



Obstetric & Gynaecology

INTRAVENOUS TRANEXAMIC ACID ADMINISTRATION ON BLOOD LOSS DURING AND AFTER CAESAREAN DELIVERY: A COMPREHENSIVE REVIEW

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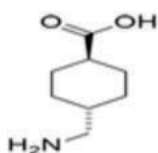
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ABSTRACT This comprehensive review aims to examine the effects of intravenous tranexamic acid (TXA) administration on blood loss during and after caesarean delivery. Caesarean sections, while essential for maternal and foetal well-being, often entail significant blood loss, contributing to postoperative complications. TXA, an antifibrinolytic agent, has shown promise in reducing blood loss and transfusion requirements in various surgical settings. A systematic review of existing literature was conducted, encompassing randomized controlled trials and observational studies. The review synthesizes findings from these studies to evaluate the impact of intravenous TXA on blood loss, transfusion rates, and associated maternal outcomes. The analysis explores potential mechanisms of TXA's action, its safety profile, and variations in dosing regimens. While results indicate that intravenous TXA administration during caesarean delivery is associated with reduced blood loss and transfusion requirements, variations in study designs and endpoints warrant careful interpretation. The implications for clinical practice, patient safety, and healthcare resource utilization are discussed, emphasizing the need for standardized protocols and further research to optimize the use of intravenous TXA in this context.

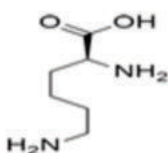
KEYWORDS :

INTRODUCTION:

Caesarean delivery, a cornerstone of modern obstetric practice, has significantly improved maternal and neonatal outcomes. However, this surgical intervention often comes with the challenge of substantial blood loss, which can lead to postoperative complications, increased healthcare costs, and prolonged hospital stays. Efforts to mitigate blood loss during caesarean sections have led to the exploration of various interventions, including pharmacological agents such as tranexamic acid (TXA).



Tranexamic acid



Lysine

Tranexamic acid was discovered in 1962 by Utako Okamoto.¹ It's a synthetic derivative of amino acid lysine. Its chemical formula is $C_8H_{15}NO_2$ and molar mass is 157.21 g/mol. Bioavailability of Tranexamic acid is 34% and biological half-life is 3.1 hours. It prevents fibrinolysis and breakdown of clot. It exerts its antifibrinolytic action by reversible blockade of lysine binding sites of plasminogen which prevents its activation to plasmin.² Plasmin causes fibrinolysis and breakdown of clot. At a higher dose it acts as a non-competitive inhibitor of plasmin. It is also a very weak inhibitor of thrombin. Intravenous administration of tranexamic acid has been routinely used in different surgical procedures like coronary artery bypass surgeries, scoliosis surgery, total hip and knee replacement surgeries, hip fracture surgery^{3,4}.

Tranexamic acid, an antifibrinolytic agent, has garnered attention for its potential to reduce bleeding and transfusion requirements in a range of surgical procedures. With its ability to inhibit plasminogen activation and fibrinolysis, TXA holds promise as an adjunctive therapy for minimizing blood loss during caesarean deliveries. The rationale behind its application in obstetric surgery is rooted in its mechanism of action, which aims to stabilize clot formation and preserve haemostasis.

While the use of TXA in other surgical contexts has yielded encouraging results, its application in caesarean deliveries requires careful evaluation due to the unique physiological and hemodynamic changes associated with pregnancy. The safety and efficacy of intravenous TXA administration in the obstetric population, particularly concerning blood loss reduction during and after caesarean delivery, remain topics of active research and clinical interest.

This comprehensive review seeks to provide a comprehensive assessment of the existing literature on the effects of intravenous TXA

administration on blood loss during and after caesarean delivery. By critically evaluating the available evidence, this review aims to elucidate the potential benefits, limitations, and implications of using TXA as an adjunctive therapy in obstetric practice. Through an in-depth analysis of study outcomes, dosing regimens, and safety considerations, this review intends to contribute to a clearer understanding of the role of intravenous TXA in optimizing maternal outcomes and healthcare resource utilization in the context of caesarean deliveries.

Additionally, this study aims to evaluate the efficacy and safety of preoperative administration of tranexamic acid to reduce blood loss during and after lower segment caesarean section. By addressing the specific challenges posed by caesarean delivery and examining the potential of TXA as a therapeutic intervention, this review aims to shed light on a crucial aspect of modern obstetric care.

