ORIGINAL ARTICLE

Prevention of bleeding in total hip and knee replacement : Contribution of combined route in tranexamic acid administration

Prévention du saignement en chirurgie prothétique en orthopédie : Apport de l'acide tranexamique par voie combinée

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Abstract

Introduction: Tranexamic acid (TXA) has revolutionized perioperative blood management of total hip (THA) and knee arthroplasties (TKA). However, there is currently no consensus on the optimal administration route.
Aim: To compare the combined administration of TXA (intravenously (IV) and topically) versus IV alone on the reduction of postoperative bleeding in THA and TKA.
Methods: A nine-month double-blind randomized trial was conducted. Adult consenting patients scheduled for primary total hip arthroplasty (THA) or total knee arthroplasty (TKA) were included. The primary outcome measure was the decrease in hemoglobin levels 24 hours after surgery. They were randomized either to the IV group (51 patients) receiving 2 doses of 1 g of IV TXA 3 hours apart, or to the Combined group (50 patients) receiving 1 g of IV TXA and a topical dose of 1.5 g.
Results: The mean decrease in hemoglobin 24 hours after surgery was similar for both groups in THA (p=0.91) and TKA (p=0.19). There was no difference in perioperative transfusion rate between the two THA groups (p=0.6). In TKA, no perioperative transfusion was required. Total and measured blood losses were similar in both groups. Immediate and 3-month postoperative complications were similar.
Conclusion: Compared to IV TXA alone, the combined route does not reduce the risk of bleeding in prosthetic surgery.

Key words: tranexamic acid, knee replacement, total hip replacement, bleeding, transfusion of red blood cells

Résumé

Introduction: L'acide tranexamique (ATX) a révolutionné les mesures d'épargne transfusionnelle lors des chirurgies de prothèse totale de hanche (PTH) et du genou (PTG). Cependant, le schéma optimal de son utilisation reste encore mal élucidé.
Objectif: Comparer L'administration combinée d'acide tranexamique (ATX) (par voie intraveineuse (IV) et topique) à la voie IV seule sur la diminution du saignement en post opératoire d'arthroplastie de la hanche ou du genou.
Méthodes: Essai randomisé en double aveugle pendant 9 mois. Etaient inclus les patients adultes, consentants, programmés pour une arthroplastie totale primaire de la hanche (THA) ou du genou (TKA). Le critère principal était la diminution de l'hémoglobine 24 heures après la chirurgie. Ils ont été randomisés soit dans le groupe IV (51 patients) recevant 2 doses de 1 g d'ATX par voie IV à 3 heures d'intervalle, soit dans le groupe Combiné (50 patients) recevant 1 g d'ATX par voie IV et une dose topique de 1,5 g.
Résultats: La diminution moyenne de l'hémoglobine 24 heures après la chirurgie était similaire pour les deux groupes en THA (p=0,91) et TKA (p=0,19). Il n'y avait aucune différence dans le taux de transfusion périopératoire entre les deux groupes de THA (p=0,6). Dans le TKA, aucune transfusion périopératoire n'était nécessaire. Les pertes de sang totales et mesurées étaient similaires dans les deux groupes.
Conclusion: Comparée à la voie IV de l'ATX, la voie combinée ne diminue pas le risque de saignement en chirurgie prothétique.

Mots clés: acide tranexamique, prothèse de genou, prothèse totale de hanche, saignement, transfusion de gobules rouges

