

Original Research Article

Tranexamic acid with vitamin K mixture decreases bleeding of total hip arthroplasty in a Jordanian population

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ABSTRACT

Background: Bleeding of total hip arthroplasty has severe consequences on postoperative recovery. 75–90% of early bleeding after surgery and during surgery is caused by operative technical issues. tranexamic acid decreases bleeding of arthroplasty. vitamin k has late and dose sensitive effect in clotting.

Methods: This retrospective investigation included subjects of middle age and of both genders scheduled for primary hip replacement at Queen Alia hospital, Jordanian Royal medical services, between March 2022 and June 2023. Subjects were classified into two groups. Group I subject were administered intravenous mixture of Tranexamic acid 10 mg/kg with vitamin K1 of 10 mg 5 min pre-skin incision followed by an infusion of Tranexamic acid 1 mg/kg/h and vitamin K1 0.2 mg/kg/h, until skin closure. Group II subjects were administered only intravenous vitamin K1 of 10 mg, 5 min pre- skin incision followed by infusion of 0.2 mg/kg/h until skin closure. Hemoglobin, packed cell volume, platelet count, prothrombin time, partial thromboplastin time and fibrinogen were tested. Bleeding and blood transfusion were remarked.

Results: Group I demonstrated a remarkable less modifications in blood tests and less bleeding than group II. Group II demonstrated less bleeding after surgery. The average Hb in group I demonstrated a remarkable less reduction after surgery compared to group II. ($p < 0.005$). No blood transfusion after surgery was needed in group I. Nine (15%) patients in group II needed one unit of blood transfusion during surgery.

Conclusion: Intravenous administration of Tranexamic acid with vitamin K mixture in total hip arthroplasty decreased bleeding during and after surgery and decreased the requirement for blood transfusion.

Keywords: Tranexamic acid, Vitamin K, Bleeding, Total hip arthroplasty, Blood transfusion

INTRODUCTION

Bleeding influences recovery following orthopedic surgery. Orthopedic surgeries occupy 10% of the requirement for blood transfusions worldwide. Excluding allogenic blood products avoids the patient from hazards of blood transfusion. 75–90% of early bleeding after and during surgery is caused by operative technical issues.¹ Uncontrolled bleeding will cause hemodilution, consumption of clotting factors and metabolic acidosis. Bleeding of total arthroplasty increases blood transfusion

in 75%.^{2,3} Different agents were used to decrease bleeding such as bone wax, fibrin glues and lysine analogs such as epsilon-aminocaproic acid (tranexamic acid).⁴

Tranexamic acid is a synthetic antifibrinolytic agent that blocks binding of plasminogen to fibrin and delaying fibrinolysis. It decreases bleeding during arthroplasty and remarkably decreases blood transfusion.^{5,6} Vitamin K1 controls hepatic production and function of clotting factors II, VII, IX, and X. It antagonizes the action of warfarin with onset of action following few hours, but the liver

requires 3–5 days to reproduce the vitamin K-dependent clotting factors. This late onset of action makes vitamin K use limited to avoid rebleeding following bleeding control and for the correction of the international normalized ratio in warfarinized patients.⁷

The aim of our investigation was to assess the influence of the intravenous administration of tranexamic acid with vitamin K1 mixture on bleeding and the requirement for blood transfusion in Jordanian subjects scheduled for primary total hip arthroplasty.

METHODS

This comparison, prospective and double-blind investigation included 120 subjects, aged 54-69 years., of both genders and assigned for primary total hip arthroplasty at Queen Alia military hospital, JRMS, Amman, JORDAN, during the period March 2022-June 2023, after obtaining approval from our local ethical and research board review committee of the Jordanian Royal medical services and written informed consent from all participants.

Subjects with a history of venous thromboembolism, platelet count under 150.000/ μ l), prothrombin time more than 16 s and partial thromboplastin time more than 60 s were ruled out

Subjects were classified in a random manner into two groups of 60 subjects each. Group I subjects (GI; n=60) had been administered intravenous mixture of Tranexamic acid 10 mg/kg with vitamin K1 of 10 mg (10 ml intravenous infusion over 10 min) 5 min pre- skin incision followed by an infusion of tranexamic acid 1 mg/kg/h and vitamin K1 0.2 mg/kg/h until skin closure and group II subjects (GII; n=60) had been administered only vitamin K1 intravenous of 10 mg (10 ml slow infusion over 10 min) 5 min pre- skin incision followed by infusion of 0.2 mg/kg/h until skin closure.

Hemoglobin, packed cell volume, platelet count, prothrombin time, partial thromboplastin time and fibrinogen were tested before, during and 3 days after surgery. Bleeding, blood tests and blood transfusion were remarked during and after surgery.

