LUMEN ET VIRTUS
ISSN: 2177-2789

EFFICACY OF TRANEXAMIC ACID IN THE MANAGEMENT OF POSTPARTUM HEMORRHAGE: AN INTEGRATIVE REVIEW OF SCIENTIFIC EVIDENCE

https://doi.org/10.56238/levv15n41-053

Submission date: 09/15/2024 **Publication date:** 10/15/2024

Mery Anne dos Santos Angelo Zamba[1], Tereza Cristina Barbosa Ribeiro do Vale[2], Antônio Luís Alves Dias Júnior[3], Igor Thiago Pinheiro Passos[4].

ABSTRACT

Postpartum hemorrhage (PPH) is a leading cause of maternal mortality, especially in low- and middle-income countries. Tranexamic acid (TXA) has been widely used as an effective intervention to reduce mortality and complications associated with PPH. This integrative review was conducted based on the PICO strategy to assess the efficacy of TXA in the management of PPH. The search was conducted in databases such as PubMed, VHL, and SciELO, covering the period from 2014 to 2024, and resulted in the inclusion of 12 studies. The results indicate that TXA, when administered within the first three hours after the onset of hemorrhage, can reduce maternal mortality by up to 31%, as evidenced by the WOMAN Trial. In addition, other studies, such as the one by Oseni et al. (2021), have shown a 50% reduction in intraoperative blood loss in cesarean sections. The study by Novikova et al. (2015) highlighted the effectiveness of TXA in preventing severe bleeding, particularly in cesarean sections, by significantly reducing blood loss in excess of 1000 mL. However, the effectiveness of TXA is limited in settings with inadequate hospital infrastructure, compromising the full implementation of the intervention in low-income countries. It is concluded that TXA is a crucial intervention in the management of PPH, but its effectiveness depends on its early administration and better hospital conditions.

Keywords: Postpartum Hemorrhage, Tranexamic acid, Maternal Mortality, Pharmacological Treatment.

[1] Medical Student - Ceuma University, São Luís - MA
[2] Medical Student - Ceuma University, São Luís - MA
ORCID: 0000-0002-5175-9426
[3] Medical Student - Ceuma University, São Luís - MA
ORCID: 0009-0009-1610-0093
[4] Medical Student - Ceuma University, São Luís - MA
ORCID: 0009-0005-2245-3486

INTRODUCTION

Postpartum hemorrhage (PPH) is one of the most serious complications of the postnatal period and one of the leading causes of maternal death in the world. Defined as the loss of more than 500 mL of blood after vaginal delivery or more than 1,000 mL after a cesarean section, PPH can worsen rapidly and, if not treated effectively, can lead to multiple organ failure and maternal death. According to the World Health Organization (WHO), PPH is responsible for about 25% of maternal deaths in the world, with a higher incidence in low- and middle-income countries, where access to emergency obstetric care is still limited (OSENI et al., 2021).

Risk factors for PPH are varied, but uterine atony – the inability of the uterus to contract properly after delivery – is the main cause, accounting for approximately 70% of cases (ALAM et al., 2023). Other causes include obstetric trauma, placental retention, and coagulation disorders. Although uterotonic agents such as oxytocin are routinely used as a first-line treatment to induce uterine contraction, there are situations in which these approaches are not sufficient to control bleeding. In these circumstances, other therapies are needed to prevent progression to more severe complications (McCormick et al., 2021).

One of the most promising therapeutic innovations in the treatment of PPH is tranexamic acid (TXA). TXA is an antifibrinolytic agent that works by inhibiting the breakdown of blood clots, helping to stabilize clots and reduce bleeding. Originally used to control hemorrhages in surgeries and severe trauma, its use in the obstetric context has shown significant results in reducing maternal mortality associated with PPH (WOMAN TRIAL COLLABORATORS, 2017). Its effective mechanism of action and safety profile make tranexamic acid an important addition to PPH management strategies (SHAKUR et al., 2017).

The most comprehensive study on the use of TXA in the management of PPH was the WOMAN Trial (World Maternal Antifibrinolytic Trial). This randomized, placebo-controlled clinical trial enrolled more than 20,000 women in 21 countries and demonstrated that early administration of TXA, especially in the first three hours after the onset of hemorrhage, reduced maternal bleeding mortality by 31% (WOMAN TRIAL COLLABORATORS, 2017). The results of this study reinforce the importance of rapid administration of TXA to maximize its beneficial effect on bleeding control (OSENI et al., 2021).

