New Trends in Anesthetic Management with Platelet Disorders

Essay

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بسم الله الرحمن الرحيم
قالُوا سُبْحَانكَ لاَ
عِلمَ لَنَا إِلاّ ما
عَلّمْتَنَا إِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيم
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List of Abbreviations

Abb.	Full word
ADP	Adenosine diphosphate
AML	Acute myelogenous leukemia
AMP	Adenosine monophosphate
Anti HPA-1a	Anti human platelet antigen-1a
aPTT	Activated partial thromboplastin time
ATP	Adenosine triphosphate
ATPase	Adenosine triphosphatase
AVWS	Acquired von Willebrand syndrome
BSA	Body surface area
BSS	Bernard-Soulier Syndrome
BT	Bleeding time
CABG	Coronary Artery Bypass Grafting
CAMP	Cyclic adenosine monophosphate
CCI	Corrected count increment
COX-1	Cyclooxygenase-1
COX-2	Cyclooxygenase-2
CXC	Chemokines
DDAVP	1-desamino-8-D-arginine vasopressin (Desmopressin)
DIC	Disseminated intravascular coagulopathy
EACA	Epsilon Amino Caproic Acid
EDTA	Ethylene Diamine Tetra Acetic Acid
FcγRII	Fc gamma receptor III (Leukocytic receptor)
FDPs	Fibrin degradation products
FPS	Familial platelet syndrome
GDP	Guanosine diphosphate
GMP	Guanosine monophosphate
GP	Glycoprotein
HELLP	Hemolysis (H), elevated liver enzymes (EL), low platelet count (LP)
HIT	Heparin induced thrombocytopenia
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen

List of Abbreviations (Cont...)

Abb.	Full word
HPA	Human platelet antigen
HSC	Hematopoietic Stem cells
HUS	Hemolytic uremic syndrome
IL	Interleukin
ITP	Immune Thrombocytopenic Purpura
IVIg	Intravenous Immunoglobulins
KMS	Kasabach Merrit Syndrome
MDS	Myelodysplastic syndrome
NO	Nitric oxide
NSAIDS	Non Steroidal Anti-inflammatory Drugs
PAF	Platelet activating factor
PC	Phosphatidyl-choline
PCI	Percutaneous coronary intervention
PDGF	Platelet derived growth factor
PF4	Platelet factor 4
PFA	Platelet activating factor
PGI2	Prostacyclin
PNH	Paroxysmal nocturnal hemoglobinuria
P-Selectin	Platelet selectin
PT	Prothrombin time
RCF	Ristocetin cofactor
RNA	Ribonucleic acid
SPD	Storage pool disease
TAR	Thrombocytopenia with absent radii
t-PA	Tissue plasminogen activator
TPO	Thrombopoietin
TSP	Thrombospondin
TTP	Thrombotic thrombocytopenic purpura
TXA2	Thromboxane A2
U	Unit
VEGF	Vascular endothelial growth factor
vWF	von Willebrand factor
WAS	Wiskott Aldrich syndrome

INTRODUCTION

Platelets contribute to the hemostatic process into two different ways. First through their adhesive and cohesive function that lead to the formation of a hemostatic plug. Second they can activate coagulation mechanisms through the exposure of an adequate phospholipid surface or exposed collagen acting as a catalytic site for the development of coagulation and the consolidation of the hemostatic plug. To promote a correct hemostasis, platelets should ideally retain their adhesive and procoagulant properties ***(Paparella et al., 2008).***

There are two main types of platelet disorders: disorders related to the number of platelets that may be caused by over or underproduction of platelets in the bone marrow along with abnormal rates of destruction or sequestration in the body which may be inherited as ITP or acquired as in case of malignancy, and problems related to the function of the platelets such as Bernard-Soulier disease and von Willebrand's disease involve platelet numbers which are normal, with a problem in the fundamental function of the platelets ***(Kaushanky et al., 2006).***

These conditions are often genetic but they can also be acquired and it may be immune mediated meaning that abnormal immune system function is involved ***(WiseGeek, 2014).***

Surgical procedures are a great challenge to the hemostatic system in which the platelets are cornerstone in this process; therefore, carefully assessing the risk of bleeding by anesthiologist in every surgically patient is important. The assessment is based on the bleeding history, the results of initial hemostatic tests (PT, aPTT, platelet count) and the type of surgery that is planned, low risk and high risk conditions of operations are categorized. A critical analysis of each potential cause of bleeding should be undertaken for the high-risk conditions. Among multiple factors, interactions of drugs used in anaesthesia with platelets have been implicated to aggravate the risk of haemorrhagic complications.

In Brief there is anesthetic considerations and precautions for patients with platelet disorders as in general anaesthesia, neuroaxial anaesthesia and peripheral nerve blocks ***(Seligsohn et al., 2006).***

Aim of the Work

The aim of the study is to review the updates in the role of platelets in hemostasis, disorders of platelets and the anesthetic considerations in patients with platelet disorders.

