Bleeding and Coagulopathies in Critical Care unit

Essay

Submitted for Partial Fulfillment of Master Degree
in Intensive Care Medicine

Presented by

Mostafa Mahmoud Meselhy

M.B., B.Ch. Faculty of Medicine, Banha University

Supervised by

Prof. Dr. Sherif Farouk Ibrahim

Professor of Anesthesiology & Intensive Care Medicine
& Pain Management
Faculty of Medicine, Ain Shams University

Prof. Dr. Karim Youssef Kamal

Assistant Professor of Anesthesiology & Intensive Care Medicine
& Pain Management
Faculty of Medicine, Ain Shams University

Dr. Mohammed Mahmoud Maarouf

Lecturer of Anesthesiology & Intensive Care Medicine
& Pain Management
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2017


بسم الله الرحمن الرحيم
وَاتَّقُوْا اللّٰهَ وَيُعَلِّمُكُمُ اللّٰهُ
وَاللّٰهُ بِكُلِّ شَيْءٍ عَلِيمٌ
صدق الله العظيم
سورة البقرة – آية ٢٨٢

Acknowledgement

First, I feel always indebted to **Allah**, the Most Kind and the Most Merciful.

I would like also to express my deep appreciation and gratitude to **Prof. Dr. Sherif Farouk Ibrahim,** Professor of Anesthesiology & Intensive Care Medicine, & Pain Management, Faculty of Medicine, Ain Shams University, for his unlimited help, great efforts and time he has devoted to accomplish this work. I really have the honor to complete this work under his supervision.

I am deeply grateful to **Prof. Dr. Karim Youssef Kamal,** Assistant Professor of Anesthesiology & Intensive Care Medicine & Pain Management, Faculty of Medicine, Ain Shams University, for his unlimited help and giving me the privilege to work under his supervision. His care and support are really valuable and precious.

I would like also to express my deep appreciation and gratitude to **Dr. Mohammed Mahmoud Maarouf,** Lecturer of Anesthesiology & Intensive Care Medicine, & Pain Management, Faculty of Medicine, Ain Shams University, for his care and support, also for the efforts and time he has devoted to accomplish this work.

Finally, I wish to extend my thanks to my **Family** for their care and support.

Mostafa Mahmoud Meselhy

List of Contents

List of Abbreviations

Abbr.	Full-term
ABCDE	: Airway, Breathing, Circulation, Disability and Exposure
APC	: Activated Protein C
aPTT	: Activated partial thromboplastin time
AST	: Aspartate aminotransferase
ATC	: Acute traumatic coagulopathy :
AXR	: Abdominal radiograph
BUN	: Blood urea nitrogen
CBC	: Complete Blood Count
CNS	: Central nervous system
COPD	: Chronic Obstructive Pulmonary Disease
CT	: Computed Tomography
CXR	: Chest radiography
DDAVP	: Desmopressin
DIC	: Disseminated intravascular coagulation
ECG	: An Electrocardiogram
ESR	: Erythrocyte Sedimentation Rate
FFP	: Fresh frozen plasma
Fp	: Fibrinopeptides
GI	: Gastrointestinal
gla	: γ-carboxyl glutamic acid
GP	: Glycoprotein
HITTS	: Heparin-induced thrombocytopenia and thrombosis syndrome
HIV	: Human immunodeficiency virus
HUS	: Hemolytic-Uremic Syndrome
INR	: international normalized ratio
ITP	: Immune thrombocytopenic purpura

IU : International units
IVIG : Intravenous immunoglobulin .
LMW : Low molecular weight
MAHA : Microangiopathic hemolytic anemia
MDS : Myelodysplastic syndrome
MRI : Magnetic Resonance Imaging
NAPs : Nematode family of anticoagulant proteins
PAI : Plasminogen activator inhibitor
PAR-1 : protease-activated receptor 1 ,
PCC : Prothrombin complex concentrates
PGI2 : Prostacyclin
PT : Prothrombin time
PTT : Partial thromboplastin time;
RBCs : Red blood cells
rFVIIa : Recombinant activated factor VII
rTM : Recombinant thrombomodulin
SIRS : Systemic inflamatory response syndrom
TAFI : Thrombin Activatable Fibrinolytic Inhibitor
TF : Tissue factor
TFPI : Tissue Factor Pathway Inhibitor
tPA : Tissue Plasminogen Activator
TTP : Thrombotic Thrombocytopenic Purpura
TXA : Tranexamic acid
vWD : Von Willebrand's disease
vWF : von Willebrand Factor
WBC : white blood cell