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Introduction

Hip and knee prosthetic surgery is one of the most performed surgeries in orthopedics. Faced with the improvement in life expectancy with the resulting aging of the population, the number of total hip and knee prostheses has increased considerably in recent years to reach 1 million/year in the United States (1). Indeed, in 2010, the prevalence of total hip arthroplasty (THA) in the United States was 0.83% or 2.5 million people per year and it is expected to reach 4 million in 2030. For total knee arthroplasty (TKA), the prevalence was 1.52% in 2010 and expected to be 7.4 % in 2030 (1). In France, the incidence of THA has increased from 222 to 241 prostheses/100000 inhabitants from 2008 to 2014 (2) with a growth of +32.2% in unicompartmental and total knee arthroplasty procedures recorded between 2012 and 2018 with a growth estimate of +33% by 2050 (3).
Blood loss continues to be a common surgical risk in THA and TKA, with estimated losses of 1188–1651 millilitres (mL) in THA and 726–1768 mL in TKA (4) and need of blood transfusion up to 42% and 34% of patients operated for total hip and knee replacement respectively (5). This blood transfusion is not without risk and may be responsible for multiple complications that may threaten both vital prognosis, such as ABO system incompatibility and acute lung oedema, and functional prognosis, by increasing the risk of infection of the prosthesis, thus increasing the length and cost of hospitalisation.
Its impact on morbidity and mortality has led to the introduction of numerous transfusion-sparing measures to improve post-operative rehabilitation. These include the use of tranexamic acid (TXA). An antifibrinolytic agent, has revolutionized perioperative blood management by minimizing blood loss and blood transfusions, leading to less transfusion related complications and periprosthetic joint infection. Because of its anti-fibrinolytic properties and low cost, it has been highly recommended in total joint replacement compared to placebo (6).
Several routes of administration have been described in the literature, but the optimal regimen for its use, indicating the most appropriate route of administration and the doses used, remains poorly elucidated.
In this context, the aim of this study was to evaluate the contribution of tranexamic acid administered by the combined route to the prevention of bleeding in patients proposed for hip or knee prosthetic surgery, compared with the intravenous route alone.

Methods

Study design

We conducted a monocentric randomized, double-blind trial over 9 months, from December 2021 to September 2022 in Mongi Slim's departments of anaesthesia and orthopaedic surgery. The study protocol was approved by the local ethics committee. All patients were included after obtaining informed consent.
We declare no conflict of interest.

We included patients aged of 18 years or more, scheduled for a primary THA and TKA in a traumatic, degenerative setting or malformations.
We did not include revisions, bilateral procedures, polytrauma, pregnant patients, contraindications for the use of TXA, coagulation disorders or anaemia with Haemoglobin (Hb) less than or equal to 9 g/dl preoperatively and patients treated with anticoagulants, Heparin, Warfarin, Oestrogen.
Exclusion criteria were serious anesthesia-related complications (impossible orotracheal intubation, anaphylactic shock) and severe transfusion reaction such as hemolysis.
Patients and surgery specific factors were collected including demographic characteristics (gender, age, height, weight and body mass index), transfusion and allergy history, calculation of scores: American Society of Anesthesiologists (ASA), LEE, STOPBANG (snoring history, tired during the day, observed stop of breathing while sleeping, high blood pressure, BMI > 35 kg/m2, age > 50 years, neck circumference < 40 cm and male gender) ; the reason for the prosthesis: traumatic, degenerative, malformations. A full clinical examination with neurological, haemodynamic and respiratory assessment (Glasgow coma score, blood pressure, respiratory rate and pulse oxygen saturation) was evaluated.

TXA administration

The eligible patients were randomized to either:
- Intravenous (IV) group: Receiving TXA at a dose of 15 mg/Kg, with a maximum dose of 1 g, diluted in 50 mL of isotonic saline solution (ISS) over 30 minutes with an electric syringe pump (ESP) 30 minutes before the incision, then 15 mg/Kg, with a maximum dose of 1 g diluted in 50 mL of ISS over 30 minutes with the ESP, 3 hours after the first dose combined with an intra-articular (IA) injection of 50 mL of ISS.
- Combined group: 15 mg/Kg of TXA was injected intravenously with a maximum dose of 1 g diluted in 50 mL of ISS over 30 minutes at the ESP 30 minutes before incision and then 50 mL of ISS at the ESP over 30 minutes, 3h after the first dose, combined with an IA administration of 1.5 g of TXA diluted in 50 mL of ISS. The topical dose was injected into the surgical site, over the posterior and anterior capsule, medial and lateral retinaculum in TKA and over the acetabulum and the femoral canal in THA for 3 minutes respectively after acetabulum and femur preparation. After this period, the joint capsule and incision were closed, and the drain was kept clamped for 30 minutes.
Neither the doctors (anesthesiologist and surgeon) nor the patient knew whether the patient had received intra-articular TXA or ISS.
TKA were performed under tourniquet in our study.

