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Topical use of tranexamic acid in primary total knee arthroplasty: a comparative study

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SUMMARY: **Topical use of tranexamic acid in primary total knee arthroplasty: a comparative study.**

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Introduction. *Perioperative blood management represents a major issue in knee arthroplasty. The aim of the present observational study is to compare two different methods of topical tranexamic acid (TXA) administration (periarticular and intraarticular) in primary knee arthroplasty.*

Patients and methods. *The present is an observational comparative study. A total of 66 consecutive patients receiving topical injection of TXA after unilateral primary knee arthroplasty due to osteoarthritis were recorded. Patients were divided into two groups: group 1; periarticular injection of TXA and group 2; intraarticular injection.*

Results. *Transfusion rate in group 1 was found to be 15%, compared to 44% in group 2 (p-value= 0.015). In transfused patients the mean received blood units were 1.2 (SD=0.44) in group 1, compared to 1.06 (SD=0.24; p-value=0.34) in group 2. The mean hospital stay of group 1 patients was 7.94 days (SD=2.79), compared to 9.58 days (SD=3.26; p-value=0.03) in group 2.*

Discussion. *The main findings of the study are that statically significant higher transfusion rates, as well as longer in-hospital stay were found in the intraarticular group, when compared to the periarticular group. According to these two parameters the present study has shown that the topical periarticular TXA injection is superior to the intraarticular one. Further research is of utmost importance in order to conclude to the optimum combination of knee arthroplasty perioperative blood management.*

KEY WORDS: Topical tranexamic acid - Intraarticular tranexamic acid - Periarticular tranexamic acid - Blood management knee arthroplasty - Knee replacement tranexamic acid.

Introduction

Perioperative blood loss represents a major issue following total knee arthroplasty. Patients often present with significant postoperative anemia and require transfusion. Transfusions may lead to infection, graft versus host disease, hemolysis, and transfusion-related acute lung injury (1-3).

Many studies, lately, have shown that tranexamic acid (TXA) seems to be effective in decreasing perioperative blood loss and transfusion requirements in knee arthroplasty. TXA is a synthetic lysine analog that can competitively inhibit the activation of plasminogen and plasmin binding protein. The intravenous (i.v.) administration of TXA has proven effective, since it significantly reduces perioperative blood loss, as well as the need for transfusion (3, 4). However, several comorbidities, often identified in patients undergoing knee arthroplasty, such as a history of cardiac and cerebrovascular disease, deep vein thrombosis and renal failure prohibit the i.v. administration of TXA. To counter these drawbacks the topical use of TXA was introduced (3, 5).

The safety, as well as the efficacy of topical TXA during primary knee arthroplasty has already been proven by previous studies (6-9). There are two methods of topical use of TXA in knee arthroplasty: the in-

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traarticular injection, following closure of the joint capsule and the periarticular injection in two stages (prior and after placement of the final prostheses) (3).

The present observational study aims to compare the results regarding perioperative blood management of these two topical methods of TXA administration in primary knee arthroplasty.

Patients and methods

The present is an observational prospective comparative study. A total of 66 consecutive patients receiving topical injection of TXA after unilateral primary knee arthroplasty due to osteoarthritis performed by senior surgeons at the Department of Orthopaedics and Traumatology were recorded. The performed topical TXA injection method was the surgeon's choice. Patients were divided into two groups: group 1; patients receiving periarticular injection of TXA and group 2; patients receiving intraarticular injection. Patients that received (i.v.) TXA prior or during the operation were excluded from the study.

Demographics of patients were recorded. The parameters that were evaluated were: preoperative hemoglobin (mg/dl), decrease of hemoglobin 6 hours and 24 hours postoperative, the need for transfusion and the blood units per transfused patient, as well as the total in-hospital stay (in days).

In all operations patients' limbs were elevated, bleeding was controlled with an Esmarch bandage, and the tourniquet was inflated to 320 mmHg. Operative techniques included a median skin incision followed by medial parapatellar approach. Cement was used for prosthetic fixation. A polyethylene liner was inserted and wounds were closed. An intra-articular drain was placed until the second post-operative day. All patients were given low-molecular-weight heparin to prevent DVT, unless they took another cardiovascular medication before surgery. All patients underwent the same postoperative recovery and rehabilitation program.

