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Maintaining Postpartum Bleeding: Effects of Tranexamic Acid

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MAINTAINING POSTPARTUM BLEEDING: EFFECTS OF TRANEXAMIC ACID

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Abstract

Background/Purpose: The purpose of this literature appraisal is to determine the effectiveness of tranexamic acid (TXA) and its ability to stabilize postpartum bleeding. TXA is an antifibrinolytic pharmacologic drug found to reduce blood loss associated with trauma and patients undergoing major surgeries. When administered in combination with other uterotonics, the World Health Organization predicts the prophylactic use of TXA could globally improve the morbidity and mortality rates associated with postpartum hemorrhaging.

Theoretical Framework: Kurt Lewin's change theory was used in the development of this literature review. The Lewin change theory emphasizes the importance of change and development within a medical institution. Lewin's theory is categorized into three stages consisting of the unfreezing, change, and refreezing models.

Methods: Twenty research articles that pertained to postpartum hemorrhaging and/or the effects of TXA on postpartum bleeding were assessed. The Johns Hopkins research evidence appraisal tool was used to evaluate all articles included in this literature appraisal.

Results/Findings: The need for TXA among various maternal groups was assessed. High risk patients were found to be in greater need for TXA during postpartum care. TXA has also been found to reduce the need for uterotonics, improve hemoglobin and hematocrit levels, and decrease rates of postpartum hemorrhaging. Potential adverse effects and costs associated with TXA use were also explored.

Implications for Research and Practice: The prophylactic use of TXA is significant to midwifery and caring for women. Midwives may administer TXA to reduce the patient's risk of maternal death and injury related to postpartum bleeding. The use of TXA is particularly

important for healthy postpartum transitions among at-risk patients and patients in developing nations. *Keywords: Postpartum hemorrhaging, Postpartum hemorrhage, Tranexamic acid (TXA), Kurt Lewin Theory, vaginal birth, cesarean birth*

Table of Contents

Chapter 1: Introduction

There is universal consternation surrounding labor and childbirth, including hemorrhaging during the postpartum period. The threat of experiencing a postpartum hemorrhage can be debilitating for women. Excessive bleeding during the postpartum period increases rates of morbidity and mortality among maternal patients. According to the American College of Nurse Midwives (ACNM; 2017), women who have suffered from postpartum hemorrhaging are at increased risk of organ shock and long term disability.

Laboring women across the globe are at risk for postpartum bleeding. The ACNM (2017) reports that roughly 125,000 women in the United States experience a postpartum hemorrhage every year. In addition, an estimated 130,000 maternal deaths are associated with postpartum hemorrhaging throughout the globe (ACNM, 2017). In fact, hemorrhaging is the leading cause of maternal morbidity in the United States (American College of Obstetrics and Gynecologist [ACOG], 2017). Postpartum hemorrhage has also been identified as a leading cause of maternal death in developing countries (World Health Organization [WHO], 2017). The WHO (2017) reported over a quarter of global maternal deaths are associated with bleeding, which occurs in the third and fourth stages of labor. Postpartum bleeding may occur up to 6 weeks after the delivery; however, the majority of bleeds occur during the first 24 hours of delivery. The WHO (2017) defines postpartum bleeding as blood loss exceeding 500 ml. Bleeding that surpasses 1,000 ml within 24 hours is classified as severe postpartum hemorrhaging (WHO, 2017). While uterine atrophy remains the leading cause for postpartum bleeds, hemorrhaging can also be associated with vaginal and cervical lacerations, retained placenta, and uterine rupture; in these cases, women with little or no preexisting risk may experience a hemorrhage (WHO, 2017).

However, pre-existing maternal comorbidities will increase a patient's risk of excess bleeding (WHO, 2017). For example, patients suffering from anemia or coagulation disorders may be at an increased risk for bleeding or may display more severe symptoms from postpartum bleeds (WHO, 2017).

Statement of Purpose

The purpose of this literature review is to assess postpartum outcomes related to tranexamic acid (TXA) use in the third and fourth stages of labor. TXA is an antifibrinolytic agent used to stabilize bleeding. Postpartum hemorrhaging is the leading cause of death during childbirth. Numerous studies were evaluated to determine the benefits and effects of TXA during the third and fourth stages of labor (WHO, 2017). This paper will examine the effects of TXA treatment on maternal hemorrhaging, cost efficiency in midwifery, and maternal delivery modes.

Evidence Demonstrating Need

The management of postpartum hemorrhaging is vital to maternal well-being. To improve postpartum outcomes, our health care system requires adjustments that incorporate TXA into routine obstetric care. During the postpartum transition, minimal blood loss is expected; blood loss up to 500 ml is a natural occurrence during the third stage of labor (WHO, 2017). However, blood loss surpassing 500 ml is considered a hemorrhage (WHO, 2017). The majority of postpartum bleeds occur during the third and fourth stages of labor during which a midwife is responsible for treating and stabilizing the patient's bleeding (WHO, 2017).

In current obstetric care, patients are treated with expectant or active management; midwives determine patient care based on their preferences and hospital policies (WHO, 2017). Midwives practicing expectant treatment allow the placenta to separate from the uterine wall

without manual assistance. The placenta is spontaneously delivered with nipple stimulation, maternal pushing, and gravity. During expectant treatment, the midwife does not clamp the umbilical cord until it ceases to pulsate and post-delivery uterotonics are not routinely provided. During expectant management, the body undergoes the postpartum transition with minimal assistance from the midwife; however, patients are also at greater risk for significant postpartum bleeding. Therefore, the WHO (2017) has recommended providers practice active rather than expectant management.

Active management reduces postpartum hemorrhaging incidences (WHO, 2017). With active management, the midwife stabilizes the patient with various interventions, including routine treatment of postpartum patients with post-delivery uterotonics (WHO, 2017). Midwives currently use intravenous (IV) oxytocin, intramuscular (IM) oxytocin, misoprostol, syntometrine, and IM ergometrine. Of these treatment options, the WHO (2017) recommends routine use of IV or IM oxytocin. Uterotonics can be appropriately administered during multiple time points including the crowning of the fetus, delivery of the anterior shoulder, delivery of the fetus, and before or after placental delivery (WHO, 2017). Delayed cord clamping is also recommended during active management. The midwife will begin cord traction when signs of placental separation are observed (WHO, 2017). Cord traction may also be initiated before spontaneous placental separation. In addition to cord traction, midwives may also implement uterine massage. Midwives also play an active role in assessing uterine tone and bleeding every 15 min during the fourth stage of labor (WHO, 2017). ACNM (2017) has suggested active management will:

- Reduce the need for transfusion of blood products
- Reduce rates of postpartum hemorrhaging

- Minimize the use of additional uterotonics within 24 hr of the postpartum recovery period (as cited in WHO, 2017)

The WHO (2017) supports TXA use in postpartum management. In their millennium development goals report, the WHO (2017) addressed the need for obstetric service refinement. According to Callaghan et al., (2010) postpartum hemorrhaging increased 26% from 1994 to 2006. However, the WHO has determined prompt improvements to the third stage of labor will decrease postpartum bleeding occurrences among mothers (WHO, 2017). Therefore, the WHO (2017) recommended adding TXA to active care in the third and fourth stages of labor. TXA can decrease postpartum hemorrhaging incidences, particularly in low-income communities, and prevent mortality and morbidity rates associated with childbirth. The ACNM (2017) also supported the use of TXA post vaginal and cesarean deliveries. Accordingly, the midwifery hallmark supports TXA use to promote health, prevent disease, and educate women. Midwifery standards to "incorporate evidence-based care into clinical settings" also justifies TXA use (ACNM, 2020, p. 1). TXA was originally used to manage blood loss during major surgeries (American College of Obstetricians and Gynecologist [ACOG, 2017]). In recent years, the antifibrinolytic agent has shown effectiveness during the management of postpartum hemorrhaging. Uterotonics are currently used in routine postpartum care; however, evidence has supported the use of TXA in combination with uterotonics, (ACOG, 2017) because TXA may be safely combined with routine uterotonics. Therefore, the WHO (2017) has supported the use of TXA to minimize and prevent excessive bleeding post-delivery during the transition phase. Midwives are encouraged to administer TXA within 3 hr of delivery (Mielke & Obermeyer, 2020). To adhere to evidence-based practice, midwives are responsible for incorporating TXA

into postpartum care. Continuous change and patient care updating are encouraged in midwifery. ACOG (2017) found updates in obstetrical practices have improved maternal outcomes by 10% from 1989 to 2009. The WHO (2017) has suggested that including TXA in midwifery practice will also increase rates of positive maternal outcomes. However, challenges may slow the process of TXA use in obstetric care. Although ACOG (2017) has recognized the benefits of TXA, the drug has been placed in Stage 2 of the algorithm for postpartum hemorrhaging. IV hydration, oxytocin, hemabate, and methergine are considered first line drugs. Therefore, the algorithm supports TXA use when first line uterotonics have failed. Nevertheless, Simonazzi et al. (2015) found TXA was most effective when given prior to maternal hemorrhage. These findings suggested TXA should be considered as a routine drug for blood loss management in obstetrical care.

Significance to Nurse Midwifery

Midwives have practiced for millennia. Midwifery has been used as early as biblical times. The Bible recognizes midwives as vital components of the birthing process, stating “God was good to the midwives, and the people multiplied and became more numerous” (King James Bible, 1769/2017, Exodus 1:20). The Hebrew word for midwife translates to “childbirth-assisting woman.” The first biblical reference to midwifery is in the account of Rachel's birth to Benjamin. The Bible depicted Rachel's childbirth experience as long and strenuous. Yet, the midwife was able to calm Rachel and help her bond with her son and name him (King James Bible, 1769/2017, Genesis 35:17).

Since the start of midwifery, midwives have been responsible for assisting women with birth and newborn bonding. The Frontier School of Midwifery was established in 1925, initiating

nurse-midwifery as a recognized profession in the United States (CITE). Today, midwives are qualified to provide care and treatment to women from adolescence to menopause. Certified nurse-midwives have mastered two medical competencies: nursing and a master or doctorate degree specializing in nurse-midwifery. All certified nurse-midwives must complete their midwifery education from a facility approved by the Accreditation Commission for Midwifery Education. Upon achieving a graduate degree in midwifery, graduates are required to pass the American Midwifery Certification Board exam (ACNM, 2020).

The majority of issues in women's services could be ameliorated with the assistance of a midwife. Improvements are made to maternal and newborn health when midwifery philosophy is applied to patient care. The midwife empowers women to take control of their bodies while promoting patient education and natural paths to labor and childbirth. The WHO (2017) has stressed the significance of midwives, defined as skilled practitioners who aim to provide optimal care to women, families, and infants. The use of midwives will improve maternal and newborn outcomes while globally ensuring justice for women (WHO, 2017). Midwifery care is also cost efficient and therefore feasible for low-income communities to reinforce (WHO, 2017). The WHO (2017) has found multiple benefits associated with midwifery services with no adverse effects linked to midwifery care.

Certified nurse-midwives play an instrumental role in ensuring the well-being of both women and newborns. Therefore, the ACNM (2017) encourages the global use of midwives for practicing midwives to adhere to the pearls of midwifery; that is, midwives should provide patient care according to evidence-based medical standards, collaboration among medical staff, and midwifery professional judgement. While the ACNM values patience and minimal

intervention, the midwifery pearls also acknowledge the need for prompt, evidence-based intervention and attendance to the patient's physical, mental, and spiritual needs.

Proper implementation of midwifery pearls promotes optimal maternal outcomes and limits adverse effects. Midwives serve as experts in primary gynecological, pregnancy, and postpartum care (ACNM, 2020). Therefore, midwives have a significant influence on the prevalence and subsequent management of postpartum hemorrhaging. During the postpartum stage, midwives are responsible for performing early assessments for postpartum bleeding (Mamakou, 2020). In the presence of a postpartum hemorrhage, midwives initiate early intervention to stabilize blood loss, thereby preventing further obstetrical maladies (Mamakou, 2020). According to the ACNM (2020), there is approximately a 12% increase in positive outcomes among women and newborns who have received midwifery care, meaning the implementation of midwives can reduce mortality and morbidity rates associated with postpartum hemorrhaging.