Anesthetic protocol

For the THA we routinely use general anesthesia. Titrated or single shoot spinal anesthesia was used for total knee arthroplasty.

We noted preoperative anemia (Preoperative anemia was defined as hemoglobin (Hb) less than 12 g/dL in women and less than 13 g/dL in men as defined by the World Health Organization (WHO) (7) and preoperative thrombocytopenia: platelet count < 150 000/ mm^3.
We calculated tolerable losses (mL) according to Gross' formula (8) =
(TBV x 2 x (Initial Hb - Threshold Hb)) / (Initial Hb + Threshold Hb)
With total blood volume (TBV) = Patient's weight in kilograms x Blood volume per kilogram.

Outcome measures

The main outcome of our study was Haemoglobin decline 24hours after surgery.
The second outcomes were postoperative hemoglobin decline 6 hours after surgery, the use of blood transfusion, total blood loss (TBL) (TBL= Total Blood Volume * (pre-operative haematocrit (Ht) - Ht at h36) + Volume of red blood cells transfused, measured blood loss (MBL) (MBL= Volume of blood drawn into the jar + compresses + into the post-operative drainage (until the drain is removed)), post-operative length of stay in hospital, post operative pain 6 hours and 24hours using visual analog scale. We evaluated also using telephone questionnaire the surgical site infections (early postoperative infections before 3 months or delayed between 3 months and 1 year or late after 1 year (9)), cardiovascular complication, thromboembolic complications including symptomatic postoperative deep vein thrombosis (DVT) or pulmonary embolism, surgical revision, respiratory complications or renal failure observed during the last surgical and biological control : defined according to KDIGO criteria (stage 1: Creatinine 1.5-1.9 times baseline, or Creatinine increase >0.3 mg/dL or urine output < 0.5 ml/Kg/h x 6-12 hours. Stage 2: creatinine 2-2.9 baseline or urine output <0.5 ml/Kg/h for > 12 hours. Stage 3: Creatinine >3xbaseline, or creatinine > 4mg/dL or initiation of dialysis or urine output <0.3 mL/Kg/h for > 24 hours or anuria > 12 hours).

Statistics

In order to calculate the number required for the study, we used the study published by Chalmers et al (10) in 2020. The fall in post-operative haemoglobin (at the first day post-surgery) from baseline in the intravenous group was 2 ± 0.9 g/dl. In order to have a fall in haemoglobin of 1.3 g/dl in the combined group with a risk α of 0.05 and a study power of 90%, the number required for the study was 76. To avoid potential exclusions, we included 102 patients.
All statistical analyses were conducted using SPSS 26.0 software (IBM SPSS Inc., Chicago, Illinois, USA). Qualitative variables were expressed as absolute numbers and percentages. After being tested for normal distribution using the Shapiro-Wilk and Kolmogorov-Smirnov tests, normally distributed continuous variables were expressed as mean ± standard deviation and non-normally distributed continuous variables were expressed as median and interquartile range. Considering the particularities between hip and knee prosthesis, the 4 groups were compared 2 to 2. Parametric data were then compared using Student's T test for independent-samples and non-parametric data were compared using the Mann-Whitney-Wilcoxon test. Qualitative variables were compared using the Chi-square test or Fisher's exact test.
For comparisons of qualitative variables between two groups, we used Pearson's Chi 2 test or Fisher's exact test. A value of $p<0.05$ was considered statistically significant.