In the periarticular group a total of 1.5 g TXA diluted in 50 ml of normal saline were injected in two stages. Prior to final prostheses placement 25 ml of the dilution were injection at the posterior knee joint capsule. Following the final prostheses placement, the remaining dilution was injection at the surrounding soft tissues for at least 5 min prior to tourniquet deflation.

In the intraarticular group, a total of 1.5 g of TXA diluted in 50 ml of normal saline was injected into the knee joint after knee capsule closure for at least 5 min prior to tourniquet deflation, while the drainage was opened 1.5 hours later.

Two-sided Fisher's exact tests were used to compare transfusion rates between the two groups, while t-tests were used for the comparison of the mean value of the remaining parameters. Statistical Analysis was carried out at the 5% level of significance using IBM-SPSS 24.

The present study was approved by the relevant bioethics' committees.

Results

Thirty-three patients were included in each group. The mean age of group 1 was 72.08 [standard deviation (SD)=6.14], while the mean age of group 2 was 72.27 (SD=7.06; p-value =0.9). The mean preoperative hemoglobin of group 1 was 12.99 (SD=1.52), compared to 13.18 (SD=0.76; p-value=0.52) of group 2. A total of 12 males (18%) and 54 females (82%) were included in the study.

Table 1 highlights the main results of the present study. The mean 6 hours postoperative decrease of hemoglobin in group 1 was 0.5 mg/dl (SD=0.7), compared to 0.33 mg/dl (SD=0.6; p-value=0.29) of group 2. The mean 24 hours postoperative decrease of hemoglobulin in group 1 was 2 (SD=0.8), compared to 1.5 (SD=1; p-value=0.02) in group 2.

Transfusion rate in group 1 was found to be 15%, compared to 44% in group 2 (p-value= 0.015). In transfused patients the mean received blood units were 1.2 (SD=0.44) in group 1, compared to 1.06 (SD=0.24; p-value=0.34) in group 2. The mean hospital stay of group 1 patients was 7.94 days (SD=2.79), compared to 9.58 days (SD=3.26; p-value=0.03) in group 2.

Discussion

Perioperative blood management of patients undergoing primary knee arthroplasty represents a major issue. Following the total knee replacement surgery,

TABLE 1 - STUDY'S MAIN FINDINGS ARE PORTRAYED. MEAN DECREASE OF HEMOGLOBIN AT 6 AND 24 HOURS POSTOPERATIVE, TRANSFUSION RATES AND BLOOD UNITS PER TRANSFUSED PATIENT AND HOSPITALIZATION LENGTH ARE COMPARED BETWEEN THE TWO GROUPS (T-TESTS).

	Group 1 (Periarticular injection)	**Group 2 (Intraarticular injection)**	**P-values**
Sample	33	33	
Mean Age	72.08 (SD=6.14)	72.27 (SD=7.06)	0.9 (n.s.)
Mean pre-operative Hemoglobin (mg/dl)	12.99 (SD=1.52)	13.18 (SD=0.76)	0.52 (n.s.)
Mean Hemoglobin (mg/dl) decrease 6 hours postoperatively	0.5 (SD=0.7)	0.33 (SD=0.6)	0.29 (n.s.)
Mean Hemoglobin (mg/dl) decrease 24 hours postoperatively	2 (SD=0.8)	1.5 (SD=1)	***0.02***
Transfusion rate	15%	44%	***0.015***
Mean blood units used (in patients receiving transfusion)	1.2 (SD=0.44)	1.06 (SD=0.24)	0.34 (n.s.)
Mean hospital stay (days)	7.94 (SD=2.79)	9.58 (SD=3.26)	***0.03***

n.s. = non-significant

blood loss may reach 2 liters, with most patients in need of transfusion (3). Bleeding control following knee arthroplasty has become a "hot" topic of research during the last years (11-15). Antifibrinolytic agents such TXA represent primary focus of clinical practice, as well as research. TXA exerts its antifibrinolytic effects by inhibiting plasminogen, prohibiting plasminogen activation and the binding of plasmin to fibrin. This leads to clot stabilization and decreases blood loss (10, 16).