In addition to reducing hemorrhage deaths, the WOMAN Trial showed that TXA also significantly decreased the need for invasive surgeries, such as laparotomy, to control bleeding (SHAKUR et al., 2017). However, the study did not observe a reduction in the rate

of hysterectomies, likely due to the fact that the decision to perform a hysterectomy is often made before TXA administration or in the most severe cases where other interventions fail (McCormick et al., 2021).

Given the proven efficacy of tranexamic acid, the WHO has included TXA in its guidelines for the treatment of PPH, recommending its use in cases where uterotonic agents fail to control bleeding or when hemorrhage is due to obstetric trauma (ALAM et al., 2023). However, the widespread implementation of this intervention in low- and middle-income countries faces challenges, such as lack of access to medicines and inadequate health infrastructure. Even so, international efforts have sought to integrate TXA into obstetric emergency clinical practices around the world (OSENI et al., 2021).

Postpartum hemorrhage is a treatable condition, and the introduction of affordable and rapidly implemented interventions such as TXA can significantly reduce maternal deaths. The use of TXA has already been incorporated into WHO guidelines, but there are still challenges to its large-scale implementation, especially in resource-limited settings (ALAM et al., 2023).

Given the growing importance of TXA in the management of PPH, how does tranexamic acid impact maternal mortality in cases of PPH, and what are the latest updates on its use and implementation?

The aim of this integrative review is to explore the efficacy of tranexamic acid in the management of postpartum haemorrhage, with an emphasis on reducing maternal mortality and updating treatment. In addition, we will discuss the challenges for the implementation of this intervention in different socioeconomic contexts, proposing solutions for a broader application in public health systems, especially in regions with a high prevalence of maternal deaths.

METHODOLOGY

This integrative review was conducted with the aim of synthesizing evidence on the efficacy of tranexamic acid (TXA) in the management of postpartum hemorrhage (PPH) and its implications for maternal mortality. To ensure methodological rigor, the integrative review model proposed by Whittemore and Knafl (2005) was followed, which involves five stages: formulation of the research question, literature search, evaluation of studies, analysis and synthesis of data, and presentation of results.

The research question was structured using the PICO (Population, Intervention, Comparison, Outcome) strategy, as described below:

- P (Population): Women in the postpartum period who suffered PPH;

- I (Intervention): Administration of tranexamic acid (TXA) in standardized doses (usually 1 g intravenously);
- C (Comparison): Women who did not receive TXA or who received only the standard treatment (uterotonics such as oxytocin);
- O (Outcome): Reduction of maternal mortality, reduction of surgical interventions and reduction of blood loss.

Based on this framework, the research question set was, "Is tranexamic acid effective in reducing maternal mortality and complications associated with postpartum hemorrhage, and how does its effectiveness vary in different socioeconomic contexts?"

The search was carried out in the PubMed, VHL (Virtual Health Library) and SciELO databases, covering the period from 2014 to 2024. The search terms were combined with Boolean operators as follows:

- ("postpartum hemorrhage" OR "hemorragia pós-parto") AND ("tranexamic acid" OR "ácido tranexâmico")
- ("maternal mortality" OR "mortalidade materna") AND ("TXA treatment" OR "tratamento TXA")

The searches resulted in 29 articles in PubMed, 11 in the VHL and 1 in SciELO. After applying the inclusion and exclusion criteria, 9 articles were selected. We included 3 studies widely recognized in the literature, totaling 12 articles analyzed.

INCLUSION AND EXCLUSION CRITERIA

- Inclusion Criteria: Peer-reviewed studies published between 2014 and 2024 that dealt with the administration of TXA in PPH were included. We considered randomised controlled trials, observational studies, and systematic reviews that assessed maternal mortality, need for surgical interventions, or reduced blood loss. The studies included samples from high-, middle- and low-income countries.
- Exclusion Criteria: We excluded studies without access to the full text, with insufficient data or that addressed non-obstetric bleeding complications. Purely theoretical reviews, studies with small samples or without statistical significance were also excluded.

The methodological quality of the studies was assessed using the Critical Appraisal Skills Programme (CASP) tool, adapted for randomised controlled trials and observational

studies. The evaluation included criteria such as methodological rigor, internal and external validity, and relevance of the results. All included studies met the minimum quality standards required for review.

Data from the selected studies were extracted by two reviewers independently, categorizing variables such as study type, population, intervention (TXA dose, time of administration), and outcomes (maternal mortality, need for surgical interventions, and complications). In case of disagreements, a third reviewer was consulted. The comparative analysis focused on differences in effectiveness between high-, middle- and low-income countries, with the aim of identifying patterns and determinants for the success of the TXA intervention.