Results

Flow chart of the study

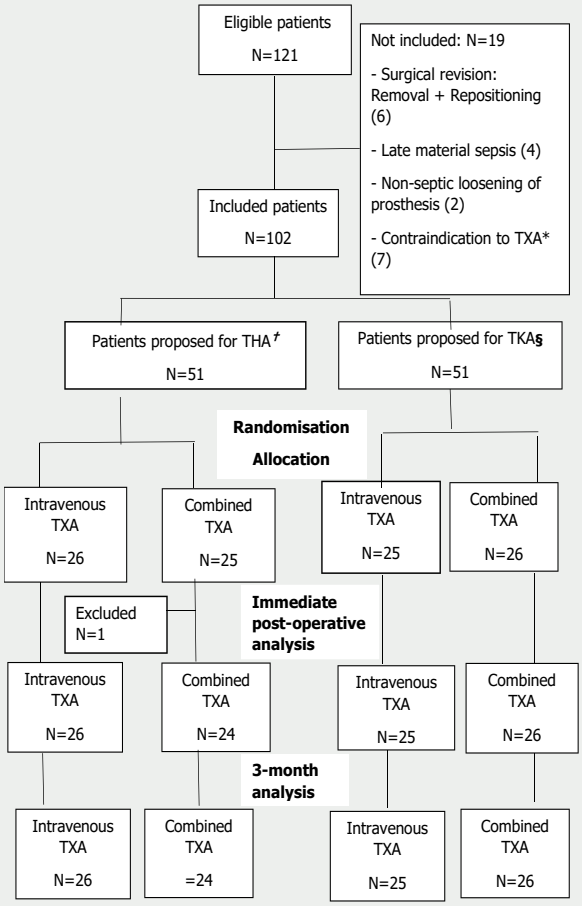

Figure 1. Flow chart of the study
***TXA**: Tranexamic acid; **†THA**: Total hip arthroplasty; **§TKA**: Total knee arthroplasty

Demographic characteristics

Demographic characteristics were comparable between the two groups of THA and TKA (Table 1).

Reasons for arthroplasty

In both THA and TKA cohorts, there was no difference mentioned in the reason for arthroplasty. The main reason for THA was traumatic in 53.8% of cases (42.3% for degenerative and 3.8% for malformation reason) with p=0.57.

TKA were performed for even degenerative or traumatic reason. In the combined group, all patients had TKA for degenerative reason and 96% in the IV group, with p=0.49. One patient in the IV group was operated for chronic post traumatic gonarthrosis

Table 1. Comparison of the means of anthropometric parameters between the two groups of patients operated on for total hip and knee replacement.

	IV* Group	Combined group	p
For total hip replacement	**N=26**	**N=24**	
Gender			0.09
Men	7(26.9%)	12(50%)	
Women	19(73.1%)	12(50%)	
Sex ratio	0.37	1	
Age (years)	57±14.7	58.63±12.41	0.68
BMI§ (Kg/m²)	27.91±4.89	26.90±4.49	0.45
Obesity (n)	9(18%)	7(14%)	0.68
For total Knee replacement	**N=25**	**N=26**	
Gender			1
Men	4(16%)	4(15.4%)	
Women	21(84%)	22(84.6%)	
Sex ratio	0.19	0.18	
Age(years)	66.36±5.9	67.37±8	0.63
BMI§ (Kg/m²)	33.54±7.47	31.87±7.94	0.44
Obesity (n)	17(33.33%)	12(23.52%)	0.11

***IV**: Intravenous; **§BMI**: body mass index

Clinical and biological characteristics

The main clinical and biological characteristics are presented in table 2.