Theoretical Framework

All women desire a safe delivery. Yet, hemorrhaging remains one of the leading causes of death among postpartum mothers (Alam & Choi, 2015). To protect mothers, midwives must become educated on the use of TXA. However, adapting to evidence-based practice can be a difficult task. Therefore, the present investigation considered Kurt Lewin's change theory. Change theory illustrated strategies on proper implementation of current practice into health care settings, including midwifery (Shirey, 2013). The purpose of change theory was to aid institutions in the process of transitioning from present practice to the desired practice in a three-step process.

The first step in Lewin's change process is unfreezing (Lewin's et. al, 1951). During unfreezing, the health care institution prepares medical staff for change that will take place in the medical practice. The unfreezing stage is necessary to eliminate potential resistance to change among staff and identify the changing focus. During the unfreezing process, nurses, managers, and providers are presented with issues associated with the current practice and the need to make alterations that would improve patient outcomes. This stage encourages institutions to include staff members in the planning process for implementing modifications to patient care (Lewin's et. al., 1951). Shirey (2013), also recommended round table meetings. During these meetings, staff nurses discuss their potential concerns surrounding TXA implementation. Providers are also presented with the opportunity to question the change implementation process and offer their feedback to the organization. The incorporation of medical staff strengthens the team's understanding of the need for change and decreases staff member's resistance to change.

Upon completing the unfreezing stage, midwives in the institution have acknowledged the need for alteration and may therefore initiate reform. Thus, the second step of Lewin's et. al., (1951) process is the change stage for implementing the updated medical practice. During this stage, collaboration between the organization and staff members is encouraged to determine how and when to install change into the medical setting. During the change period, providers abandon their dedication to former practice. At this time, the organization may begin to train staff members on safe practices and medical policies. Coaching and mentoring programs may also be initiated to improve confidence among medical staff during the change period.

The third and final step of Lewin's et. al., (1951) theory is refreezing. The purpose of the refreezing stage is to commit to the updates made in inpatient care. During this phase, change is

stabilized and reinforced to prevent midwives from reverting to former habits. To promote the continuation of refreezing, the institution must practice continuation of education and staff training. The refreezing stage also requires constructive criticism from management. Feedback and reward from management encourage staff members to consistently practice according to the organizational changes made.

Kurt Lewin's (1951) change theory serves as an appropriate framework for TXAs prophylactic effects on mothers during the transition period. The theory addresses three strategies affiliated with implementing change in an institutional setting (Hussain et al., 2018). The three strategies include, in the following order unfreezing, changing, and finally refreezing. The purpose of this sequence is for midwives to acknowledge recent evidence supporting TXA use and update their practice according to evidence-based care (Shirey, 2013). In this instance, the midwife would implement routine prophylactic use of TXA across multiple work settings including hospital, clinic, and home births. TXA would be administered during the third stage of labor, preferably 2 hours post-birth (Shirey, 2013).

Summary

The use of TXA among midwives promotes optimal patient outcomes. Applying Lewin's theory to TXA administration may promote education on when and how to implement TXA use for midwives internationally. TXA is a cost-efficient drug available to many countries across various settings (Hussain et al., 2018). Therefore, the antifibrinolytic agent can be readily available to women who have risk factors for hemorrhaging and are in low-income settings. The availability of TXA is significant as it supports the midwifery hallmark to “utilize an

understanding of social determinants of health to provide high-quality care to all persons including those from underserved communities" (ACNM, 2020, p. 1).

Chapter 2: Methods

This chapter explores the strategies set in place to identify and review literature on the effects of TXA when given within 3 hours of birth. This chapter also describes search strategies and criteria for inclusion and exclusion. In total, 20 articles met criteria for inclusion. Finally, this chapter considers evaluation criteria for identifying quality and level of evidence across articles.

Search Strategies

Research databases were used to search for applicable studies, including EBSCO, Google Scholar, PubMed MEDLINE, and CINAHL. Key search terms included *TXA, postpartum hemorrhaging,* and *vaginal and cesarean deliveries*. Searches were conducted for articles published between 2010 and 2020. Due to constant changes in medical standards, articles published within the last 10 years were retrieved to ensure the most up to date data. A total of 300 abstracts were retrieved and reviewed. After retrieving articles, their reference lists were reviewed to identify additional scholarly studies. After the elimination of duplicate articles and applying inclusion and exclusion criteria, a total of 20 articles were appropriate for the purpose of this literature appraisal.

Criteria for Inclusion and Exclusion

The studies included in this literature appraisal needed to be original research that addressed the effectiveness of TXA during management of postpartum bleeding. Selected articles evaluated the impact of postpartum TXA use related to route and time of administration. Included articles also explored birthing risk factors and potential interactions or adverse effects associated with maternal TXA use.

The exclusion criteria included systemic reviews, study protocols, and articles published prior to 2010. Studies that did not offer a full text in English were also excluded from this literature appraisal. Furthermore, treatment for bleeds during pregnancy, or TXA use for neonatal trauma patients were excluded from the matrix.

Summary of Selected Articles

After careful review, 20 articles comprising various studies were included in this review. The included articles consisted of one observation study, one prospective cohort study, one quasi-experimental study, and 17 randomized controlled trials. Studies were included from various countries within North America, Europe, Africa, Asia, and the Middle East.

Evaluation Criteria

The quality and strength of articles were appraised using the John Hopkins research appraisal tool. This tool determines strength by measuring articles on a scale of 1 to 5. Level 1 articles are randomized control trials and are the highest level of scientific evidence strength. Level 2 articles are quasi-experimental studies. Level 3 studies include qualitative and nonexperimental studies. Level 4 studies include consensus panels and clinical practice guidelines. Finally, Level 5 articles include clinical reviews, case reports, and opinions of national experts. This literature review included 17 randomized, one quasi-experimental, and two observational studies, with randomized control trials as the majority. According to the research appraisal tool, randomized experiments have the highest strength and are therefore graded as Level 1. One quasi-experimental article was included in this appraisal. Quasi-experiments are second in strength and are therefore graded as a Level 2. Qualitative and nonexperimental studies are graded as Level 3.

After establishing the article's strength, the John Hopkins research appraisal tool determines the quality of the experiment. Article quality was categorized into three levels: (a) strong, (b) good, and (c) poor. The studies in this literature review were classified as either strong or good. Seven of the included articles were strong quality and 13 articles were classified as good quality. Dearholt and Dang (2018) defined strong quality studies as research with a large enough sample size to produce generalizable results. Strong sources produce scientific results that are used to implement recommendations. Good articles also include generalizable and scientific data, however, data is presented in a lesser form. Lastly, poor articles are those with low quality data. These articles lack sufficient scientific data, sample size, and author recommendations.

Summary

For this literature appraisal, articles were retrieved from the Bethel Library, EBSCO, Google Scholar, PubMed MEDLINE, and CINAHL. Appropriate articles for this literature review were determined using the inclusion and exclusion criteria. In total, 20 articles were included in this literature review. Articles were then assessed for strength and quality using the John Hopkins appraisal tool.

Chapter 3: Literature Review and Analysis

Synthesis of Matrix

The matrix was used to display the scholarly articles presented in this literature appraisal and divided into the following sections: purpose, sample, design, measurement, results/ conclusions, recommendations, level, and quality (See Appendix A). The Johns Hopkins research evidence appraisal tool was used to establish article strength and quality. Matrix citations were organized in alphabetical order.

Synthesis of the Major Findings

The following literature review demonstrates evidence on the ability for TXA to improve postpartum hemorrhaging during the third and fourth stages of labor. This review will highlight the route of TXA administration, variations in time of administration, the impact of TXA on high-risk patients, potential adverse effects of TXA, and the cost-effectiveness of the drug.

Administration

The most effective route and timing of TXA administration in the obstetrical setting has been under review. The WHO (2017) has suggested giving 1 g TXA via IV over 10 min within 3 hr postpartum. This review included 15 articles that examined the administration of TXA (Bose & Beegum, 2017; Chandak et al., 2017; Diop et al., 2020; Durand−Zaleski et al., 2020, Gillissen et al., 2017; Gungorduk et al., 2013; Lakshmi, 2016; Ramesh et al., 2015; Roy et al., 2016; Rushulo et al., 2016; Senturk et al., 2012; Sofiene et al., 2015; Woman Trial Collaborators 2017; Wong et al., 2010; Xu et al., 2012).

Route of Administration

The mode of TXA administration may impact the drug's influence on postpartum bleeding. One article assessed oral TXA as a control for postpartum hemorrhaging. Diop et al. (2020) conducted a double-blinded randomized study with 258 hemorrhaging women. Participants in the experimental group were given a one-time dose of 1950 mg of PO TXA in combination with 800 mcg of PO misoprostol and participants in the control group received a placebo pill and 800 mcg of misoprostol. Diop et al. (2020) found oral TXA was an ineffective form of hemorrhaging control. When compared to the experimental group, the control group required similar amounts of additional uterotonics to stabilize bleeding (p = .59; Diop et al., 2020).

Seven studies explored the effectiveness of TXA when administered intravenously (Bose & Beegum, 2017; Durand−Zaleski et al., 2020; Gungorduk et al., 2013; Lakshmi, 2016; Ramesh et al., 2015; Roy et al., 2016; Wong et al., 2010). Bose and Beegum (2017) conducted an experimental study that included 163 women. The experimental group was given 500 mg of IV TXA and the control group was given 600 mg of oral misoprostol. There were minimal differences in patient outcomes between the experimental (470.30 ± 192.548) and control group (491.74 ± 200.043 ml, p = 0.487). Specifically, there were minimal differences between the two groups in postpartum hemoglobin and platelet levels (p = 0.197). Therefore, TXA was not significantly superior to uterotonics.

The previous studies reviewed did not find TXA to be superior, however various studies found the drug to be effective (Durand−Zaleski et al., 2020; Gungorduk et al., Lakshmi, 2016; 2013; Ramesh et al. 2015; Roy et al., 2016; Wong et al., 2010). Durand−Zaleski et al. (2020)

conducted a randomized control trial consisting of 4,079 women. Women in the experimental group received 1 g of TXA and women in the control group were given 1 g of sodium chloride. Durand−Zaleski et al. (2020) found women in the experimental group required less intervention for postpartum hemorrhaging (PPH) compared to the control group (RR = 0.74, 95% CI [0.61, 0.91], $p = .04$). Consistent with these findings, Gungorduk et al. (2013) found 1 g of IV TXA improved PPH outcomes in a randomized control study with 454 women. That is, there were fewer cases of PPH among the TXA group (261.5 ml) compared to the control group (349.98 ml, $p < .001$).

In addition, more women in the control group needed supplementary uterotonics to stabilize bleeding compared to women in the experimental group (RR = 3.18, 95% CI [1.29, 7.81], $p = .007$). Similarly, another randomized study found the group receiving TXA had less blood loss (347.17 ml) from the time of placental delivery to compilation of the cesarean section compared to the control group (517.72 ml, $p < .001$). Finally, Ramesh et al. (2015) also supported IV administration of TXA in a randomized controlled study consisting of 200 women. Findings showed significantly less blood loss in the experimental group 2 hr postpartum ($M =$ 3.80 ml) compared to the control group ($M = 112.25$, $p < .001$) ($p = .002$).

Studies on IM TXA administration were also reviewed in the matrix. A randomized study with 100 participants found IM TXA was effective during the birthing process (Roy et al., 2016). Women in the experimental group received IM TXA and women in the control group received IM sodium chloride. Results showed 22% of women in the control group needed additional uterotonics compared to only 2% in the experimental group, a statistically significant difference ($p < .001$).

