Magdalena Kwiatkowska[1, 2], Muhammad Alam Hashmi[2], Luoise Grimes[2], Anant Mahapatra[2], Jarosław Czubak[1]

Tranexamic acid combined with iron pathway may significantly decrease the postoperative rate of transfusion after elective total hip and knee replacement

Kwas tranexamowy połączony z przedoperacyjną suplementacją preparatami żelaza zmniejsza liczbę pooperacyjnych transfuzji u pacjentów po endoprotezoplastyce biodra i kolana

[1]Department of Orthopaedics, Pediatric Orthopaedics and Traumatology, Centre of Postgraduate Medical Education, Gruca Teaching Hospital, Otwock
Head of Department: Associate Professor Jarosław Czubak, MD, PhD
[2]Department of Orthopaedic Surgery, Our Ladys Hospital, Navan, Ireland
Head of Department: Alan Walsh MBBS, MSc. (Orth), FRCSI, FRCS (Ed)

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Adres/address:

*Magdalena Kwiatkowska
Klinika Ortopedii,
Ortopedii i Traumatologii Dziecięcej,
Centrum Medyczne
Kształcenia Podyplomowego,
Samodzielny Publiczny Szpital Kliniczny
im. prof. Adama Grucy
ul. Konarskiego 13, 05-400 Otwock
tel. +48 (22) 779-40-31
kootd@cmkp.edu.pl

S u m m a r y

Introduction. Transfusion associated with joint replacement surgery has long been recognized as a substantive issue.

Aim. In the present study, we compared blood loss, Hb levels, and transfusion requirements after elective primary total hip and knee arthroplasty when tranexamic acid (TXA) and iron pathway when indicated were used as a routine prophylaxis.

Material and methods. A total of 2416 consecutive patients, with the diagnosis osteoarthritis undergoing unilateral primary hip (n = 1509) or knee (n = 907) arthroplasty at Our Ladys' Hospital, Navan, Ireland were included in the study between January 2010 and December 2015.

The patients were divided into two groups:

A. Patients operated on between January 2010 and December 2012 before the introduction of tranxemic acid and iron pathway.
B. Patients operated on between January 2013 and December 2015 when tranxemic acid was used routinely as prophylaxis and iron pathway when needed.

Results. During the period of observation, 2416 patients underwent total joint arthroplasty performed by participating surgeons. Among these, 1262 patients received perioperative TXA (treatment group) and 74 entered the iron pathway. The average increase in Hb level was 0.8 g/dl.

Group A patients (patients treated before TXA and iron pathway introduction 2010-2012): Among 1154 patients undergoing joint replacement 648 (56.1%) were transfused with RBC units.

Group B patients (patients treated after TXA and iron pathway introduction 2013-2015): Among 1262 patients undergoing joint replacement 240 (19.01%) were transfused with RBC units.

Conclusions. The introduction of tranxemic acid and iron pathway has reduced transfusion rates with improved outcomes and cost reduction

The level of post operative Hb level was higher after the introduction of tranxemic acid.

Patients who fail to respond to iron treatment should be followed up to ensure no serious pathology.

S t r e s z c z e n i e

Wstęp. Zastosowanie transfuzji po endoprotezoplastykach stawów kolanowych i biodrowych wciąż pozostaje istotnym elementem opieki pooperacyjnej.

Cel pracy. Celem badania było porównanie utraty krwi, wartości Hgb oraz konieczności przeprowadzenia transfuzji po planowanych endoprotezoplastykach stawów biodrowych i kolanowych po rutynowym zastosowaniu okołooperacyjnej suplementacji preparatami żelaza oraz kwasu tranexamowego.

Materiał i metody. Badanie przeprowadzono w sposób retrospektywny. Analizie poddano historie chorób 2416 pacjentów hospitalizowanych w Klinice Ortopedii Our Ladys'

Hospital, Navan w Irlandii przyjętych w celu wykonania planowych zabiegów endoprotezoplastyki stawów biodrowych (n = 1509) oraz kolanowych (n = 907) w okresie 2010-2015.