Table 2. Comparison of pre-operative clinical and biological data

	IV* Group	Combined group	P
Total hip replacement	**N = 26**	**N = 24**	
ASA Score §	2 [1 ;3]	2 [1 ;3]	0.10
Lee Score	0 [0 ;0]	0 [0 ;1]	0.06
Preoperative sytolic pressure (mmHg)	132.96±15.81	131.33±11.62	0.67
Preoperative heart rate (bpm)	80.12±9.20	83.33±12.41	0.3
Haemoglobin (g/dl)	12.44±1.42	13±1.41	0.17
Hematocrit (%)	37.53±3.84	38.50±3.95	0.38
Platelet count (10^9/mm³)	262.5±659.9	257.62±64.88	0.79
Prothrombin (%)	93.57±7.04	91.63±10.22	0.44
Activated partial thromboplastin time	1.07±0.12	1.06±0.13	0.89
Tolerable blood loss (mL)	2247.1±862.4	2307.1±771.6	0.79
Total Knee replacement	**N = 25**	**N = 26**	
ASA Score §	2 [1 ;3]	2 [1 ;3]	0.78
Lee Score	0 [0 ;3]	0 [0 ;1]	0.80
Preoperative sytolic pressure (mmHg)	139.92 ±17.18	143.27±16.90	0.48
Preoperative heart rate (bpm)	76.04±12.32	71.38±9.23	0.13
Haemoglobin (g/dl)	12.86±1.30	12.90±1.529	0.93
Hematocrit (%)	38.93±3.64	38.44±3.60	0.63
Platelet count (10^9/mm³)	238.4±522.2	230.15±743,2	0.65
Prothrombin (%)	96.16±6.52	95.95±6.93	0.91
Activated partial thromboplastin time	1.01±0.06	1±0.03	0.54
Tolerable blood loss (mL)	2395.8±667.9	2387.5±814.9	0.96

***IV** : intravenous ; **§ASA** : Physical status score

Anaesthetic and surgical management

Anaesthetic technique was comparable between the two kinds of arthroplasties (p=0.07 and p=0.63 for THA and TKA respectively). All patients proposed for traumatic THA were operated on within 48 hours.

For THA, 24(92.3%) patients of the IV group had general anaesthesia versus 21(87.5%) patients in the combined group. Single shot spinal anaesthesia was used only with 2 patients (7.7%) of IV group. Titrated spinal anaesthesia was used only with 3(12.5%) patients of the combined group.

For TKA 6(24%) patients of IV Group had general anaesthesia versus 5(19.2%) patients in the combined group. Single shot spinal anaesthesia was used with 15 patients (60%) of IV group versus 14 (53.8%) in the combined group. Titrated spinal anaesthesia was used with 15(60%) patients of IV group versus 14 (53.8%) of the combined group.

In the IV THA group, 19 patients (73%) had a cemented prosthesis and 19 patients (79%) in the combined one. The difference was not statistically significant between the 2 groups p=0.61.

In the TKA group, all patients had a cemented prosthesis with tourniquet placement.

Haemoglobin decline 24 hours after surgery

There was no difference in the principal outcome in the two cohorts. Mean haemoglobin decline 24 hours after surgery was statically similar for both groups in THA and TKA (Figure 2).

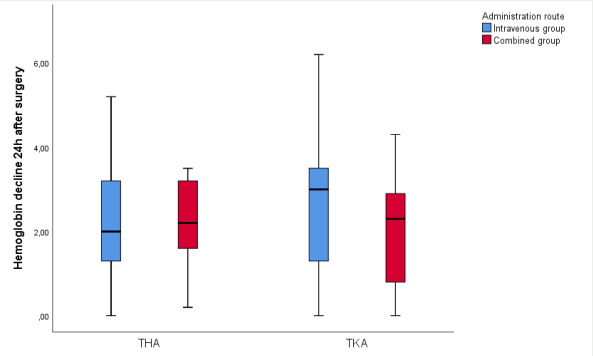

Figure 2. Mean Haemoglobin decline 24 hours after surgery

Haemoglobin decline 6 hours after surgery

Mean haemoglobin decline 6 hours after surgery was statically similar for both groups in THA with p= 0.78 (1.4 [0.5; 2.7] g/dL in IV group versus 1.6 g/dL [0.7; 2.7] in the combined group) and for TKA with p=0.41 (1.4 [0.8; 2.7] g/dL in IV group versus 1.3 [0.27 ;2.22] g/dL in the combined group).

