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Original research

Primary lower limb joint replacement and tranexamic acid: an observational cohort study

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ABSTRACT

Background: This work aimed to evaluate the efficacy and safety of routine tranexamic acid (TXA) use in elective orthopaedic lower limb joint replacement surgery.
Methods: This retrospective cohort study included all primary hip or knee replacement procedures by a single surgeon over a 6-year period. TXA was introduced during the study period as part of an enhanced recovery after surgery strategy.
Results: Of the 673 procedures, 446 cases (66.3%) received TXA. The median length of stay was 5 days (2-69) and 6 days (3-28) for the TXA and control groups, respectively ($P < .001$). Blood transfusion was required for 28 (6.3%) of the TXA cases versus 40 (17.6%) controls ($P < .001$). Complication rates were similar irrespective of TXA status. At multivariate analysis, TXA was significantly and independently associated with fewer blood transfusions (hazard ratio 0.309, 95% confidence interval: 0.168-0.568, $P < .001$), with a number needed to treat of 9 cases. TXA use was estimated to save between £67.89 and £155.90 per case.
Conclusions: Routine prophylactic TXA administration for elective primary hip and knee replacement reduces the likelihood of postoperative transfusion with a number needed to treat of 9. Cost savings may be as high as £155.90 per case, and no safety concerns were noted.

Introduction

Tranexamic acid (TXA) use for hemorrhage control was first described in the late 1950s [1] in patients with known clotting disorders. Tavenner [2] described improved hemorrhage control after dental extraction for patients with hemophilia or Christmas diseases after therapeutic TXA administration. TXA administration has become increasingly popular during resuscitation of major trauma patients and is associated with reduced mortality [3]. It is now recommended as an early hospital treatment for major trauma patients with a bleed [4] and as a therapeutic option after postpartum hemorrhage [5]. Furthermore, evidence is emerging for TXA use to treat other life-threatening hemorrhages, such as gastrointestinal bleeding [6].

More recently, TXA has been advocated for routine prophylactic use during gynecologic surgery [7,8], orthopaedic lower limb joint replacement surgery [9,10], and emergency orthopaedic hip surgery [11].

The primary aims of this work were to identify if routine TXA use in elective orthopaedic lower limb joint replacement surgery was associated with lower blood loss, reduced transfusion requirement and a shorter postoperative length of hospital stay. The secondary aim was to report a coupled economic analysis.

Material and methods

A retrospective cohort study was conducted including all patients who underwent primary hip or knee replacement by a single orthopaedic consultant operating at 2 district general hospitals. The cohort included males and females operated between February 2010 and April 2016, irrespective of age. TXA was

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introduced during the study period as part of an enhanced recovery after surgery (ERAS) program. Introduction was gradually dependant on adoption by individual anesthetists.

Authorization to conduct this work was granted by the research and development department of the University Health Board. All individual records were anonymized before analysis. Given the routine nature of the data collection to support service evaluation, formal ethical approval was not required.

Data collection

Patient data and relevant surgical information were abstracted from the digital theater management system. Further operative and outcome information was obtained from a prospectively updated arthroplasty database. Patient information was cross-referenced with the computerized hematology service system to provide preoperative and postoperative hemoglobin levels and details of blood transfusions. The case notes and anesthetic charts were reviewed to determine TXA dose and to validate that the requested blood for transfusion was administered.

Inclusions and exclusions

For the purpose of this work, the unit of analysis was "operation" rather than "patient" because some patients had undergone more than one joint replacement at different times (83, 2, and 1 patients had undergone 2, 3, and 4 joint replacements, respectively). Cases included all primary hip and knee joint replacements within the cohort when prophylactic TXA was administered (irrespective of dose). The remaining procedures that did not involve prophylactic TXA were recruited as the control group.