Pacjentów podzielono na 2 grupy:

A. Pacjenci operowani w okresie od stycznia 2010 do grudnia 2012 roku – przed wprowadzeniem rutynowej suplementacji preparatami żelaza oraz kwasem tranexamowym.
B. Pacjenci operowani w okresie od stycznia 2013 do grudnia 2015 roku – po wprowadzeniu rutynowej suplementacji preparatami żelaza oraz kwasem tranexamowym.

Wyniki. Podczas okresu obserwacji 1246 pacjentów otrzymało kwas tranexamowy okołooperacyjnie, a 74 zostało zakwalifikowanych do suplementacji preparatami żelaza. Średni wzrost poziomu Hgb wynosił 0.8 g/dl.

W grupie A (okres 2010-2012 – przed wprowadzeniem rutynowej profilaktyki) 1154 pacjentów, u których przeprowadzono operacje endoprotezoplastyki, 648 (56.1%) poddano transfuzji z powodu wskazań klinicznych i labolatoryjnych.

W grupie B (okres 2013-2015 – po wprowadzeniu rutynowej profilaktyki) 1262 pacjentów, u których przeprowadzono operacje endoprotezoplastyki, 240 (19.01%) poddano transfuzji z powodu wskazań klinicznych i labolatoryjnych.

Wnioski. Zastosowanie rutynowej okołooperacyjnej profilaktyki z użyciem kwasu tranexamowego oraz suplementacji preparatami żelaza zmniejszyło liczbę koniecznych transfuzji krwi po planowych operacjach endoprotezoplastyki biodra i kolana.

Pooperacyjny poziom Hgb był wyższy u pacjentów z grupy B.

Pacjenci, u których poziom Hgb nie uległ poprawie po zastoowaniu suplementacji żelazem, powinni być poddani badaniom diagnostycznym w celu określenia przyczyny niedokrwistości.

INTRODUCTION

Transfusion associated with joint replacement surgery has long been recognized as a substantive issue. Investigations performed in the 1980s revealed that intraoperative blood losses in total knee arthroplasty (TKA) averaged more than 1000 mL per procedure (1). More recent studies have shown that non-visible blood loss such as bleeding into tissues and hemolysis with reinfusion typically accounts for volume losses equivalent to an additional 500 mL (2-11).

AIM

In the present study, we compared blood loss, Hb levels, and transfusion requirements after elective primary total hip and knee arthroplasty when tranexamic acid (TXA) and iron pathway when indicated were used as a routine prophylaxis.

MATERIAL AND METHODS

A total of 2416 consecutive patients, with the diagnosis osteoarthritis undergoing unilateral primary hip (n = 1509) or knee (n = 907) arthroplasty at Our Ladys' Hospital, Navan, Ireland were included in the study between January 2010 and December 2015. Exclusion criteria were known liver disease or coagulation disorder.

Patients greater than 18 years of age who underwent joint reconstruction at Our Lady of Lourdes Hospital, Navan, Ireland between January 2010 and December 2015 were identified by review of computerized inpatient and their medical records were retrospectively examined. Patients were included if they received primary, revision, or bilateral TKA or THA performed by either of six participating orthopedic surgeons. The patients were divided into two groups:

A – patients operated on between January 2010 and December 2012 before the introduction of tranexamic acid and iron pathway,

B – patients operated on between January 2013 and December 2015 when tranexamic acid was used routinely as prophylaxis and iron pathway when needed.

The following baseline variables were recorded in group A and B: age; gender; BMI; medication prior to surgery, including the use of acetylsalicylic acid (ASA), nonsteroidal anti-inflammatory drugs (NSAIDs), or selective serotonin receptor inhibitors (SSRIs); type of surgery; and thrombosis prophylaxis. Patients on ASA or NSAIDs were urged to discontinue these medications 3 days before surgery. Medication with potent platelet inhibitors, such as clopidogrel, were stopped at least 1 week before surgery. Blood samples from a peripheral vein for hemoglobin (Hb), platelet count, activated partial thromboplastin time (aPTT), and prothrombin time (PT) analyses were obtained < 24 h before surgery. Hemoglobin level was also measured 24-48 h postoperatively in order to calculate blood loss.