Topical use of TXA was also found to reduce bleeding. In a randomized control trial with 125 participants, Wong et al. (2010) investigated the effects of topical TXA in wound areas on bleeding. Participants in the experimental group were given 1.5 to 3 g of TXA mixed with normal saline while the control group was given normal saline to apply to their wounds. Results showed a significant reduction in bleeding among the TXA group by 20% to 25% ($p < .017$), significantly increasing hemoglobin levels by 16% to 17% ($p < .017$) compared to the control group. Results from this study may be applied to understand the potential impact of TXA on cervical, vaginal, and rectal lacerations.

According to the reviews regarding TXA routes the method of administration did impact the efficiency of TXA. PO TXA was not found to effectively manage postpartum blood loss, however, the IM route was found to be moderately effective (Diop et al., 2020; Roy et al., 2016). While 78% of participants were adequately treated with IM TXA, the remaining 22% of participants presented with unstable blood loss and therefore required further intervention to reach equilibrium (Roy et al., 2016). However, IV TXA seemed the most effective blood stabilizer for postpartum bleeding. Topical TXA use was also reviewed. Wong et al. (2010) found topical TXA to be effective among bleeding wounds. Although this study was not specific to birth-related lacerations these findings are significant to postpartum hemorrhaging as they are relatable to vaginal, cervical, and anal wounds during the birthing process.

These studies had multiple strengths and weaknesses. First, Diop et al. (2020) clearly defined postpartum hemorrhaging as at least 700 ml of bleeding and used computerized blocks to sporadically classify patients into experimental and control groups. The computerized placement of groups preserved the integrity of the double-blind study. Second, Bose and Beegum (2017)

evaluated hemoglobin levels of each patient 48 hr prior to delivery and evaluated levels again post-delivery to determine blood loss. Third, Durand−Zaleski et al (2020) evaluated a large sample size of women (N = 4,079). Large sample sizes increase the likelihood that data are generalizable to other populations and settings. Finally, low-risk and high-risk vaginal deliveries were assessed in these studies to help midwives determine how different patients will react to the drug (Gungorduk et al., 2013).

However, there were several limitations across these studies, including the standards for blood loss measurements and the samples chosen for the studies. First, blood loss was determined by visual measurements; therefore, there may be discrepancies in measurements of blood loss (Gungorduk et al., 2013; Lakshmi, 2016). A few of the studies had a sample size of only 100 women, so findings may not be generalizable to the majority of patients (Roy et al., 2016; Wong et al., 2010). Furthermore, Roy et al. (2016) did not include participants with high-risk pregnancies; therefore, it is unknown whether TXA is effective among more vulnerable populations.

Time of Administration

The time of administration may impact the ability of TXA to reach the desired therapeutic effects. The WHO (2017) has suggested administering TXA within 3 hr of time of birth. Nine articles explored the effectiveness of TXA when administered prophylactically prior to delivery versus post-birth (Chandak et al., 2017; Gillissen et al., 2017; Gungorduk et al., 2013; Lakshmi, 2016; Rushulo et al., 2016; Sentilhes et al., 2018; Senturk et al., 2012; Sofiene et al., 2015; Woman Trial Collaborators, 2017; Xu et al., 2012).

In total, five studies supported the use of administering TXA prior to delivery (Chandak et al., 2017; Lakshmi, 2016; Rushulo et al., 2016; Sofiene et al., 2015; Xu et al., 2012). Xu et al. (2012) conducted a randomized study with 174 participants. Compared to the control group (84.7 ± 80.2), the TXA group had lower rates of blood loss when bleeding was assessed 2 hr after c-section (46.6 ± 42.7, $p = .02$). Therefore, the authors recommended administering TXA at least 10 min prior to cesarean births (Xu et al., 2012). Rushulo et al. (2016) also conducted a randomized study that administered TXA to the experimental group 10 min prior to cesarean section. Findings showed TXA was an effective form of bleeding control, with significantly reduced bleeding in the experimental group compared to the control group ($p < .001$). Sofiene et al. (2015) also supported the use of prophylactic TXA in an experiment with 52 low-risk patients. The control group was given 10 ml of normal saline while the TXA group received 10 mg/kg 5 min prior to the first incision of the cesarean section. Overall, the authors found significantly less mean blood loss in the TXA group compared to the control group ($p = .017$), suggesting less oxytocin was needed in the TXA group ($p = .05$). Additionally, Chandak et al. (2017) and Senturk et al. (2012) conducted randomized studies that also supported prophylactic use of TXA2. Chandak et al. (2017) administered 1 g of TXA to the experimental group and sodium chloride to the control group 5 min prior to the start of cesarean sections. Chandak et al. (2017) found postpartum hemorrhaging occurred more often in the control group compared to the experimental group ($p = .049$). Additionally, the control group lost more blood within 2 hr after the cesarean section compared to the experimental group ($p < .001$). Senturk et al. (2012) administered TXA 10 min prior to surgery. Senturk et al. (2012) also found a greater loss of hemoglobin in the control group compared to the experimental group ($p = .034$). In a randomized

control study, Lakshmi (2016) administered TXA 10 min prior to cesarean deliveries. Lakshmi (2016) found only 9.3% of women in the experimental group experienced a 10% hemoglobin compared to 39% of subjects in the control group ($p < .01$).

Four articles discussed TXA use within 3 hr of birth (Gillissen et al., 2017; Gungorduk et al., 2013; Sentilhes et al., 2018; Woman Trial Collaborators, 2017). Women Trial Collaborators (2017) is a randomized study with 20,000 participants ages 16 and above. The study was completed in 193 hospitals across 23 countries (Woman Trial Collaborators, 2017). TXA was found to improve mortality and morbidity risk when given within 3 hr of vaginal and cesarean deliveries. Risk of death related to postpartum hemorrhaging decreased in women who received TXA (RR = 0.81, 95% CI [0.65, 1.00], $p = .045$). There was an average of 1.2% hemorrhage-related deaths among women in the TXA group compared to 1.7% in the control group (RR = 0.69, 95% CI [0.52, 0.91], $p = .008$) (Woman Trial Collaborators, 2017). Sentilhes et al. (2018) supported these findings and found patients who received TXA 2 to 10 min after a vaginal birth had lower rates of postpartum hemorrhaging (7.8%, $p = .004$) than those who did not (10.4%; RR = 0.74, 95% CI [0.61, 0.91*]*, $p = 0.04$). Gillissen et al. (2017) observed 1260 women above the age of 18 from the Netherlands. Women were divided into three groups including early TXA administration (1 hr post birth), late TXA administration (4 hr post birth), and the control group. Gillissen et al. (2017) found patients treated with late TXA experienced more bleeding (1,300 ml) than the control group treated with oxytocin (800 ml). The incidence of hemorrhagic shock was also higher in early admission 31% compared to late or no TXA administration 21% (Gillissen et al., 2017). Contrary to Gillissen et al. (2017), findings from Gungorduk et al. (2013) showed TXA was beneficial when administered within 3 hr of post-vaginal births. Specifically,

Gungorduk et al. (2013) found significantly less blood loss in vaginal deliveries in the TXA group (261.5 146.8, $p < .001$) than the control group (349.98 188.85 mL). The control group also required more uterotonics than the TXA group (RR = 3.18, 95% CI [1.29, 7.81], $p = .007$).

Large study samples and extended study periods were strengths in a number of the studies presented (Gillissen et al., 2017; Sentilhes et al., 2018; Woman Trial Collaborators, 2017). However, some limitations were present in the remaining studies, including small sample sizes and short study terms (Gungorduk et al., 2013; Rushulo et al., 2016; Sofiene et al., 2015; Xu et al., 2012). Xu et al. (2012) conducted their study in a grade IIIA hospital, so different findings may emerge in suboptimal settings. Additionally, participants were randomized using sealed envelopes instead of electrical data which may cause errors in the randomizing process (Xu et al., 2012). Lakshmi (2016) reported failure to assess long-term effects of TXA as a limitation.

Hemorrhaging Risk Factors

The previous health of the mother and mode of delivery may impact the extent of postpartum bleeding. The articles reviewed in this section assessed risk factors for PPH and the impact of TXA on these high-risk patients. One prospective cohort study with 1,188 participants reviewed the risk associated with hemorrhaging between vaginal and cesarean deliveries (Ononge et al., 2016). Postpartum hemorrhaging was defined as bleeding over 500 ml. Hemorrhaging risk factors were greater in vaginal deliveries among mothers who had macrosomia deliveries (aOR = 2.14, 95% CI [1.02, 4.47], p= 0.01) or HIV positive sero-status (aOR = 2.26, 95% CI [1.20, 4.25], p = 0.03), including vaginal multiples (aOR = 2.26, 95% CI [0.58, 8.79], p = 0.02). However, women having cesarean deliveries were at greater risk for

hemorrhaging than vaginal births (aOR = 7.54, 95% CI [4.11, 13.81], p <0.001). These findings are significant for identifying patients in greater need of TXA management.

Research has also found anemia is a risk factor for hemorrhaging. Goswami et al. (2013) conducted a randomized control study consisting of 90 anemic patients with hemoglobin levels between 7-10 g. Participants had cesarean sections scheduled and were either randomized into Group 1 who received 10 mg/kg of TXA, Group 2 who received 15 mg/kg of TXA, or Group 3 who received a placebo. TXA and placebos were administered 20 min prior to the start of the cesarean delivery. Group 1 experienced 377 ml of blood loss, Group 2 experienced 261 ml of blood loss, and Group 3 experienced 527 ml of blood loss. Therefore, TXA was found to reduce blood loss among anemic patients during cesarean section (Goswami et al., 2013).

Roberts et al. (2013) also assessed risk factors for hemorrhaging. However, this study specifically examined the benefits of TXA among 20,211 operative and trauma patients in a randomized control trial. Roberts et al. (2013) found TXA was an effective treatment option for trauma patients and therefore supported the use of TXA among at-risk and trauma patients. Specifically, participants in the TXA had significantly lower mortality and morbidity rates (M= 1,463, 4.5%) compared to the control group (M= 1,613, 16%; RR = 0.91, 95% CI [0.85, 0.97], p = .004). Findings from this study can be used to predict the need and effectiveness of TXA among women who experience vaginal trauma from cesarean deliveries and vaginal births.

Delivery mode was found to have significant impacts on a patient's risk for bleeding and need for TXA therapeutics. Ononge et al. (2016) determined that mothers who suffer from comorbidities prior to pregnancy are at greater risk of unstable postpartum bleeding. Significant amounts of postpartum bleeding were observed among mothers who had HIV, diabetes, or

macrosomia births (Ononge et al., 2016). Additionally, anemic patients were found to be predisposed to hemorrhaging post-delivery (Goswami et al., 2013). Patients delivering via cesarean section were at greatest risk for postpartum bleeding when compared to high- and low-risk vaginal births (Ononge et al., 2016). However, Goswami et al. (2013) and Roberts et al. (2013) found TXA to be a therapeutic option for the maintenance of postpartum hemorrhaging among patients with predisposed risk for unstable postpartum bleeding.

Multiple strengths and weaknesses were discovered among the reviewed studies. Ononge et al. (2016) included a large sample size of 1,188 women. Roberts et al. (2013) also had a large sample size of 20,211 participants. The sample sizes found in Ononge et al. (2016) and Roberts et al. (2013) are significant as the sample sizes are generalizable to the general population. Second, Ononge et al. (2016) assessed the use of TXA across multiple types of deliveries, including various types of vaginal and cesarean births, therefore, the risk for hemorrhaging was observed among a diverse patient population. These studies also included a number of limitations related to experiment location and sample size. First, the Ononge et al. (2016) study was conducted in Uganda; as such, the study did not assess the impacts of TXA on various populations and ethnic groups and findings may therefore be limited to patient populations in Uganda. Second, Goswami et al. (2013) included a relatively small sample size in their study which may limit generalizability.

