DOI: 10.21276/sjams.2017.5.3.6

Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2017; 5(3A):711-716 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Original Research Article

Interest of tranexamic acid in total hip arthroplasty

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Abstract: Total hip arthroplasty (THA) is one of the most frequent interventions in orthopedics. This is a surgical procedure at high risk of bleeding. Tranexamic acid (ATX), a synthetic antifibrinolytic, is an option of choice in the blood economy. It is therefore felt necessary to initiate the study on the interest of the ATX in the prevention of bleeding during the implantation of primary THA. A retrospective study subjects exposed and unexposed single-center, comparative between January 1, 2013 and March 31, 2014. All patients who had undergone primary total hip arthroplasty were enrolled and divided into 2 groups of 30:- Group ATX + patients received the administration of tranexamic acid in perioperative - Group ATX - patients didn't receive tranexamic acid as the control group. Sixty patients had received primary THA, divided into two groups of 30. The mean age of patients was comparable in both groups. The sex ratio was 1.1 with no significant gap between the two groups (p = 0.2). The average BMI was 23.60 ± 3.5 kg / m² in ATX + Group and 24.2 ± 3.5 kg / m² in ATX – group (P = 0.6). The average hemoglobin was 12.9 ± 1.1 g / dL in all patients. The surgical indications were identical in the two groups. Both anesthetic methods were practiced, spinal anesthesia and general anesthesia with no significant difference in both groups (P = 0.9). The mini-invasive incision was made more than 70% in both groups (P = 0.9). The average Blood loss was 459.6 ± 102 ml in the ATX + group and 750.8 ± 247.34 ml in the ATX- group. The overall transfusion rate was 30%, including 8.3% in the ATX+ group and 21.7% in the ATX- group. We noticed a reduction in the postoperative bleeding in the ATX + group in the D0-D1 interval with a difference significant (P = 0.0002). This work confirms the Eficacy of tranexamic acid in the transfusional saving strategy in major orthopedic surgery such as total hip arthroplasty and should be used systematically in the management of anesthesia in high-risk patient's Haemorrhagic fever.
Keywords: Acid tranexamic- Blood loss- Hip arthroplasty- Transfusion saving

INTRODUCTION

Total hip arthroplasty (HIP) is one of the most frequent interventions in orthopedic surgery. It is a surgical procedure with a high haemorrhagic risk per and postoperative with a major haemorrhage index of 1.4 [1]. It consumes an average of 8% of erythrocytic concentrates delivered and is one of the first causes of surgical transfusion in programmed surgery [2]. Transfusion of red blood cells is currently the only treatment for poorly tolerated acute anemia. Its complications, its cost as well as problems of supply of labile blood products, lead to promoting a strategy of transfusion saving [3]. Thus, tranexamic acid (ATX) which is a synthetic antifibrinolytic inhibiting the degradation of fibrin and delaying degradation of the haemostasis clot is an option of choice. However, it is used only in 17% of its theoretical indications due to the great variability of the protocols of use [4, 5]. It was therefore necessary to initiate this study on the place of ATX in the prevention of bleeding during primary implantation PTH.

PATIENTS AND METHODS

Inclusion, Non-Inclusion Criteria

This is a retrospective study exposed subjects and unexposed subjects monocentric, comparativ ranging from January 2013 to March 31, 2014 being a duration of 15months. All patients with first-line THP were included and divided into two groups of thirty. Patients with ATX contraindications were not included: coagulopathy, Prior history of venous or arterial thromboembolic events, stroke, epilepsy, creatinine

clearance <40ml / min. Repeats of PTH also whatever the indication were also not included.

Anesthesia

All patients had systematically benefited from a large caliber peripheral venous pathway with a 500-ml prefilling of SSI or RL prior to anesthetic induction and cefuroxime-based antibiotic prophylaxis 1.5 g thirty minutes before the incision with re-injection of 750mg every two hours. Monitoring was performed with a multiparameter monitor ECG CM (DII derivative), SPO2, PANI taken immediately after anesthetic induction and every five minutes until the end of surgery.