The following perioperative variables were recorded in group A and B: duration of operation, bleeding during surgery (intraoperatively), transfusion requirements intraoperatively, and postoperatively until discharge or until reoperation and autologous transfusion of wound blood after cell saver processing. Intraoperative bleeding was calculated from blood retrieved from wound suction plus the estimated amount of blood in the swabs.

Additionally to the above mentioned measures the group B patients were pre-assessed at least 28 days before the date of the surgery. The FBC was obtained and anemic patients were identified. The anemia was diagnosed according to WHO as Hb level < 12 g/dl in adult females and Hb < 13 g/dl in adult males. The results were forwarded to the GPs with guidance for treatment. The patients were commonly prescribed with Ferrous Sulphate 200 mg TDS or Ferrous Fumarate 325 mg BD-TDS.

The average increase in Hb level was 0.8 g/dl. Patients with no increase in hemoglobin were interviewed and asked about compliance with oral iron; follow up was arranged as appropriate.

A standardized prescribing regimen was established in which patients received TXA 1gram as a direct intravenous (IV) injection immediately prior to skin incision and once again immediately after the surgery was complete.

With the exception of insertion of drains in TKAs, all participating reconstructive orthopedic surgeons used identical operative techniques for joint reconstruction. All surgeons used similar postoperative pain management techniques, antithrombotic therapy (subcutaneous enoxaparin 40 mg daily beginning on postoperative day 1), and rehabilitation strategies and both employed a standardized protocol for daily laboratory monitoring. All surgeons routinely followed identical criteria for decisions regarding blood transfusion (hemoglobin < 8.0 g/dL, unless anemic symptoms are present).

The primary outcome was objective measures of perioperative blood loss and prevalence of blood transfusion among patients undergoing total joint arthroplasty. Accordingly, preoperative and nadir postoperative (usually postoperative day 1) hemoglobin and hematocrit levels were recorded and differences were determined. Blood product administrations were identified and recorded, including volumes or amounts and types of transfusion according to allogeneic or autologous blood. Secondary outcomes of interest included length of stay, relative health condition as described in the hospital discharge summary, and in-hospital occurrence rates for thrombotic, hemorrhagic, and other serious complications.

RESULTS

During the period of observation, 2416 patients underwent total joint arthroplasty performed by participating surgeons. Among these, 1262 patients received perioperative TXA (treatment group) and 74 entered the iron pathway. The average increase in Hb level was 0.8 g/dl.

Group A patients (patients treated before TXA and iron pathway introduction 2010-2012): among 1154 patients undergoing joint replacement 648 (56.1%) were transfused with RBC units.

Group B patients (patients treated after TXA and iron pathway introduction 2013-2015): among 1262 patients undergoing joint replacement 240 (19.01%) were transfused with RBC units.

74 patients entered the iron pathway. Among this population 6 patients did not improve and were diagnosed with severe medical condition or referred to other specialty: 1 case of chronic lymphocytic leukemia, 1 case of multiple myeloma, 1 case of bowel cancer and 1 of esophageal cancer, 2 patients were referred for further hematology evaluation.

None of the patients experience complications associated with TXA administration.

DISCUSSION

Our evaluation of joint reconstruction surgery revealed that intraoperative TXA administration and implementation of iron pathway were associated with decreased blood loss and diminished transfusion requirements. These patient safety considerations are consistent with previous experience reported by others.

