International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 4 July-Aug 2023, pp: 1930-1934 www.ijprajournal.com ISSN: 2249-7781

Systematic Review on Effects and Outcomes of Concomitant Tranexamic Acid and LMWH in Arthroplasty

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Submitted: 10-08-2023 Accepted: 20-08-2023

ABSTRACT
Cases witnessing total hip and knee arthroplasty are at greater risk for venous thromboembolism (VTE). It is a serious and potentially fatal complication that can occur during hospital for surgery. In order to drop blood loss,tranexamic acid has been extensively applied in total knee arthroplasty significantly to reduce peri-operative blood loss. The choice of anticoagulants for venous thromboembolism prevention after tranexamic acid is controversial. Therefore this study aimed to evaluate the outcome of tranexamic acid and LMWH as chemoprophylaxis in arthroplasty.

Key words: Anti-coagulants, Arthroplasty, Tranexamic acid, Venous thromboembolism.

I. INTRODUCTION

The incidence of venous thromboembolism in arthroplasty is around 40-60%, with no measure(s) to prevent venous thromboembolism with appropriate prophylaxis use, the incidence falls around 0.6 – 1.4%. They may include use of anticoagulants or mechanical agents on both [(1)]. On the other side, there is also a risk of excessive blood loss. Direct blood loss during surgery and indirect loss through drain during the perioperative period, which may subsequently result in the need for blood transfusion(s) [(2)]. To minimize blood transfusions, clinicians opt to use tranexamic acid during the time of incision with post- closure, thereby reducing the blood loss. Theoretically, tranexamic acid use is associated with VTE events [(11)]. Studies have shown that TXA reduces blood loss and blood transfusion rates without any VTE events [(12)]. This confounding evidence may influence the clinical use of TXA. This systematic review aims to evaluate the outcomes of low molecular weight heparin and tranexamic acid as chemoprophylaxis in arthroplasty.

II. METHODOLOGY

Search strategy: An electronic literature search was performed on pubmed with emphasis on studies that included anticoagulants and tranexamic acid in arthroplasty. Preference was given to randomised and controlled trials, meta-analysis and comparative studies.

Study selection: 78 relevant studies were obtained following the search. The results were filtered and selected based on the inclusion and exclusion criteria.

Inclusion criteria

- ✓ Patient who underwent unilateral/bilateral/arthroplasty (TKA), THA.
- ✓ Each patient must have received TXA/placebo with anticoagulant(s).

Exclusion criteria

- ✓ Patient who are undergoing revision of arthroplasty were excluded.

Among the 78 published articles, only 7 studies fulfilled the criteria; out of which 4 were randomised and controlled studies, 3 were comparative studies.

Characteristics of studies

Amid four RCTs, only one trial was found to be double blinded, the rest three RCTs were single blinded. Two RCTs compared outcomes of TXA+LMWH and placebo [(3)] [(9)]; one RCT compared outcomes of TXA+LMWH with placebo and Rivaroxabon[(4)]. The last RCT compared outcomes of TXA with LMWH, RIV and ASA [(5)]. Two comparative studies collated outcomes of TXA and LMWH with TXA and RIV. One comparative study juxtaposed TXA+LMWH with

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TXA+RIV and TXA+APX. All studies evaluated equivalent doses of LMWH.
RCT – Randomised and Controlled Trials
RIV – Rivaroxaban
ASA – Aspirin/Acetyl Salicylic acid
APX – Apixaban
LMWH – Low Molecular Weight Heparin (which includes Enoxaparin, Nadroparin, Dalteparin and Fondaparinux)