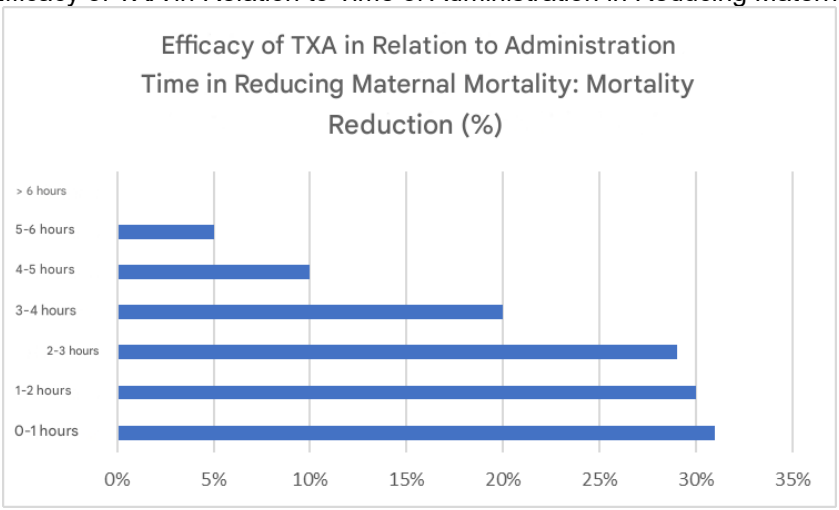
DEVELOPMENT OF THE REVIEW

Postpartum hemorrhage (PPH) is one of the leading causes of maternal death globally, with the greatest impact in low- and middle-income countries. Tranexamic acid (TXA), an antifibrinolytic agent, has been shown to be an effective intervention to reduce maternal mortality associated with PPH, especially when administered early, in the first three hours after the onset of bleeding. In this section, we explore key findings on the efficacy, safety, and challenges for implementing TXA in different socioeconomic contexts.

EFFICACY OF TRANEXAMIC ACID IN THE CONTROL OF PPH

The WOMAN Trial, conducted by Shakur et al. (2017), is the largest and most robust study to date on the use of TXA in the management of PPH. This randomized clinical trial, with the participation of more than 20,000 women in 21 countries, revealed a 31% reduction in maternal mortality when TXA was administered in the first three hours after the onset of hemorrhage.

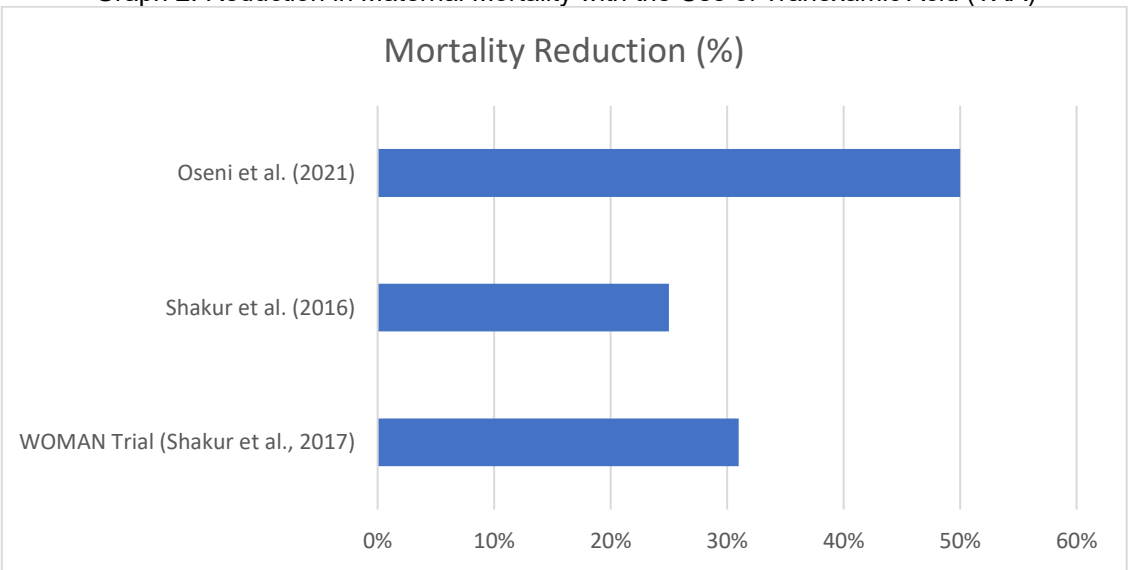
Graph 1 - Efficacy of TXA in Relation to Time of Administration in Reducing Maternal Mortality.



