The Clinical Uses Of Sealants for Hemostasis In Cardiac Surgery

Essay

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ACT	Activated clotting time
ADP	Adenosine diphosphate
BSA	Bovine serum albumin
CPB	Cardiopulmonary bypass
CABG	Coronary artery bypass graft
DIC	Disseminated intravascular coagulation
EU	Europe
FS	Fibrin sealant
FDA	Food and Drug Administration
FFP	Fresh frozen plasma
GPs	Glycoproteins
Ig	Immunoglobulin
ICU	Intensive care unit
ITA	Internal thoracic artery
IOALs	Intraoperative air leaks
LIMA	Left internal mammary artery

ORC	Oxidized regenerated cellulose
PEG	Polyethylene glycol
PCR	Polymerase chain reaction
PITLs	Post intubation tracheobronchial lacerations
RBCs	Red blood cells
RIMA	Right internal mammary artery
TAFI	Thrombin-activated fibrinolysis inhibitor
TF	Ttissue factor
UV	Ultraviolet
US	United states
vWF	Von Willebrand factor

Introduction

Hemostasis means the arrest of bleeding from an injured blood vessel ***(Moake, 2015)***

An important complication of cardiac surgical procedures, specially after cardiopulmonary bypass, is bleeding that results from an alteration in the haemostatic mechanisms, which include: (1) the loss of platelets and impairment of platelet function caused by cardiopulmonary bypass, (2) hemodilution with associated decreased plasma concentrations of coagulation factors, (3) incomplete neutralization of heparin given during cardiopulmonary bypass, and (4) an inadequate function of the fibrinolytic system ***(Levi and van der Poll, 2008)***.

A wide range of surgical hemostatic agents for use in cardiovascular surgery have been developed recently. These agents vary widely in their mechanism of action, composition, ease of application, adherence to wet or dry tissue, immunogenicity and cost. These agents can be divided into three broad categories: hemostats, sealants and adhesives. ***(Katayama et al., 2009)***

Sealant is a liquid , paste ,or coating ,or tape that fills small gaps between mating parts ***(Gooch ,2014)***

Sealants can be further subdivided as fibrin sealants and synthetic sealants. ***(Katayama et al., 2009)***

Fibrin sealant is a two-component material consisting of fibrinogen and thrombin. In the presence of small amounts of calcium and factor XIII, the thrombin converts fibrinogen into insoluble fibrin, the final stable form of the agent ***(Spotnitz, 2014).***

Synthetic sealants are composed of polyethylene glycol (PEG) polymers and at least one additional component. They are biodegradable agents that are used to act both as a fluid barrier and as hemostatic agents. They quickly form an adhesive bond and degrade in 1 – 6 weeks. They may be more expensive than other products ***(Reuters,2014).***

The ideal sealant should be safe (its components and degradation products do not induce immunological reaction and viral infection), efficient (inducing healing, clot formation, and strong superficial adhesion), easy to use (rapid solidification, ready to use, multiuse) and cheap ***(Lodi et al., 2012).***

Aim of the work

The aim of this article is to review the clinical applications of the most diffused surgical sealants (fibrin sealants and synthetic sealants) in cardiac surgery, highlighting their advantages and disadvantages .

Chapter 1
Hemostasis

Hemostasis preserves vascular integrity by balancing the physiologic processes that maintain blood in a fluid state under normal circumstances and prevent excessive bleeding after vascular injury. Preservation of blood fluidity depends on an intact vascular endothelium and a complex series of regulatory pathways that maintains platelets in a quiescent state and keeps the coagulation system in equilibrium. In contrast, arrest of bleeding requires rapid formation of hemostatic plugs at sites of vascular injury to prevent exsanguination. Perturbation of hemostasis can lead to bleeding or thrombosis. Bleeding will occur if there is failure to seal vascular leaks either because of defective hemostatic plug formation or because of premature breakdown of the plugs ***(White et al., 2013)***.

The normal hemostatic system comprises four compartments: the vasculature and platelets (primary hemostasis), the coagulation proteins (secondary hemostasis), and the fibrinolytic system.

When a blood vessel is injured, all four components interact in a coordinated manner to prevent blood loss by forming a clot and localizing this to the area of injury ***(Chee, 2014)***.

I-Primary Hemostasis

The term “primary hemostasis” encompasses all aspects of platelet adhesion and aggregation. Apart from platelets, components of the vessel wall – subendothelial matrix components in particular – and von Willebrand factor (vWF) are involved in this process (fig.1) ***(Berndt and Metharom , 2014).***

a-Vascular Endothelium:

A monolayer of endothelial cells lines the intimal surface of the circulatory tree and separates the blood from the prothrombotic subendothelial components of the vessel wall. Rather than serving as a static barrier, the healthy vascular endothelium is a dynamic organ that actively regulates hemostasis by inhibiting platelets, suppressing coagulation and promoting fibrinolysis .

