

# **The Efficacy of preoperative Tranexamic acid administration on the amount of blood loss during and after elective cesarean sections**

*Thesis submitted for Partial fulfillment of  
Master Degree in Obstetrics and Gynecology*

By

**Mohammed Gaafar Osman Ali**  
*(M.B., B.Ch. 2004-Assiute University)*  
*Resident in Luxor General Hospital*

Under SupervisionOf

**Prof. Dr. Mohamed Alaa Mohy El-Din El-Ghannam**  
*Professor of Obstetrics and Gynecology*  
*Ain Shams University*

**Dr. Ahmed Abd El-Kader Fahmy**  
*Assistant Professor of Obstetrics and Gynecology*  
*Ain Shams University*

**Dr. Sayed Korany Mohamed**  
*Lecturer in Obstetrics and Gynecology*  
*Ain Shams University*

Faculty of medicine  
Ain Shams University  
2010

# Acknowledgment

First and foremost I would like to thank "Allah" for every thing. This would not be achieved without the support of "Allah".

I would like to express my deepest gratitude to **Prof. Mohamed Alaa Mohy El-Din El-Ghannam**, Professor of Obstetrics and Gynecology, Faculty of medicine, Ain Shams University, for his constant help, encouragement, meticulous constructive advice, keen supervision to me.

I am greatly honored to express my deep gratitude to **Dr. Ahmed Abd El-Kader Fahmy**, Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University. He gave me much of his time, experience and endless support that can not be expressed in words.

I wish to express my great gratitude and ultimate thanks to **Dr. Sayed Korany Mohammed**, Lecture in Obstertrics and Gynecology, Faculty of Medicine Ain Shams University, for his encouragement, help , without his help this work would never be completed.

Lastly, I would be remiss if failed to acknowledge **my Family**, for their tolerance and their emotional support pushing me to finish this work, many thanks.

Mohammed Gaafar Osman

## List of Table

Table No.	Title	Page No.
<b>Table (1):</b>	Indications for elective cesarean section. ....	12
<b>Table (2):</b>	Indication for urgent and emergency cesarean section.....	13
<b>Table (3):</b>	The obstetric concepts and their parameters. ....	15
<b>Table (4):</b>	The ten-group classification. ....	17
<b>Table (5):</b>	Pharmacodynamic properties of tranexamic acid in patients. Effects described are relative to those seen in untreated control or placebo groups. ....	31
<b>Table (6):</b>	Population estimates ( <i>Stafford et al., 2008</i> ). ....	50
<b>Table (7):</b>	HCT, vEBL, and cEBL values and degree of perineal laceration. ( <i>Stafford et al., 2008</i> ). ....	51
<b>Table (8):</b>	HCT, vEBL, and cEBL values and mode of delivery. ....	53
<b>Table (9):</b>	HCT, vEBL, and cEBL values with vaginal and cesarean deliveries ( <i>Stafford et al., 2008</i> ). ....	55
<b>Table (10):</b>	Calculated and estimated blood loss and duration of hospital stay by t-test ( <i>Lapaire et al., 2006</i> ). ....	61
<b>Table (11):</b>	Initial Characteristics of Included Women.....	65
<b>Table (12):</b>	Indications of CS in Included Women .....	66
<b>Table (13):</b>	Difference between Study Groups concerning Preoperative Vital Signs and Laboratory Investigations.....	68
<b>Table (14):</b>	Difference between Study Groups concerning Intra- and Postoperative and Total Blood Loss .....	69
<b>Table (15):</b>	Difference between Cases of Primary CS among Study Groups concerning Intra- and Postoperative and Total Blood Loss .....	72

Table No.	Title	Page No.
<b>Table (16):</b>	Difference between Cases of Repeat CS among Study Groups concerning Intra- and Postoperative and Total Blood Loss.....	73
<b>Table (17):</b>	Difference between Study Groups concerning Vital Signs 1 and 2 hours Postoperatively.....	74
<b>Table (18):</b>	Difference between Study Groups concerning Postoperative Hemoglobin Concentration and Haematocrit Value.....	75
<b>Table (19):</b>	Difference between Study Groups concerning Postoperative Blood Chemistry.....	77