The choice of anesthesia technique was based on the patient's condition and preference. The preferred technique was spinal anesthesia in the absence of contraindications. The anesthetic solution used was a mixture of 15mg hyperbaric bupivacaine and fentanyl 25ug. In case of contraindications or failure to spinal anesthesia, conversion to general anesthesia with orotracheal intubation was performed. The morphine used was fentanyl at 3 µg / kg. The hypnotic was propofol at 2.5 mg / kg or by titration depending on the cardiovascular condition of the patient. Myorelaxation was provided by vecuronium bromide at 0.1 mg / kg. Maintenance of hypnosis was provided by 2MAC isoflurane and reinfusions of curare and fentanyl. Unbolus of 5mg of ephedrine was administered in the event of a PAS fall of more than 25% of the basic PAS or if the PAS was less than 90mmHg.

Injectable tranexamic acid (ATX) was administered according to this schedule: bolus of 1g over 15min before incision, 0.5g if the surgery reached 2 hours and 2g within 8 hours postoperatively in patients who benefited from PTH. This allowed us to define two groups:

• 1st group: ATX + denoted the group of patients who benefited from the administration of tranexamic acid in perioperative
• 2nd group: ATX - designated the patient group that did not benefit from tranexamic acid as the control group.

The postoperative analgesia was multimodal intravenously initiated as soon as the surgical site was closed with intravenous paracetamol 1g / 6h associated with nefopam 20mg / 8h in case of contraindication of tramadol 100mg / 8h in case of contraindication and with ketoprofen 100mg / 12h in the absence of blood-vessel disorders and renal insufficiency. Prevention of venous thromboembolic disease was provided by enoxaparin 40mg / d subcutaneously from the 6th postoperative hour under control of the redon drain and platelet count.

Surgical Technique

It was stereotyped and performed by the same surgeon. This was a postero-external approach to a patient in lateral decubitus. The incision was minimally invasive (less than 10cm) or classic. The implants used were non-cemented (AMPLITUDE®) or cemented. At the end of the procedure, an intra-articular aspiration duct was placed systematically for 48 hours.

Blood transfusion protocol

The operative intraoperative bleeding was evaluated after measuring the amount of blood drawn in peroperatively and collected in the compresses. Postoperative bleeding was estimated by the amount of blood collected through the redon drains.

The transfusion thresholds were:
- 7g / dl in the absence of a specific antecedent
- 8 to 9 g / dl for poor tolerance of anemia, heart failure or coronary artery disease
Oral iron of 180mg / d was administered systematically to all patients the day after surgery. At the end of the procedure, patients were all transferred to SSPI after table extubation for GA. 2-5 The data collected.

For each patient were collected age, sex, morphological data, usual treatment, medical and orthopedic history. Elements of preoperative clinical and biological evaluation as well as surgical indications were also noted. We observed the surgical technique, the equipment used and the duration of the intervention. On the anesthetic level, we noted the type of anesthesia, the type and quantity of filling solutes, the intraoperative and postoperative blood loss, the blood products administered and finally the postoperative evolution.

STATISTICAL ANALYSIS

The values were represented as an average plus or minus standard deviations and percentages. The quantitative parameters were compared by the Student's T-test and the qualitative parameters were compared by the Chi2 test in univariate analysis. The threshold of significance was lower than 0.05.

RESULTS:

During the study period, 60 patients had first-line PTH divided into ATX + (n = 30) and ATX - (n = 30). The ATX + group consisted of patients who received tranexamic acid and the ATX group were not operated without tranexamic acid.

Table I illustrates the demographic and medical characteristics of the study population. Table I represents the demographic and medical characteristics of our patients. The indications for PTH were identical

in the two groups of patients. They were dominated by aseptic necrosis of the femoral head (ATX + 50% versus 40% ATX -) followed by osteoarthritis (43% versus 50%) and fracture of the femoral neck (7% versus 10%).

We found four areas: HTA, Sickle Cell Disease, Diabetes and Asthma, divided into the two groups according to Table II. Table II reproduces the peculiarities of the patient's grounds. In the study of intraoperative blood loss, an average loss of 459.6 ± 102 ml (range of 150 to 1000 ml) was detected in the ATX + group and 750.8 ± 247.34 ml (range of 200 and 1800ml) in the ATX group.