The use of blood transfusion

There was no difference in the rate of transfusion during and after surgery between the two groups of THA. Indeed, a single patient in group IV versus 2 patients in

the combined group required per-operative transfusion (p=0.6). Only one patient in group IV required transfusion by post-operative and none in the combined group (p=1). In TKA no peri nor post operative transfusion was needed in the two groups.

Total and measured blood loss

For THA, total blood loss was comparable with both routes of administration, estimated at 308.71 [185.22 ;536.77] mL in the IV group versus 300.87 [137.08 ;480.45] mL in the combined group with p=0.31. Similarly for measured blood loss estimated at 520 [417.5 ;625] mL in the IV group versus 410 [320 ;590] in the combined group with p=0.65.
For TKA, total blood loss was comparable between the two routes of administration. It was estimated at 359.16 [217.16 ;490.93] mL for the IV route versus 274.32 [153.87 ;524.05] mL for the combined route with p=0.37. Measured blood loss was estimated at 400 [320 ;520.5] mL for the IV route versus 355 [247.5 ;495] mL for the combined route, with p= 0.06.

Length of stay in hospital

The intra-hospital length of stay was 2 days [2; 2] for both groups of patients undergoing THA. However, there was a significant difference between the IV and combined groups in patients undergoing TKA, with a longer length of stay in the IV group (2 days [3; 2] versus 2 days [2; 2] in the IV and combined groups respectively with p =0.03).

Postoperative pain

Tranexamic acid had the same effect in terms of post-operative pain at H6 and H24 between the two groups of THA with a comparable visual analogue scale (VAS) with p= 0.45 and p=0.14 respectively (figure 3).

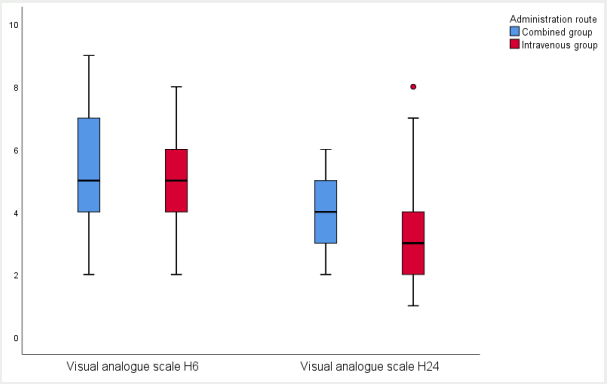

Figure 3. Mean post operative visual analogue scale in THA

In the TKA group, the difference was statistically significant between the two groups at H6 and H24 post-operatively and was higher in the combined group with p=0.001 and p=0.007 respectively (figure 4).

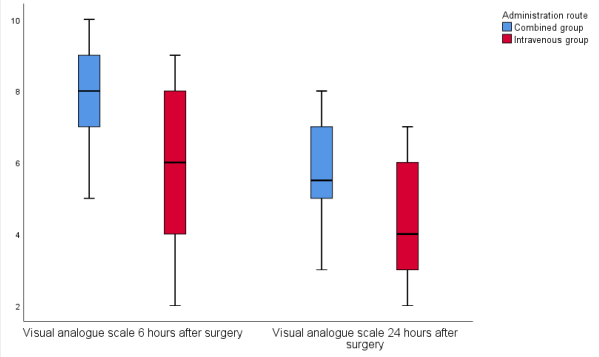

Figure 4. Mean post operative visual analogue scale in TKA

Immediate and 3 months post operative complications

In patients undergoing THA the findings are shown in the table below (table 3).

Table 3. Comparison of immediate and three months after total hip replacement complications

	IV* group N = 26	Combined group N = 24	P
Immediate complications			
Surgical site infections	1(4.2%)	1(2%)	**0.48**
Deep vein thrombosis	0	0	**1**
Surgical revision	0	1(4.2%)	**0.48**
Three months post operative complications			
Surgical site infections	1(3.8%)	1(4.2%)	**1**
Deep vein thrombosis	1(3.8%)	1(4.2%)	**1**
Surgical revision	2(7.7%)	0(4.2%)	**0.49**

***IV** : Intravenous

No complication was observed immediately nor 3 months after surgery in patients undergoing TKA.