Caption: The efficacy of TXA in reducing maternal mortality is greatest in the first three hours after the onset of hemorrhage, decreasing significantly thereafter.

The study demonstrated that TXA reduced the need for invasive surgical interventions, such as hysterectomies, without increasing the risk of thromboembolic complications (SHAKUR et al., 2017). The study conducted by Oseni et al. (2021), focused on women undergoing cesarean sections in a low-income context in Nigeria, also showed significant results. The administration of TXA reduced intraoperative blood loss by up to 50%, evidencing its effectiveness in resource-limited settings, where the ability to respond quickly to obstetric emergencies is critical for patient survival (OSENI et al., 2021).

Graph 2: Reduction in Maternal Mortality with the Use of Tranexamic Acid (TXA)



Caption: The WOMAN Trial demonstrated a 31% reduction in maternal mortality, while the study by Shakur et al. (2016) reported a 25% reduction in hysterectomies and bleeding complications. The study by Oseni et al. (2021) reported a reduction of up to 50% in intraoperative blood loss during cesarean sections.

In addition to the therapeutic use of TXA in situations of established postpartum hemorrhage, tranexamic acid has been investigated for prophylactic use. A recent

systematic review and meta-analysis, published by Assis et al. (2023), evaluated the efficacy of TXA in preventing postpartum bleeding in vaginal and cesarean deliveries. The study included 16 randomized controlled trials with 6,731 patients and demonstrated that the prophylactic use of TXA was a protective factor against excessive bleeding (mean difference: -131.07 mL; 95% CI: -170.00 to -92.78; $p < 0.001$), in addition to presenting positive results in hemoglobin variation. These findings suggest that TXA may be an effective intervention to reduce blood loss in preventive settings, especially in cesarean sections, where bleeding is more profuse.

COMPARISON OF EFFECTIVENESS IN DIFFERENT SOCIOECONOMIC CONTEXTS

Although TXA is a low-cost intervention and proven to be effective in reducing maternal mortality related to postpartum hemorrhage (Shakur et al., 2017; Roberts et al., 2013), its large-scale implementation in low- and middle-income countries presents challenges. Studies suggest that TXA is economically viable, especially when compared to the cost of more invasive surgical interventions, such as hysterectomies, and the need for blood transfusions (Franchini et al., 2018).

However, the lack of adequate infrastructure and the need for specialized training for the early administration of TXA in obstetric emergencies still pose significant barriers, as highlighted by Sentilhes et al. (2018). These disparities are especially evident when comparing the effectiveness of the TXA in high-income countries with low- and middle-income countries.

Chart 1 below illustrates the impact of TXA administration in different socioeconomic contexts, highlighting critical factors such as access to transfusions, thrombotic complications, and availability of emergency surgeries:

Chart 1: Impact of TXA Administration in Different Socioeconomic Contexts

RATED FACTOR	HIGH-INCOME COUNTRIES	LOW- AND MIDDLE-INCOME COUNTRIES
ACCESS TO TRANSFUSIONS	Wide access, allowing effective control of hemorrhages.	Limited access, undermining the full effectiveness of TXA.
THROMBOTIC COMPLICATIONS	Reduced and non-significant risk, as evidenced.	No increase observed, however, robust data is lacking in regions with fewer resources.
AVAILABILITY OF SURGERIES	Complete infrastructure for emergency surgeries.	Limited infrastructure, making it difficult to carry out complementary interventions, such as emergency surgeries.

The adoption of protocols that include the use of TXA can be facilitated by investments in training health professionals and by improving access to care centers, especially in remote areas.

The positive results observed in high-income countries indicate that, with the right infrastructure and support, TXA can be a highly effective intervention to reduce maternal mortality in cases of postpartum hemorrhage. However, it is essential to prioritize actions to improve health infrastructure and specialized training so that these results can be replicated in low- and middle-income countries.

In low-income countries, such as Nigeria, the study by Oseni et al. (2021) highlighted that despite the effectiveness of TXA, the lack of adequate resources for blood transfusions and surgical interventions limits the full impact of the intervention. Similarly, Picetti et al. (2020) analyzed data from the WOMAN Trial in low- and middle-income countries and concluded that the lack of hospital infrastructure compromises outcomes, even when TXA is properly administered (PICETTI et al., 2020).

