

## INFLUENCE OF DIFFERENT ADMINISTRATION METHODS OF TRANEXAMIC ACID ON BLOOD LOSS VOLUME AND COMPLICATIONS IN ELDERLY PATIENTS WITH AO2.2~3 INTERTROCHANTERIC FRACTURE IN INTERNAL FIXATION

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### ABSTRACT

**Objective:** To investigate the influence of different administration methods of tranexamic acid on blood loss volume and complications in elderly patients with AO2.2~3 intertrochanteric fracture in internal fixation.

**Methods:** Clinical data of 174 elderly patients with AO2.2~3 intertrochanteric fracture admitted to our hospital from March 2015 to October 2020 were retrospectively analyzed and all patients divided into three groups: Group A (without tranexamic acid, 70 cases), Group B (tranexamic acid injection through medullary cavity, 55 cases) and Group C (intravenous injection of tranexamic acid, 49 cases). The perioperative blood loss volume, postoperative drainage volume, blood transfusion rate, Hb level, HCT level and incidence of thrombosis related complications among the 3 groups were compared.

**Results:** The perioperative blood loss volume and blood transfusion rate of Group B and Group C were significantly less than those of Group A ( $P < 0.05$ ). There was no significant difference in blood loss volume and postoperative drainage volume among 3 groups ( $P > 0.05$ ). The levels of Hb and Hct of Group B and Group C in 1d, 3d and 5d after operation were significantly higher than those of Group A ( $P < 0.05$ ). Color Doppler ultrasound of lower extremity blood vessels reexamined in 5d and 4w after operation showed that there were 2 cases and 3 cases of intramuscular venous thrombosis in Group A and Group B respectively, with the incidence of 2.86% and 5.45% respectively. No thrombotic complications such as deep vein thrombosis, pulmonary embolism, ACS and stroke were found.

**Conclusion:** Intravenous injection and intramedullary administration of tranexamic acid in the treatment of elderly patients with AO2.2~3 intertrochanteric fracture in internal fixation can effectively decrease the total blood loss volume and hidden blood loss volume in the perioperative period, reduce the blood transfusion rate, without the increase of the risks of thrombosis related complications.

**Keywords:** Internal fixation, tranexamic acid, elderly, intertrochanteric fracture, blood loss, complications.

DOI: 10.19193/0393-6384\_2021\_2\_180

Received March 15, 2020; Accepted October 20, 2020

### Introduction

Intertrochanteric fracture is one of common fracture types in elderly people. The proportion of unstable fractures due to the combination of osteoporosis is as high as 30%~45%. Meanwhile, the incidence of postoperative complications is higher than that of other fracture types<sup>(1)</sup>. Proximal femoral nail antiro-tation (PFNA) operation is a main treatment method of intertrochanteric fracture, with the advantages of iatrogenic mild trauma, small incision and strong

stability<sup>(2)</sup>. It is currently believed that the blood loss volume (mainly hidden blood loss) increases in the patients with unstable intertrochanteric fracture during the perioperative period due to fracture reduction difficulty and operation time extension, while massive blood transfusion during the perioperative period may increase the risks of surgical treatment and postoperative immunohemolysis<sup>(3,4)</sup>. Tranexamic acid belongs to a derivative synthesized by lysine, with the effect of inhibiting protease degradation. It has been widely applied in bleeding prevention in the periop-

erative period, but there is still no definite conclusion in the method of administration<sup>(5)</sup>. Clinical data of 174 elderly patients with AO2.2~3 intertrochanteric fracture admitted to our hospital from March 2015 to October 2020 were retrospectively analyzed to explore the influence of different administration methods of tranexamic acid on blood loss volume and complications in elderly patients with AO2.2~3 intertrochanteric fracture in internal fixation.

## Data and methods

### Demographics

Clinical data of 174 elderly patients with AO2.2~3 intertrochanteric fracture admitted to our hospital from March 2015 to October 2020 were retrospectively analyzed and all patients divided into three groups: Group A (without tranexamic acid, 70 cases), Group B (tranexamic acid injection through medullary cavity, 55 cases) and Group C (intravenous injection of tranexamic acid, 49 cases). In Group A, there were 36 males and 38 females, with the average age of (67.84±5.12) years, and the average time from the injury to the operation was (7.46±1.24)h. According to the position of fracture, 32 cases and 38 cases suffered fracture at the left side and right side, respectively. According to AO type, there were 18 cases of A2.2 type, 18 cases of A2.3 type, 14 cases of A3.1 type, 12 cases of A3.2 type, and 8 cases of A3.3 type. According to the reasons for fracture, 50 cases got injured due to tumbles; 8 cases got injured due to traffic accidents and 10 cases got injured due to other reasons. According to the types of combined chronic diseases, 17 cases had cardiovascular and cerebrovascular diseases and 6 cases had diabetes.