## List of Figure

Figure No.	Title	Page No.
<b>Fig. (1):</b>	Structural formula of tranexamic acid. ....	28
<b>Fig. (2):</b>	Antifibrinolytic action of tranexamic acid. Normally, plasminogen binds to fibrin at a lysine binding site and is converted in the presence of tissue plasminogen activator (t-PA) to plasmin. Tranexamic acid blocks the lysine binding site and prevents access of plasminogen to the fibrin molecule.....	29
<b>Fig. (3):</b>	Degree of perinatal laceration in all vaginal deliveries.....	52
<b>Fig. (4):</b>	Mode of delivery.....	54
<b>Fig. (5):</b>	Bar-Chart showing Age Group Distribution of Included Women.....	66
<b>Fig. (6):</b>	Pie-Chart showing Indications of Cesarean Section in Included Women.....	67
<b>Fig. (7):</b>	Box-Plot Chart showing Difference between Study Groups concerning Estimated Intraoperative Blood Loss .....	70
<b>Fig. (8):</b>	Box-Plot Chart showing Difference between Study Groups concerning Estimated Postoperative Blood Loss.....	70
<b>Fig. (9):</b>	Box-Plot Chart showing Difference between Study Groups concerning Estimated Total Blood Loss .....	71
<b>Fig. (10):</b>	Box-Plot Chart showing Difference between Study Groups concerning Postoperative Hemoglobin Concentration.....	76
<b>Fig. (11):</b>	Box-Plot Chart showing Difference between Study Groups concerning Postoperative Haematocrit .....	76

# List Of Abbreviations

CS:	Cesarean Section
BCE:	Before christion era
CE:	CHRISTION ERA
n:	THE NUMBER
Kd:	dissociation constant
t-pA:	tissue plasminogen activator
$\alpha$ :	Alpha
CPB:	Cardiopulmonary bypass
CBC:	Complete blood count
CSF:	Cerebrospinal fluids
aPTT:	activated partial thromboplastion time
PT:	Prothrombin time
CD:	Cesarean delivery
OVD:	Operative vaginal delivery
SVD:	Spontaneous Vaginal delivery
LO:	No perineal lacerations
L1:	first perineal lacerations
L2:	Second perineal lacerations
L3:	third perineal lacerations

L4:	fourth perineal lacerations
vEBL:	visualized estimated blood loss
cEBL:	calculated estimated blood loss
HCT:	Haematocrite level
S.D.:	standard deviation
vs:	Versus
INR:	International normalized ratio
AST:	aspartate transferase
ALT:	Alanin transferase

## List of Contents

Title	Page No.
<b>Introduction.....</b>	<b>1</b>
<b>Aim of the work.....</b>	<b>4</b>
<b>Review of literature .....</b>	<b></b>
♦ <b>History of Cesarean Sections.....</b>	<b>5</b>
- Incidence of Cesarean Birth .....	8
- Indications of Cesarean sections .....	12
- Classification of Cesarean sections.....	13
- Complications of Cesarean Sections.....	19
♦ <b>Blood Coagulation and the Fibrinolytic System .....</b>	<b>26</b>
♦ <b>Tranexamic acid .....</b>	<b>28</b>
♦ <b>Estimation and Calculation of blood loss in vaginal         and cesarean delivery .....</b>	<b>48</b>
<b>Patients and methods .....</b>	<b>62</b>
<b>Results .....</b>	<b>65</b>
<b>Discussion.....</b>	<b>78</b>
<b>Summary.....</b>	<b>84</b>
<b>Conclusions and recommendation .....</b>	<b>89</b>
<b>References .....</b>	<b>90</b>
<b>Arabic Summary .....</b>	<b></b>



## Introduction

Cesarean section (CS) rate has increased to as high as 25 to 30% in many areas of the world (*Kambo et al., 2002*). Delivery by CS can cause more complications than normal vaginal delivery and one of the most common complications is postpartum bleeding, which can be life threatening. To reduce maternal mortality and morbidity caused by bleeding, it is important to reduce the extent of bleeding during and after CS (*Declercq et al., 2007*).

To control the bleeding after CS, some medications such as oxytocin, prostaglandins (E1, E2 and F2 $\alpha$ ) and methylergometrine have been used (*Munn et al., 2001*).

Excessive bleeding is one of the major threats to women at childbirth, during vaginal delivery there was no correlation between estimated and measured blood loss, and in women delivered by elective CS, the correlation was moderate (*Larsson et al., 2006*).

Sublingual misoprostol appears to be as effective as intravenous infusion of oxytocin in reducing blood loss at CS. However, occurrence of transient side effects such as shivering and pyrexia were noted more frequently with the use of misoprostol (*Vimala et al., 2006*).

Oral misoprostol appears to be safe and as effective as intravenous syntocinon in reduction of intraoperative blood loss during elective CS under regional anesthesia and merits further investigation (*Acharya et al., 2001*).

General anesthesia resulted in significantly more blood loss, lower postoperative haematocrit, and higher proportion of patients who had postoperative haematocrit < 30 per cent than epidural anesthesia and spinal anesthesia. Regional anesthesia is a better choice of anesthesia for CS than general anesthesia. However, the availability of different technique and ability to change the technique when needed were very useful and important (*Lertakyamanee et al., 1999*).

Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect through the reversible blockade of the lysine binding sites on plasminogen molecules (*Wellington and Wagstaff, 2003*).