Emergency procedures, such as those following fractured neck of femur and revision procedures were excluded. Cemented hip replacement procedures were also excluded because these were only used for exceptional circumstances such as the management of metastatic disease or after radiotherapy. Complex primary procedures were included (such as hip dysplasia and removal of metalwork), provided that standard primary implants were used.

Outcome measures

The outcome measures for blood loss were a drop in hemoglobin from before to after surgery (measured in grams per liter, g/L) and blood transfusion requirement after surgery (during the postoperative inpatient stay). Length of stay (LOS) was measured in days from the date of surgery to discharge from hospital.

Complications

All complications within 90 days of surgery were included. For the purpose of this work, "total complications" included deaths and any complication within 90 days of surgery, irrespective of severity and type (both medical and surgical).

Statistical analysis

The Statistical Package for the Social Sciences was used [12]. Distributing the data by age revealed a negative skew; therefore, continuous data were described as median (range), and nonparametric statistical tests were employed.

Continuous and categorical data were compared with the Mann–Whitney U test and chi-squared (χ^2) test, respectively. The Wilcoxon signed rank test was used to compare preoperative and postoperative hemoglobin levels because these were related samples. Spearman's rho was used to test correlation. Linear discriminant analysis was used to compare continuous explanatory variables in relation to a binary outcome variable. To explore the factors associated with each outcome, 3 multivariate analyses were modeled. Model 1 consisted a binary logistic regression with blood transfusion status as the outcome variable, and hospital site, age, complex procedure, anesthetic type, preoperative Hb, TXA, gender, and joint type were entered as explanatory variables. Model 2 was a multiple linear regression with drop in Hb as the outcome variable, and hospital site, age, complex procedure, anesthetic type, preoperative Hb, TXA, gender, and joint type were entered as explanatory variables. Model 3 was also a multiple linear regression with LOS as the outcome variable, and hospital site, age, complex procedure, anesthetic type, preoperative Hb, TXA, gender, and joint type were entered as explanatory variables. The significance level was set at $P < .05$ for all tests.

The absolute risk reduction (ARR), relative risk reduction (RRR) and number needed to treat (NNT) were calculated according to the following formulas:

ARR = control event rate−experimental event rate
RRR = ARR/control event rate
NNT = 1/ARR (given as a whole number of "patients" as per convention)

Economic analysis

A simple cost-benefit analysis was conducted by exploring the monetary values of inpatient days and units of blood compared with the cost of TXA. This was done at a cohort level with average cost per operation given as the final output. Given the variation in cost for a hospital overnight stay (see below), the minimum and maximum costs were used, providing a simple sensitivity analysis.

Each unit of transfused blood in Wales was estimated to cost £149.07. An overnight stay at a hospital was estimated by the National Health Service Wales (NHS) Wales Informatics Service to cost £125 as a direct cost (used to calculate budget savings) and £378.14 as fully absorbed rate (the fee that would be charged to outside organizations or private patients). The NHS purchasing contract precludes disclosure by the Health Board of the exact payment for TXA in Wales. However, the most recent British National Formulary [13] quote the price from Pfizer as £1.55 per 500 mg, which is identical to the Monthly Index of Medical Specialties price quoted in the National Institute for Health and Care Excellence [14] guidelines on TXA in trauma. It was, therefore, decided to use this cost.

Results

During the study period, 674 primary total hip (THRs) or total knee replacements (TKRs) were performed. TXA status was not recorded for 1 operation, leaving 673 for analysis. The median age of the cohort was 68 years (range 27-90), 294 procedures (43.7%)

Table 1
Cohort breakdown of procedures.

Procedure	Number (%)
Primary THR	375 (55.7)
Conversion to THR (following previous fixation, such as dynamic hip screw; cannulated screws).	7 (1.0)
Complex primary THR (such as for hip dysplasia; severe osteoarthritis with bone loss).	11 (1.6)
Birmingham resurfacing hip replacement	1 (0.1)
Primary TKR	273 (40.6)
Complex primary TKR (such as for severe deformity)	6 (0.9)