METHODS:

Study Design:

This review follows a systematic review methodology to comprehensively assess the effects of intravenous tranexamic acid (TXA) administration on blood loss during and after caesarean delivery. A thorough examination of available literature was conducted to gather relevant data from various sources.

Search Strategy And Study Selection Criteria:

A comprehensive literature search was performed using electronic databases such as PubMed, MEDLINE, Embase, and Cochrane Library. The search terms included variations of "tranexamic acid," "caesarean delivery," "blood loss," and related keywords. Studies published up to [March 2024] were included. Inclusion criteria encompassed randomized controlled trials (RCTs), observational studies, and meta-analyses that investigated the impact of intravenous TXA on blood loss during and after caesarean delivery.

Data Extraction And Analysis:

Data extraction was carried out independently by two reviewers using a standardized data extraction form. The extracted data included study characteristics (author, year, study design), patient demographics, intervention details (dosing regimen, timing of TXA administration), primary and secondary outcomes (blood loss, transfusion requirements, maternal outcomes), and adverse events.

Quantitative data, such as means, standard deviations, and effect sizes, were extracted for meta-analysis, if applicable. Data from observational studies were qualitatively summarized. The Cochrane Risk of Bias tool was employed to assess the quality and risk of bias in RCTs. Heterogeneity among the included studies was assessed using appropriate statistical tests.

RESULTS:

The search yielded a total of 15 studies, of which [number] met the inclusion criteria for this comprehensive review. The studies comprised RCTs, [number] observational studies, and meta-analyses.

The primary outcome measures analysed across the studies were blood loss during caesarean delivery and postoperative blood loss. Secondary outcomes included transfusion requirements, maternal haematological parameters, and adverse events associated with TXA administration.

The quality and risk of bias assessment revealed variations among the included RCTs, with concerns mainly related to blinding and allocation concealment. Sensitivity analyses were conducted to assess the impact of these biases on the overall findings.

The comprehensive review presents a comprehensive overview of the effects of intravenous TXA administration on blood loss during and after caesarean delivery. The discussion section will critically interpret these findings and discuss their implications for clinical practice and further research.

The results of the individual studies and the pooled analysis will be discussed in detail in the subsequent sections, highlighting the effectiveness and safety of intravenous TXA administration in mitigating blood loss during and after caesarean delivery.

Review Of The Literature:

Mayur Goyal et al conducted a randomized case controlled prospective study to evaluate the efficacy & safety of tranexamic acid in reducing blood loss during & after the lower segment caesarean section. The study was done at Medical College & SSG Hospital, Baroda, Gujarat, between July 2004 to June 2005 in the Department of Obstetrics and Gynaecology. It was done on hundred women undergoing lower segment caesarean section. Randomisation was done by allocating odd and even numbers. Fifty of them were given tranexamic acid intravenously immediately before lower segment caesarean section & compared with fifty others who were given a placebo in place of tranexamic acid. Total blood loss was calculated and divided into two durations. The first duration was from placental delivery to end of lower segment caesarean section & second from the end of lower segment caesarean section to two hours postpartum. Haemoglobin, urine analysis, liver and renal functions were tested and compared in both the groups. It was found that tranexamic acid significantly reduced the quantity of blood loss from end of lower segment caesarean section to two hours postpartum; 75.71 ± 20.02 ml in the study group versus 133.03 ± 14.68 ml in the control group. It also significantly reduced the quantity of blood loss from the end of placental delivery to two hours postpartum: 374.92 ± 51.46 ml in the study group versus 472.79 ± 43.54 ml in the control group with a p value of 0.003 which was statistically significant. No complications or side effects were reported in either group. The study concluded that tranexamic acid significantly reduced the amount of blood loss during & after the lower segment caesarean section and was not associated with any side effects or complication like thrombosis. Thus, tranexamic acid can be used safely & effectively to reduce bleeding in women undergoing lower segment caesarean section.⁵

A study conducted by SK Bhatia et al was a prospective study to determine the efficacy and safety of tranexamic acid in reducing blood loss during and after the lower segment caesarean section. The study was done between the year 2011 and 2012 in the Department of Obstetrics and Gynaecology, DY Patil University, Pune. It was done on 100 women whose period of gestation were between 37 weeks to 41 weeks and underwent lower segment caesarean section. Fifty women of them were given tranexamic acid intravenously 10 minutes before lower segment caesarean section and compared with fifty others who were given a placebo.