Table-1: Demographic and medical characteristics of patients

	ATX +	ATX -	P
Age (an)	46,3±15,3	47,3±12,5	0,8
Sex (F/M)	14/16	13/17	0,2
Weight (kg)	67,15±12,5	69±12,6	
IMC (kg/m2)	23,6±3,5	24,2±3,5	0,6
ASA (I/II/III)	17/12/1	17/13/0	
Hb (g/dl)	12,76±1,13	13,05±1,23	0,45
HCT (%)	40,15±1,1	40,39±3,05	0,84
Clairance (ml/min/1,73m2)	130	142	0,87
Anesthetic technique (%)			
RA	80	80	
AG	20	20	
Filling (ml)			
Cristalloïde	1250±325	1600±185	0,22
Gélatine	1100±150	1300±210	0,45
Incision (%)			0,9
Mini-invasive	90	79	
Classic	10	21	
Matyriel (n)			
Ciment	5	4	0,28
No ciment	25	26	0,51
Operating time (min)	101±14,3	100,3±15,2	0,58

Table II: Distribution of patients with particular terrain

errains	ATX^+ (n)	ATX^- (n)
Sickle cell disease	**4**	**1**
High blood pressure	**3**	**6**
Diabete	**2**	**-**
Asthm	**1**	**3**

Table III: Postoperative blood loss following Redon drain

Day	ATX^+ (ml)	ATX^- (ml)	P
D0 – D1	208,66 ± 56,62	284 ± 70,8	0,0002
D1 – D3	90,7 ± 32,7	101,43 ± 61,4	0,54

We found no relationship between blood loss and incision type (p> 0.05) in the two groups. The type of anesthesia was also not correlated with an increase in bleeding (p> 0.05) in both groups. The implants used were predominantly non-cemented with no direct relationship to bleeding in both groups (p> 0.05). Five patients, or 16.7% in the ATX + group, used transfusion during the operation compared with 13 in the ATX group - 43.3% (p = 0.02). In the majority of cases (85%) the transfusion threshold was 10 g / dl associated with poor clinical tolerance. Postoperative blood loss was assessed by the amount of blood collected by redon drains. We observed a reduction in postoperative bleeding in the ATX + group for the J0-J1 interval with a significant difference (p = 0.0002). Table III: Redon drains production The overall postoperative blood transfusion rate was 15%. In all patients

transfused after surgery, the transfusion threshold was 7 g / dl.

DISCUSSION:

The management of hemorrhagic surgeries must balance the morbidity and mortality associated with anemia and the risk of transfusion [6]. Indeed, postoperative anemia, present in 90% of patients after arthroplasty, leads to an increased risk of myocardial infarction due to inequality between intake and oxygen requirements in the perioperative phase and is the leading cause of death After major orthopedic surgery [7, 8]. However, the adoption of restrictive thresholds is not associated with an increase in mortality [9]. In order to reduce blood loss during a number of haemorrhagic surgical procedures, the ATX has been advocated. ATX is a synthetic analogue of lysine, an amino acid that acts by binding to lysine binding sites on plasminogen molecules. It reversibly and competitively decreases the binding affinity of plasminogen for fibrin, decreases the plasminogen activation to plasmin and decreases the local degradation of fibrin by plasmin. Since its development in the early 1960s, it has been shown that ATX is a remarkably effective drug for the reduction of perioperative blood loss and therefore the use of transfusions [10, 11]. This has never been more evident than in orthopedic surgery, especially in patients undergoing major arthroplasty procedures. Several clinical studies have reported beneficial effects on perioperative bleeding in hip arthroplasty [12, 13]. Reduction of postoperative bleeding was achieved when ATX was administered. On the other hand, Benoni et al do not objectify any reduction in losses when administered at the end of surgery [14]. Sukeik *et al.;* concluded in a meta-analysis to a reduction in total average blood loss of 289ml. Recently, 46 randomized controlled trials involving 2,925 patients undergoing orthopedic surgery were identified and included in a meta-analysis. In 21 studies, ATX was administered at doses of 15 mg.kg-1 and in 18 studies it was administered at doses of 15 mg.kg-1. A single bolus was administered preoperatively in 20 studies while repeated boluses were administered in 26 studies. After collection of all doses and conditions of administration, ATX was associated with a mean total reduction in blood loss of -408 ml (95% confidence interval [CI]: -506 to -311), resulting in Halving the probability of an allogeneic blood transfusion (relative risk: 0.51, 95% CI, 0.46 to 0.56) [15].