Table 2: Comparison of Major Studies on the Use of Tranexamic Acid (TXA) in PPH

Study	Type of study	Intervention (txa)	Results	Conclusions
WOMAN TRIAL (SHAKUR ET AL., 2017)	Randomized, multicenter clinical trial	1 g IV TXA administered within 3 hours	31% reduction in maternal mortality due to PPH	TXA is effective when administered early. There was no increase in thromboembolic complications.
OSENI ET AL. (2021)	Randomized controlled trial	1 g TXA by cesarean section	50% reduction in intraoperative blood loss	Effective in low-income contexts, reducing the need for transfusions.
SHAKUR ET AL. (2016)	Randomized multicenter study	1 g of TXA i.v. administered after vaginal delivery or cesarean section	25% reduction in hysterectomies and bleeding complications	TXA reduces the need for hysterectomies and serious complications. Safe in obstetric emergencies.
PICETTI ET AL. (2020)	Qualitative analysis of the WOMAN Trial	1 g TXA in low/middle-income settings	Limited impact in places with inadequate hospital infrastructure	Lack of access to transfusions and surgery impairs effective management with TXA.

Chart 2 highlights a comprehensive comparison of major studies on the use of tranexamic acid (TXA) in the management of postpartum hemorrhage (PPH), making it easier to visualize the different contexts and interventions. The WOMAN Trial (Shakur et al., 2017), being one of the largest multicenter clinical trials conducted, demonstrated that TXA is highly effective in reducing maternal mortality, especially when administered within the first three hours after the onset of hemorrhage.

Oseni et al. (2021), in turn, evidenced that TXA is also effective in low-income contexts, significantly reducing intraoperative blood loss during cesarean sections, but its full effectiveness depends on access to other resources, such as blood transfusions. The study by Shakur et al. (2016) reinforces the safety of TXA in obstetric emergencies, with a reduction of up to 25% in hysterectomies and serious complications.

However, the qualitative analysis by Picetti et al. (2020) points out that the lack of adequate hospital infrastructure can limit the impact of TXA in low- and middle-income countries, hindering the effective management of PPH. These findings underscore the importance of early administration and hospital support to ensure the best clinical outcomes.

In contrast, Alam et al. (2023), in a study conducted in Canada, showed that TXA was highly effective in reducing postpartum hemorrhage in a setting with advanced hospital infrastructure. The study highlighted that in high-income settings, where there is adequate access to blood transfusions and surgical support, TXA can be safely administered without increased thromboembolic complications (ALAM et al., 2023).

Table 1: Comparison of TXA Effectiveness in High- and Low-Income Contexts

Context	Countries	Key findings	Conclusions
High income	Canadá (Alam et al., 2023)	TXA reduced postpartum hemorrhage without increasing complications	TXA was safe and effective, with adequate support from hospital infrastructure.
Low/middle income	Nigéria (Oseni et al., 2021); Países do WOMAN Trial	Limitations due to lack of blood and hospital resources	Even effective, the lack of infrastructure compromises early management and its impact.

SAFETY AND COMPLICATION CONSIDERATIONS

The safety of TXA was a central point in the reviewed studies. Both the WOMAN Trial and the study by Alam et al. (2023) confirmed that TXA does not significantly increase the risk of thromboembolic complications, which makes it a viable option in obstetric emergencies. The study by Shakur et al. (2016) also demonstrated that, when administered at recommended doses, TXA is safe, with no increased risk of thrombosis in women suffering from PPH (SHAKUR et al., 2016; ALAM et al., 2023).

However, studies conducted in low-income countries highlight that while TXA is safe, the lack of access to emergency care, such as surgeries and blood transfusions, limits its impact. This situation is exacerbated in regions where hospital infrastructure is fragile, as indicated by Picetti et al. (2020). This context reveals the need to improve health infrastructure in these countries to maximize the potential of interventions such as TXA (PICETTI et al., 2020).

Chart: Safety and Complications Associated with the Use of Tranexamic Acid (TXA) in the Management of Postpartum Hemorrhage

Study	Key Findings	TXA Security	Limitations
WOMAN Trial (Shakur et al., 2017)	TXA reduced maternal mortality without increasing the risk of thromboembolic complications.	Safe when administered within the first three hours of the onset of bleeding.	Efficacy decreases if administered after three hours.

