Ain Shams University
Faculty Of Medicine
Department Of Anesthesiology And Critical Care

Hemostatic Effects of Hemodilution in Orthopedic Surgery Assessed by Thromboelastography

Thesis submitted for partial fulfillment of M.D. degree in anesthesiology
Presented by:

Mahmoud Abdalla Ahmed Hassan
M.B.B.Ch. – M.Sc in Anesthesia

Supervised By :

Professor Dr./ **Amr Essam El-Din Abd El-Hamid**
Professor of Anesthesia and Critical Care
Faculty of Medicine – Ain Shams University

Dr./ **Ahmed Mohamed Khamis**
Lecturer of Anesthesia and Critical Care
Faculty of Medicine – Ain Shams University

Dr./ **Walid Ahmed Mansour**
Lecturer of Anesthesia and Critical Care
Faculty of Medicine – Ain Shams University

Ain Shams University
Faculty of Medicine
2012

وَمَا أُوتِيتُمْ مِنَ الْعِلْمِ إِلَّا قَلِيلًا

صدق الله العظيم

(سورة الإسراء، اللآية ٨٤)

Acknowledgement

Thanks are all to **God**, the beneficent and the merciful, for giving me the power to finish this work and for his generous help throughout my entire career.

I would like to express my deepest gratitude to **Prof. Dr. Amr Essam**, Professor of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, for his patience, support and encouragement.

It has been an honor working under the supervision of **Dr. Ahmed Khamis**, Lecturer of Anesthesia and Intensive Care, Faculty of Medicine, Ain Shams University, who helped me in every way he could.

I'm greatly indebted to **Dr. Walid Mansour**, Lecturer of Anesthesia and Intensive care, Faculty of Medicine, Ain Shams University, who provided me with intellectual and technical support from the very beginning till the end.

Mahmoud Abdalla
October, 2012.

Contents

List of Tables

List of Figures

List of Abbreviations

- µl: microliter
- µm: micrometer
- ABD: autologous blood donation
- ACT: Activated clotting time
- ADAMTS-13: a disintegrin like and metalloproteinase with thrombospondin motif, member 13.
- ADP: Adenosine diphosphate
- Alb: serum albumin
- ALT: alanine transaminase
- ANH: Acute normovolemic hemodilution
- ANOVA: analysis of variance
- aPTT: Activated partial thromboplastin time.
- AST: aspartate transaminase
- ATP: Adenosine triphosphate
- BUN: blood urea nitrogen
- CPDA: citrate, phosphate, dextrose adenine.
- D_5W: Dextrose 5% in water
- D5W: Dextrose 5% in water.
- Da: Daltons.
- DDAVP: Desamino D-arginine Vasopressin.
- Desmopressin: DDAVP
- EDTA: ethylene diamine tetra-acetate
- FDPs: fibrin degradation products.
- GP: glycoprotein
- HES: hydroxyethyl starch

- HiTT: high dose thrombin time
- HMWK: high molecular weight kininogen
- INR: international normalized ratio
- K: coagulation time.
- K: potassium
- kDa: kilo Dalton.
- L: liter
- MA: maximum amplitude.
- MABL: Maximum allowable blood loss.
- Mg: magnesium
- Mg: milligram
- MW: molecular weight
- Na: sodium
- NS: Normal saline
- PACU: post-anesthesia care unit
- PO4: phosphorus
- PPF: Plasma protein fraction.
- PPF: plasma protein fraction.
- PT: Prothrombin time.
- R: reaction time.
- ROTEG: Rotational thromboelastogram
- SCr: serum creatinine
- SD: standard deviation
- SPSS: statistical program for social science
- TBil: total bilirubin
- TCT: Thrombin clotting time.
- TEG: thromboelastograph.

- t-PA: tissue plasminogen activator
- TXA_2: Thromboxane A_2.
- VIII-c: factor VIII, coagulant part.
- vWF: von Willebrand factor
- VWF: Von Willebrand Factor.