In Group B, there were 20 males and 25 females, with the average age of (68.61±5.40) years, and the average time from the injury to the operation was (7.27±1.39)h. According to the position of fracture, 22 cases and 23 cases suffered fracture at the left side and right side, respectively. According to AO type, there were 12 cases of A2.2 type, 16 cases of A2.3 type, 10 cases of A3.1 type, 10 cases of A3.2 type, and 7 cases of A3.3 type. According to the reasons for fracture, 41 cases got injured due to tumbles; 6 cases got injured due to traffic accidents and 8 cases got injured due to other reasons. According to the types of combined chronic diseases, 13 cases had cardiovascular and cerebrovascular diseases and 5 cases had diabetes. In Group C, there were 25 males and 24 females, with the average age of (66.25±5.68) years, and the average time from the injury to the op-

eration was (7.71±1.40)h. According to the position of fracture, 22 cases and 27 cases suffered fracture at the left side and right side, respectively.

According to AO type, there were 13 cases of A2.2 type, 14 cases of A2.3 type, 10 cases of A3.1 type, 8 cases of A3.2 type, and 4 cases of A3.3 type. According to the reasons for fracture, 37 cases got injured due to tumbles; 5 cases got injured due to traffic accidents and 7 cases got injured due to other reasons. According to the types of combined chronic diseases, 12 cases had cardiovascular and cerebrovascular diseases and 4 cases had diabetes. The comparison differences in demographics among the 3 groups were not statistically significant ( $P>0.05$ ).

### Inclusion and exclusion criteria

#### Inclusion criteria:

- Definitely diagnosed as intertrochanteric fracture;
- AO type was AO 2.2~3<sup>(6)</sup>;
- Age ≥60 years;
- Unilateral closed fracture;
- The time from injury to the operation ≤14d.

#### Exclusion criteria:

- Had allergic history of tranexamic acid or relevant contraindications;
- Pathological fracture;
- Abnormal coagulation function prior to the operation;
- Took anticoagulant drugs in recent 4 weeks;
- Accompanied with intra-articular fracture;
- Hip surgery history;
- Important organ dysfunction.

The research scheme conformed to the requirements of Declaration of Helsinki, and patients or their family members were informed and consented.

### Methods

The operation was completed by the same surgeon. The surgical incision was from the greater trochanter of femur to the tip of the greater trochanter, with the length of about 6-8cm. the guide pin was placed in the medullary space via the incision under X-ray perspective, and PFNA-II main nail was inserted after proximal medullary space expansion. The spiral guide pin was screwed in with the help of the proximal sighting device, and the tip-apex distance was ensured within 30mm. after the screw blade was punched in, the interlocking screw was placed with the help of the proximal sighting device, and the alignment of the fracture end was confirmed to be satisfactory. Finally, the operative region was

thoroughly washed with normal saline and the incision was sutured. Tranexamic acid was not used in Group A. Group B was given tranexamic acid injection through the medullary space. Prior to medullary space expansion, the mixed liquid (2g+20ml) of tranexamic acid and normal saline was injected into the medullary space through the fracture end. Group C was given intravenous injection of tranexamic acid (20mg/kg) 30min before operation. After operation, the drainage tube was routinely occluded for 120min.

The patients conducted functional exercise in the bed in 2d after operation. The patients with extramedullary fixation walked on ground with other's help in 14d after operation, and those with intramedullary fixation walked on ground in 7d after operation. Besides, they received intravenous drip of low molecular heparin for 7d. After discharge, they continued to take rivaroxaban orally for 4 weeks.

**Outcome measure**

The blood loss volume in the perioperative period, explicit blood loss volume, postoperative drainage volume, blood transfusion in the perioperative period, laboratory index and postoperative complications were recorded by looking up case records. Blood loss volume included aspirator and gauze, and the blood loss volume was calculated according to Cross equation. The calculation formula of operative blood loss volume was preoperative blood volume (preoperative Hct + operative Hct). The calculation formula of explicit blood loss volume was negative pressure drainage volume + postoperative 33d drainage volume + amount of bleeding from dressing<sup>(7)</sup>.

**Statistical processing**

SPSS24.0 software was used to analyze data. One-way analysis of variance was used to compare measurement data conforming to normal distribution, and LSD-t test was used for pairwise comparisons in case of homogeneous variance, expressed with ( $\bar{x}\pm s$ ). Enumeration data were compared with  $\chi^2$  test or Fisher exact probability method, expressed with %.  $P<0.05$  was considered to be statistically different.

