EFFECT OF TRANEXAMIC ACID USE ON POSTOPERATIVE BLOOD LOSS IN TOTAL KNEE ARTHROPLASTY

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EFFECT OF TRANEXAMIC ACID USE ON POSTOPERATIVE BLOOD LOSS IN TOTAL KNEE ARTHROPLASTY (Abstract). **Aim**: To monitor the effect of tranexamic acid use (Exacyl) on postoperative bleeding (aspiration), autologous blood transfusion (autotransfusion), allogeneic blood transfusion and postoperative anemia (difference between preoperative and immediate postoperative hemoglobin levels) in total knee arthroplasty. **Material and methods**: This retrospective observational study was conducted on a sample of 457 patients who underwent endoprosthetic knee arthroplasty in the interval January 1, 2008-July 30, 2014 at the Traumatology-Orthopedics Clinic of the Iasi Rehabilitation Hospital. The mean age of the study group was 66 years (range 32-84 years), 74.4% were female, 39.8% presented varus and 6.1% valgus malalignment. The study group was subdivided into two groups: **Group 1** served as controls and underwent surgery without the administration of tranexamic acid and **Group 2** received tranexamic acid. **Results**: In group 1 the average amount of blood lost was significantly higher than in group 2, 1168.94 ml vs 452.9 ml (p < 0.001). The use of a cell saver was required in 70% of group 1 patients with an average amount of auto transfused blood of 480.70 ml, significantly more frequent and in greater amounts than in group 2 (below 10%) with an average of 15.05 ml (p < 0.001). In this study tranexamic acid had not a statistically significant favorable effect on blood transfusion requirements and anemia syndrome. **Conclusion**: Tranexamic acid has a favorable effect on postoperative blood loss and its associated complications, with a favorable impact on both early clinical and functional recovery. **Keywords**: TRANEXAMIC ACID, TOTAL KNEE ARTHROPLASTY, TOURNIQUET, BLOOD LOSS.

Knee osteoarthritis is one of the most common causes of pain and loss of joint function, the risk of disability being as high as that attributable to cardiovascular diseases and higher than in any other disease in the elderly (1). The disease is more common in women (2). In the advanced stages of knee osteoarthritis endoprosthetic arthroplasty is the gold standard treatment, the technique being customized according to the associated deformity and individual joint architecture (bone and ligaments) (3).

The use of a tourniquet induces local fibrinolysis in the operated lower leg and increased fibrinolytic activity causes significant postoperative blood loss. Blood loss causes such postoperative complications as anemia (4), cardiovascular complications, post transfusion reactions (post transfusion shock, transfusion transmitted diseases, postoperative infection) (5,6), with a direct
impact on the early postoperative course and functional recovery. Tranexamic acid, a synthetic analogue of lysine which competitively inhibits the activation of plasminogen to fibrin (7.8) is used to reduce postoperative blood loss. The aim of this study was to assess the effect of tranexamic acid (Exacyl) use on postoperative bleeding (aspiration), autologous blood transfusion (use of cell saver) and allogeneic blood transfusion on postoperative anemia syndrome (difference between preoperative and immediate postoperative Hb levels, D Hb).

**MATERIALS AND METHODS**

The retrospective observational study was conducted on a sample of 457 patients diagnosed with advanced knee osteoarthritis who underwent endoprosthetic knee arthroplasty in the interval January 1, 2008 - July 30, 2014 at the Traumatology-Orthopedics Clinic of the Iasi Rehabilitation Hospital. The mean age of the study patients was 66 years (range 32-84 years), 74.4% of them being female. The study group was subdivided into two groups: group 1 (78.11%) - patients who were not given Exacyl and group 2 (21.89%) - patients who received intravenous tranexamic acid intraoperatively and immediately postoperatively.

Also evaluated was blood loss depending on the presence or absence of frontal plane deformities, as evidenced by the calculation of hip-knee-ankle (HKA) angle on long leg X-ray (fig.1.a, b). 53.6% of the patients had proper knee alignment, while varus and valgus malalignment was present in 39.8% and 6.1%, respectively.

Sagittal plane malalignment, in flexum, was associated with varus misalignment in 97% of the cases, being the sole finding in only two cases. Of the study patients with genu varum 44% presented a mild deformity of 8 degrees and 18% of over 15 degrees. In genu valgum patients, the three categories were in almost identical percentages.

![Fig. 1. a) Preoperative planning: Digital long leg X-ray of the lower limb in upright position; b)Advanced secondary knee osteoarthritis on genu valgum (HKA- 152°)](image1.jpg)
RESULTS

1. Aspiration: Comparing the blood loss in the two groups we found a statistically significant difference (p < 0.001). If in group 1 the average blood loss was of 1168.94 ml (highest: 4150 ml), the analysis of data from group 2 showed an average blood loss of 452.9 ml (highest: 1100 ml) (fig. 2.) Blood loss was not influenced either by age (p = 0.336) or sex parameters (p = 0.512).

