Efficacy of Intravenous Tranexamic acid in Reducing Blood Loss During and After Elective Caesarean Section

Thesis

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By

Zarafshan Mohammad Raqeeb

M.B.B.,Ch (2008)

Under Supervision of

Dr./ Ahmad Hamdi Nagib Abdul Rehman

Assistant Professor of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Dr./ Ahmad Mohammad Mamdouah

Lecturer in Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
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Introduction

Caesarean section is the most common major surgical procedure performed on women worldwide and its rates continue to rise steadily in both developed and developing countries ***(Gibbons et al., 2012).***

Epidemiologic data reports a C.S incidence of 20-30 % worldwide with comparable rate in high income and low income countries ***(Khawaja et al., 2009).***

The current rate of C.S, Which is approximately 4-5 folds greater than that of the 1970s, can be attributed to facts such as assumed benefit to the fetus, low maternal risk and social preference ***(Toy et al., 2011).***

The hematocrit falls by 10% and the blood transfusion is required in 6% of women undergoing Caesarean delivery compared with 4% of women who have a vaginal delivery, Numerous methods for performing Caesarean section exist; The aim is a safe delivery for the infants with minimum maternal morbidity. Operative morbidity includes hemorrhage, anemia, blood transfusion and the risks associated with receiving donor blood products ***(Asicioglu et al., 2010).***

Caesarean section is as high as 25-30 % in many areas of the world, In Egypt the Caesarean section rate is 27, 6% ***(WHO report, 2010).***

The national US caesarean section rate leveled off at 32,8% in 2010 & 2011 ***(Hamilton et al., 2012).***

caesarean section accounts for 20 -25% of all deliveries in UK ***(Fairley et al., 2011).***

In many areas of china the caesarean section rate is as high as 40-50% ***(Zhang, 2008).***

Maternal morbidity following Caesarean section is much higher than that following a vaginal delivery, generally, it is 2-4 times higher than vaginal delivery, the main cause of death following Caesarean section are infection, hemorrhage pulmonary embolism and anesthesia - associated complications, the most frequent being aspiration pneumonia and cardio pulmonary arrest. Caesarean section has been an important underlying cause of death in Norway and contributed to the increased maternal death ratio in the last decade ***(Vangen and Bergsjo, 2003).***

The average blood loss during caesarean section is (1000 ml) which is double the amount of blood lost during vaginal delivery (500 ml) ***(Magann, 2005).***

In severe cases, caesarean section may result in major obstetric hemorrhage, hysterectomy, admission to an intensive care unit, or maternal death. Medication, such as Oxytocin, Misoprostol, Prostaglandin F2α, and Methylergonovine has

been used to control bleeding after caesarean section ***(RCOG 2004)*** and ***(Asicioglu et al., 2010).***

But still the post-partum hemorrhage remaining a leading cause of maternal mortality, especially in developing countries ***(Ronsmans, 2006).***

In order to reduce maternal mortality and morbidity caused by bleeding, it is important to reduce the amount of bleeding during and after caesarean section ***(Kambo et al., 2002).***

Tranexamic acid (TXA) is a synthetic derivative of the amino acid Lysine, which is an anti-fibrin lytic that reversibly inhibits the activation of plasminogen. Thus inhibiting fibrinolysis and reducing bleeding. Tranexamic acid may enhance the effectiveness of the patient's own hemostatic mechanism (***Bolton et al., 2003).***

Tranexamic acid has been routinely used for many years to reduce hemorrhage during and after surgical procedures, such as Coronary artery bypass, pediatric cardiac operations, and scoliosis surgery and hip & knee arthroplasty. It has been shown to be very useful for reducing blood loss and blood transfusion ***(Ido et al., 2000).***

In gynecology and obstetrics, Tranexamic acid is most commonly used to treat idiopathic menorrhagia and is an

effective & well tolerated treatment when administrated orally ***(Novikova et al., 2010).***

Bleeding associated with pregnancy (placenta abruption, placenta Previa) has been treated with Tranexamic acid ***(Sekharat et al., 2009).*** Furthermore multiple small randomized studies have shown that Tranexamic acid reduce blood loss during and after caesarean section.

Systematic review of Tranexamic acid showed no statistically significant increase in the risk for the thrombo embolic event assessed ***(Henry et al., 2001);*** and no significant change in PT or PTT ***(Gungorduk et al., 2011).***

Tranexamic acid acts within 2-3 hours after oral administration and immediately after intra venous administration, and its half-life is 2-10 hours ***(Jurema, 2008).***

In this study the efficacy of Tranexamic acid in reducing blood loss during and after caesarean section will be invistegated.

Aim of the Work

Determination of the efficacy of using Tranexamic acid pre-operatively on decreasing the amount of blood loss during and within the first 24 hours after elective caesarean section.