Discussion

We conducted a nine-month double-blind randomized trial to compare the combined administration of TXA versus IV alone on the reduction of postoperative bleeding in THA and TKA. The main results concluded that in the THA Group: The hemoglobin decline at 24 hours postoperative compared to the pre-operative value was comparable in both groups 2 [1.17; 3.27] g/dL in group IV versus 2.2 [1.55; 3.2] g/dL in the combined group with p=0.91.
In the TKA group: The hemoglobin decline at 24 hours postoperative compared to the pre-operative value was comparable with the two routes of administration 3 [1.25; 3.6] g/dL versus 2.3 [0.8; 2.9] g/dL (with p=0.19).

Weaknesses and strengths of the study

This study has some limitations that should be mentioned: the limited number of patients and the inclusion of patients with degenerative and traumatic causes. Indeed, bleeding can occur preoperatively in traumatic context.
Trying to overcome this limit, traumatic causes were comparable in the 2 groups and these operated on within the first 48 hours after trauma.

The double-blind randomized trial and the follow-up of all patients at 3 months without losing sight were our main strengths.
Another strength of this study was represented by the results of two secondary endpoints, namely surgical site infection (SSI) and postoperative pain. SSI is
a major concern for orthopedic surgeons. According to our study, intra-articular administration did not increase the risk of infection. Post-injection pain in total
knee arthroplasty could be a barrier to the use of the combined approach.

Bleeding risk in prosthetic surgery

Intra-operative blood loss can reach 315 to 929 mL during THA and 220 to 4340 mL during TKA (11). These data, reported by the French National Authority for Health in 2006, come from old studies published between 1992 and 2003.
During THA, the risk of haemorrhage reaches its maximum intra-operatively, particularly during reaming of the acetabulum and femoral shaft, which is often underestimated despite monitoring of the operating field and surgical aspiration, with the risk of damage to the gluteal or obturator artery (11). The risk of haemorrhage may persist until the third post-operative day.
During TKA, the use of a tourniquet makes it possible to underestimate intra-operative bleeding and leads to greater activation of fibrinolysis by the intense vascular ischaemia induced (12), which manifests itself above all during the first 24 hours and persists until the 3rd day.

The role of tranexamic acid in blood savings during arthroplasty

TXA inhibits the binding of plasminogen to fibrin, preventing the formation of an active serine protease, plasmin, and subsequent fibrinolysis (13). The conversion of inactive plasminogen to fibrinolytically active plasmin by tissue plasminogen activator (t-PA) is catalysed by the binding of t-PA-plasminogen to the lysine residues of fibrin. TXA binds reversibly to the lysine-binding sites of plasminogen, blocking its conversion to plasmin.

The choice of dose administred

The choice of tranexamic acid dose was based on studies which showed that the increase in the occurrence of complications was correlated with the dose administered. In fact, the majority of studies have concluded that a cumulative dose of 3mg should not be exceeded, as in the case of the metaanalysis of Jashvant Poeran et al (14) which looked at the occurrence of new-onset “composite complications” (venous thromboembolism, myocardial infarction, seizures, and ischemic stroke/transient ischemic attack) and the need for blood transfusions in 3 groups of patients, group 1 with a history of thromboembolism, group 2 with a history of renal failure and group 3 with a history of atrial fibrillation, with cumulative doses of 1, 2 and 3 mg in each group.
The results concluded that tranexamic acid use was associated with decreased odds of blood transfusion and no increased odds of composite complications were in all groups.