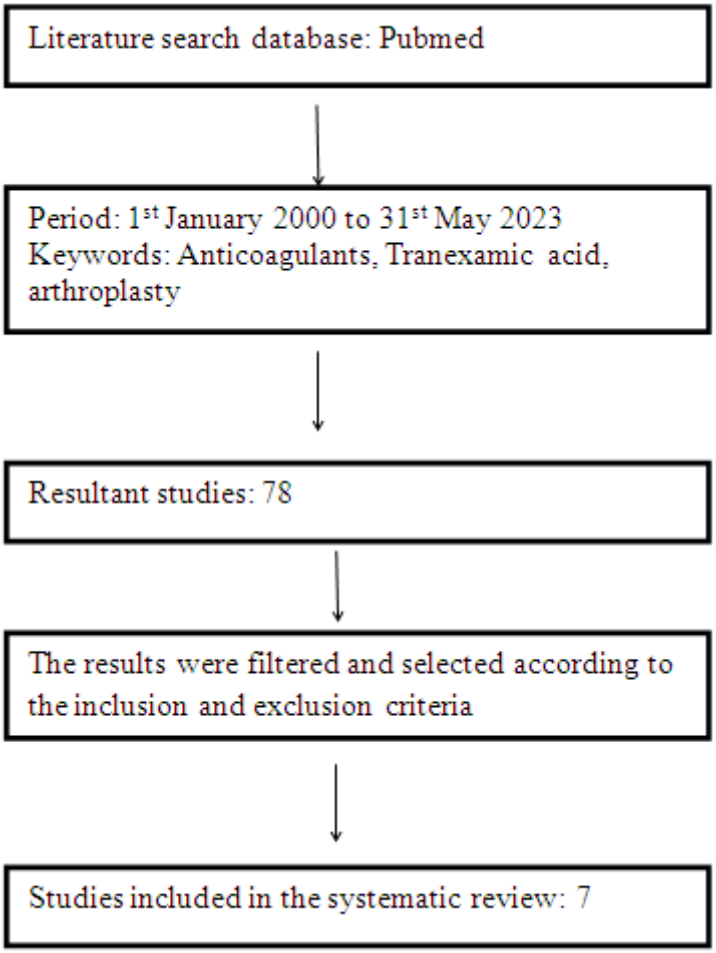

Figure 1: Literature search strategy

III. RESULTS:

The outcomes of the studies are tabulated (Table 1). Due to the extreme heterogeneous nature of the studies, compiling and deriving outcomes as a whole from the studies may increase the chances of bias. Hence, a qualitative narrative approach has been undertaken. All of these studies warrant the use of TXA and LMWH as a strategy to minimize blood loss and need for allogeneic blood transfusions. Furthermore, none of the studies found any evidence of serious VTE events (such as Deep vein thrombosis, Pulmonary embolism, Cerebrovascular events, Myocardial Infarction, Renal or Liver failure), whereas mild problems (such as wound complication, intramuscular venous thrombosis, hematomas, ecchymosis, Sepsis-induced coagulopathy) showed statistically no difference between the control groups and placebo, except in one comparative study, the TXA+RIV group had increased events of minor VTE, which resolved after withholding RIV [(6)]. Statistically significant reduction in blood loss and need for blood transfusions were noted in all 3 trials that compared with placebo [(3) (4) (9)]. In one RCT, the events of blood transfusions were higher in the TXA+LMWH group. Confounding data exist regarding the use of TXA+RIV, comparable to TXA+LMWH.

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Reference No.	Total Population	Population in the study arm	Total Blood Loss	Requisition for Transfusion	Symptomatic/ Asymptomatic	Male/ Female	Average age	Study Type	Control group / Arm
3	105	52	1130 ± 0.311	1	0/NR	26/28	58.8±9.7	RCT, DB	Placebo
			1.48 ± 0.510	5	0/NR				
4	158	58	511ml	1	0/0	23/35	72	RCT	RIV & Placebo
			440ml	0	0/1				
			763ml	2	0/3				
5	180	60 Dalte	959 ± 131.9	12	0/5	29/31	64.1±6.7	RCT	RIV & ASA
			902.1±129.5	4	0/4				
			833.2±115.0	3	0/7				
6	113	52	1035 ± 259	2	0/10	9/43	70.6±8	Comparative study	RIV
			1085 ± 260	4	0/28				
8	184	Nadro - 46	1247.6 ± 370.6	1	0/3	23/23	58.71±12.7	Comparative study	RIV & APX
		Enox - 45	1235.5 ± 583.1	3		19/26	57.2±11.3		
				6	0/1				
9	72	36 Fondaparinux	306 ± 214	4	0/3	5/31	69.7±7.9	RCT	Placebo
			590 ± 287	15	0/4				
10	150	Nadro - 50	1207±509.5	3	0/4	25/25	58.8±12.3	Comparative study	RIV
		Enox - 50	1132±512.3	5	0/1	21/29	58.0±11.2		
			1124.5±507.5	4	0/1				

Table 1: Outcomes of the studies

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IV. DISCUSSION

The mechanism of action of LMWH is to inhibit the activity of coagulation factors; while the mechanism of action of TXA is to inhibit the activation of plasminogen and the dissolution of fibrin. In theory, antifibriolysis and LMWH do not antagonise each other [(8)]. However, previous studies have shown risk of thrombosis in post-operative patients while resisting fibrinolysis [(11)]. The use of anticoagulants as chemoprophylaxis to prevent VTE events in post-operative patients has become inevitable in clinical practice. Despite novel oral anticoagulants, LMWH still remains as the most preferred chemo prophylactic agent for VTE. There seems to be a clear lack of evidence to support the use of both these agents concomitantly. The dose, titration and duration of TXA are still uncertain with being mentioned. Several studies are underway to establish the aforementioned grey areas of TXA use in peri-operative period.

Limitations:

i. The dose, frequency and duration of TXA were not compared and established among the studies due to lack of consistency.
ii. Variability in surgeon's skillset and regional guidelines on drug use.
iii. Co-morbid patients and patients who were on post medications were not strained, which may influence the outcome.

V. CONCLUSION:

The use of tranexamic acid and LMWH may reduce perioperative blood loss and need for blood transfusions. There appears to be no significant difference in VTE events with this combination.

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