Chapter One

ROLE OF PLATELETS IN HEMOSTASIS AND MONITORING ITS FUNCTION

Physiology of platelets:

Platelets are not actually cells, but cytoplasmic fragments of large cells known as megakaryocytes. The platelets themselves are incapable of mitotic division since they lack a nucleus and have no DNA. Contained within the platelets are cytoplasmic granules which can release biochemical mediators when stimulated by an injury to a blood vessel. The disc-shaped platelets circulate in an inactive state as long as the endothelium lining of the blood vessels is intact and remain in circulation for about 10 days before being removed from circulation by the spleen. When the blood vessel is damaged, the blood is exposed to the subendothelial layer of the vessels. The platelets become spherical and extend pseudopods, which adhere to vessel walls and each other, and hemostasis is initiated in conjunction with coagulation factors. These events lead to the formation of a fibrin plug that stops bleeding from the injured vessel ***(Michiels et al., 2006).***

The earliest blood cells develop from endothelial cells within the walls of the newly forming vessels of the cardiovascular system. These vessels begin forming within the walls of the yolk sac and allantois around the end of the third

week of gestation. Blood formation begins in the embryo during the fifth week of gestation, occurring in various parts of the embryonic mesenchyme. Platelets are first noted in the fetal circulation by the fifth to sixth week of gestation. The transition to hepatic hematopoiesis may involve stem cell migration from the yolk sac to the liver. Megakaryocytes can be found in the liver/spleen tissue by 10 weeks' gestation ***(Bick and Murano, 2005).***

Megakaryocytes were recognized as the source for platelets in the early 1900s, almost 100 years after platelets were first described. They make up 0.02 to 0.1% of the total nucleated bone marrow cells and are large in size. Neonatal megakaryocytes are smaller than adult megakaryocytes, and their size increases with advancing gestational age ***(Bick and Murano, 2005).***

The progenitors of megakaryocytes arise from pluripotent hematopoietic stem cells by a process that is not yet well understood. The burst forming unit-megakaryocyte (BFU-MK) is the earliest identifiable megakaryocyte progenitor. The later progenitor is the colony forming unit-megakaryocyte (CFU-BK). Both BFU-MK and CFU-MK can be quantified and have proliferative potential ***(Bick and Murano G, 2005).***

CFU-MK are more plentiful in the bone marrow; BFU-MK are more plentiful in circulating peripheral blood Interleukin 3 (IL-3) stimulates megakaryocytopoiesis progenitor cells.

Interleukin 6 (IL-6) and interleukin 11 (IL-11) act with IL-3 to stimulate CFU-MK proliferation. Interleukin 1 (IL-1), IL-6, IL-11, and leukemia-inhibiting factors are active in the latter stages of megakaryocyte maturation. Thrombopoietin (TPO), stimulates all stages of megakaryocyte growth and development ***(Bick and Murano, 2005).***

Each day the adult human produces approximately 10,000/mm^3 platelets, a level of production that can be increased 10 to 20 fold in times of increased demand. The circulatory half-life of a platelet is approximately 10 days in humans with normal platelet counts but is somewhat shorter in patients with moderate (7 days) to severe (5 days) thrombocytopenia, as a higher proportion of the total platelet mass is consumed in the day-to-day function of maintaining vascular integrity ***(Bick and Murano, 2005).***

The transit time from megakaryocyte progenitor cell to release of platelets into the circulation ranges from 4 to 7 days ***(Bick and Murano, 2005).***

Hemostasis:

Hemostasis is a process which causes bleeding to stop, meaning to keep blood within a damaged blood vessel. It is the response for the body to stop bleeding and loss of blood. It is the first stage of wound healing. This involves blood changing from a liquid to a gel. Intact blood vessels are mild to

moderating blood's tendency to clot. The endothelial cells of intact vessels prevent blood clotting with a heparin-like molecule , thrombomodulin and prevent platelet aggregation with nitric oxide and prostacyclin. When endothelial injury occurs, the endothelial cells stop secretion of coagulation and aggregation inhibitors and instead secrete von Willebrand factor which initiate the maintenance of hemostasis after injury ***(Coughlin and Camerer, 2007).***

Platelets are a large factor in the hemostatic process. They allow for the creation of the "platelet plug" that forms almost directly after a blood vessel has been ruptured. Within seconds of a blood vessel's epithelial wall being disrupted platelets begin to adhere to the sub-endothelium surface. It takes approximately sixty seconds until the first fibrin strands begin to intersperse among the wound. After several minutes the platelet plug is completely formed by fibrin ***(Coughlin and Camerer, 2007).***

Hemostasis is maintained in the body via three mechanisms:

1) **Vascular spasm** - Damaged blood vessels constrict. Vascular spasm is the blood vessels' first response to injury. The damaged vessels will constrict (vasoconstrict) which reduces the amount of blood flow through the area and limits the amount of blood loss. This response is triggered by factors such as a direct injury to vascular smooth muscle, chemicals