COMPARATIVE STUDY OF CLINICAL AND LABORATORY FINDINGS IN POSTPARTUM HAEMORRHAGE

Thesis

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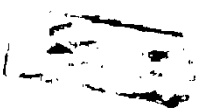
OBSTETRICS & GYNAECOLOGY



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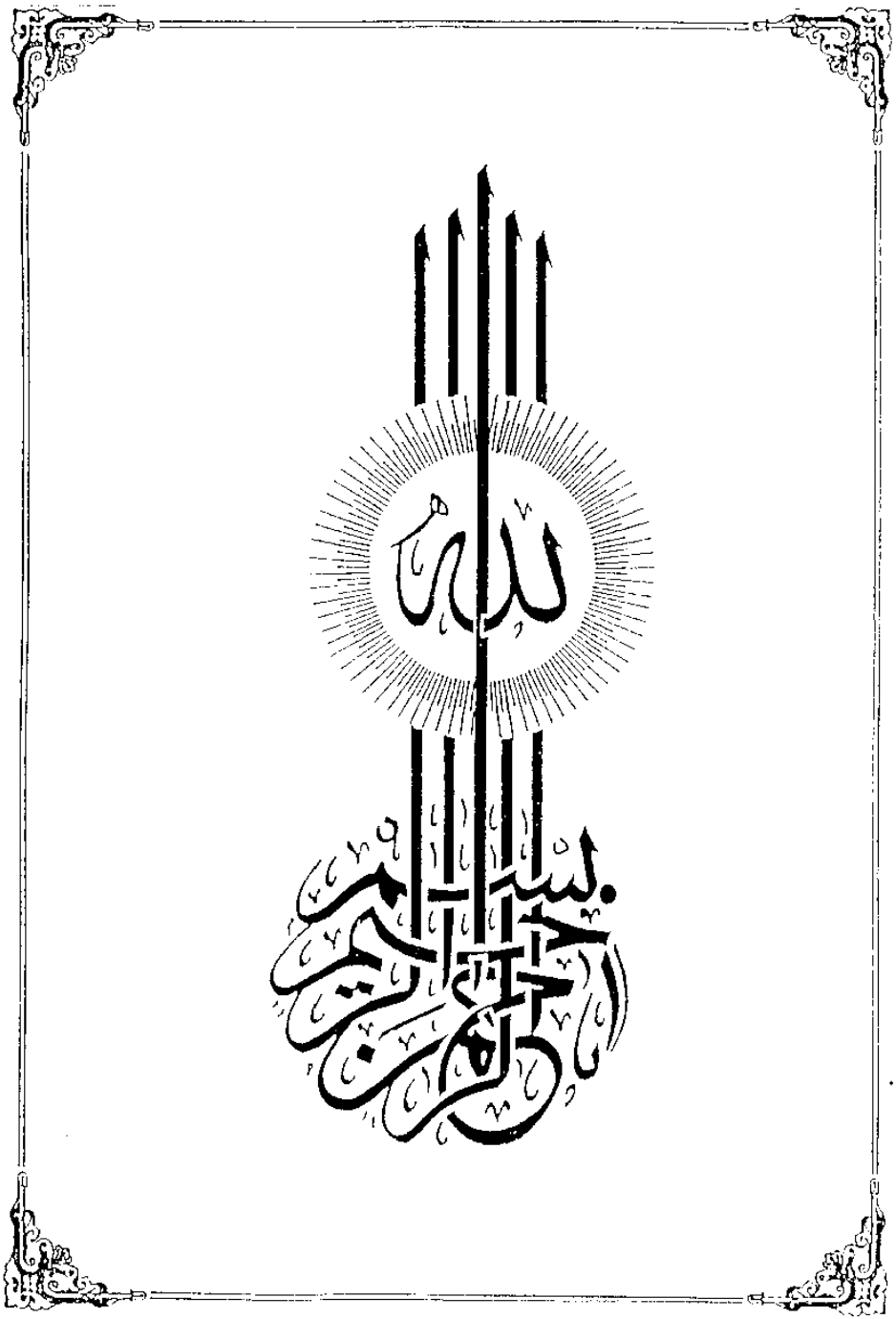
To

My beloved Parents



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C O N T E N T S

INTRODUCTION

Postpartum haemorrhage is one of the most serious and critical event that may face the obstetrician, and be a cause of maternal mortality. As a direct factor in maternal mortality, it is a cause of about one quarter of deaths from deaths of obstetric haemorrhage in a group that includes postpartum haemorrhage, placenta praevia, placental abruption, ectopic pregnancy, haemorrhage from abortion and rupture of uterus (Pritchard and Macdoland, 1975).