The first controlled trial of TXA administration in orthopedics was conducted in the early 1990s. In this report, 29 patients undergoing TKA were randomly assigned to receive a direct IV injection of TXA 15 mg/kg or an identical volume of normal saline placebo a few minutes before tourniquet deflation. Measured total postoperative blood loss was 1549 ± 574 mL in the placebo group and 847 ± 356 mL in the TXA group ($p < 0.001$). During hospitalization, patients in the placebo group received a mean 3.3 ± 1.8 units of pRBCs as compared with 1.5 ± 1.3 units in the TXA group ($p < 0.005$). Two patients in the placebo group experienced a thrombotic complication as compared with none in the TXA group.

This initial experience in which operative blood loss and requisite blood replacement were approximately halved with use of TXA was replicated by others in successive years. Since then, nationwide surveys (12-20) and numerous additional controlled trials have confirmed these findings in both TKA and THA. These trial results have been systematically reviewed in at least six meta-analyses. Findings of these analyses of pooled data from 15 to as many as 46 clinical trials are congruent with regard to conclusions that TXA is effective and safe in reducing blood loss and transfusions in TKA and other major orthopedic procedures. Directed studies have shown TXA to be cost-effective in these procedures. Further investigations have shown that TXA is effective in minimizing blood loss in concurrent (21) and staged bilateral TKAs as well as revision TKA. Finally, clinical trials have evaluated the comparative effectiveness of differing numbers of intraoperative doses of IV TXA and differing routes of administration including IV injection, IV infusion, intra-articular or topical application, oral ingestion, and various combinations of these. Although some trials present data favoring multiple-dose regimens, the overall clinical effects of TXA in orthopedics appear favorable. In total, evidence concerning perioperative TXA in orthopedics has been categorized by the American Society of Anesthesiologists as A1 for strength and quality of research design and, due to this high regard, worthy of consideration as a means to prevent excessive bleeding in essentially all patients (22-30).

Our study confirms the above findings. To our knowledge we are the first to introduce the patient centered approach to blood management and incorporate iron pathway together with TXA administration. The iron pathway helps not only to treat the anemia but also to discover early enough the underlying severe pathology and avoid serious complications.

TXA is a lysine analog procoagulant that acts by inhibiting fibrinolysis. Prominent adverse effects of

procoagulants include thrombotic complications associated with excessive blood coagulation. However, when used as a blood conservation modality during primary TKA in conjunction with postoperative antithrombotic medications including aspirin, warfarin, or parenteral low-molecular-weight heparin, TXA has been associated with occurrence rates of symptomatic deep vein thrombosis of 0.5% and non-fatal pulmonary embolism (PE) of less than 0.4% Odds ratios for venous thromboembolism and mortality were shown to be equal in large cohorts of patients undergoing TKA or THA with and without TXA. These reassuring incidence rates for serious thrombotic complications are juxtaposed by a recent report describing a 65-year-old male with a previously undiagnosed patent foramen ovale who suffered bilateral PE and an acute symptomatic cerebrovascular infarct following synchronous bilateral TKA in which IV TXA was administered.

Our study has several important limitations. It was performed with a retrospective, non-randomized design, and an assessment of care provided at the discretion of autonomous physicians. This study had relatively small sample sizes and it was performed at a single institution. The medical records used to identify signs and symptoms of venous thromboembolism, hemorrhage, or other complications did not always address specific clinical criteria required for systematic evaluation of these issues. Nonetheless, this assessment of case findings offers a clinical perspective taken from typical contemporary acute patient care and, as such, it is representative of a broad spectrum of orthopedics practice in hospitals. To our knowledge, this is the first evaluation that assessed the impact of TXA combined with on iron pathway on postoperative need for blood transfusion.

In conclusion, perioperative administration of IV TXA and implementation of iron pathway was associated with diminished perioperative blood loss and lesser transfusion requirements in patients undergoing joint replacement surgery. No serious treatment-related adverse effects were identified.

CONCLUSIONS

The introduction of tranexamic acid and iron pathway has reduced transfusion rates with improved outcomes and cost reduction

The level of postoperative Hb level was higher after the introduction of tranexamic acid.

Patients who fail to respond to iron treatment should be followed up to ensure no serious pathology.

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