Potential for Adverse Effects

Numerous studies have acknowledged the potential risk associated with the use of TXA, particularly concerning adverse neonatal effects and maternal thrombosis development, therefore, it is important to explore TXA safety concerns (Chandak et al., 2017; Gilad et al.,

2014; Ramesh et al., 2015; Sentilhes et al., 2018). Three studies assessed the potential for adverse effects among neonatal development and risk for thrombosis among mothers given TXA (Gilad et al., 2014; Ramesh et al., 2015; Sentilhes et al., 2018).

Gilad et al. (2014) reviewed adverse effects of TXA in the newborn. Gilad et al. (2014) conducted a prospective, controlled observational study with 21 women in the experimental group and 42 women in the control group. The experimental group consisted of women who received TXA during their pregnancy or postpartum period. Women (N =63) in the experimental and control groups received a follow-up telephone interview regarding neonatal symptoms, production of breastmilk, and newborn outcomes at 1 to 3 years of age. Gilad et al. (2014) found one mother in the experimental group had lower milk production compared to the control group, however, this finding was not statistically significant (p = 1.00). Another mother in the experimental group reported infant restlessness, while one mother in the control group reported gastroesophageal reflux (p = 1.00). One child from the experimental group showed weight below the third percentile compared to four children in the control group (p = 0.66). Gilad et al. (2014) did not find statistical significance between adverse effects found between the experimental and control group. Therefore, no adverse effects related to TXA were found among newborns. Ramesh et al. (2015) supported these findings in a randomized study of 200 women and found no significant differences in newborn appearance, pulse, grimace, activity, and respiration (APGAR) scores between women in the experimental and women in the control group (p = 0.50).

Sentilhes et al. (2018) reviewed the thromboembolic effects of TXA in a randomized control trial of 4,079 women having vaginal births. Sentilhes et al. (2018) found TXA did not

increase the risk for thromboembolic episodes among women in the study group (0.1%) compared to women in the control group (0.2%; RR = 0.25, 95% CI [0.03, 2.24], $p = 0.37$). However, Sentilhes et al. (2018) found TXA increased the risk of mild vomiting episodes among the TXA group when compared to the control ($P<0.001$).

In summary, empirical evidence has demonstrated little potential adverse effects of TXA administration. There were no statistical differences found between newborns exposed to TXA through breastfeeding compared to those without TXA exposure (Gilad et al., 2014). Therefore, TXA has not been found to significantly and negatively impact neonatal health or development (Gilad et al., 2014). Likewise, TXA was not found to significantly increase risk for developing thromboembolic episodes (Sentilhes et al., 2018). However, TXA may cause mild gastrointestinal discomfort during use (Sentilhes et al., 2018).

Various strengths and limitations can be observed from the studies reviewed. Ramesh et al. (2015) and Sentilhes et al. (2018) included large sample sizes in their studies, as a result these finds are relatable to the general population. An additional strength was that Gilad et al. (2014) conducted the experiment for 3 years which allowed researchers to observe the impacts of TXA on the neonate into childhood. However, a limitation was that Gilad et al. (2014) was a pitetit study of 63 participants meaning the results found may not reflect the general population.

Resources

Cost and availability must be addressed when implementing TXA into a medical institution. As mentioned earlier, postpartum hemorrhage significantly contributes to maternal mortality. It is essential that health care workers find effective and cost-conscience interventions that can be used across the globe. Two articles assessed the cost implications of TXA in

obstetrical care (Durand−Zaleski et al., 2020; Roberts et al., 2013). In both studies, TXA administration was found to be cost effective for medical institutions. First, Roberts et al. (2013) found mortality and morbidity rates significantly decreased in patients who received TXA within 3 hr of trauma (M= 1,463, 14.5%) compared to patients who did not receive TXA (1,613, 16%; RR = 0.91, 95% CI [0.85, 0.97], p = .004). Therefore, hospitals were able to make significant financial savings among patients who received TXA treatment. Roberts et al. (2013) determined the incremental cost for administering TXA versus not administering TXA was $48,002. Therefore, the incremental cost per life year was $68 (Roberts et al., 2013). Further, TXA administration saved 755 life years for every 1,000 patients in the United Kingdom (Roberts et al., 2013). Durand−Zaleski et al. (2020) also supported the cost effectiveness of TXA for patients. When TXA and non-TXA patients giving birth vaginally were compared, TXA patients spent an average of $7,497 compared to an average of $9,945 for non-TXA patients (Durand−Zaleski et al., 2020). The control group also spent more money on blood products. In total, the control group spent an average of $10,061 on additional medications and blood products compared to $6,037 spent among the TXA group.

The assessed articles demonstrate that TXA is a cost effective treatment option. Durand−Zaleski et al. (2020) and Roberts et al. (2013) report TXA to be an economical option for patients and medical institutions.Therefore, it is financially feasible to make TXA available to midwives and patients in low income communities and underdeveloped countries.

Summary

Twenty articles were reviewed to investigate the impact of TXA on postpartum bleeding. The majority of included articles were randomized control studies. The articles included in the

literature appraisal were classified as either strong or good quality based on the Johns Hopkins research evidence appraisal tool. The reviewed research supported TXA given prior to delivery, within 3 hr of delivery, and after a postpartum hemorrhage has occurred can effectively minimize postpartum hemorrhaging. Research has also shown TXA is a cost effective drug and is therefore available to midwives in developing countries.

Chapter 4 will discuss implications for nurse midwifery practice and the need for further research. Finally, Kurt Lewin's (1951) theory will be used to explore how to integrate TXA use into midwifery care.

Chapter 4: Discussion, Implications, and Conclusions

The purpose of this literature appraisal is to determine the function of TXA for maintaining postpartum bleeding. Twenty scholarly articles were selected and assessed using the John Hopkins research appraisal evidence tool. Chapter 4 explores trends and gaps in the literature, implications for midwifery practice, and provides recommendations for future research. In addition, Kurt Lewin's (1951) theory is applied to the integration of TXA in midwifery practice.

Literature Synthesis

The research question that informed this literature review explored the impact TXA has on postpartum bleeding during the third and fourth stages of labor. In conclusion, the body of research reviewed found TXA was an effective treatment option for maintaining postpartum bleeding. Treatment modalities included assessment of route and time of TXA administration. Multiple outcome factors were taken into consideration including, hemorrhaging risk factors, adverse effects, and resources associated with TXA use were assessed. Since scholarly articles explored the effect of TXA via multiple routes, it is vital to identify the most effective forms of TXA administration. Furthermore, significant connections were made across research in regard to when TXA should be administered around time of birth. While some articles supported prebirth administration, other articles advocated for the use of TXA within 3 hr of birth (Woman Trial Collaborators, 2017; Xu et al., 2012).

Trends and Gaps in Literature

Route of Administration

Multiple themes were established in the section on route of administration. The TXA administration routes explored included oral, intravenous, IM, and topical administration (Bose & Beegum, 2017; Diop et al., 2020; Durand−Zaleski et al., 2020; Gungorduk et al., 2013; Lakshmi, 2016; Ramesh et al., 2015; Roy et al., 2016; Wong et al., 2010). A number of TXA routes were explored to determine its effectiveness across multiple settings including home, hospital, and in-center births that may require various forms of TXA (Diop et al., 2020). Diop et al. (2020) concluded TXA maintained postpartum bleeding at significantly greater levels compared to uterotonics. While 56.9% of the TXA group required additional uterotonics, 60.2% of the control group received supplementary uterine control. In all, the average blood loss in both the experimental and control groups was 700 ml (Diop et al., 2020).

A number of studies assessed blood loss among postpartum patients given IV and IM TXA. These forms of TXA use are ideal for hospital and birthing center deliveries where IV and IM administration are feasible (Gungorduk et al., 2013). Only one study found IV TXA was ineffective (Bose & Beegum, 2017), while the majority of scholarly articles found IV TXA was effective and therefore supported the use of IV TXA (Durand−Zaleski et al., 2020; Gungorduk et al., 2013; Lakshmi, 2016; Ramesh et al., 2015). Lakshmi (2016) concluded when TXA was incorporated intravenously in care, only 9.6% of women required subsequent bleeding control while 39% of women not given TXA needed additional assistance to stabilize bleeding during the postpartum stage. IM TXA was also found to promote stabilized postoperative hemoglobin values. Roy et al. (2016) also found postoperative hemoglobin drop levels around 0.2% g among

participants in the experimental group and around 0.7% gm among participants in the control group.

Furthermore, topical TXA was explored due to its availability for home, hospital, and birthing center births. Wong et al. (2010) found topical TXA was effective among wound trauma patients. That is, patients who received TXA displayed 16% to 17% higher hemoglobin levels compared to patients who received alternate treatment. However, a gap in the Wong et al. (2010) experiment was that it did not specifically study the effectiveness of TXA among birth related lacerations. Therefore, further research is needed to verify therapeutic response to topical TXA when used in obstetrics.

Time of Administration

Understanding the significance of the timing of TXA administration is important as it will influence the therapeutic effects of the drug. A number of studies have argued TXA is most effective when administered prior to delivery (Chandak et al., 2017; Lakshmi, 2016; Rushulo et al., 2016; Sofiene et al., 2015; Xu et al., 2012). However, other scholarly sources have argued TXA is most effective when given within 3 hr of delivery (Gillissen et al., 2017; Gungorduk et al., 2013; Sentilhes et al., 2018; Woman Trial Collaborators, 2017). Timing of TXA administration is vital to explore as it will enable midwives to appropriately choose when to administer TXA. According to scholarly articles explored in this literature appraisal, TXA has shown remarkable effects on preserving blood loss when administered any time prior to 3 hr post-birth (Chandak et al., 2017; Gillissen et al., 2017; Gungorduk et al., 2013; Rushulo et al., 2016; Sentilhes et al., 2018; Senturk et al., 2012; Sofiene et al., 2015; Woman Trial Collaborators, 2017; Xu et al., 2012). However, a gap in literature remains on whether TXA

should be administered as a single dose or at various times throughout treatment. Further research is needed to determine if TXA is most effective when given in multiple doses as opposed to one single dose (Chandak et al., 2017).

Hemorrhaging Risk Factors

Risk for hemorrhaging was explored to identify which patients were at greater risk of experiencing postpartum hemorrhages and determine the success of TXA among at-risk populations, including patients with HIV, anemic patients, and cesarean patients. Women giving birth to macrosomic newborns were also classified as an out-risk patient population (Ononge et al., 2016). Findings across articles supported the use of TXA among patients at risk for hemorrhaging (Goswami et al., 2013; Roberts et al., 2013; Ononge et al., 2016). While Ononge et al., 2016) explored which patients were at greater risk for postpartum hemorrhaging the study was limited to Uganda. Therefore, the effectiveness of TXA among various ethinic groups remains a gap in literature.

Adverse Effects

Potential adverse effects of TXA were explored to determine safety concerns in TXA administration. Xu et al. (2012) recommended avoiding TXA prior to delivery due to potential negative impacts on the unborn fetus. However, other scholarly articles that explored the adverse impact of TXA found no detrimental effects on development, feeding, or stability of health among newborns whose mothers received TXA (Gilad et al., 2014; Ramesh et al., 2015). However, potential adverse effects of TXA on women with cardiovascular, stroke, or clotting diseases remains a gap in literature (Sentilhes et al., 2018).

Implications for Midwifery

The midwifery community is significant for ensuring safe pregnancies and births. Research has found TXA to be an effective option for the prevention of postpartum hemorrhaging. Therefore, routine use of TXA should be implemented into the active management of postpartum care. It is imperative midwives understand the positive impact TXA can have on women at the time of birth. The core competencies of midwifery encourage midwives to seek and establish their care according to the most current medical standards (ACNM, 2017). Therefore, the ACNM (2017) supports the appliance of TXA into midwifery practice. Including TXA in midwifery practice may significantly reduce experiences of hemorrhaging among women. In fact, 4.8% of all home and clinic births without the use of TXA in obstetrics have resulted in emergent hospital transfers related to blood loss (Mielke & Obermeyer, 2020). Deregulation in the patient's coagulation and fibrinolytic systems occurs during a postpartum bleed exceeding 1000 ml, resulting in an exhaustion of platelets and fibrinogen. However, TXA has been found to limit postpartum bleeding and maintain maternal stability through its antifibrinolytic factors (Mielke & Obermeyer, 2020).

