Comparison of Oral versus Topical/Intravenous Tranexamic Acid in the Prevention of Blood Loss in Total Knee Replacements

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Summary

- Tranexamic acid is an antifibrinolytic used to reduce blood loss in total knee arthroplasty
- Current practice utilises topical/intravenous administration of tranexamic acid but this regime is invasive and expensive
- This study aimed to demonstrate the non-inferiority of an oral tranexamic acid regime compared to the topical/intravenous (IV) regime
- No significant difference was found between the groups in terms of volume of blood loss, haemoglobin changes, or incidence of deep vein thrombosis
- Oral tranexamic acid was non-inferior to the current topical/IV regime and provided improved convenience for nursing staff and patients
- Substantial monetary savings for healthcare facilities may be achieved by implementing oral TXA to reduce blood loss in total knee arthroplasty

Background

- Tranexamic acid (TXA) is an anti-fibrinolytic which reduces blood loss and the need for blood transfusions post total knee arthroplasty (TKA).
- Evidence supports the use of topical or intravenous (IV) TXA[1] but Zohar et al[2] demonstrated that an oral regime of TXA produced equivalent blood-sparing effects to intravenous regimes.
- The use of oral TXA has the potential to provide significant financial savings to healthcare facilities, with equivalent quantities of IV TXA ampoules being almost 40-fold more expensive than oral tablets.[3]

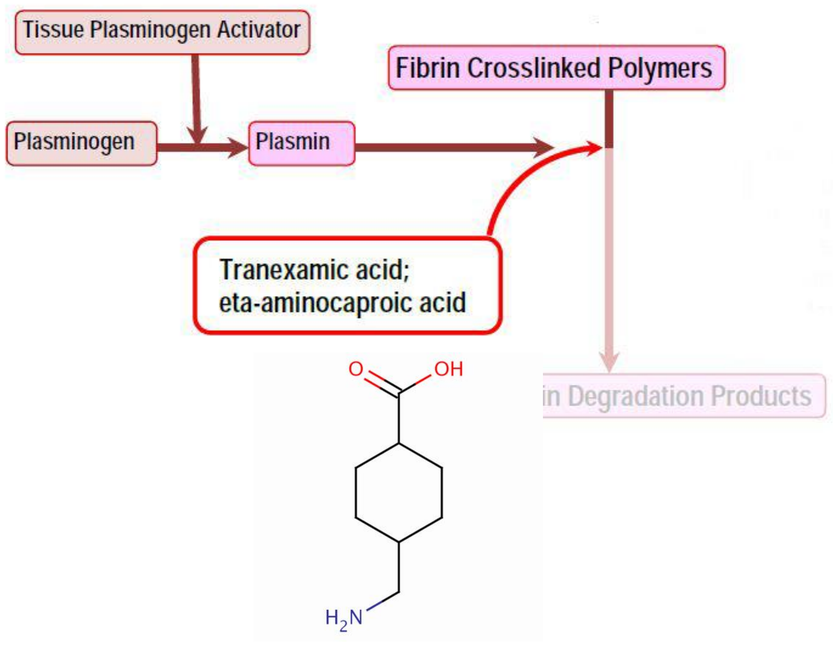

Figure 1 : Structure and Mechanism of action of tranexamic acid

Aim

- The aim of this study was to investigate the non-inferiority of an oral TXA regimen to the currently used topical/IV TXA protocol.
- The primary outcome was haemoglobin change and blood loss due to surgery as measured by the amount of blood loss in theatre and volume collected from the joint drain by ten hours post surgery.
- Secondary measures were safety as measured by reported by incidence of adverse effects including deep vein thrombosis (DVT) determined by Doppler ultrasound at six weeks post surgery.