The antifirinolytic effect of tranexamic acid results from the formation of a reversible complex of the drug with plasminogen. Human plasminogen contains lysine binding sites that are important for interactions not only with synthetic antifibrinolytic amino acid derivatives but also with  $\alpha$ 2-antiplasmin and fibrin (*Thorsen, 1975*).

Tranexamic acid has been routinely used for many years to reduce hemorrhage during and after surgical procedures, such as coronary artery bypass, scoliosis surgery and knee arthroplasty. It has been shown to be very useful for reducing blood loss and blood transfusion (*Asada et al., 2000*). There are some reports on the use of tranexamic acid in prevention of blood loss in many gynaecologic diseases such as menorrhagia (*Srinil et al., 2005*), and also CS (*Gai et al., 2004 and Gohel et al., 2007*).

Tranexamic acid statistically reduces blood loss from end of CS up to 2 hours after CS and its use was not associated with any side effects or complications. Consequently, tranexamic acid can be used safely and effectively to reduce bleeding resulting from CS (*Sekhavat et al., 2009*).

## **Aim of the Work**

Determination of the efficacy of using tranexamic acid preoperatively on decreasing the amount of blood loss during and within the first two hours after elective cesarean sections.

## **History of Cesarean Sections**

Cesarean delivery was practiced for ages and is referred to in the myths and folklore of many ancient nations. The evidence that cesarean section was performed arises from legal texts: a cuneiform tablet dealing with the adoption of a small boy during the 23rd year of the renowned king (*Lurie and Mamet, 2001*).

Hammurabi of Babylon (1795-1750 BCE), (*Oppenheim, 1960*), “Lex Regia” (the Law of the Kings) proclaimed by Numa Pompilius, an ancient Roman king (716-673 BCE) and Mishna, the collection of ancient Jewish laws (2nd century BCE to 6<sup>th</sup> century CE). Unfortunately, no ancient medical documents mentioning the techniques or exact indication for cesarean section are extant (*Lurie and Mamet, 2001*).

The surgical technique could have been used by the Banyoro tribe surgeons for centuries: “The patient was a healthy-looking primipara (1<sup>st</sup> pregnancy) of about twenty years of age and she lay on an inclined bed, the head of which rested against the side of the hut. She was half-intoxicated with banana wine, was quite naked and was tied down to the bed by bands of bark cloth over the thorax and thighs. Her ankles were held by a man while another man stood on her right steadying her abdomen the surgeon was standing on her left side holding the knife aloft and muttering an incantation (*Field, 1988*).

He then washed his hands and the patient's abdomen first with banana wine and then water. The surgeon made a quick cut upwards from just above the pubis to just below the umbilicus severing the whole abdominal wall and uterus so that amniotic fluid escaped. Some bleeding points in the abdominal wall were touched with red hot irons. The surgeon completed the uterine incision, the assistant helping by holding up the sides of the abdominal wall with his hand and hooking two fingers into the uterus.

The child was removed, the cord cut, and the child was handed to an assistant. The report goes on to say that the surgeon squeezed the uterus until it contracted, dilated the cervix from inside with his fingers (to allow postpartum lochia to escape), removed clots and the placenta from the uterus, and then sparingly used red hot irons to seal the bleeding points. The peritoneum, the abdominal wall, and the skin were approximated back together and secured with seven sharp spikes. A root paste was applied over the wound and a bandage of cloth was tightly wrapped around it. Within 6 days, all the spikes were removed. Felkin observed the patient for 11 days, and when he left mother and child were alive and well.

The salient points of the cesarean technique of the Banyoro tribe surgeons are anesthesia (banana wine), antisepsis (banana wine), low midline abdominal incision, good hemostasis (red hot iron), blunt incision of the uterus (minimizing hemorrhage), non-suturing of the uterus with

---

manual massage and cautery of uterine incision bleeding points (minimizing hemorrhage), suture of abdominal wall, and wound care (root paste) (*Field, 1988*).

Currently, uterine suture is thought to reduce the amount of blood loss and to enhance uterine healing. Nonsuture of the uterus is apparently associated with greater hemorrhage that may even lead to exsanguination. Conversely, recent experimental data in dogs reveal that nonclosure of a low transverse uterine incision after safe hemostasis and administration of uterotropins is associated with good outcome and might even be preferable in appropriate cases (*Gul et al., 2000*).

### **History of cesarean section in Africa:**

Cesarean section is not a new procedure in the health care system, even in the developing world. For instance, experience with abdominal child deliveries in Africa predates colonialism (*Chip, 1989*).

On January 9, 1884, a Scottish final year medical student, Robert Felkin gave a lecture to the Edinburgh Obstetrical Society about his experience of observing cesarean section in Africa. The title of the lecture was, “Notes on Labor in Central Africa”. He narrated how, while in Uganda in 1879, he had observed the Bagandas performing a successful emergency cesarean section using a large knife and alcohol as anesthetic, analgesic, and antiseptic. This was probably the first record on