Effect of route of administration on bleeding and transfusion sparing

The meta-analysis by Sun (15) compared the efficacy and safety of combined IV and topical TXA versus IV TXA alone in reducing blood loss after primary THP and TKP.
The results concluded that the intravenous route did not differ substantially from the topical route with respect to the total blood loss volume (p=0.31), drain blood loss (p=0.50), postoperative Hb levels (p=0.96), Hb decline (p=0.08), length of hospital stay (p=0.38), transfusion rate (p=0.75) and VTE occurrence (p=0.15). Compared with the combined-delivery group, the single-route group had significantly increased total blood loss volume ($p<0.05$), greater Hb decline ($p<0.05$) and higher transfusion rates ($p<0.05$). However, no significant difference was noted in the drain blood loss, postoperative Hb levels and VTE events between the two groups.

Effect of route of administration on adverse reactions

Seizures
The increased incidence of seizure disorders may be explained by the fact that TXA crosses the blood-brain barrier and interacts with glycine receptors (14). Post-operative seizures have been reported in patients with renal dysfunction following administration of high doses of TXA (50 mg/kg). Colour vision and visual disturbances could also be caused by the use of TXA. After a review of the literature, we did not find any studies indicating that the different routes of application of TXA may cause higher complication rates. According to Gilbody et al (16), topical use of TXA may be safer than IV in patients with an increased risk of thromboembolic events or renal impairment. This is probably due to the fact that after topical administration, the rate of absorption from the joint is very low. In our study, none of the patients in the two cohorts experienced a convulsive seizure, which may be due to the low dose administered by both the IV and combined routes.

Thromboembolic diseases
Despite the existence of a proposed mechanism of action for TXA as a fibrin clot stabiliser, the use of any antifibrinolytic drug in patients considered to be at "high risk" of thromboembolic events (e.g. history of thromboembolic venous disease, myocardial infarction with vascular stents, cerebrovascular occlusion) remains contraindicated. This continues to limit the use of TXA in hip and knee arthroplasty (17). In our study, in the THA cohort, one patient in group IV and one patient in the combined group developed deep vein thrombosis. This was explained by poor compliance with thromboprophylaxis.

Post-operative pain
In our study, postoperative pain at H6 and H24

postoperatively was without significant difference between the two THA groups with p=0.45 and p=0.14 respectively. On the other hand, pain was statistically significantly greater in the combined TKA group at H6 and H24 with p= 0.001 and 0.007.

The results of our study are in line with those of the study by Wei et al (18) in which TXA was incriminated in the increase in postoperative pain at H24 and H48 if administered topically compared with the IV route with p=0.001 and 0.008. No significant difference was observed at H48 post-operatively. On the other hand, in the study of TKA by Guerreiro et al (19), topically applied TXA caused less post-operative pain at 24 and 48 h post-operatively compared with the IV route (p<0.01) and there was no significant difference at D7, D21 and D60 post-operatively.

In the literature, studies confirming the hyperalgesic effect of locally administered TXA were carried out on THA, unlike our study which showed no difference in the two groups of this type of arthroplasty. The study by Wurtz et al compared 169 patients undergoing THA who had received intra-articular TXA versus 213 patients who had received SSI. The results showed greater post-operative pain in the TXA group (p=0.006) with earlier use of morphine (p=0.03) and higher doses (p=0.001) (20). These results have been explained by the inhibition of GABA and glycine receptors, which are linked to hyperalgesia and allodynia according to animal experiments carried out on rats (21,22). Ex vivo and in vitro studies carried out on human tendon, synovial and cartilage tissues harvested respectively during repair of the anterior cruciate ligament, hip arthroplasty and hip hemiarthoplasty showed a significant decrease in synoviocyte viability within four hours of exposure to 1 mg/mL TXA, and significant decreases in chondrocyte and tenocyte viability after four hours exposure to 100 mg/mL TXA (23). This effect on post-operative pain was not demonstrated when TXA was administered IV, despite its role in reducing post-operative haematoma (24,25).

Conclusion

Combined administration of TXA during hip and knee arthroplasty appears to be an effective and safe technique.

At present, this route is still little known and little used.

Further randomised, multicentre studies are needed to reinforce our results and potentially offer this technique in routine practice.

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