The definition of postpartum haemorrhage is arbitary, some refers it primarily to bleeding which occurs immediately after the placenta is delivered. In practical terms however we may consider under this heading all haemorrhages from the time the child is delivered until the puerperium is ended. These occurring after the first 24 hours are late or puerperal haemorrhage (Greenhill, 1974).

Dewhurst (1981) reported that primary postpartum haemorrhage is excessive bleeding from or into the genital tract within twenty four hours of the birth of the child. The average blood loss in normal labour does not usually exceed 10 ounces (300 ml).

The cardinal cause of primary postpartum haemorrhage is anything which interferes with retraction of the uterus as a whole and placental site in particular. The majority of cases are due to imperfect retraction as a result of uterine atony, less commonly mechanical factors, may play a part in interfering with proper uterine action. Other causes are trauma to the genital tract and coagulation defects (Pritchard and Macdoland,1973).

Late postpartum haemorrhage as a common belief is due to retained placental tissue. Also it may be due to failure of thrombosis of blood vessels at the placental site. Although it is rare to find placental tissue when the uterus is curreted for late post-partum haemorrhage (Greenhill, 1974).

Other causes of late postpartum haemorrhage are stilbesterol and other oestrogen used to suppress lactation which are a fairly common causes. fibromyoma, an overlooked haematoma, cascinoma of the cervix, rupture and inversion of the uterus and too early coitus (Doland, 1974).

Defective coagulation leading to severe post-partum haemorrhage occur as a result of consumption of the coagulation factors and platelets by a process

PHYSIOLOGY OF HAEMOSTASIS

There is, nowadays, a considerable amount of knowledge on the mechanisms of haemostasis, but not all is of practical importance in dealing with patients (Ingram and Brozovie, 1982).

In man, and many other animals, haemostasis is achieved by a highly integrated process involving the blood vessels themselves, together with the blood platelets and a number of plasma proteins which participate in the coagulation and fibrinolytic pathways.

However, the fundamental principles of haemostasis are more readily appreciated if the process is divided into arbitary stages and each considered independently. The three major aspects are (Hutton, 1981):

1. The role of the blood vessels and blood platelets in the formation of a haemostatic plug.
2. Interactions between the soluble coagulation factors leading to the formation of a fibrin clot.
3. Interactions between the components of the fibrinolytic system.

Role of blood vessels:

The intact intimal surface of blood vessels was long thought to be inert with respect to blood coagulation, but recent evidences indicate that this may not be the case (Hutton, 1981).

Both antithrombin III and plasminogen activator have been identified in endothelial cells especially in veins, and the release of the latter into the blood stream following venous occlusion was readily demonstrated by Nalbandian and Henry in 1979.

Endothelial cells in culture also synthesize a protein which, although lacking procoagulant activity, has many of the antigenic characteristics of factor (VIII, Ag.) (Nalbandian, 1979).

Moreover, the detection of prostacyclin (prostaglandin I_2), an inhibitor of platelet aggregation in vascular tissues, suggests that the blood vessels possess a mechanism for actively retarding platelet deposition on their walls (Griffin and Cochrane, 1979).

It was reported that if the endothelial cells are damaged, basement membrane elastin and sub-endothelial microfibrils are exposed, platelets

promptly adhere to these structures, with the assistance of a plasma factor which is defective in Von Wilebrand's disease. More trauma exposes deeper layers, including the collagen in the media (Baumgartner et al., 1971).

Collagen causes rapid platelet aggregation and the release of active components, and at the same time activated factor XII in the plasma. The interaction between platelets and subendothelium at the site of injury is essential for normal haemostasis as it allows the accumulation of platelet masses which was called plugs (Ingram, 1982). Moreover, the transient vasoconstriction which may later be sustained by 5-hydroxy tryptamine (5-H.T.) released from platelets shares in the haemostatic process (Hutton, 1981).

Role of blood platelets in haemostasis:

The platelets are fragments of the cytoplasm of the megakaryocytes; they are non-nucleated and formed chiefly in the bone marrow.

The rate of which platelets are produced appears to be under hormonal control, the agent responsible being called thromboplastin (Henry, 1977). Recently produced platelets tend to be larger, denser and more metabolically active than those in the circulation (Mibashan, 1977).

By means of some unidentified feedback mechanism the platelet count in the peripheral blood is maintained at a fairly constant level which ranges between 150 and 400 x 10^9/liter in normal subjects (Henry,1977).