Statistics analysis

The average discrepancies in blood tests, blood transfusion and bleeding were assessed using the post-hoc test.

RESULTS

There were no remarkable discrepancies according to demographics between groups. The average age was 61.5 years. There were 65 (54.2%) men and 55 (45.8%) women (Table I) $p>0.05$. There was a remarkable discrepancy between groups in terms of the average of surgery duration $p<0.05$.

The average Hb in group I demonstrated a remarkable less reduction after surgery compared to group II ($p<0.005$). The average PCV after surgery demonstrated more remarkable discrepancy between group I ($p<0.005$) and group II. The average Hb and PCV modifications demonstrated remarkable reductions in group I more than in group II. The average decrease in Hb was 0.48 g/dl in group I and 1.58 g/dl in group II. The average platelet counts after surgery on the third day had a remarkable less reduction in group I than in group II ($p<0.05$). The platelet counts after surgery had a remarkable reduction in group II. The average PT and PTT after surgery had an unremarkable reduction between the two groups. There was no remarkable discrepancy between groups in terms of modifications in prothrombin time after surgery ($p>0.05$). Groups I and II had a decrease in the average prothrombin time after surgery. There was no remarkable discrepancy between groups according to PTT ($p>0.05$). There was no remarkable discrepancy between groups in terms of the fibrinogen level ($p>0.05$). The average fibrinogen was less in group II than in group I (Tables II and III). There was a remarkable discrepancy between groups ($p<0.005$) according to the overall average bleeding. Group I demonstrated the least overall bleeding and then group II. The average bleeding after surgery in group II was less than group I (289-168=121 ml less than group I). No blood transfusion after surgery was needed in group I. Nine (15%) patients in group II needed one unit of blood transfusion during surgery. The average bleeding during surgery was 363.1 ml in group I and 907.8 ml in group II. Groups I and II demonstrated less bleeding, while group I had less during surgery and overall bleeding (Table IV).

Table 1: Demographic data.

	I	II	P value
Intravenous drugs	Tranexamic+Vitamin K1	K1	
Number	60	60	
Gender (%)			
Female	26 (43.3)	29 (48.3)	>0.05
Male	34 (56.7)	31 (51.7)	>0.05
Age (years) average ($\pm$SD)	56 (9.1)	57 (8.3)	>0.05
Surgery duration (hour) average ($\pm$SD)	1.58 (0.2)	2.21 (0.25)	<0.05

Table 2: Blood profile before surgery.

	I	II	P value
Hb (g/dl) average (±SD)	12.01 (0.376)	11.89 (0.312)	<0.005
PCV (%) average (±SD)	44.7 (2.063)	39.6 (1.359)	<0.005
Platelet (10⁶/ml) average (±SD)	345 (34.95)	333 (30.7)	<0.05
PT (s) average (±SD)	14.29 (0.51)	12.75 (0.48)	>0.05
PTT (s) average (±SD)	30.94 (1.93)	31.72 (1.71)	>0.05
Fibrinogen (mg/dl) average (±SD)	336.4 (33.2)	332.7 (26.4)	>0.05

Table 3: Blood profile after surgery.

	I	II	P value
Hb (g/dl) average (±SD)	11.53 (0.223)	10.31 (0.236)	<0.005
PCV (%) average (±SD)	40.87 (1.565)	33.82 (0.961)	<0.005
Platelet (10⁶/ml) average (±SD)	343 (34.05)	331 (30.22)	<0.05
PT(s) average (+/-SD)	12.04 (0.39)	10.45 (0.2)	>0.05
PTT(s) average (+/-SD)	27.98 (1.54)	28.69 (1.51)	>0.05
Fibrinogen (mg/dl) average (+/-SD)	268.8 (11)	230.4 (10.8)	<0.005

Table 4: Bleeding profile.

	I	II	P value
Bleeding during surgery (ml) average (±SD)	363.1 (67.9)	907.8 (58.4)	<0.005
Drain after surgery (ml) average (±SD)	289 (34.9)	168 (36.5)	<0.005
Overall bleeding (ml)	585.5	1020.1	<0.005
Patients who required transfusion	0	9	<0.005