Alam et al. (2023)	TXA was found to be safe in advanced hospital settings, with adequate infrastructure.	There was no significant increase in thromboembolic complications.	Limitations in access to rapid surgical care and transfusions can affect effectiveness.
Shakur et al. (2016)	The study demonstrated that TXA, at recommended doses, is safe and effective, with no increased risk of thrombosis.	Safe in obstetric emergencies when administered early.	The need for adequate infrastructure to maximize effectiveness was underscored.
Picetti et al. (2020)	In low-income countries, TXA is safe, but lack of access to emergency care limits its impact.	Although safe, the absence of hospital infrastructure compromises the potential of the intervention.	Weak infrastructure, absence of transfusions, and emergency surgeries reduce the overall effectiveness of TXA treatment.

GAPS IN THE LITERATURE AND AREAS FOR FUTURE STUDIES

Although tranexamic acid has been shown to be effective in reducing maternal mortality, there are significant gaps in the literature that need to be addressed. First, there is a lack of studies investigating the long-term impact of TXA use in women with comorbidities, such as severe anemia and hypertension, conditions common in low-income countries. In addition, it is necessary to assess the cost-benefit of administering the TXA in contexts with limited hospital infrastructure, to ensure its sustainable viability (PICETTI et al., 2020; OSENI et al., 2021).

DISCUSSION

The reviewed studies largely demonstrate the efficacy of tranexamic acid (TXA) in the management of postpartum hemorrhage (PPH), with robust evidence of its ability to reduce maternal mortality and the need for invasive surgical interventions such as hysterectomies. However, this efficacy presents significant variations depending on the socioeconomic context and the available health infrastructure, resulting in important agreements and counterpoints between the findings.

AGREEMENT BETWEEN STUDIES

Major peer-reviewed studies, such as the WOMAN Trial (Shakur et al., 2017) and the study by Shakur et al. (2016), agree in pointing to TXA as an effective intervention to reduce maternal mortality associated with PPH. In the WOMAN Trial, which involved more than 20,000 women in 21 countries, early administration of 1 g of intravenous TXA reduced maternal hemorrhage mortality by 31%, when administered within the first three hours after bleeding onset (SHAKUR et al., 2017). Similarly, Shakur et al. (2016) confirmed that TXA is also effective in reducing the need for hysterectomies by up to 25%, which reinforces the safety of TXA as a first-line intervention for the management of obstetric emergencies.

The study conducted by Oseni et al. (2021), conducted in Nigeria, highlights the effectiveness of TXA in intraoperative settings, especially in cesarean sections, where a reduction of up to 50% in intraoperative blood loss has been observed. This finding is consistent with the idea that TXA is an effective intervention in different clinical settings, even in regions with limited resources. All reviewed studies agree that the use of TXA does not significantly increase the risk of thromboembolic complications, a frequent concern when using antifibrinolytics in obstetric emergencies (OSENI et al., 2021; SHAKUR et al., 2017).

COUNTERPOINTS AND CONTEXTUAL DIFFERENCES

Despite the promising results, the studies highlight significant differences in the impacts of TXA in high- and low-income countries. The study by Alam et al. (2023), conducted in Canada, demonstrated that TXA is extremely effective and safe when administered in contexts with adequate hospital infrastructure, without an increase in thromboembolic complications (ALAM et al., 2023). In contrast, the analysis by Picetti et al. (2020), based on data from the WOMAN Trial, pointed out that in low-income countries, where hospital infrastructure is inadequate, the impact of TXA is limited by lack of access to blood transfusions and emergency surgical interventions. Even with the correct administration of the TXA, the absence of essential resources compromises the results (PICETTI et al., 2020).

Another point of divergence is in the early administration of TXA. The WOMAN Trial was clear in demonstrating that TXA is most effective when administered within the first three hours after the onset of hemorrhage. After this period, the effectiveness of the drug decreases significantly (SHAKUR et al., 2017). In low-income countries, however, the lack of emergency infrastructure can delay the administration of TXA, reducing its potential effectiveness. As noted by Picetti et al. (2020), in many regions, delays in treatment due to a lack of trained health professionals and logistical difficulties can hinder the beneficial effect of the intervention.

DETERMINING FACTORS FOR THE EFFECTIVENESS OF TXA

One of the most determining factors for the success of the TXA is the administration time. The WOMAN Trial (Shakur et al., 2017) showed that the maximum efficacy of TXA occurs when administered within three hours of the onset of hemorrhage. After this period, the benefits decrease substantially, which highlights the importance of rapid response protocols in obstetric emergencies. Early administration reduces maternal mortality and

decreases the need for invasive surgical interventions, such as hysterectomies, in addition to minimizing the risk of severe complications (SHAKUR et al., 2017).