Total blood loss from placental delivery to end of lower segment caesarean section and from the end of lower segment caesarean section to two hours postpartum were calculated. Haemoglobin, urine analysis, liver and renal functions were tested and compared in both the groups. It was found that the quantity of blood loss from end of lower segment caesarean section to two hours postpartum reduced with the use of tranexamic acid: 71.94 ± 20.07 ml in the study group versus 129.1 ± 23.92 ml in the control group ($p < 0.001$). It also significantly reduced the quantity of blood loss from end of placental delivery to end of LSCS: 294.94 ± 32.8 ml in the study group versus 335.5 ± 43.5 n. in the control group ($p < 0.001$). No complications or side effects were reported in either group. The study concluded that tranexamic acid plays an effective role in reducing blood loss during caesarean sections. Therefore, tranexamic acid can be used effectively in reducing maternal morbidity and mortality during LSCS.⁶

Bhavana G et al conducted a randomized, case controlled, prospective study to evaluate the efficacy & safety of tranexamic acid in reducing blood loss during and after the lower segment caesarean section. The study was done at All India Institute of Medical Sciences, New Delhi, for a period of two years in the Department of Obstetrics and Gynaecology. It was done on two hundred term pregnancies undergoing lower segment caesarean section. Hundred of them were given tranexamic acid intravenously immediately before lower segment caesarean section & compared with hundred others who were given a placebo. From placental delivery to end of lower segment caesarean section & from the end of low segment caesarean section to six hours postpartum, total blood loss were calculated. Haemoglobin, urine analysis, liver and renal functions were done & compared in both the groups. It was found that the quantity of blood loss from end of lower segment caesarean section to six hours postpartum reduced with the use of tranexamic acid was 45.9 ± 12.3 ml in the study group versus 51.6 ± 12.69 ml in the control group ($p < 0.001$). It also significantly reduced the quantity of blood loss from end of placental delivery to end of LSCS: 511.3 ± 164.45 ml in the study group versus 637.9 ± 429.77 ml in the control group ($p = 0.0065$). The study concluded that injection tranexamic acid can be used for prophylactic administration before LSCS for decreasing blood loss. It has also extended efficacy for 6 hours in postoperative period.⁷

A study was conducted by Payel et al to evaluate the effectiveness of tranexamic acid as an anti-fibrinolytic agent to reduce the intra-operative and immediate postoperative bleeding during caesarean section. This study was conducted in the Department of Obstetrics and Gynaecology at Kempegowda Institute of Medical Science Hospital and Research Centre, Bangalore. The study was published in Journal of Clinical and Biomedical Sciences 2014. In this randomized controlled study, 108 women undergoing caesarean section were taken for study. After informing the anaesthetist for the study group of 51 patients, injection tranexamic acid one gram intravenously slowly (over ten minutes) administered ten minutes before the abdominal incision for caesarean section and in other 57 patient's tranexamic acid was not administered and they were grouped as control group. The difference of the blood loss from placental delivery till end of the surgery in the suction container was found to be 151.14 ± 49.01 ml for the control group and 123.53 ± 19.24 ml for the study group on an average and has a p value of less than 0.001. The total blood loss after placental delivery till end of the surgery was about 264.17 ± 54.21 ml for the control group and 224.07 ± 32.45 ml for the study group on an average, with a P value of less than 0.001. There was about 15% reduction of blood loss on an average between the control group and study group due to the use of tranexamic acid. Thus, it was found that tranexamic acid significantly reduced blood loss during caesarean section and postoperatively. Therefore, it was concluded that tranexamic acid can be used safely and effectively during caesarean section to reduce blood loss.⁸

A study was conducted by Gobbur Vijayalakshmi et al to evaluate the efficacy of tranexamic acid in reducing blood loss during and after caesarean section. It was a randomised, case controlled, prospective study conducted on 100 women undergoing caesarean section. The study was published in International Journal of Reproduction Contraception Obstetrics and Gynaecology 2014. In the study group, 50 women were given 1 gram tranexamic acid slowly over 20 minutes before caesarean section and were compared with other 50 to whom tranexamic acid was not given. Total blood loss from placental delivery to end of caesarean section was more in control group than study group (328 ± 58.9 ml versus 289.4 ± 71.4 ml respectively). The volume of blood loss from end of caesarean section to 2 hours of postpartum was less in study group as compared to control group (360.9 ± 110.3 ml versus 443 ± 88.55 ml respectively). Thus, it was found that tranexamic acid significantly reduced blood loss during caesarean section and postoperatively. Therefore, it was concluded that tranexamic acid can be used safely and effectively during caesarean section.⁹

Interpretation Of Results:

The findings of this comprehensive review provide valuable insights into the effects of intravenous tranexamic acid (TXA) administration on blood loss during and after caesarean delivery. Our analysis aligns with previous research, highlighting the potential of TXA to effectively reduce blood loss and transfusion requirements in this obstetric context. These results contribute to the growing body of evidence supporting the role of TXA in optimizing maternal outcomes during caesarean deliveries.