Platelet ultrastructure by electron microscope, showed that, beside the cytoplasmic contents of other cells, such as mitochondria and lysozymes, there are a number of features which have a role in the hemostatic process which are: (Henry, 1977)

1. Dense bodies which are the primary secretory organells of platelets and are responsible for secondary platelet aggregation. They contain ADP (adenosin diphosphate), catezolamine, calcium and 5-H.T. which, in addition to being a potent vasoconstrictor, also aggregates platelets (White, 1968).

2. α -granules: These are a heterogenous group of granules, some of which are lysosomes. Others produce catalase and are called peroxosomes, and yet others contain fibrinogen and possibly platelet factor 4 and B-thromboglobulin (Austen, 1975).

3. Surface connecting system:
This is an extensive system of invaginations of

the plasma membrane, which serves to increase the surface area across which membrane transport can be affected and through which products of the release reaction can more rapidly reach the outside of the cell. It is formed of exterior coat, the unit membrane of the submembranal area (Naka and Anfnist, 1968 and Cooper, 1976).

4. Peripheral band of microtubules:
These structures are generally regarded as the cell's skeleton. During aggregation they move towards the centre of the cell, entrapping many of the granules. The function of this change is unknown (White, 1968).

5. Platelet microfibrils:
These contain the contractile protein thrombothenin (platelet actinomycin) which has been identified both on the outer surface and in the platelets cystoplasm. It is believed that the latter is responsible for the platelet-dependant phenomenon of clot retraction (Bettet-Galland and Luscher, 1959).

Some of the constituents of platelets relevant to thrombosis together with their possible location and function, are listed in table (1), from post-graduate hematology by Hoffbrad (1981).

Table (1): Some of platelets constituents relevant to thrombososis, possible location and function.

Constituent	Localisation	Possible function
- Nucleotides:		
ATP I	- Cytosol, mitochondria	- Cellular metabolism
ATP II	- Dense bodies	?
ADP	- Dense bodies	- Secondary aggregation
Cyclic AMP	- Membranes	- ? Depresses release reaction
- 5-hydroxy-tryptamine	- Dense bodies	- Vasoconstriction and aggregation
- Phosphatidyl serine - Phosphatidyl ethanolamine	- Membranes	- Coagulant activity
- Phosphatidyl inositol	- Membranes	- Membrane repair
- Arachidonic acid	- Phospholipids	- Prostaglandin synthesis
- Thrombosthenin (Actinomycin)	- Membrane cytoplasm	- Shape change and release reaction
- Fibrinogen	- α -granules	- Aggregation
- Platelet factor 4	- α -granules	- Heparin neutralizing
- B-thromboglobulin	- α -granules	-
- Platelet factor 3	- Phospholipids	- Enhances blood coagulation

Haemostatic properties of platelets:

Platelet adhesion:

Platelets escaping from an injured blood vessels come into contact with, and adhere to a number of tissues, in particular to collagen and subendothelial microfibrils that serve to plug small gaps in the endothelium resulting from mechanical distortion and vasodilatation. Using the Baumgarter model of arterial strips denuded of endothelial cells, the process of adhesion to microfibrils has been shown to require factor VIII R : WF (the Von Willebrand factor), together with platelet membrane glycoprotein 1, and calcium ions (Tschopp and Baumgartner, 1979).

The platelet release reaction:

Within second of their adhesion to collagen and other foreign surfaces, the platelets undergo a change in shape from disc to a spiny sphere and this is followed by a release reaction which reaches a peak in 3-5 minutes. With weak stimuli only dense bodies' contents are released, with strong stimuli, such as thrombin, release of some of the α-granules constituents occurs as well (Pollar, 1977).

The released substances are mainly ATP (adenosin-triphosphate) and ADP (adenosine-diphosphate). The

released ADP induces secondary platelet aggregation and this, together with the vasoconstriction induced by the released 5-H.T. (hydroxy tryptamine) is the major factor of primary hemostatic response. Platelet factor 4 is also released which has been shown to inhibit thrombin absorption to fibrin and may thus pontentiate the action of the protease (Zucker, 1980).

Platelet aggregation:

ADP is a powerfull inducer of platelet aggregation and its release from the dense bodies following adhesion, leads to platelet clumping which itself causes further release.

Thus a self-sustaining cycle of events are set up rapidly leading to the formation of platelet plug in the immediate vicinity of the site of injury (Shattil and Bennet, 1980).

Platelet coagulant activities:

Within minutes of the onset of aggregation (and to a lesser extent of adhesion) coagulant activity can be detected and this is generally referred to as platelet factor 3 (PF3). It reaches a peak level after around 15 minutes and particularly all the PF3 is sedimentable with the platelets (Zwaal, 1980).