List of Tables

List of Figures

Abstract

Introduction: Bleeding is the second leading cause of death after trauma. Initial care of the patient with hemorrhage focuses on restoring circulating blood volume and reversing coagulopathy. Trauma and injury can initiate the coagulation cascade. Patients with massive bleeding should be resuscitated with goal-directed therapy, applying recent recommendations of goal-directed therapy, massive transfusion protocols, fixed ratios, markedly impact the outcome.

Objectives: This review aims to study the physiology of hemostasis and coagulation cascade, causes, pathophysiology and management of disorders of hemostasis in critical care unit.

Data sourses: Medline databases (PubMed, Medscape, Science Direct) and all materials available in the Internet till 2017.

Study Selection: This search presented 150 articles. The articles studied the causes, pathophysiology and management of disorders of hemostasis in critical care unit.

Data extraction: If the studies did not fulfill the inclusion criteria, they were excluded. Study quality assessment included whether ethical approval was gained, eligibility criteria specified, appropriate controls, and adequate information and defined assessment measures.

Conclusion: Massive bleeding with coagulopathy and hemorrhagic shock poses a potential threat to life in numerous clinical settings. Optimal treatment including the prevention of exsanguination necessitates a standardized and interdisciplinary approach. Several studies have shown the importance of massive transfusion protocols and standardized coagulation algorithms to improve survival of severely bleeding patients and to avoid secondary complications.

Key words: coagulopathies ICU, hemorrhagic shock

Introduction

The definition of coagulopathy is "a condition in which the blood ability to clot is impaired." However, for some clinicians, the term also covers thrombotic states, and because of the complexity of the hemostatic pathways, the two conditions can exist simultaneously. Such states are common in patients in the intensive care unit and require a clinicopathological approach to ensure that the correct diagnosis is made and the appropriate treatment administered ***(Orfanakis and Deloughery, 2013).***

Hemostasis is the process that maintains the integrity of a closed, high-pressure circulatory system after vascular damage. Vessel-wall injury and the extravasation of blood from the circulation rapidly initiate events in the vessel wall and in blood that seal the breach. Circulating platelets are recruited to the site of injury, where they become a major component of the developing thrombus; blood coagulation, initiated by tissue factor, culminates in the generation of thrombin and fibrin ***(White and Newton, 2015).***

Bleeding is the second leading cause of death after trauma. Initial care of the patient with hemorrhage focuses on restoring circulating blood volume and reversing coagulopathy. Trauma and injury can initiate the coagulation cascade. Patients with massive bleeding should be resuscitated with goal-directed

therapy, applying recent recommendations of goal-directed therapy, massive transfusion protocols, fixed ratios, markedly impact the outcome ***(Paterson and Stein, 2014).***

Hemostatic disorder is common in critical ill patient and may be complex and multifactorial in pathogenesis. As disorder of hemostasis may complicate a wide range of medical, surgical and obstetric disorders, definitive diagnosis and specific therapy can significantly impact the outcome ***(Hart and Spannagl, 2014).***

Massive bleeding with coagulopathy and hemorrhagic shock poses a potential threat to life in numerous clinical settings. Optimal treatment including the prevention of exsanguination necessitates a standardized and interdisciplinary approach. Several studies have shown the importance of massive transfusion protocols and standardized coagulation algorithms to improve survival of severely bleeding patients and to avoid secondary complications ***(Grottke et al., 2013).***

Aim of the Work

The aim of this essay is to study the physiology of hemostasis and coagulation cascade, causes, pathophysiology and management of disorders of hemostasis in critical care unit.