Vascular tone and permeability. Defective vascular function can lead to bleeding if the endothelium becomes more permeable to blood cells, if vasoconstriction does not occur, or if premature degradation of hemostatic plug opens seals in the vasculature ***(Van Hinsbergh , 2012).***

b-Platelets:

Ordinarily platelets circulate in a quiescent state, near the endothelial cells lining the blood vessels without forming stable adhesions. However, after breaches of the vasculature, a number

of highly reactive subendothelial matrix proteins become exposed including vWF, collagen, fibrinogen, and fibronectin. Damage to the intimal lining of the vessel exposes the underlying subendothelial matrix. Platelets home to sites of vascular disruption and adhere to the exposed matrix proteins. Initial platelet adhesion is mediated principally by platelet surface receptors interacting with their cognate ligands. Initial platelet-adhesive interactions are mediated by platelet surface glycoproteins (GPs) including GPVI and GPIbα interacting with endothelial-bound collagen and VWF, respectively. Adherent platelets undergo activation and not only release substances that recruit additional platelets to the site of injury but also promote thrombin generation and fibrin formation. The excretion of the content of the platelets' α- and δ-granules leads to the release of a variety of components (e.g., coagulation factors, calcium, ADP) and modulators of hemostasis, such as thromboxane A2 and platelet-activating factor, both of which are potent platelet activators and promote vasoconstriction. Upon activation, platelets also exhibit a more thrombogenic surface by exposing a negatively charged phospholipid layer, providing the catalytic surface for the binding of coagulation factors and, thus, the process of fibrin formation and stabilization. Furthermore, externalization, clustering, and activation of receptors on the platelets' surface occur, allowing for a complex and intense

interaction of platelets with matrix proteins and other platelets. In this process, platelets aggregate by cross-linking the highly expressed GP IIb/IIIa aggregation receptors on the platelet surfaces via vWF or fibrinogen. As a result of primary hemostasis, a primary platelet plug forms on the injured endothelium, mainly consisting of platelets and vWF. This platelet clot is further modified and stabilized by cross-linking of fibrin ***(McFadyen and Kaplan 2015) .***

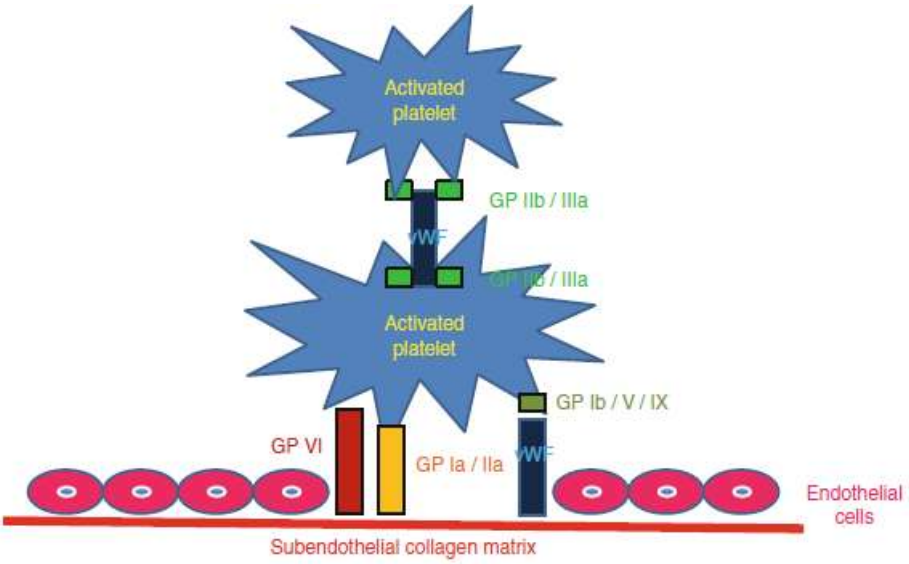

Figure 1 Schematic view of platelet adhesion and aggregation. Following endothelial injury, platelets adhere to collagen by interaction of the receptor glycoprotein (GP) Ib/V/IX with von Willebrand factor which is bound to collagen. This adhesion is stabilized by direct interaction of platelet collagen receptors GP Ia/IIa and GP VI with collagen. Following activation of the aggregation receptors GP IIb/IIIa, platelets aggregate, mediated by von Willebrand factor or fibrinogen **(Berndt and Metharom , 2014).**