I. INTRODUCTION & AIM OF THE WORK

Introduction & Aim of the work

Certain surgical procedures are associated with significant bleeding, with the possible consequences of hypotension and tissue ischemia, as well as coagulopathy due to consumption of platelets and clotting factors, which leads to a vicious circle. Putting into consideration that blood transfusion isn't also completely safe, various blood – sparing techniques have evolved over the years *(Mittermayr et al, 2007).*

One modality uses the principle of "hemospasia" and "sequestration," in which manipulation of the patient's intravascular compartment with colloids or crystalloids produces hemodilution. This maneuver has various names, including intraoperative autologous donation, acute normovolemic hemodilution (ANH), isovolemic or isovolumic hemodilution *(Loubser & Chan, 2006).*

ANH is an effective blood conservation strategy in procedures with an expected blood loss of more than one liter. By this way, blood that is lost during surgery has a reduced hematocrit, which effectively reduces the need for allogenic blood transfusion and the associated risks. In addition, the intraoperative administration of fresh whole blood containing platelets and coagulation factors augments coagulation and reduces surgical blood loss *(Van Der Linden & Icks, 2006).*

ANH involves the removal of blood from the patient shortly after the induction of anesthesia and before the start of major surgical blood loss. A replacement fluid is simultaneously transfused to maintain intravascular volume. The stored blood is returned to the patient when a threshold hematocrit is reached, or

sooner, if clinically indicated. Ideally, this is after most of the blood loss has occurred. Both crystalloid and colloid replacement fluids have been used to maintain normovolemia during ANH, but few data are available to justify the use of a particular replacement fluid, especially when considering their haemostatic effects *(Jones et al, 2003).*

The type of intravenous fluids used during surgery has always been – and is still – a matter of debate. To date, the ideal intravenous fluid is not available. Controversy regarding crystalloids versus colloids has been the subject of many in vivo and in vitro studies. The enhancement or impairment of coagulation following hemodilution is a unique phenomenon, which is not fully understood yet.

Some studies support the use of colloids, as they are highly effective volume expanders, but there has been a recurring question about their negative effects on coagulation. On the contrary, many studies demonstrated, in vitro and in vivo, that hemodilution with crystalloid solutions enhances coagulation *(Ruttmann et al, 2002).*

Understanding of blood coagulation has evolved significantly in recent years due to the development of various new diagnostic coagulation tests. Also many promising haemostatic drugs agents are currently used for prophylaxis and treatment of bleeding, while many others are still under trials *(Bombeli & Spahn, 2004).*

In our study, we proposed enhanced coagulation with the use of normal saline and impaired coagulation with the use of gelatin and starch. Many studies failed to prove such relationship due to the lack of appropriate methodology. Measuring plasma concentrations of specific markers of coagulation appears to be too simple to assess the full spectrum of changes in the hemostatic process.

We designed a prospective, randomized study to determine if the replacement fluid choice impacts measured coagulation values and perioperative blood loss. We also decided to use thromboelastography, which is a well established tool in monitoring dynamics and kinetics of the coagulation process. TEG examines total blood coagulation; the interplay of the protein coagulation cascade, fibrinogen, and platelet function. TEG has been found to correlate best with postoperative blood loss, which makes it helpful to reduce the use of blood products.

II. REVIEW OF LITERATURE

A: Physiology of Coagulation.

B: Monitoring of Coagulation.

C: Pharmacology of Intravenous Fluids.

D: Blood Conservation Strategies.

A: Physiology of Coagulation

Hemostasis means prevention of blood loss. Normal hemostasis involves series of physiologic processes that keep blood in an invariably liquid state as it circulates throughout the body. Once the vascular network is violated, it transforms rapidly to a solid state through coagulation *(Drummond et al, 2009).*

Whenever a vessel is injured, hemostasis is achieved by several mechanisms: (1) vascular constriction, (2) formation of a platelet plug, (3) formation of a blood clot as a result of blood coagulation, and (4) eventual growth of fibrous tissue into the blood clot to close the hole in the vessel permanently *(Ganong, 2011).*

I. Vascular Constriction

Immediately after a blood vessel has been cut, the trauma to the vessel wall itself causes the smooth muscle in the wall to contract; this instantaneously reduces the extravasation of blood.

The contraction results from:

1. Local myogenic spasm,
2. Local autacoid factors from the traumatized tissues and blood platelets (thromboxane A_2:TXA_2)
3. Nervous reflexes, initiated by pain nerve impulses from the traumatized vessel or nearby tissues *(Guyton& Hall, 2006).*

II. Formation of the Platelet Plug

Platelets (thrombocytes) are minute discs 1 to 4 µm in diameter, formed from the bone marrow megakaryocytes. The normal concentration of platelets in the blood is 150,000 and 400,000/µl. It has a half-life in the blood of 8 - 12 days. They have