Haemostatic Failure in Critically Ill Patients

An Essay

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in Intensive Care

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بِسْمِ اللّهِ الرّحمَنِ الرّحيمِ

[...رَبِّ أَوزِعنِي أَن أَشكُرَ نِعمَتَكَ
الَّتِي أَنْعَمْتَ عَلَيَّ وعَلى والِدَيَّ
وأَنْ أَعْمَلَ صَالِحاً تَرْضَاهُ
وأَدْخِلْنِي بِرَحْمَتِكَ فِي
عِبَادِكَ الصَّالِحِينَ]

صدق الله العظيم

النمل.. اية رقم ١٩

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List of Abbreviations

AABB : American Association of Blood Banks
ACoTS : Acute Coagulopathy of Trauma-Shock
ACS : Acute coronary syndrome
ADP : Adenosine diphosphate
APLA : Antiphospholipid antibody
APTT : Activated partial thromboplastin time
AT3 : Antithrombin III
ATP : Adenosine triphosphate
BT : Bleeding time
CBC : Complete blood count
CCI : Corrected count increment
CFT : Clot firmness time
DDAVP : 1-deamino-8-D-arginine Vasopressin
DIC : Disseminated intravascular coagulation
DITP : Drug-induced immune thrombocytopenic purpura
EACA : e-aminocaproic acid
ELT : Euglobulin lysis time
FFP : Fresh frozen plasma
GAGs : Glycosaminoglycans
GVHD : Graft-vs-host disease
HELLP : Syndrome of haemolytic anaemia, elevated liver enzymes and low platelets
HIPA : Heparin-induced platelet activation
HIT : Heparin-induced thrombocytopenia
ICU : Intensive care unit
INR : International normalized ratio

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ISTH : International Society of Thrombosis and Haemostasis
ITP : Immune thrombocytopenic purpura.
JAAM : Japanese Association for Acute Medicine
LMWH : Low molecular weight heparin
PAI-1 : Plasminogen activator inhibitor
PCC : Prothrombin Complex Concentrate
PF4 : Platelet factor-4
PFA-100 : Platelet function analyzer-100
PT : Prothrombin time
RBCs : Red blood cells
rFVIIa : Recombinant factor VIIa
SDPs : Single donor platelets
SIRS : Systemic inflammatory response syndrome
TAFI : Thrombin activatable fibrinolysis inhibitor
TCT : Thrombin clotting time
TEG : Thrombelastography
TFPI : Tissue factor pathway inhibitor
tPA : Tissue plasminogen activator
TTP : Thrombotic thrombocytopenic purpur
TXA : Tranexamic acid
UFH : Unfractionated heparin
uPA : Urokinase-type plasminogen activator
VKA : Vitamin K antagonism
VTE : Venous thromboembolism
vWD : Von Willebrand disease
vWF : Von Willebrand factor
α2-PI : Alpha2-plasmin inhibitor

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Introduction

Haematologic factors, in particular platelets and the coagulation system, play an important role in the pathogenesis of organ failure in the intensive care unit ***(Levi and Schultz, 2011).***

Platelets are irregularly shaped, disk-like fragments of the membrane of their precursor cell, the megakaryocyte. Megakaryocytes shed platelets in the bone marrow sinusoids. From there the platelets are released to the blood, where they function in hemostasis. Several factors stimulate megakaryocytes to release platelets, including the hormone thrombopoietin, which is generated and released into the bloodstream when the number of circulating platelets drops. Platelets have no defined nucleus. They are one fourth to one third the size of erythrocytes. Platelets possess physiologically important proteins, stored in intracellular granules, which are secreted when the platelets are activated during coagulation ***(English, 2003).***

The liver plays a major role in haemostasis, as most of the coagulation factors, anticoagulant proteins and components of the fibrinolytic system are synthesized by hepatic parenchymal cells. Additionally, the reticuloendothelial system of the liver

helps to regulate coagulation and fibrinolysis by clearing these coagulation factors from the circulation ***(De Sancho and Pastores, 2005).***

Failure of these haematologic systems is common in intensive care patients and may range from isolated thrombocytopenia or prolonged global clotting tests to complex defects, such as disseminated intravascular coagulation. There are many causes for a deranged coagulation in critically ill patients, and each of these underlying disorders may require specific therapeutic management. Hence, a proper differential diagnosis and initiation of adequate (supportive) treatment strategies are crucial to reduce morbidity and mortality in critically ill patients with coagulation abnormalities ***(Levi and Schultz, 2011).***

Many critically ill patients in the intensive care unit (ICU) present with failure of haemostatic system, most prominently platelets and the coagulation system. In general, coagulation abnormalities require prompt and proper identification of the underlying cause because many of these disorders may necessitate very different therapeutic management strategies ***(Levi and Opal, 2006).***

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 ***(Guyton and Hall, 2006).***

Failure of haemostasis is common in critically ill patients and may be complex and multifactorial in pathogenesis. As haemostatic failure may complicate a wide range of medical, surgical and obstetric disorders, definitive diagnosis and specific therapy can significantly impact on outcome. Frequently, complex tests are required for definitive diagnosis, but the urgency of the situation cannot always wait for the results, and therapy may be initiated on clinical evidence with minimal laboratory information. Consultation with a clinical haematologist is strongly recommended ***(Bersten and Soni, 2009).***

The incidence of thrombocytopenia (platelet count $<150\times10^9$/L) in critically ill medical patients is 35 to 44%.A platelet count of $<100\times10^9$/L is seen in another 30 to 50% of patients. A prolonged global coagulation time such as the prothrombin time (PT) or the activated partial thromboplastin time (aPTT) occurs in 14 to 28% of intensive care patients ***(Levi and Opal, 2006).***

Thrombocytopenia is important because it increases the risk of bleeding, alters plans for care, and serves as a marker of morbidity and mortality. Thrombocytopenia may also be a manifestation of a disease that promotes clotting, such as heparin-induced thrombocytopenia (HIT) or disseminated intravascular coagulation (DIC) ***(Strauss et al., 2002).***

Thrombocytopenia is one of the most common laboratory abnormalities in intensive care unit (ICU) patients. Thrombocytopenia can be a result of increased (nonimmune or immune) platelet destruction, haemodilution, platelet sequestration (as in hypersplenism), or decreased platelet production ***(Vanderschueren et al., 2000).***

The most common causes of acquired coagulation disorders include DIC, trauma, liver disease, vitamin K deficiency and exposure to anticoagulants ***(Irwin and Rippe, 2014).***

In general, there may be clinical features suggesting local or generalized failure of the haemostatic system. Clinical history is important, especially with respect to previous bleeding problems, family history, comorbid medical conditions and medications. The nature of surgery or

an invasive intervention may have haemostatic issues that need specific consideration ***(Bersten and Soni, 2009).***

In most clinical settings, laboratory haemostatic screening tests are readily available, with near-patient testing techniques continuing to improve. A full blood count, prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen level, D-Dimer, thrombin clotting time (TCT) provide a broad screen for most clinically significant haemostatic disorders. Based on these results, and following consultation with a haematologist, further specific tests of haemostasis may be performed (e.g. mixing studies, factor assays, platelet function tests and test of fibrinolytic function) ***(Rochon and Shore-Lesserson, 2006).***

The laboratory investigation of a patient with a potential haemostatic defect depends on the degree of urgency. It may be necessary to administer blood component therapy without a definitive haemostatic defect being established. A detailed clinical history and screening laboratory investigations prior to elective procedures will often avert undiagnosed emergency haemostatic crises ***(Bersten and Soni, 2009).***