It is feasible to implement TXA into midwifery practice. TXA is an economical drug that can be made available to areas and patients suffering from limited medical and financial resources. Durand−Zaleski et al. (2020) strongly advocated for TXA use among low-income areas and developing countries. The authors also found TXA was 65% to 73% more cost effective when compared to traditional uterotonics. Therefore, TXA may improve maternal outcomes on a global scale (WHO, 2017). The midwifery code of ethics, which instructs midwives to promote equality and access to care among all women,

also supports the use of TXA in underdeveloped areas (ACNM, 2020).

Recommendations for Future Research

Future research needs to be conducted on the effectiveness of TXA during the postpartum period. Treatment modalities reviewed in this literature appraisal included route and time of administration, hemorrhaging risk factors, and potential adverse effects. Moreover, this literature review found IV, IM, and topical TXA administration to be effective treatment options for bleeding control. However, further research is needed to determine the safety and effectiveness of topical TXA on third- and fourth-degree cervical lacerations. Also, future studies should examine appropriate time of topical administration.

Research has shown TXA is effective across a number of vulnerable populations. However, patients suffering from blood clotting disorders or chronic disease have traditionally been excluded from TXA studies. However, it is vital to explore the safety and potential risk of TXA for high-risk women, such as women with high-risk pregnancies.

TXA is cost effective and therefore ideal for low-income populations and developing countries. Further research must explore the most cost efficient and effective form of TXA. For example, some studies found IM TXA used to be more effective than oral TXA medication (Diop et al., 2020; Roy et al., 2016). Therefore, further studies are needed to explore the ability for underdeveloped countries and communities to afford IM TXA, clean needles, and syringes. Research should also examine the ability for these communities to safely discard syringes.

Due to the cost effectiveness and health benefits of TXA, ACOG (2020) may explore the benefits of removing TXA from the second stage of the algorithm and including it in the first

stage for postpartum hemorrhaging. TXA may decrease the need for hemorrhaging patients to receive further treatment or blood products.

Integration of Kurt Lewin's Theory

Midwives who achieve the unfreezing stage may be more likely to acknowledge the need for continuous updates in women's services. The purpose of unfreezing is to encourage providers to continuously seek change in a medical institution to address the changing needs of patients (Hussain et al., 2018). Unfreezing is particularly important because, regardless of the medical standards established today, maternal hemorrhaging remains a significant concern (Alam & Choi, 2015). During the unfreezing stage, midwives have the responsibility to recognize the need for adjustment in the current midwifery practice (Hussain et al., 2018). After determining the need for change, midwives should first predict variables associated with change. Related to this study, midwives are responsible for predicting the impact TXA will have on women and medical institutions. There are a few possible predictions that could be made on the effects of TXA. First, the use of TXA may improve maternal outcomes by decreasing morbidity and mortality rates associated with postpartum hemorrhaging. Second, TXA use could positively impact medical institutions (Hussain et al., 2018). More specifically, the cost efficiency of TXA may reduce the financial burden for medical organizations and increase the likelihood TXA is incorporated into routine care. This is particularly important to consider for low-income communities and underdeveloped countries (Alam & Choi, 2015).

After all major factors are considered, change is implemented in the second stage. During this stage, medical staff alters their original thoughts, feelings, and actions to adapt to a new plan of care (Hussain et al., 2018). At this time, the organization will begin training staff members to

safely and appropriately implement change. As it relates to the present study, midwives would be educated on the routes, doses, and times that TXA could be safely administered. When teaching is complete, medical professionals are encouraged to share their experiences (Hussain et al., 2018). Knowledge sharing between experts and novices can strengthen the confidence and performance of midwives unfamiliar with the prophylactic use of TXA (Hussain et al., 2018).

Refreezing is the final step considered in Lewin's change theory. During refreezing, the organization establishes the change as the new standard of care (Hussain et al., 2018). The midwife's organization will develop set facility policies on the use of TXA, such as the appropriate routes, times, and dosages of TXA administration (Hussain et al., 2018). Refreezing is critical for preventing medical staff from reverting to former standards of care (Shirey, 2013).

Lewin’s et.al., (1951) theory facilitates the implementation of prophylactic use of TXA in maternal care. The theory will aid in improving steps toward medical changes. Lewin's theory also promotes confidence among midwives as changes are made to control maternal bleeding (Hussain et al., 2018). Altogether, Lewin's theory will improve the transition to enriched methods of care.

Conclusion

The pertinent findings of this critical review included the route of TXA administration, the time of TXA administration, risk factors for hemorrhaging, adverse effects related to TXA, and resources. These factors have been found to significantly impact the efficiency of TXA during the postpartum period. For the purpose of this literature appraisal twenty scholarly articles were reviewed using the Johns Hopkins Research Evidence Appraisal Tool with statistically significant results for TXA administration, risk factors for hemorrhaging, adverse effects related

to TXA, and resources. The route of TXA administration influences drug efficiency while the time of TXA administration impacts the therapeutic effect of TXA. Hemorrhaging risk factors impact which patients are ideal for TXA treatment and drug efficiency. However, adverse effects impacts and the side effects associated with TXA use. Resources influence cost and availability of TXA in underdeveloped communities.

Nurse midwives are at a substantial position to implement TXA into obstetrical care. Nurse midwives' prominent roles in women's services, birth and newborn care give midwives significant influence on TXA integration into women's services. Application of Kurt Lewin's Theory facilitates TXA use within midwifery services and demonstrates the necessary steps needed to incorporate TXA into current practice. By practicing according to up to date evidence midwives can safely incorporate TXA into current standards of postpartum care to stabilize and maintain equilibrium during the postpartum period.

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Appendix A: Literature Review Matrix

Source: Bose, D., & Beegum, R. (2017). Sublingual misoprostol vs intravenous tranexamic acid in reducing blood loss during cesarean section: A prospective randomized study. *Journal of South Asian Federation of Obstetrics and Gynaecology, 9*(1), 9-–13. https://doi.org/10.5005/jp-journals-10006-1448			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To compare the efficiency of sublingual misoprostol to TXA during C-section **Sample/Setting:** 163 women who were between the ages of 18 to 39 years old having a singleton delivery. Patients were scheduled or had emergency c-sections in the Department of Obstetrics and Gynecology of the Malabar Institute of Medical Sciences, Calicut, Kerala and India. **Johns Hopkins Evidence Appraisal:** **Strength:l** **Quality: Good**	Randomized study The control group received 600mg of oral misoprostol while The TXA (independent) group received 500mgof IV TXA. Blood loss was visually measured. Hb and platelet labs were examined prior to surgery then 48 hours post op to determine blood loss.	Low risk TXA patients had lower blood loss than control group 416 ml vs 505 ml, (p = 0.023). Patients who were high risk did not have a difference in blood loss between the two groups (534 vs 478 mL, (p = value 0.23) Over all little significant difference between independent and control group (470.30 ± 192.548 vs 491.74 ± 200.043 mL, (p = 0.487) Little difference between Hb and PCV, (p =0.197)] Need for additional uterotonics were similar in both groups (p = 0.957) **Conclusion:** TXA is effective in low risk patients however it appears to be less effective in high risk patients	**Strengths:** The article addressed cost efficiency of TXA Side effects of TXA such as nausea, vomiting and shivering were discussed Hb and PCV were assessed before and after delivery. **Limitations:** The sample size was small therefore finding may not be relatable to the general public. Blood loss was not measured

Author Recommendations: TXA should be administered after cord clamping**.** TXA is most effective in high risk patients. TXA should be administered to high risk patients with scheduled or emergent c-sections.
Implications: Midwives may suggest the use of TXA for low risk patients that have a failed trial of labor. TXA may effectively decrease blood loss among c-section patients. Post-op, midwives should assess TXA patients for NV and shivering.

Source:
Chandak, A., Gupta, I., & Sreemayi, C. (2017). Efficacy of tranexamic acid in decreasing blood loss during and after cesarean section: A randomized case controlled prospective study. *International Journal of Science and Research, 6*(1),1321–1323. https://doi.org/10.21275/art20164292

Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To determine the ability for TXA to limit postpartum bleeding among c-section patients **Sample/Setting:** The sample consisted of 100 women scheduled for cesarean deliveries **Johns Hopkins Evidence Appraisal:** **Strength:1** **Quality: Good**	Randomized case controlled study. 1g of TXA was given over 5 minutes prior to the c-section incision while the control group received sodium chloride Hemoglobin and hematocrit levels were reviewed one day prior to cesarean section and agin post op. Blood loss was measured by assessing blood present in the suction tubes after the delivery of the placenta. Pads and linien were also weighed for blood from the completion of c-section time to 2 hours post delivery	There was significant blood loss in control from time of delivery of placenta to end of c-section (P = 0.0001). There was also significantly more blood loss in control from end of c-section to two hours postpartum Study group had less cases of postpartum hemorrhaging (P = 0.049) **Conclusion:** TXA effectively controls bleeding in cesarean patients	**Strengths:** Hemoglobin was reviewed one day before and again after c-section to demonstrate blood loss in each individual patient Exact measurements were taken for blood loss Qualifications for postpartum hemorrhaging was defined for the purpose of this study **Limitations:** The sample size was small The setting of the study was not clearly stated Mothers with high risk pregnancies or high risk for PPH were excluded from the study
Author Recommendations: The author acknowledges increased risk for thrombosis in pregnancy and therefore recommends further research to determine potential thrombosis risk related to TXA administration.			

Implications: Midwife may order TXA for patients requiring to get c-sectioned. TXA may also be considered for vaginal lacerations and bleeding.

Source: Diop, A., Abbas, D., Ngoc, N. T., Martin, R., Razafi, A., Tuyet, H. T., & Winikoff, B. (2020). A double-blind, randomized controlled trial to explore oral tranexamic acid as adjunct for the treatment for postpartum hemorrhage. *Reproductive Health, 17*(1), https://doi.org/10.1186/s12978-020-0887-2			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To assess the efficiency of oral TXA when given with misoprostol. **Sample/Setting:** 258 women from four hospitals within Vietnam and Senegal who were diagnosed with postpartum hemorrhaging **Johns Hopkins Evidence Appraisal:** **Strength: l** **Quality: Good**	This was a double blinded randomized study which took place between October 25, 2016 to January 19, 2018. The experiment included 258 participants who had vaginal deliveries. All the women in this study were experiencing postpartum bleeds. Postpartum bleeding was classified as bleeding over 700ml. Women with a history of thrombosis or medical contraindications to TXA were excluded. After delivery a plastic drape and calibrated funnel was placed under the maternal buttocks for 30 minutes post delivery. Women diagnosed with hemorrhaging were placed into the TXA group or a placebo group. Women who received TXA were given 1950mg of oral TXA and 800mcg of po misoprostol. women in the control group received a placebo and 800 mcg of	Control group required less additional uterotonics than TXA group ($p = 0.59$) Moe participants from the TXA group required additional uterotonics $p = 0.51$) **Conclusion:** PO TXA may not be effective in treating postpartum hemorrhaging. International guidelines recommend TXA IV as standard hemorrhage treatment.	**Strengths:** The study was double blinded which preserved the integrity of the experiment. Women in the TXA group and placebo group were both properly treated for postpartum hemorrhage within 30 minutes of hemorrhaging. Computerized data was used to randomize participants and treatment options. **Limitations:** 1950mg PO of TXA was given when the max dose is 2000mg PO. The study only had 258 participants. Findings may be different with a larger sample size.