2. Autotransfusion: The need for a cell-saver and the amount of autotransfused blood were significantly higher in group 1 (p < 0.001). In group 1 a cell-saver was used in 70% of the cases and the average amount of autotransfused blood was 480.70 ml. In group 2 the average amount of autotransfused blood was of only 15.05 ml, and cell saver was used in less than 10% of patients.

3. Blood Transfusion: The difference between the two groups was not statistically significant (p = 0.436). A lower rate of allogeneic blood transfusion was recorded in group 1 (20% of cases, average amount 68.91 ml) compared to group 2 (32% of cases, average amount 99.5 ml).

4. Anemia syndrome: Mean $D Hb$ was 3.27 mg/dl in group 1 and 2.74 mg/dl in group 2. The highest level was 8.10 mg/dl in group 1 compared to 4.90 mg/dl in group 2. Despite the values differed, the difference did not meet statistical significance (p = 0.514).

5. The presence of deformities: These variables for quantifying blood loss were also checked within the context of present or absent joint deformities, without noticing significant differences (tab. I). We noted that frontal plane deformities greater than 15 degrees were often associated with an increase in the amount of blood loss.

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<td>Average values of blood loss variables according to the presence/absence of diforimity</td>
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<td>Diforimity</td>
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DISCUSSIONS

Endoprosthetic knee arthroplasty is accompanied by minimal intraoperative bleeding due to the use of pneumatic tourniquet but by important postoperative blood loss.

This study shows that the use of tranexamic acid results in a significant decrease
in postoperative blood loss and hence in the use of cell saver, but has no impact on allogeneic blood transfusion. Our results are in agreement with literature data in terms of the amount of blood collected during suction drainage (4,7,9,10-12) but not in terms of the amount of blood needed for allogenic blood transfusion (11,12). In our study group the amount of transfused blood did not differ significantly between the two groups, the decision to resort to this therapy being more frequent in group 2, probably due to the fact that cell-saver in more rarely used in this category of patients. It is worth mentioning that although in group 2 the average blood loss was small, anemia syndrome was not statistically more significant in group 1. This mismatch between the amount of drained blood and postoperative anemia raises the suspicion of an additional blood loss. Sehat (13) speaks of a hidden blood loss of 700 ml, probably from hematoma formation.

Tranexamic acid, a synthetic inhibitor of fibrinolysis which acts by competitively blocking the lysine binding sites on plasminogen (7), reduces blood loss and financial cost in orthopedic surgery (hip and knee replacement surgery, spinal surgery) (4,9) and cardiovascular surgery (cardiopulmonary bypass) (14) but only insignificantly the hidden blood loss. This phenomenon probably represents the extravasations of red cells after tourniquet release, hemostasis being by primary hemostatic mechanisms, before fibrinolysis has any effects (15).

CONCLUSIONS
Our study highlights the importance of using tranexamic acid in knee arthroplasty as it significantly decreases the postoperative blood loss and financial cost given the fact that the use of cell-saver is less frequently required. This research demonstrates that tranexamic acid does not have a significant impact on allogeneic blood transfusion and anemia syndrome. Tranexamic acid is an essential drug product in total knee arthroplasty as it reduces postoperative blood loss and its associated complications, with a favorable impact on early recovery of joint function.

REFERENCES
Effect of tranexamic acid use on postoperative blood loss in total knee arthroplasty


ANTIMICROBIAL ROLE OF FILAGGRIN-2 PROTEIN

Filaggrin-2 (FLG2) is a water-insoluble 248 kDa S100 fused-type protein found in the upper epidermis and eccrine sweat glands. A study by Hansmann et al. tested the antimicrobial activity of filaggrin-2 against Pseudomonas aeruginosa and other Pseudomonads and found that recombinant FLG2 C-terminal protein fragments have potent antimicrobial activity against P. aeruginosa and after cultivation of P. aeruginosa on stratum corneum, antimicrobially active FLG2 fragments are released from insoluble material by the bacteria themselves. These FLG2 C-terminal fragments have an alternative mode of action different from most other antimicrobial peptides, as they do not induce pore formation, but membrane blebbing. According to Hansmann et al., FLG2 fragments interfere with bacterial replication, inhibit their growth on skin surfaces and contribute to the skin's antimicrobial defense, explaining why Pseudomonas infections of healthy skin are very rare. Also, the absence of filaggrin 2 at certain body surfaces and in the case of burned skin seems to be responsible for the higher susceptibility to these infections. The study concluded that FLG2 C-terminal fragments could represent new Pseudomonas-targeting antimicrobials (Hansmann B, Schröder JM, Gerstel U. Skin-Derived C-Terminal Filaggrin-2 Fragments Are Pseudomonas aeruginosa-Directed Antimicrobials Targeting Bacterial Replication. PLoS Pathog. 2015;11(9):e1005159. doi: 10.1371/journal.ppat.1005159).

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