However, in many low- and middle-income countries, early administration of TXA is hampered by a lack of hospital infrastructure and trained medical staff, as pointed out by Picetti et al. (2020). The study suggests that even when TXA is available, the absence of adequate support for transfusions and surgical interventions compromises its full effectiveness. Therefore, in addition to ensuring access to the drug, it is essential that there is training of health teams and adequate infrastructure to treat bleeding complications.

CHALLENGES TO GLOBAL IMPLEMENTATION

Implementing TXA on a global scale faces several challenges, especially in low-income regions. While TXA has proven effective in low-resource settings, as demonstrated by Oseni et al. (2021) in Nigeria, logistical challenges continue to hinder its efficient application. The main obstacle is the lack of access to surgical care and transfusions, which are essential for the complete management of postpartum hemorrhage (OSENI et al., 2021).

As pointed out by Picetti et al. (2020), the implementation of TXA in poorer regions requires significant investments in hospital infrastructure. The absence of health policies that promote the use of antifibrinolytic drugs, combined with the lack of adequate training of health teams, contribute to the fact that TXA does not reach its full potential to save lives in obstetric emergency contexts (PICETTI et al., 2020). This scenario underlines the need for international cooperation to improve access to and effective use of TXA in countries with high maternal mortality.

STUDY LIMITATIONS

Despite the positive results, all studies face limitations. The WOMAN Trial, for example, involved a wide variety of countries, which made it possible to observe TXA in different contexts. However, differences in health systems and available resources in each country make it difficult to generalize the results.

The lack of long-term data on the effects of TXA in women with comorbidities, such as severe anemia and hypertension, also represents an important limitation. These conditions are common in low-income countries and may influence the long-term efficacy and safety of TXA (SHAKUR et al., 2017; PICETTI et al., 2020).

The study by Oseni et al. (2021), while relevant for highlighting the effectiveness of TXA in low-income settings, was conducted at a single institution in Nigeria, which may limit

the extrapolation of results to other regions with similar challenges. Another important limitation is that few peer-reviewed studies address the cost-effectiveness of TXA administration in low- and middle-income countries, where health systems often operate with limited resources.

PRACTICAL AND THEORETICAL IMPLICATIONS

The revised results have important practical implications. The use of TXA should be integrated in a standardized way into PPH management protocols, especially in low- and middle-income countries, where maternal mortality is high. However, it is essential that these regions invest in improving hospital infrastructure, ensuring adequate access to blood transfusions and surgical support.

Early administration of TXA, as demonstrated by the WOMAN Trial, should be a priority to ensure maximum treatment efficacy (SHAKUR et al., 2017; ALAM et al., 2023). From a theoretical point of view, the reviewed studies suggest the need for new models of obstetric intervention, which take into account regional disparities in access to health care.

Incorporating TXA as part of routine obstetric care can save thousands of lives, but it must be accompanied by investments in infrastructure and training of health teams in low- and middle-income countries.

GAPS IN THE LITERATURE AND AREAS FOR FUTURE STUDIES

While the results so far are promising, there are significant gaps that need to be addressed. First, the lack of studies on the long-term effects of TXA use in vulnerable populations, such as women with severe comorbidities, should be explored. Further studies are needed to investigate the cost-effectiveness of administering TXA in fragile health systems, where resources are limited and emergency response capacity is reduced.

Future studies should also focus on developing improved protocols for the use of TXA in complex obstetric emergencies, such as multiple or preterm births, where hemorrhages can be more severe and difficult to control. Another important field of research would be adapting public health policies that promote the equitable distribution of treatments like TXA around the world, especially in regions that still struggle with high maternal mortality rates.

CONCLUSION

The present integrative review demonstrated that tranexamic acid (TXA) is an effective and safe intervention in the management of postpartum hemorrhage (PPH), and is

especially effective in reducing maternal mortality when administered early, in the first three hours after the onset of hemorrhage.

Studies such as the WOMAN Trial (Shakur et al., 2017) showed a 31% reduction in maternal mortality, while Shakur et al. (2016) evidenced a significant reduction in hysterectomies and severe bleeding complications. These findings were corroborated by studies conducted in both high- and low-income countries, such as the study by Oseni et al. (2021), which pointed to a 50% reduction in intraoperative blood loss in cesarean sections in Nigeria.