DISCUSSION

Bleeding in total arthroplasty reduces the Hb and early rehabilitation. Tranexamic acid decreases bleeding in orthopedic surgeries by minimizing clot breakdown without improving clot formation via fast action but with a short half-life, and not interfering with the antithrombotic prevention.^{8,9} Intravenous vitamin K1 action is present in 1-2 hours. Bleeding is controlled in 3-8 hours and prothrombin normalizes following 12-14 hours. Intravenous vitamin K has rapid onset of action and a maximum action in 6-12 hours. The indication of vitamin K in surgery is to antagonize warfarin and avoid re-bleeding following bleeding is controlled.¹⁰ Tranexamic acid administration decreased blood transfusion.^{10,11} Tranexamic acid decreases bleeding following total hip or knee arthroplasty.¹²⁻¹⁶ Tranexamic acid is more efficient than fibrin sealant in decreasing hemorrhage in hip arthroplasty.^{17,19}

In this investigation, the bleeding during and after surgery was decreased in the drains of the total bleeding in group I compared to group II as in other investigations where a tranexamic acid 15 mg/kg single- dose decreased bleeding after surgery, overall bleeding and packed cell transfusion with total hip arthroplasty.^{15,20} The average bleeding during surgery was 363.1 ml in group I and 907.8 ml in group II, which was less than other investigations where 15 mg/kg tranexamic acid single intravenous dose was administered 15 min pre- skin incision in primary total hip

arthroplasties and recorded an average of 410 ml bleeding during surgery compared to 615 ml in the control group.¹⁴ Tranexamic acid 10 mg/kg single dose at induction of anesthesia for total hip arthroplasty recorded no remarkable discrepancy with the control group in terms of bleeding and Hb after surgery and more of patients needed blood transfusion. The discrepancy between this and our investigation is due to administration of a single, low, and early dose of tranexamic acid.¹⁶

The average Hb and PCV modifications demonstrated remarkable reductions in group I more than in group II as in other investigation with remarkable increase in the average bleeding during surgery and reduction in Hb in the control group finding that a single dose of intravenous Tranexamic acid 10 mg/kg 10 min pre- skin incision in total hip arthroplasty reduced bleeding, decreased Hb and the requirement for blood transfusion.¹⁵

The average decrease in Hb was 0.48 g/dl in group I and 1.58 g/dl in group II. No patient in group I needed transfusion during surgery, while 9 patients in group II needed one unit of transfusion during surgery, better than others who recorded an average decrease in Hb at the fifth day after surgery of 2.5 g/dl in the study group and 3.4 g/dl in the control group.⁸ The platelet counts after surgery had a remarkable reduction in group II because of increased bleeding during surgery and consumption of platelets in the unopposed normal clotting as in others, who found that tranexamic acid might protect the platelet count and

function and decrease blood transfusion.²¹ In elective orthopedic surgeries, bleeding of more than 500 ml was correlated with an increase in platelet aggregation by day 1 and day 7 postoperatively and a remarkable reduction in platelet count with the PCV by day 1 after surgery.³ The average PT and PTT after surgery had an unremarkable reduction between the two groups as in other patients who received only tranexamic acid or received both tranexamic acid and vitamin K.²² Patients in the second group had a mild more reduction in PT and PTT because of vitamin K. The average fibrinogen was less in group II than in group I as in others, who recorded less fibrin degradation products in the tranexamic acid group and a remarkable reduction in fibrinogen in the control group.⁵

Oral, intravenous or combined routes were used for tranexamic acid administration and all were efficient in decreasing overall bleeding.¹⁷ One dose before surgery and three doses of tranexamic acid were used for total hip replacement. One dose of intravenous tranexamic acid was as efficient as two doses in decreasing bleeding and transfusion following hip or knee arthroplasty.¹⁹ In our investigation, tranexamic acid with vitamin K were used intravenously primarily then by an infusion until wound closure to attain the controlling bleeding during surgery by the fast effect of tranexamic acid, and by the late effect of vitamin K1 after surgery.

Tranexamic acid did not interfere with the administration of anticoagulants and was efficient for decreasing of bleeding after surgery in hip and knee arthroplasty.²³ Because of the late effect of vitamin K, there was no influence of it on minimizing bleeding during surgery in group II, but the important action was on decreasing bleeding after surgery in the drain. Less bleeding was recorded with the combined tranexamic acid with vitamin K1 than in the hypotensive anesthesia.²⁴ In this investigation, groups I and II demonstrated less bleeding after surgery because of the late action of vitamin K, while group I had less during surgery and overall bleeding because of the rapid effect of tranexamic acid and the late effect of vitamin K. This permitted early rehabilitation instantly postoperatively.

CONCLUSION

The administration of intravenous Tranexamic acid with vitamin K1 mixture in total hip arthroplasty decreases the requirement for blood transfusion and bleeding during and after surgery via the rapid effect of Tranexamic acid and the late effect of vitamin K1. The enhanced recovery program started instantly after surgery.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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