The i.v. administration of TXA has already proven effective in bleeding control following knee arthroplasty. However, due to the relative inability to use in many patients undergoing total knee replacement surgery, such as those suffering from renal failure, or those having a history of deep vein thrombosis, cardiac or cerebrovascular episode, the question whether topical TXA administration has equal results has been raised (17-19).

The purpose of this comparative study was to evaluate two methods of topical TXA administration; the periarticular and the intraarticular. The demographics and the preoperative hemoglobin values of the patients between the two groups did not exhibit statistically significant difference. Therefore, these two groups (group 1: periarticular TXA administration and group 2: intraarticular administration) could be considered homogenous.

The main findings of the present study are that statically significant higher transfusion rates were found in the intraarticular group, when compared to the periarticular group (Table 1; transfusion rate of group 1= 15%, compared to 44% of group 2; p-value=0.015). It is of note that the intraarticular group had very high transfusion rates, comparable to control groups of patients, reported in the literature, not receiving TXA (3, 20). A distinct advantage of periarticular TXA injection, when compared to intraarticular injection, seems to be that the orthopaedic surgeon may target specific areas, prompt to postoperative bleeding, such as sites of soft tissue release and incisal edges in the synovial membrane. Additionally, it is not yet clarified whether the volume of intraarticular solution is sufficient to immerse the anterior tissues, especially since the patient is placed supine during knee replacement surgery (10). It is of note that a solution of 50 ml was used in the present study, while most studies in the literature have reported a volume of 5-25ml

(21, 22). It is also of note, that due to extensive soft tissue release, leakage of the injected intraarticular TXA solution may be observed.

Furthermore, this study has revealed a statistically significant longer in-hospital stay of patients undergoing the intraarticular TXA administration [Table 1; in-hospital stay of group 1= 7.94 (SD=2.79), compared to 9.58 (SD=3.26) of group 2; p-value= 0.03]. Longer hospitalization increases the burden on the health care system, by raising costs, as well as the risk for complications, such as endonosocomial infections, while control of perioperative bleeding in patients undergoing total knee replacement surgery has already been associated with shorter length of hospitalization (23, 24).

Similar studies in the literature have revealed comparable results between these two methods (periarticular and intraarticular) of topical administration of TXA (3), whereas the present study showed superiority of the periarticular method.

This comparative study has some limitations. It has a relatively small sample and it is observational. Indications for blood transfusion in the department are hemoglobin < 8.0 g/dl or hemoglobin < 10.0 g/dl with concomitant symptoms of anemia (tachycardia, tachypnea, decreased exercise tolerance) or anemia-related organ dysfunction. However, since this was an observational study, no interventions were performed and it was the surgeon's decision to transfuse a patient. As a result, there was no monitoring of these decisions.

Currently, perioperative blood management following primary knee arthroplasty still represents a major clinical issue, controlled by tourniquet, hypotension, re-infusion drains, bipolar radiofrequency ablation and antifibrinolytic drugs such as TXA (3, 10). Many areas in the blood management following knee arthroplasty remain unexplored or require further investigation. Experience and further research are needed towards issues such as the administration of i.v. TXA prior to incision and avoidance of tourniquet application, or combined i.v. and topical TXA use, with or with tourniquet application.

Conclusions

Allogeneic blood transfusions represent a major economic burden and may result in the transmission of bloodborne pathogens, an immunomodulatory response, and periprosthetic joint infection. Control of perioperative blood loss following total knee replacement surgery is associated with lower transfusion rates and shorter length of hospital stay. According to these two parameters (transfusion rate and in-hospital stay) the present study has shown that the topical periarticular TXA injection is superior to the topical intraarticular one. Further research is of utmost importance in order to conclude to the optimum combination of knee arthroplasty perioperative blood management.

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Conflict of interest

The Authors declare that there is no conflict of interest.

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Contributors

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Authors' contributions

GB, CK, KR, KV for the literature search and analysis, and manuscript writing. AK, DT, IK, OP, KK, AK for the final manuscript revision. All Authors have read and approved the final manuscript.

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