In our clinic, the use of ATX perioperatively resulted in a significant transfusion saving similar to that found in Sukeik's meta-analysis [16]. However, in our series, the estimate of postoperative blood losses by redon drainage remained inadequate because the postoperative hematoma was not taken into account in this method. The postoperative hemoglobin or hematocrit is more reliable in estimating these losses in this situation. Several studies have also proved the reduction of the homologous transfusion rate related to the administration of the ATX [16-18]. In our study, the use of ATX significantly reduced the incidence of homologous transfusion in our patients, ie 16.7%. According to Irrison et al the volume of bleeding is significantly decreased, and this is prolonged until the third postoperative day [19]. This study confirms the efficacy of ATX in major orthopedic surgery in terms of homologous and autologous transfusion reductions [16, 20, 21]. Despite this efficiency, its low cost and little side effect, the ATX remains little used in our practice. Elsewhere, in an analysis of the economic impact of ATX, Irisson et al find a direct financial saving generated within the budget for blood saving techniques of 25% per patient in the literature. This impact is reported in Term reduction in length of stay [22]. Until recently, questions regarding the theoretical risk of seeing TXA increased the number of postoperative venous thrombotic events (ETVs) have delayed or even prevented its wider use in patients undergoing arthroplasty. Venous thrombotic events remain a concern in patients undergoing arthroplasty who are particularly prone to postoperative thrombotic complications [15].

The great risk mentioned with antifibrinolytics is the possibility of venous thrombosis during their use. In the Norio *et al.;* study, all patients underwent body scan to detect not only deep venous thrombosis but also pulmonary embolism [23]. It was found that administration of ATX did not increase the incidence of deep thrombosis or pulmonary embolism contrary to the arguments of other studies [16, 24, 25]. In the meta-analysis of Huang *et al.;* the authors did not observe statistically significant increases in thromboembolic events. Deep venous thrombosis (DVT) rates were similar in the ATX and control groups [respectively: 30/1 376 (2.18%) patients and 26/1 313 (1.98%) patients; Relative risk: 1.11; 95% CI: 0.69 to 1.79 [15]. In our study, no patient presented a sign related to venous thromboembolic event or pulmonary embolism with clinical expression. The ATX remains an antifibrinolytic that stabilizes the haemostasis clot by preventing its degradation but also prevents the formation of other clots [20, 26, 27]. This clinical study, the purpose of which was to confirm the benefit of the use of perineal and postoperative ATX as reported recently by Raveendran in his editorial [28], compared two groups of exposed and non-exposed subjects ATX, operated with a PTH of first implantation in programmed surgery. It has some limitations related to its retrospective nature and a slightly inhomogeneous patient population. Nevertheless, we consider that the strength of this study, despite its relatively modest population, lies in the uniformity of the surgical and anesthetic procedures performed by the same team. It was a standardized protocol of the ATX for the usual

contraindications of this drug, including in the non-exposed subjects who served as a witness in this work.

CONCLUSION:

The reduction of the incidence of blood transfusion in major orthopedic surgery is based on a true policy of transfusion-specific economy adapted to each service and adapted to each patient. Our study confirms the beneficial interest in transfusion saving by a clear decrease in bleeding. For this purpose, tranexamic acid should be integrated into our protocols for the management of hip prosthetic surgery because of intravenous 1g for 10min, fifteen minutes before the incision and then 0.5g at the second hour, Intervention and finally 0.5g at the sixth hour after surgery.

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