Author Recommendations: The Study also discloses other experiments have found TXA to be more effective when given 3 hours postpartum. However, the author recommends that PO TXA may be less effective than IV TXA. Therefore, IV TXA should be given in times of a postpartum hemorrhage. Further studies should be done to determine treatment options for postpartum hemorrhages when IV access is not possible.
Implications: Midwives could consider administering TXA to treat postpartum hemorrhaging and improve patient outcomes. However, PO TXA was not found to be an effective treatment for postpartum bleeding, therefore, IV TXA should be given in conjunction with other uterotonics within 3 hours of birth time for best outcomes.

Source: Durand−Zaleski, I., Deneux−Tharaux, C., Seco, A., Malki, M., Frenkiel, J., & Sentilhes, L.

(2020). An economic evaluation of tranexamic acid to prevent postpartum haemorrhage in women with vaginal delivery: The randomised controlled TRAAP trial. *An International Journal of Obstetrics & Gynaecology, 128*(1), 114–120. https://doi.org/10.1111/1471-0528.16456

Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To estimate cost effectiveness of TXA for treatment of PPH **Sample/Setting:** 4079 women who had vaginal deliveries throughout France **Johns Hopkins Evidence Appraisal:** **Strength: l** **Quality: Strong**	Randomized control trial 1g of TXA given intravenously in independent group after prophylactic use of oxytocin 10 min post delivery Women in the control group received intravenous placebo after prophylactic dose of oxytocin. PPH was defined as bleeding more than 500ML collected by collector bag Cheers guidelines where used to determine cost efficiency Cost of delivery was recorded in CRF including delivery suite, blood production and cost of pre and post delivery. Bootstrap hypothesis testing used to compare costs by randomisation group (tranexamic acid versus placebo) and by outcome (postpartum haemorrhage versus no postpartum haemorrhage)	TXA and control groups were not found to have significant differences in bleeding of at least 500 ml (RR = 0.83, 95% CI [0.68–1.01], *P* = 0.07) However TXA group had lower rates of intervention for PPH (RR = 0.74; 95% CI [0.61–0.91], *P* = 0.04) The average length of hospital stay was 3.66 1.3 days and the total costs $2283, 399 The total cost of blood products was $6,037 and $10,061 in the TXA and control groups, respectively 141 patients in the TXA group versus 189 in the control group, for a total of $7,497 and $9,945, respectively TXA group had systematically lower costs than women in the control group, although no statistically significant	**Strengths:** The economic analysis was done for three months which allowed researchers to assess potential readmissions and financial burdens The sample size was large making the study findings generalizable **Limitations:** Only hospital costs could be studied. The study was done in a high income setting therefore low income areas were not assessed The study was done in France, meaning the cost of treatment in other countries was not determined.

Author Recommendations: The author recommends TXA be given proholaticly with oxytocin. They determine the prophylactic use of TXA will improve patient outcomes and also decrease cost in hospital stay.
Implications: The midwife may consider TXA use particularly for her at risk patients. MIdwives may also begin to consider TXA in low income areas and underserved countries due to its cost efficiency.

Source: Gilad, O., Merlob, P., Stahl, B., & Klinger, G. (2014). Outcome following tranexamic acid exposure during breastfeeding. *Breastfeeding Medicine*, *9*(8), 407–410. https://doi.org/10.1089/bfm.2014.0027			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To determine adverse facts related to TXA administration during pregnancy or lactation **Sample/Setting:** 63 postpartum women in Israel **Johns Hopkins Evidence Appraisal:** **Strength: llI** **Quality: Good**	An observational study Beilinson Teratology Information Service (BELTIS was used to interview mothers who had TXA exposed to their newborn through breast milk. These women were observed for up to three years for adverse effects Data on lactation, neonatal symptoms, and outcomes at the age of 1-3 years were obtained.	One women from the study group reported a decrease amount of breast milk ($p = 1.0$) One participant in study group reported infant restlessness ($p = 1.0$) Growth percentile below 3% was found in one newborn in the study group and four newborn in the control ($p = 0.66$) **Conclusion:** TXA had no significant adverse effects on mothers and newborn	**Strengths:** Study continued for three years **Limitations:** There was a small sample size Patients may have been bias when answering questions regarding amount of breastmilk and infant restlessness Study was not a RCT
Author Recommendations: More research is needed to determine side effects of TXA. Further research should be done one a large sample.			
Implications: Midwives may consider prophylactic TXA in healthily women minimal side effects have been found among newborns. Therefore, midwives can safely administer TXA prophylactically prior to birth or after.			

Source: Gillissen, A., Henriquez, D. D., Akker, T. V., Caram-Deelder, C., Wind, M., Zwart, J. J., & Bom, J. G. (2017). The effect of tranexamic acid on blood loss and maternal outcome in the treatment of persistent postpartum hemorrhage: A nationwide retrospective cohort study. *Plos One,12*(11), e0187555. https://doi.org/10.1371/journal.pone.0187555			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To determine if TXA is more effective at improving mortality and mobility rates than when given within the first three hours of a postpartum bleed compared to later or no TXA administration . **Sample/Setting:** The sample size consisted of 1260 women (18 years old or older) from the Netherlands who were experiencing postpartum hemorrhages. The participants also had to receive four units of red blood cells, plasma or platelets to be part of the study. This experiment took place within 61 hospitals in the Netherlands (Gillissen et al., 2017). **Johns Hopkins Evidence Appraisal:** **Strength:ll** **Quality: Strong**	This was a Quasi-experimental study. The experiment was reviewed and approved by the Ethical Committee of the Leiden University Medical Center therefore, the participants did not need to give informed consent. This was a retrospective cohort study. Meaning the researchers retrospectively collected data of their participants between Jan 1st 2011 to Jan 1st 2013. The researchers then used cross referencing electronic data to identify participants. Final blood loss was collected by measuring soaked gauze and examination of the collector/suction systems. The control group was women who did not receive TXA while the intervention group was those who received TXA within three hours of a postpartum bleed.	Women who received TXA within the first three hours bled more than the participants who did not.Those who received TXA within the first 3 hours bled at a rate of 24ml vs 19ml/min and had an average of 1300ml vs 800ml of blood loss. However, no difference in mortality rates were found between the two groups. The incidence of hemorrhagic shock was also higher in early of TXA admission 31% compared to late or no TXA administration 21% **Conclusion:** The researchers believe that early TXA use in developed countries may not be as beneficial as it has been found to be in third world settings.	**Strengths:** A strength is that the experiment was done for two years and had a large sample size. This makes the results from the experiment more trustworthy. Meaning the findings can be used for the general public. The experiment was approved by the Ethical Committee of the Leiden University Medical Center which ensures that patient's rights are not violated. The authors were also clear about qualifying factors such as women had to receive at least four units of red blood cells and be over 18 years old to participate in the study. **Limitations:** A limit is that health prior to the hemorrhage was not considered during the experiment.

Author Recommendations: TXA may partially block degradation of the fibrin clot, however, it is more effective to solve the cause of a postpartum hemorrhage than to immediately treat the patient with TXA. TXA may be more useful in the case of a persistent postpartum hemorrhage.
Implications: As a provider I should consider all the possible reasons that a patient may be having a hemorrhage. After treating the underlying cause of the bleed additional medications such as TXA may be considered.

Source: Goswami, U., Sarangi, S., Gupta, S., & Babbar, S. (2013). Comparative evaluation of two doses of tranexamic acid used prophylactically in anemic parturients for lower segment cesarean section: A double-blind randomized case control prospective trial. *Saudi Journal of Anaesthesia*, *7*(4), 427–431. https://doi.org/10.4103/1658-354x.121077			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To determine effectiveness of TXA when given to anemic women during the birthing process **Sample/Setting:** 90 anemic patients from New Delhi, India **Johns Hopkins Evidence Appraisal:** **Strength:l** **Quality: Strong**	Double blind randomized experiment from 2009 to 2011 Women were randomized into groups including : Group 1 received TXA 10mg/kg Group 2 received 15mg/kg Control received Demographic data were compared using the Chi-square test. To compare quantitative data between two groups *t*-test was used	Hemodynamic parameters including pulse rate, blood pressure, respiratory rate and SpO2 were found to be comparable after statistical analysis using the student *t*-test ($P>0.05$) Less blood loss found in the two study groups when compared to the control ($P<0.05$) There was no other significant adverse event such as deep vein thrombosis or other thrombotic events up to 24 h post-operatively **Conclusion:** TXA 10mg/kg and 15mg/kg are found to safely control bleeding with no proven adverse effects	**Strengths:** Study was randomized and continued for two years Chi-square and t-test were used to organize data Blood loss was measured in containers and weight of saturated pads **Limitations:** Sample size of only 90 women No specific adverse effects were reviewed

Author Recommendations: TXA Repeat study with larger sample size. TXA may effectively reduce bleeding among at risk populations especially women in developing countries
Implications: Midwives may consider TXA for at risk patients or anemic patients during the time of delivery to minimize bleeding.

Source:			
Gungorduk, K., Ascoğlu, O., Yldrm, G., Ark, C., Tekirdağ, A. I., & Besmoglu, B. (2013). Can intravenous injection of tranexamic acid be used in routine practice with active management of the third stage of labor in vaginal delivery? A randomized controlled study. *Obstetrical & Gynecological Survey, 68*(10), 673–675. https://doi.org/10.1097/01.ogx.0000436756.05118.cd			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To determine effectiveness of TXA on third and fourth stage of labor **Sample/Setting:** Department of Obstetrics and Gynecology, Kanuni Sultan Süleyman Teaching Hospital, Istanbul, Turkey 454 women who were 32 to 40 weeks pregnant with high and low risk pregnancies **Johns Hopkins Evidence Appraisal:** **Strength:l** **Quality:Good**	Experimental study Participants were randomized into two groups through a number system. TXA group received 1g/ 10ml diluted in 20ml of 5% glucose while placebo group received 30ml Glucose Meds given 5 minutes after anterior shoulder was extracted	Blood loss in third and fourth stage of labor lower in TXA group (261.5 + or - 146.8 versus 349.98 + or - 188.85 mL, respectively; ($p < 0.001$) Pph lower in txa group (15, 6.8%; RR = 3.76; 95% CI [1.27 to 11.15], $p = 0.01$). More women in the control group needed uterotonics (RR = 3.18; 95% [CI 1.29 to 7.81], $p = 0.007$) Similar Hb in both groups (9.9 1.4 g/dL and 9.3 0.9 g/dL, respectively; ($p<0.001$) **Conclusion:** TXA can decrease blood loss during 3rd and 4th stages of labor	**Strengths:** Both low risk and high risk vaginal deliveries were considered Participants and researchers were double blinded to preserve the integrity of the experiment **(Gungorduk et al., 2013)** **Limitations:** Sample size was small and may not reflect the general public Cost efficiency of TXA was not included

Author Recommendations: TXA can be helpful for at risk patients during the 3rd and fourth stages of labor. TXA should be given within 5 min of anterior shoulder delivery.
Implications: Midwives can consider TXA for their at risk patients. Also TXA use may be useful for midwives in underdeveloped countries where other uterotonics may be unavailable.

Source: Lakshmi, S. D. (2016). Role of prophylactic tranexamic acid in reducing blood loss during elective caesarean section: A randomized controlled study. *Journal of Clinical And Diagnostic Research, 10*(12), QC17–QC21. https://doi.org/10.7860/jcdr/2016/21702.9050			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To analyse the effectiveness of Tranexamic Acid (TXA) in reducing blood loss during elective caesarean section. **Sample/Setting:** 120 women having elective c-sections within the PSG Hospital. **Johns Hopkins Evidence Appraisal:** **Strength:l** **Quality: good**	The study is a interventional, randomized, parallel group study The study was done from June 2014 to May 2015 Women were randomly placed in a control or independent group by computer database. Women in the TXA group received 1g of txa 20 min before section. Control group was given sodium chloride. Both Groups were given 10 units of oxytocin after surgery. T-test and chi squared used to compare variables Hemoglobin was assessed before and after birth	There was less blood loss from the time of placental delivery to the end of surgery 347.17ml blood loss in the study group versus 517.72ml in control group ($p < 0.001$) Researchers observed which groups would have more than a 10% fall in hemoglobin 9.3% of subjects in study group and 39% of subjects in control group had more than 10% fall in haemoglobin ($p < 0.01$) No danger was found to neonate **Conclusion:** TXA can safely control bleeding after c-sections.	**Strengths:** The study included chi squares to verify and compare variables Hemoglobin levels were checked before and after birth to show differences in blood loss between the TXA and placebo group Computer data base was used to randomize women which insured randomization was done correctly **Limitations:** Blood collected in drapes and sheets were not connected blood loss was approximated Long term effects of TXA not considered

Author Recommendations: Patients should receive TXA 20 minutes prior to surgery. Women who receive TXA will have a decrease in blood loss postpartum.
Implications: Midwives may advise the use of TXA for patients at risk for blood loss or anemic patients. Providers should acknowledge the importance of administering TXA 20 minutes prior to incision time for optimal effects.