Chapter (1):

CAESAREAN SECTION

Caesarean section has been classically defined as delivery of a fetus through a surgical incision in the anterior abdominal wall, as Caesarean and section both refer to an incision; some prefer to use the term Caesarean birth or Caesarean delivery to describe the procedure. Primary Caesarean is the first-time operation, while repeat Caesarean refers to the operation done after a prior Caesarean ***(Berghella and Landon, 2012).***

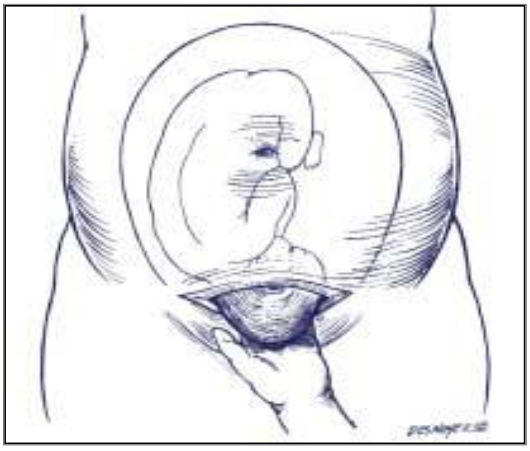

Figure (1): Lower segment caesarean section ***(Hofmeyr et al., 2009).***

History of Caesarean section:

Caesarean section has been part of human culture since ancient times and there are tales in both Western and non-Western cultures of this procedure resulting in live mothers and offspring. According to Greek mythology

Apollo removed Asclepius, founder of the famous cult of religious medicine, from his mother's abdomen. Numerous references to caesarean section appear in ancient Hindu, Egyptian, Grecian, Roman, and other European folklore. Ancient Chinese etchings depict the procedure on apparently living women.

Figure (2): One of the earliest printed illustrations of caesarean section. Purportedly the birth of Julius Caesar. A live infant being surgically removed from a dead woman. From Suetonius' *Lives of the Twelve Caesars*, 1506 woodcut.

Yet, the early history of caesarean section remains shrouded in myth and is of dubious accuracy. Even the origin of "caesarean " has apparently been distorted over time. It is commonly believed to be derived from the surgical birth of Julius Caesar; however this seems unlikely since his mother

Aurelia is reputed to have lived to hear of her son's invasion of Britain. At that time the procedure was performed only when the mother was dead or dying, as an attempt to save the child for a state wishing to increase its population. Roman law under Caesar decreed that all women who were so fated by childbirth must be cut open; hence, caesarean . Other possible Latin origins include the verb "caedare," meaning to cut, and the term "caesones" that was applied to infants born by postmortem operations. Ultimately, though, we cannot be sure of where or when the term caesarean was derived. Until the sixteenth and seventeenth centuries the procedure was known as caesarean operation. This began to change following the publication in 1598 of Jacques Guillimeau's book on midwifery in which he introduced the term "section." Increasingly thereafter "section" replaced "operation ***(http://www.nlm.nih.gov/exhibition/Caesarean/part1.html)***

By the middle ages, delivery of a baby through an incision in the mother's abdomen was well described-and so was the subsequent death of the mother. In the nineteenth century, the method of caesarean delivery was well-known in medical practice, yet rarely performed. Prior to the mid-nineteenth century, caesarean delivery was associated with an essentially 100% death rate for the mother. Looking back at medical practice at that time, it is not hard to understand why?

First, doctors had no understanding of what today is called the **germ theory of disease** (the theory that diseases are due to the presence of microorganisms in the body); therefore, they made no attempts to sterilize surgical instruments or wash their hands. Thus, many women acquired serious infections during the birthing process and, since antibiotics were unknown until a century later, these infections resulted in many deaths.

Second, blood transfusions were not performed until the twentieth century, and many women died from blood loss during delivery before this time. Even today, blood transfusions are sometimes necessary as a result of blood loss at the time of caesarean section; in the past, there was no way to help these women.

Finally, until well into the twentieth century, anesthetic techniques were very primitive. This not only made the operation more difficult for the doctor but also made it a horrendous experience for the mother. Undoubtedly, this also increased the rate of complications.

For the most part, these problems have been solved today and death or serious disability resulting from caesarean section is an extremely rare event. On the contrary, caesarean section can be credited with saving the lives of innumerable mothers and infants over the past century, and it can truly be

considered one of the major achievements of modern medicine ***(http://www.healthline.com/health/pregnancy/history-Caesarean -section)***

The first successful caesarean section was performed in America took place in what formerly Mason county, Virginia (now Mason county West Virginia), in 1794. The procedure was performed by Doctor Jesse Bennett on his wife Elizabeth ***(Woman's IIIs, 2009).***

Incidence and Rate of Caesarean Section:

The total caesarean section rate, defined as the percentage of caesarean deliveries out of all birth in a given year, similar to the total Caesarean section rate, the primary Caesarean delivery rate, defined as the percentage of Caesarean deliveries out of all births to women who have not had a previous Caesarean delivery also has increased ***(MacDorman et al., 2011).***

