endothelins, which induce vasoconstriction, and PGI_2 and NO, which produce vasodilation ***(Colman et al., 2006).***

Endothelial cells are highly negatively charged, a feature that may repel the negatively charged platelets. This anionic surface, as well as other antithrombotic properties of endothelium, could be important in limiting the intravascular extension of the haemostatic reaction induced by vessel injury ***(Ofosu et al., 1989).***

TM and heparan sulfate, the two endothelial surface-bound thrombin inhibitors, could limit the intravascular spread of fibrin beyond the confines of the haemostatic plug**.** Heparan sulfate, a glycosaminoglycan, activates antithrombin III (ATIII) and, therefore, catalyzes the inhibition of thrombin and factor Xa. Endothelial cell-associated adenosine diphosphatase (ADPase) cleaves adenosine diphosphate (ADP) to adenosine monophosphate (AMP), thereby modulating this stimulatory agonist ***(Marcus et al., 1991).***

TM binds thrombin and inhibits the ability of the enzyme to cleave fibrinogen and activate platelets and factors Va and VIIIa. TM also markedly enhances