Methods

- The study comprised two arms, a study arm treated with an oral TXA regime and a control arm treated with currently used topical/IV TXA regime as follows:
  - Study : 1g oral TXA two hours prior to surgery, 1g oral TXA two hours post-surgery, 1g oral TXA six hours post surgery
  - Control : 3g topical TXA peri-operatively, 1g IV TXA two hours post-surgery, 1g oral TXA six hours post surgery
- Both groups received apixaban 2.5mg twice daily for 15 days commencing eight hours post surgery as prophylactic antithrombotic therapy.
- All procedures were conducted by the same orthopaedic surgeon at John Flynn Private Hospital.
- Data collected included blood loss, haemoglobin change, and incidence of adverse events and incidence of DVT at six weeks post surgery.
- Ethics approval was obtained by Greenslopes Research and Ethics Committee (Protocol 17/25) and Griffith University Ethics Committee (2017/541).

Results

- A total of 53 patients were recruited with 25 patients in the study group and 28 in the control group.
- There was a slightly higher percentage of males in the study group (56.0% male, 44.0% female) compared to the control group (41.4% male, 58.6% female) but this was not statistically significant.
- There was no significant difference between the study and control group in terms of age (64.8 ± 8.8 years vs 63.8 ± 9.7 years respectively) or weight (90.2 ± 16.7 kilograms vs 86.4 ± 16.3 kilograms respectively)
- No significant difference was found between groups in total blood loss or haemoglobin changes (Table 1)
- One blood transfusion was administered being to a patient in the control group but this was determined to be unrelated to the surgery

Table 1 : Measures of efficacy in study and control groups. Data is shown as mean (standard deviation) or number (percentage)

Adverse Event	Study Oral TXA	Control Topical/IV TXA	P value
Haemaglobin g/dL	32.9 (8.9)	31.7(10.2)	0.651
Blood loss (mL)	640.0 (291.1)	538.3 (270.2)	0.173
Blood Transfusion			
Yes	25 (100%)	27 (96.4%)	
No	0 (0.0%)	1 (3.6%)	

- No cases of DVT occurred during the study period for either groups (Table 2)
- There were no statistical differences in adverse events but the incidence of constipation in the study group neared significance

Table 2 : Measures of safety in study and control groups. Data is shown as number (percentage). DVT = deep vein thrombosis, N/A = not applicable

Adverse Event	Study Oral TXA	Control Topical/IV TXA	P value
DVT	0 (0.0%)	0 (0.0%)	N/A
Acute nausea	9 (36.0%)	9 (31.0%)	0.700
Delayed nausea	8 (32.0%)	9 (31.0%)	0.938
Headache	1 (4.0%)	0 (0.0%)	N/A
Hypotension	8 (32.0%)	11 (37.9%)	0.654
Dizziness	0 (0.0%)	2 (6.9%)	N/A
Constipation	5 (20.0%)	1 (3.5%)	0.055

Discussion & Conclusion

- Past research which has demonstrated oral TXA to be non-inferior to IV TXA[2]
- This study found oral TXA compared to topical/IV TXA regimes for TKA resulted in no significant difference in haemoglobin change, total blood loss, or incidence of adverse events including DVT
- This could result in significant cost savings to healthcare facilities in terms of drug costs as the oral regime is less than three times the cost of the topical/IV
- Burden to nursing staff would be reduced plus oral administration is less invasive for patients
- In conclusion, this study demonstrates for the first time that oral TXA was non-inferior to a topical/IV regime in terms of efficacy and safety

References

1. Xiang, S., Dong, Q., and Zhang, Y. Intravenous versus topical tranexamic acid in primary total hip replacement: A systematic review and meta-analysis, *International Journal of Surgery*,2016:32: 10-18.
2. Zohar, E., Ellis, M.,Ifrach, N., Stern, A., Sapir, O., Fredman, B. The Postoperative blood-sparing efficacy of oral versus intravenous tranexamic acid after total knee replacement. *Anesthesia & Analgesia* 2004; 99:1679-83
3. Merlin Catalogue, Aug 2016, *Ramsay Pharmacy Services*