Epidemiologic data report a Caesarean section incidence of 20- 30 % worldwide, with comparable rate in high-income and low-income Countries ***(Khawaja et al., 2009).***

The current rate of Caesarean section which is approximately 4-5 folds greater than that of the 1970s, can be attributed to factors such as assumed benefit to the fetus, low maternal risk, and social preference ***(Toy et al., 2011).***

This increasing incidence has been observed despite the recommendation of the World Health Organization (WHO) to keep it below 10-15 % ***(Rozenberg, 2004).***

Caesarean delivery rates have risen in the United States in a dramatic fashion from less than 5 % in the 1960s to 32.8% by 2008.

Among the reasons for this increase are:

1) Continued increase in primary caesarean deliveries for dystocia, failed induction and abnormal presentation;
2) An increase in the proportion of woman with obesity, diabetes mellitus and multiple gestation, which predispose to Caesarean delivery;
3) Increased practice of Caesarean delivery on request;
4) Limited use of trial of labor after caesarean delivery (TOLAC), owing to both safety and medico legal concerns ***(Berghella and London, 2012).***

Indications for caesarean section:

American College of Obstetricians and Gynecologists (ACOG) mapped the indications for primary caesarean section in to 15 predefined categories as follows:

Failure to progress (arrest of dilatation in the first stage of labor or arrest of decent in the second stage of labor) and

cephalo pelvic disproportion; non reassuring fetal heart rate tracing and fetal distress; fetal mal presentation; suspected fetal macrosomia; preeclampsia and eclampsia; chorioamnionitis; fetal anomaly; multiple gestation; obstetric factors (uterine rupture, cord prolapse, placenta Previa, vasa Previa,placenta abruption, or other obstetric emergency) previous uterine scar (including hysterotomy or myomectomy);human immuno-deficiency virus and herpes simplex virus; history of shoulder dystocia and shoulder dystocia with this pregnancy ***(Boyle et al., 2013).***

Other indication in the elective category included maternal request, multi parity-women desiring tubal ligation, advanced maternal age, diabetes mellitus, human papilloma virus, post term or postdates, pregnancy remote from term group B streptococcus, polyhydramnios, fetal death and social or religious concerns, other indications include all maternal factor not elsewhere specified ***(Boyle et al., 2013).***

CAESAREAN SECTION FOR DIFFICULT LABOUR OR DYSTOCIA:

In the developed world the increasing caesarean section rate for dystocia or poor progress in labor contributes at least a third to the overall caesarean section rate, and repeat caesarean section following primary caesarean section contributes at least another third ***(Penn et al., 2001).***

Protraction disorders (e.g., slower than normal progress) or arrest disorders (e.g., complete cessation of progress).These disorders are the most common indication for primary caesarean delivery. In one study of 733 women who had unplanned caesareans, 68 percent of the deliveries were due to lack of progress in labor ***(Gifford et al., 2000).***

Protraction and arrest disorders are common. Reported incidences vary among studies due to differences in the author's definition of dystocia, as well as differences among study populations (e.g., gestational age range, personal characteristics). About 20 percent of all labors ending in a live birth involve a protraction and/or arrest disorder ***(Zhu et al., 2006).***

The risk is highest in nulliparous women with term pregnancies. As an example, a prospective Danish study in low risk nulliparous at term reported an incidence of 37 percent ***(Kjaergaard et al., 2009).***

CAESAREAN SECTION FOR FETAL DISTRESS;

Fetal distress is a widely used but poorly defined term. Current methods of assessing the condition of the fetus as non-stress test and biophysical profile are poorly predictive of those who are genuinely compromised, and end-point assessment of the neonatal condition by Apgar scores or umbilical blood gas data is poorly predictive of long-term neuro-developmental defect ***(Penn et al., 2001).***

The most common fetal heart rate abnormality was persistent bradycardia followed by late deceleration and decreased beat to beat variability ***(Roy et al., 2008).***

CAESAREAN SECTION FOR PREVIOUS CAESAREAN SECTION;

One of the most common indications for caesarean section is repeat caesarean section. It is normal practice to advice women with two or more previous CS to have a repeat elective CS at term because there are concerns about an increased risk of uterine rupture with multiple prior caesareans ***(Landon, 2010).***

CAESAREAN SECTION FOR BREECH PRESENTATION;

Perinatal mortality, neonatal mortality, or serious neonatal morbidity was significantly lower for the planned caesarean section group than for the planned vaginal birth group. No differences between groups in terms of maternal mortality or serious maternal morbidity ***(Hannah et al., 2000).***

CAESAREAN SECTION FOR THE DELIVERY OF THE PREMATURE FETUS;

Premature breech presentation;

In common with all premature births, the antecedents of premature breech delivery are often morbid. It is often the