Chapter (1)
Physiology of Hemostasis and Coagulation Cascade

With the evolution of vertebrates and their pressurized circulatory system, there had to arise some method to seal the system if injured; hence, the hemostatic system. Interestingly, there is nothing quite comparable to the vertebrate hemostatic system in invertebrate species. In all vertebrates studied, the basic constituents of the hemostatic system appear to be conserved.

Each element of the hemostatic system occupies a site at the vertex of an equilateral triangle. This representation implies that each system constituent interacts with and influences all other constituents. In the normal resting state, these interactions conspire to maintain the fluidity of the blood to ensure survival of the organism. Normally, only at the site of an injury will the fluidity of the blood be altered and a blood clot form (figure 1) ***(Colman et al., 2006).***

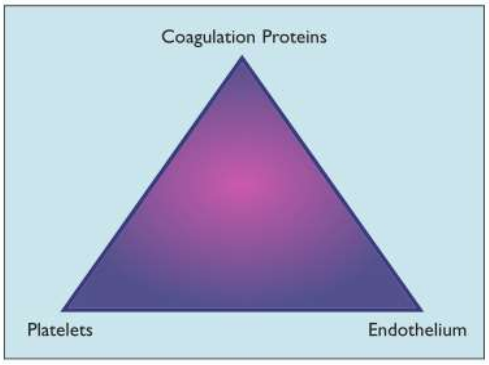

Figure (1): Basic representation of the elements of hemostasis ***(Colman et al., 2006)***

Constituents of the hemostatic system:

1- Endothelium:

The endothelium normally promotes blood fluidity, unless there is an injury. With damage, the normal response is to promote coagulation at the wound site while containing the coagulation response and not allowing it to propagate beyond this site (figure 2) ***(Aird, 2005)***.

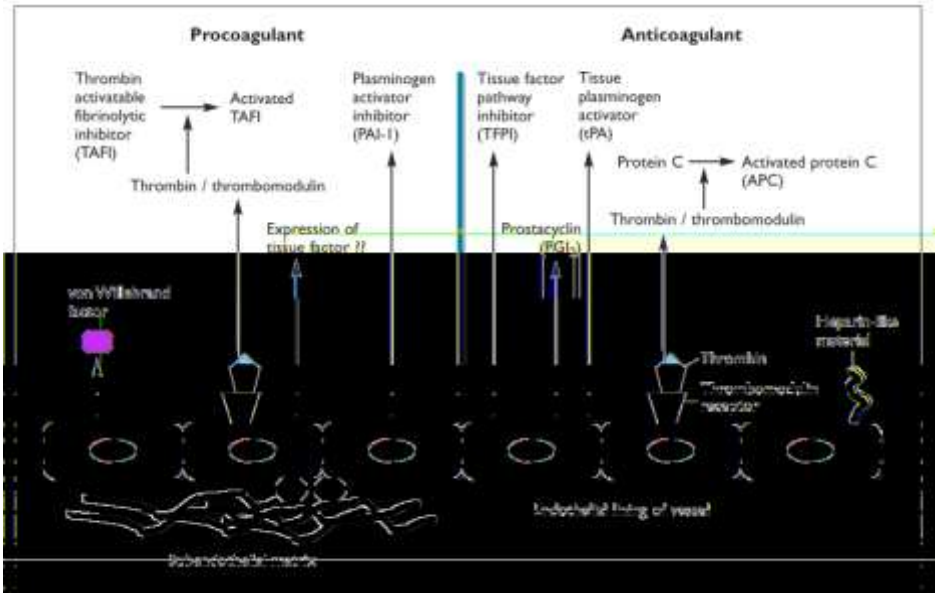

Figure (2): A stylized view of endothelial functions related to procoagulation and anticoagulation. The subendothelial matrix, represented by the purple interlocking lines, is a complex of many materials.The most important constituents of the subendothelial matrix related to coagulation function are collagen and vonWillebrand factor ***(Aird, 2005)***.

Until recently, the dogma of blood clotting suggested that the single, major procoagulant function of the endothelium is to make and express tissue factor with injury.