However, the effectiveness of TXA is directly associated with the quality of hospital infrastructure and the availability of medical resources, such as blood transfusions and trained emergency teams. In low- and middle-income countries, lack of access to these resources limits the impact of intervention, as evidenced by Picetti et al. (2020), who showed that the absence of adequate hospital support compromises effective TXA administration.

These challenges point to the need for investments in healthcare infrastructure and specialized training to ensure that TXA can reach its full potential in these regions. Early administration of TXA, within the first three hours after the onset of hemorrhage, has been identified as a determining factor for the effectiveness of the intervention. After this period, the TXA's ability to prevent deaths and serious complications decreases significantly, reinforcing the need for rapid response protocols in obstetric emergencies, especially in countries with fragile health systems.

Despite the advances, there are still gaps in the literature that need to be filled through new studies. Robust data on the long-term effects of TXA use are lacking, particularly in women with comorbidities such as severe anemia and hypertension, conditions often present in low-income countries.

In addition, there is a lack of studies investigating the cost-benefit of implementing TXA in health systems with limited resources, and also the need to develop specific protocols for the use of TXA in more complex obstetric emergencies, such as multiple or premature births.

Therefore, the review points out that, although TXA plays a crucial role in the management of PPH, its effectiveness depends on early administration, adequate infrastructure, and training of health professionals. Widespread adoption of TXA, especially in regions with high maternal mortality rates, requires not only the availability of the drug, but also structural reforms in health systems and international cooperation to ensure that women around the world have access to this life-saving treatment. Future studies should

explore ways to optimize the implementation of TXA in diverse contexts, ensuring its safe and effective use in all regions.

REFERENCES

1. Alam, A., et al. (2023). Tranexamic acid for the prevention of postpartum haemorrhage: The TAPPH 1 pilot randomized trial and lessons learned for trials in Canadian obstetrics. Scientific Reports, 13(4512). https://doi.org/10.1038/s41598-023-30947-3. Accessed on September 8, 2024.

2. Assis, I. C., Govêia, C. S., Miranda, D. B., Ferreira, R. S., & Riccio, L. G. C. (2023). Analysis of the efficacy of prophylactic tranexamic acid in preventing postpartum bleeding: Systematic review with meta-analysis of randomized clinical trials. Brazilian Journal of Anesthesiology, 73(4), 467-476.

3. Franchini, M., Mengoli, C., Cruciani, M., Marano, G., Puppe, S., Grazzini, G., et al. (2018). Safety and efficacy of tranexamic acid for prevention of obstetric haemorrhage: An updated systematic review and meta-analysis. Blood Transfusion, 16(4), 329-337. https://doi.org/10.2450/2018.0154-17.

4. McCormick, M., et al. (2021). Maternal health outcomes and blood transfusion in obstetric emergencies: Impact of tranexamic acid administration. Journal of Maternal-Fetal & Neonatal Medicine. https://doi.org/10.1080/14767058.2021.1977987. Accessed on September 8, 2024.

5. Oseni, R. O., et al. (2021). Effectiveness of preoperative tranexamic acid in reducing blood loss during caesarean section at Aminu Kano Teaching Hospital, Kano: A randomized controlled trial. Pan African Medical Journal, 39(34). https://doi.org/10.11604/pamj.2021.39.34.21060. Accessed on September 8, 2024.

6. Picetti, R., et al. (2020). Tranexamic acid for the treatment of postpartum haemorrhage: An exploratory analysis of the WOMAN trial. BMC Pregnancy and Childbirth, 20(1). https://doi.org/10.1186/s12884-020-03091-8. Accessed on September 8, 2024.

7. Roberts, I., et al. (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, 17(10), 1-79. https://doi.org/10.3310/hta17100.

8. Sentilhes, L., et al. (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.

9. Shakur, H., et al. (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. The Lancet, 389, 2105-2116. https://doi.org/10.1016/S0140-6736(17)30638-4. Accessed on September 6, 2024.

10. Shakur, H., et al. (2016). WOMAN Trial: The World Maternal Antifibrinolytic Trial (WOMAN) Protocol. Trials, 17(249). https://doi.org/10.1186/s13063-016-1332-2. Accessed on September 8, 2024.

11. Whittemore, R., & Knafl, K. (2005). The integrative review: Updated methodology. Journal of Advanced Nursing, 52(5), 546-553. https://doi.org/10.1111/j.1365-2648.2005.03621.x. Accessed on September 6, 2024.