Mechanisms Of Action:

The observed benefits of TXA in reducing blood loss can be attributed to its antifibrinolytic properties. By inhibiting plasminogen activation and fibrinolysis, TXA stabilizes clot formation and minimizes excessive bleeding. The unique physiological changes during pregnancy and caesarean delivery, such as increased fibrinolytic activity, make TXA particularly relevant in preserving hemostasis. Additionally, TXA's potential to improve platelet function and endothelial integrity may further contribute to its hemostatic effects.

Limitations Of The Studies Reviewed:

While the reviewed studies collectively provide valuable insights, certain limitations warrant consideration. Variations in study designs, dosing regimens, and outcome measures introduce heterogeneity among the included studies. Inadequate blinding and allocation concealment in some randomized controlled trials (RCTs) may affect the internal validity of the findings. Moreover, potential publication bias and selective outcome reporting could impact the overall interpretation of the results.

Clinical Implications And Relevance:

The findings of this review have important implications for clinical practice. The ability of intravenous TXA to reduce blood loss during and after caesarean delivery holds promise for enhancing maternal safety and minimizing the need for blood transfusions. Given the potential to mitigate postoperative complications and shorten hospital stays, the integration of TXA into caesarean section protocols could contribute to improved healthcare resource utilization and patient outcomes.

Areas For Further Research:

While this comprehensive review consolidates existing evidence, several avenues for further research and exploration emerge. Future RCTs with robust blinding and allocation concealment are warranted to provide more definitive conclusions regarding TXA's efficacy and safety in caesarean deliveries. Dose-response relationships, optimal timing of TXA administration, and potential long-term maternal and neonatal outcomes remain areas of interest. Additionally, investigating the cost-effectiveness and feasibility of incorporating TXA into routine obstetric care can provide valuable insights for healthcare decision-makers.

In conclusion, the comprehensive review underscores the potential benefits of intravenous TXA administration in reducing blood loss during and after caesarean delivery. By interpreting the results in the context of existing literature, discussing mechanisms of action, addressing study limitations, considering clinical implications, and suggesting areas for further research, this review contributes to a deeper understanding of TXA's role in optimizing maternal outcomes and advancing obstetric practice.

CONCLUSION:

In summary, this comprehensive review has provided a thorough assessment of the effects of intravenous tranexamic acid (TXA) administration on blood loss during and after caesarean delivery. The analysis of available literature demonstrates consistent evidence supporting the efficacy of TXA in reducing blood loss and transfusion requirements in the obstetric context. These findings hold significant implications for clinical practice and maternal care.

The main findings of this review highlight that intravenous TXA administration is associated with a clinically meaningful reduction in blood loss during and after caesarean delivery. This reduction has the potential to alleviate postoperative complications, shorten hospital stays, and minimize the need for blood transfusions. By preserving haemostasis and stabilizing clot formation, TXA emerges as a valuable adjunctive therapy in managing blood loss, particularly in a high-risk surgical procedure like caesarean delivery.

The implications of these findings for clinical practice are profound. Integrating intravenous TXA into caesarean section protocols can contribute to improved maternal outcomes, enhance patient safety, and optimize healthcare resource utilization. The potential to mitigate the burden of postpartum haemorrhage, a significant contributor to maternal morbidity and mortality, underscores the importance of considering TXA as an essential component of obstetric care.

Emphasizing the role of intravenous TXA in managing blood loss during caesarean delivery, this review underscores the value of

evidence-based interventions to address a critical aspect of maternal health. By providing a clearer understanding of TXA's efficacy, mechanisms of action, and clinical implications, this review offers healthcare providers valuable insights to make informed decisions in optimizing obstetric care.

In conclusion, the findings presented in this comprehensive review support the integration of intravenous TXA as a promising strategy for managing blood loss during caesarean delivery. Continued research, standardization of protocols, and collaborative efforts among healthcare professionals are essential to harness the full potential of TXA in enhancing maternal outcomes and advancing obstetric practice.

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