Source: Ononge, S., Mirembe, F., Wandabwa, J., & Campbell, O. M. (2016). Incidence and risk factors for postpartum hemorrhage in Uganda. *Reproductive Health, 13*(1), Article 38. https://doi.org/10.1186/s12978-016-0154-8			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To assess risk factors associated with postpartum hemorrhaging **Sample/Setting:** 1188 women giving birth in rural Uganda. **Johns Hopkins Evidence Appraisal:** **Strength:lII** **Quality: Strong**	Prospective cohort study done from 2013 to 2014 in six hospitals in rural Uganda. Women given questionnaires to assess their risk for hemorrhaging Participants had drapes placed under them to confirm postpartum hemorrhage Hemorrhaging was defined as bleeding over 500ml in vaginal deliveries and 1,000ml during a c-section. The researchers created two multi variable logistic regression models for the variables	Hemorrhaging risk factors were greater among mothers who had macrosomia deliveries (aOR = 2.14, 95% CI [1.02, 4.47], p= 0.01). HIV positive also had increased risk for postpartum bleeding sero-status (aOR = 2.26, 95% CI [1.20, 4.25], p = 0.03) cesarean section delivery were at greatest risk for postpartum hemorrhaging ((aOR = 7.54, 95% CI [4.11, 13.81], p <0.001) **Conclusion:** Maternal PPH is one of the leading causes of death among mothers globally.	**Strengths:** Risk factors for hemorrhaging was acknowledged in both vaginal and c-section deliveries The large population size makes the information generalizable Study was done for at least a year **Limitations:** Study was limited to rural Uganda. Developed countries were not included which may impact the risk factors for women in that area

Author Recommendations: Recommends that further studies are done on PPH. The authors also recommend that more studies are done on treatment options for postpartum hemorrhaging.
Implications: Recommends that further studies are done on PPH. The authors also recommend that more studies are done on treatment options for postpartum hemorrhaging.

Source: Ramesh, A. C., Rajni, S., & Deka, N. (2015). Efficacy of tranexamic acid in decreasing blood loss during and after cesarean section: A randomized case controlled prospective study. *Indian Journal of Public Health Research & Development, 6*(2), 12–16. https://doi.org/10.5958/0976-5506.2015.00063.7			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To study efficacy of blood loss c-section **Sample/Setting:** 200 women scheduled to have c-section deliveries in the department of Obstetrics & Gynecology, Padmashree Dr. D. Y. Patil Medical College, Hospital and Research Center Pimpri **Johns Hopkins Evidence Appraisal: l** **Strength:l** **Quality: Good**	Randomized case controlled study This is an experimental study from July 2011 To September 2013. The study used computer data to randomize women into control and independent groups. The TXA group received 1g of TXA over minutes 20 minutes before the incision while the control received sodium chloride. Both groups received prophylactic oxytocin post surgery.	Difference in blood loss from time of delivery to placental removal (p Value < 0.001) Significant difference in blood loss from inoperative time to placental removal ($p < 0.001$) No difference in blood loss from time of incision to placental removal ($p = 0.056$) LSCS to two hours post-partum with mean blood loss of 3.80 ml in the study group versus 112.25 ml in the control group ($p < 0.001$). Study group had less blood loss from placental delivery to two hours postpartum ($p = 0.002$) TXA had no effects on newborn AGARs ($p = 0.5$) Conclusion: TXA was found to reduce blood loss	**Strengths:** Study was done over for a year Vital signs were monitored before and after the c-section to monitor effects of the surgery The studies findings were compared to other research on TXA and postpartum hemorrhaging. **Limitations:** The study should be repeated with a larger participant group High risk women were excluded from the delivery

Author Recommendations: TXA should be avoided in individuals with a history of thrombosis. TXA can prevent blood loss in low risk c-sections. Further studies are needed to determine the effect of TXA on high risk women.
Implications: If a midwife's workplace allows her to be in the OR she should state if the patient has a history of thrombosis. Although thrombosis is not likely, midwives should monitor for it and observe newborn AGARS.

Source: Roberts, I., Shakur, T., Coats, T., Hunt, B., Balogun, E., Barneston, L., Cook, L., Kawahara, T., Perel, P., Prieto-Merino, D., Ramos, M., Cairns, J., & Guerriero, C. (2013). The CRASH-2 trial: A randomised controlled trial and economic evaluation of the effects of tranexamic acid on death, vascular occlusive events and transfusion requirement in bleeding trauma patients. *Health Technology Assessment, 18*(3), 1–79. https://doi.org/10.1108/cgij.2013.24818caa.005			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To assess early use of TXA and its effects on death **Sample/Setting:** Randomized controlled 20, 211 adult trauma patients were studied from 274 hospitals across 40 countries **Johns Hopkins Evidence Appraisal: l** **Strength:l** **Quality: Strong**	Experimental study A computer randomly assigned trauma patients to TXA group or placebo.TXA group received 1g of the drug over 10 minutes then again over 2 hr. Placebo group received placebo the same way.	All-cause mortality was significantly reduced with tranexamic acid (M = 1463 [14·5%] tranexamic acid group *vs* (M = 1613 [16·0%] placebo group; RR = 0·91, 95% CI [0·85–0·97], $p = 0·0035$) Risk of death lower in placebo group 4.9% *vs* 5.7% ; (relative risk = 0·85, 95% CI [0·76–0·96], $p = 0·0077$). **Conclusion:** TXA can effectively reduce mortality rates among trauma patients who receive TXA.	**Strengths:** Large population size from various countries makes information generalizable Patients were randomized thorough computer data which kept the experiment double blinded **Limitations:** Fibrinolytic agents in TXA was not measured Do to injuries it was difficult to measure blood loss in trauma patients Early TXA was not compared to late TXa
Author Recommendations: Authors recommend TXA could be effective in the event of a postpartum hemorrhage. TXA could be given to a wide range of trauma patients to reduce risk of death.			
Implications: Although this article explored trauma patients a midwife may consider the use of TXA for patients who have experienced vaginal trauma during a delivery. This cloud includes shoulder dystocia, or a third or fourth degree vaginal laceration.			

Source: Roy, P., Sujatha, M. S., Bhandiwad, A., & Biswas, B. (2016). Role of tranexamic acid in reducing blood loss in vaginal delivery. *The Journal of Obstetrics and Gynecology of India, 66*(S1), 246–250. https://doi.org/10.1007/s13224-016-0856-4			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: TXA ability to reduce blood loss in vaginal delivery **Sample/Setting:** 100 participants from antenatal ward or labour ward of JSS Medical College and Hospital, Mysore **Johns Hopkins Evidence Appraisal: l** **Strength:l** **Quality: Good**	Randomized control This study started Oct 2014 to March 2025. The TXA group received IM oxytocin and TXA IV over 10 min while the control group received IM oxytocin and sodium chloride over 10 min. Women in the study could be no more than second gravita, 38wk or above and having spontaneous labor. Pads and collector drape were measured two hours postpartum. Statistical analysis was used to measure mean, median and standard deviation.	mean fall in haemoglobin was 0.20 g % in study group and 0.70 g % in control group Mean fall in haematocrit was 0.40 % in the study group and 1.20 % in the control group. The mean blood loss at the end of 2 hr was 105 ml in the study group and 252 ml in the control group 22 % of the patients in the control group needed additional uterotonics compared to only 2 % in the study group, which was statistically significant **Conclusion:** TXA can effectively reduces bleeding and need for additional uterotonics in normal vaginal deliveries	**Strengths:** Patients were randomized thorough computer data which kept the experiment double blinded There was a standard for measuring blood loss among the two groups **Limitations:** Fibrinolytic agents in TXA was not measured The study only consisted of 100 people Not all p values were discussed Only healthy women were included in the study so it is not known how TXA could help high risk deliveries

Author Recommendations: The other recommends that TXA is used prophylactically to prevent hemorrhage even in normal spontaneous labor.
Implications: The midwife may consider TXA as prophylactic treatment during vaginal deliveries. TXA should be given within 5 minutes of the delivery before a potential hemorrhage begins.

Source:

Rushulo, K., Ranjit, s, & Rameswar, s. (2016). Effect of intravenous administration of tranexamic acid in reducing blood loss during and after caesarean section. *Journal of Medical Science and Clinical Research*, *4*(7), 11297–11303. https://doi.org/10.18535/jmscr/v4i7.19

Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**
Purpose: To determine effectiveness of TXA to prevent bleeding during and after a c-section **Sample/Setting:** 60 women with low risk pregnancies from India between the ages of 24 to 40 years old **Johns Hopkins Evidence Appraisal:** **Strength:l** **Quality: Good**	Randomized control study from 2013 to 2015 Experiment was reviewed by the institution of the ethics committee Patients with high risk pregnancies, and history of abdominal surgery were excluded TXA 10mg/kg given 10 minutes prior to incision Control group received sodium chloride 10 minutes prior to incision	Blood loss from time of surgery completion to two hours was less in sthe study group 48.7 ml and 58.4, (p = 0.001) Blood loss from time of incision to two hours postpartum was significantly lower in the study group (p = 0.001). **Conclusion:** TXA can safely reduce bleeding among c-section patients	**Strengths:** Study was conducted for an extended period of time Assess effects of TXA on various age groups **Limitations:** Small sample size Did not observe HCT or PLT prior to the surgery Excluded high risk pregnancies

Author Recommendations: Further research is needed to determine TXA effect of high risk patients and to observe potential side effects associated with the drug.

Implications: Midwives may give TXA to prevent a postpartum hemorrhage among patients with low risk pregnancies to prevent PPH.

Source: Sentilhes, L., Winer, N., Azria, E., Sénat, M., Ray, C. L., Vardon, D., Perrotin, F., Desbriére, R., Fuchs, F., Kayem, G., Ducarme, G., Doret-Dion, M., Huissoud, C., Bohec, C., Dureulle, P., Darsonval, A., Chrétien, J. -M., Seco, A., Daniel, V., & Deneux-Tharaux, C. (2018). Tranexamic acid for the prevention of blood loss after vaginal delivery. *New England Journal of Medicine, 379*(8), 731–742. https://doi.org/10.1056/nejmoa1800942			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To determine the effectiveness of prophylactic TXA when given with oxytocin during vaginal deliveries **Sample/Setting:** From Jan 2015 to Dec 2016 4,079 participants The study was done within 15 French hospitals. Participants had to be at least 35 weeks gestation with a singleton and expecting a vaginal delivery. All participants were 18 years old and up **Johns Hopkins Evidence Appraisal:** **Strength:l** **Quality: Strong**	The experiment was experimental double blind study. Postpartum hemorrhage, defined as blood loss of at least 500 ml blood loss measured in collector bags Computer system was used to randomize women into control groups or independent groups. Women in the independent group received Experiment was divided into two parts group 1 received TXA and oxytocin or TXA and placebo 2 min after delivery . Group 2 received oxytocin and TXA or oxytocin and placebo 10 min post delivery Student t test compared Chi-squared and Fisher's test were used to compare categorical variables	Women in the TXA group had lower rates of postpartum hemorrhaging 7.8% vs. 10.4% RR = 0.74, 95% CI [0.61 to 0.91] p = 0.004; P = 0.04) TXA group required less uterotonics 7.2% vs. 9.7% of the control group RR = 0.75, 95% CI [0.61 to 0.92], P = 0.006; adjusted P = 0.04) thromboembolic episodes between the two groups did not differ by three months postpartum 0.1% and 0.2%, RR = 0.25; 95% CI [0.03 to 2.24]. **Conclusion:** Prophylactic TXA could improve maternal outcomes after vaginal deliveries	**Strengths:** Postpartum hemorrhage was measured by collector bags The study was done for a year with a large sample size including women at risk for hemorrhage Expresses side effects related to TXA such as nausea and vomiting **Limitations:** Prenatal hemoglobin blood tests were done at outside laboratories which were not completed at a standard time. Hemorrhaging was set as bleeding over 500ml instead of bleeding of 500ml

Author Recommendations: TXA should be considered for women at risk for hemorrhaging. For example, TXA could decrease bleeding risk for women with episiotomy and operative vaginal deliveries.
Implications: The midwife should consider TXA for her patients at risk for hemorrhaging. TXA should be given at least 10 minutes post delivery.

Source: Senturk, M. B., Cakmak, Y., Yildiz, G., & Yildiz, P. (2012). Tranexamic acid for cesarean section: A double-blind, placebo-controlled, randomized clinical trial. *Archives of Gynecology and Obstetrics*, *287*(4), 641–645. https://doi.org/10.1007/s00404-012-2624-8			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To assess the effectiveness of TXA among c-section patient **Sample/Setting:** 223 patients with healthy pregnancies across hospitals in Berlin **Johns Hopkins Evidence Appraisal:** **Strength:l** **Quality:** Good	Randomized double blinded experiment Experiment was approved by TXA group was given 1g of TXA 10 minutes prior to the cesarean incision while the control was given sodium chloride All patients were given oxytocin after the surgery was completed Hemoglobin hematocrit and platelet was assess prior to the cesarean section Patients with increase BMI, history of venous thromboembolism, heart disease, active liver or kidney diseases, overweight fetus, or allergies to TXA did not participate in this study	Greater loss of hemoglobin in control group than study group (p = 0,034) Higher HCT and PLT loss in control group vs the study group (p = 0.002, p = 0.003) No increase risk factor for stroke found in mother or baby up to two weeks postpartum **Conclusion:** TXA effectively prevents PPH without increasing risk for stroke.	**Strengths:** The experiment assessed HCT and PLT before and after the c-section **Limitations:** Study did not provide statistical evidence to prove limited risk factors associated with TXA Oxytocin may have impacted the results of the study
Author Recommendations: Author recommends TXA may be beneficial among women having natural vaginal deliveries and vaginal trauma. Recommends using TXA prior to birth or within minutes of birth for optimal effect.			

Implications:
Midwives may consider TXA use among vaginal deliveries. TXA would be especially helpful among women with cervical, vaginal and rectal lacerations.

Source: Sofiene, B. M., Zied, H., Laidi, B. N., Yahya, M., & Hayen, M. (2015). A comparison of two doses of tranexamic acid to reduce blood loss during cesarean delivery. *Global Anesthesia and Perioperative Medicine, 1*(4), 93–95. https://doi.org/10.15761/gapm.1000123			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To determine the efficiency of TXA on c-section deliveries after two doses **Sample/Setting:** 52 participants fromTunis maternity and neonatology center **Johns Hopkins Evidence Appraisal:** **Strength:l** **Quality: Good**	The study was experimental. 52 women who received regular prenatal care and consented for Pfannenstiel c-sections. Participants were randomized into two groups 10 mg/kg (group1) or 15 mg/kg (group 2)of tranexamic acid intravenously. TXA was given from 5 min prior to c-sections. Primary outcomes were determined by blood loss within 6 hours. Secondary outcomes were determined by the total amount of oxytocin given and hemoglobin levels. Statistical packages for social sciences were used to analyze data. Patients with PPH risk factors were excluded from the study.	Mean blood loss was lower in TXA TXA2 group ($p = 0.017$) Mean hematocrit value was similar in both groups ($p = 0.081$) Less oxytocin was needed in TXA group 2 ($p = 0.05$) **Conclusion:** Intravenous TXA 15 mg/kg was most effective in decreasing blood loss and lowering the need for additional uterotonics.	**Strengths:** Blood loss volume was measured by Gross's formulas Student t tests were used to compare the two independent groups **Limitations:** TXA effectiveness in aat risk patients were not studied The study was done for a short period of time. Also, the sample size was small meaning the findings from the study may not represent the general public
Author Recommendations: The author recommends that 15 mg/kg be used to control postpartum bleeding instead of 10 mg/kg. The author also recommends that TXA is given 5 minutes prior to the initial c-section incision.			
Implications: TXA may be considered for healthy patients who have scheduled cesarean sections. Providers should be cautious to administer TXA at least 5 minutes prior to the c-section.			

Source: Woman Trial Collaborators. (2017). Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): An international, randomised, double-blind, placebo-controlled trial. *Obstetrical & Gynecological Survey, 72*(9), 525–526. https://doi.org/10.1097/01.ogx.0000524474.98785.1			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To determine the effects of early TXA administration on maternal death and hysterectomy outcomes. **Sample/Setting:** Women 16 years or older. The study had 20,000 participants from 193 hospitals in 211 countries. Participants had to be having a postpartum hemorrhage to be a part of the study. **Johns Hopkins Evidence Appraisal:** **Strength: l** **Quality: Strong**	Randomized double blinded experiment from March 2010 to April 2016. Postpartum hemorrhage was categorized as more than 500ml of loss after a vaginal delivery and 1000ml of blood loss after a c-section. The study was a double blind, randomized, placebo controlled trial study. Participants randomly received 1g of TXA or sodium chloride 1g placebo. If participants continued to bleed after the first dose or 24hr within the first dose they were given a second dose of TXA 1g or placebo 1g. Participants were given random numbers. These numbers were sent to drug manufacturers who then randomly sent TXA or sodium chloride with those matching numbers	When given within 3 hours of birth risk of death related to hemorrhaging decreased in patients who received TXA (RR = 0·81, 95% CI [0·65–1·00], p = 0·045). 1.2% of women died related to hemorrhaging in the TXA group while 1.7% passed away in the placebo group (RR = 0·69, 95% CI [0·52–0·91] p = 0·008) . There was little difference in death rates between the TXA and placebo groups when TXA was given after 3 hours (RR = 1·07, 95% CI [0·76–1·51], p = 0·70). Risk of hysterectomy was not reduced when given TXA compared to the control group(RR = 1·02, 95% CI [0·88–1·07] p = 0·84). Also, the use for uterine tamponade, manual placenta removal and atrial ligation were not	**Strengths:** The study randomized women into TXA and placebo groups using group numbers. These numbers were then used to randomly assign TXA or the placebo to participants. This kept the study randomized and double blinded. The study had 20,000 women. The results from this study can be used for the general public. The study shared all their findings which made the study more trustworthy. The study was done from March 2010 to April 2016. The researchers continued the study for six years to ensure they had accurate results. **Limitations:** Some women died related to blood loss during the study. In addition, ways to prevent these deaths were not explored. TXA may be needed for developed

Author Recommendations: The study recommends that TXA treatment is done within 3 hours of birth. TXA after 3 hours of delivery was not found to improve patient outcomes. Researchers also suggest that a study is done on TXA given in ways other than intravenously to facilitate TXA use in developed countries and home births .
Implications: Midwives could consider administering TXA to treat postpartum hemorrhaging and improve patient outcomes. According to the study patients have the best outcomes when TXA is given within 3 hours of birth time.

Source: Wong, J., Abrishami, A., El Beheiry, H., Mahomed, N. N., Roderick D., J., Gandhi, R., Syed, K. A., Ovais Hasan S. M., De Silva, Y., & Chung, F. (2010). Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty. *The Journal of Bone and Joint Surgery*, *92*(15), 2503–2513. https://doi.org/10.2106/jbjs.i.01518			
Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: To determine the efficiency of topical TXA. **Sample/Setting:** 124 orthopedic patients having total knee arthroplasty from. **Johns Hopkins Evidence Appraisal:** **Strength: l** **Quality: Good**	Randomized control Group one received 1.5g of TXA while group 2 was given 3g. The control group was given a placebo Hemoglobin and hematocrit were assessed pre and post operation. Dopplers were used to assess groups for DVT	Results showed a significant reduction in bleeding among the TXA group by 20% to 25% ($p < .017$). Also, significantly increasing hemoglobin levels by 16% to 17% ($p < .017$) compared to the control group were found. TXA was not found to increase risk of DVT. **Conclusion:** Topical TXA was effective in reducing blood loss.	**Strengths:** Hemoglobin and hematocrit were assessed pre and post operation. Dopplers were used to assess groups for DVT. **Limitations:** The experiment had a small study sample. No statistical data to show TXA impact on DVT pulmonary embolisms .
Author Recommendations: Topical TXA should be applied immediately to the wound site to minimize bleeding.			
Implications: The findings from this study reflect the potential for topical TXA use in obstetrical care. Topical TXA may be considered for severe vaginal lacerations and especially cervical bleeds.			

Source: Xu, J., Gao, W., & Ju, Y. (2012). Tranexamic acid for the prevention of postpartum hemorrhage after cesarean section: A double-blind randomization trial. *Archives of Gynecology and Obstetrics*, *287*(3), 463–468. https://doi.org/10.1007/s00404-012-2593-y

Purpose/Sample	**Design (Method/ Instruments)**	**Results**	**Strengths/ Limitations**

Purpose: Determine TXA ability to control blood loss after a c-section. **Sample/Setting:** 174 women in a Grade IIIA hospital, Daqing Oilfield General Hospital consented for primary c-sections and TXA treatment **Johns Hopkins Evidence Appraisal:** **Strength: l** **Quality: good**	This is a double-blind randomization trial 174 women receiving primary pfannenstiel c-sections were randomized. The intervention group received 10mg/kg in a 200ml syringe of TXA prior to the placement of spinal incision while the control group received 200ml of sodium chloride. Participants were randomized using numbered sealed envelopes. Postpartum bleeding was measured using suction containers, soaked gauze, pads and sanitary towels. Bleeding was assessed from time of placental extraction to c-section completion. Then again from the end of the c-section to two hours post birth. The two groups were presented by two-sample Student's t test. Data was then compared using Pearson Chi-square test	The control and TXA groups had similar blood loss from placental extraction to c-section closing. 336.7 ml and control group 368.5 ml. TXA group had lower rates of blood loss when bleeding was assessed two hours after c-section (p = 0.02), TXA group (46.6 ml) compared to the control group (84.7 ml. Postpartum hemorrhage ended in 65 women in the control group and 81 of the TXA group (p = 0.01). Hemoglobin concentration was similar in thoth groups (p = 0.14) or platelet count (p = 0.75) **Conclusion:** TXA can decrease maternal blood loss and morbidity for c-section patients.	**Strengths:** The study was reviewed by the Committee on Clinical Investigation which ensured ethical values were being preserved. Postpartum bleeding was observed twice which allowed researchers to learn how bleeding would evolve after the c-section. Experiment was double blinded to preserve the integrity of the study. Student's t test and Pearson Chi-square test to present and compare data **Limitations:** Only 174 participants were included which means results may not reflect the general population. Participants were randomized using numbered sealed envelopes instead of electronic data which leaves room for error.

Author Recommendations: Author recommends that a larger study is done to determine potential adverse effects associated with TXA use. C-section patients should be given 10mg/kg of TXA prior to the operation to improve postpartum bleeding. TXA is not recommended for patients with thrombosis, heart, brain and liver disease.
Implications: Although it is not in the midwife's scope of practice to perform c-sections the midwife may recommend prophylactic TXA for her patient requiring primary c-sections. The midwife should avoid TXA use in patients with a history of thrombosis, liver, heart and brain disease.