**Results**

**Comparison of blood loss volume in the perioperative period, postoperative drainage volume and blood transfusion rate among three groups**

The perioperative blood loss volume and blood transfusion rate of Group B and Group C were significantly less than those of Group A ( $P<0.05$ ). There

was no significant difference in blood loss volume and postoperative drainage volume among 3 groups ( $P>0.05$ ), as shown in Table 1.

| Group                  | No. | Blood loss volume in the perioperative period (ml) | Explicit Blood loss volume (ml) | Postoperative drainage volume (ml) | Blood transfusion rate in the perioperative period [n,%] |
|------------------------|-----|--|---------------------------------|------------------------------------|--|
| Group A                | 70  | 955.96±123.30                                      | 164.19±46.82                    | 104.30±22.41                       | 27 (38.57)   |
| Group B                | 55  | 748.23±110.47                                      | 158.94±41.52                    | 101.69±24.68                       | 6 (10.91)  |
| Group C                | 49  | 711.82±104.74                                      | 152.60±40.34                    | 96.94±18.06                        | 4 (8.16)   |
| <i>F/χ<sup>2</sup></i> |     | 4.82   | 0.97                            | 0.81                               | 8.33   |
| <i>P</i>               |     | 0.00   | 0.39                            | 0.53                               | 0.01   |

**Table 1:** Comparison of blood loss volume in the perioperative period, postoperative drainage volume and blood transfusion rate among three groups.

**Comparison of Hb level in the perioperative period among three groups**

The Hb level of Group B and Group C in 1d, 3d and 5d after operation was significantly higher than that of Group A ( $P<0.05$ ), as shown in Table 2.

| Group    | No. | Before operation | 1d after operation | 3d after operation | 5d after operation |
|----------|-----|------------------|--------------------|--------------------|--------------------|
| Group A  | 70  | 106.77±10.55     | 94.30±12.41        | 87.20±10.92        | 85.13±10.45        |
| Group B  | 55  | 105.49±11.42     | 91.69±14.68        | 85.49±11.30        | 84.48±12.23        |
| Group C  | 49  | 107.04±10.29     | 84.94±15.06        | 78.54±13.73        | 76.89±11.70        |
| <i>F</i> |     | 1.89             | 7.30               | 8.55               | 10.21              |
| <i>P</i> |     | 0.15             | 0.00               | 0.00               | 0.00               |

**Table 2:** Comparison of Hb level in the perioperative period among three groups (g/L).

**Comparison of Hct level in the perioperative period among three groups**

The Hct level of Group B and Group C in 1d, 3d and 5d after operation was significantly higher than that of Group A ( $P<0.05$ ), as shown in Table 3.

| Group    | No. | Before operation | 1d after operation | 3d after operation | 5d after operation |
|----------|-----|------------------|--------------------|--------------------|--------------------|
| Group A  | 70  | 38.57±0.36       | 28.06±2.31         | 25.06±3.90         | 24.89±3.70         |
| Group B  | 55  | 39.72±0.43       | 33.19±3.35         | 30.34±4.67         | 29.48±3.23         |
| Group C  | 49  | 38.64±0.29       | 32.96±2.15         | 29.29±3.16         | 28.13±4.45         |
| <i>F</i> |     | 1.26             | 6.59               | 8.13               | 8.76               |
| <i>P</i> |     | 0.52             | 0.00               | 0.00               | 0.00               |

**Table 3:** Comparison of Hct level in the perioperative period among three groups (%).

**Comparison of incidence of thrombosis related complications among three groups**

Color Doppler ultrasound of lower extremity blood vessels reexamined in 5d and 4w after oper-

ation showed that there were 2 cases and 3 cases of intramuscular venous thrombosis in Group A and Group B respectively, with the incidence of 2.86% and 5.45% respectively, and they improved after oral administration of antithrombotic drugs.

No thrombotic complications such as deep vein thrombosis, pulmonary embolism, ACS and stroke were found.

## Discussion

Intertrochanteric fracture was common in elderly people, and patients are often combined with multiple underlying diseases, with a significant decrease in somatic functions. For unstable intertrochanteric fracture, internal fixation has become the first choice in clinical practice, but it should be noted that hidden blood loss in the perioperative period is more likely to lead to hypovolemic anemia, which is adverse to early postoperative rehabilitation<sup>(8, 9)</sup>. Some studies have proven that, the explicit blood loss volume during intramedullary fixation represented by PFNA is less than that during extramedullary fixation, but the hidden blood loss volume in the perioperative period is often more<sup>(10, 11)</sup>. Besides, the hidden blood loss volume caused by unstable intertrochanteric fracture was more than that caused by stable fracture.

This is mainly related to multiple factors such as larger external impacts that the patients with unstable fracture suffer, severer soft tissue injury, the increase in the difficulty of restoration and operation or extension of operation time. The increase in the hidden blood loss volume may lead to anoxic state of tissues and difficulty of postoperative incision and fracture recovery<sup>(12)</sup>. How to effectively hidden blood loss volume of elderly patients with intertrochanteric fracture in the perioperative period so as to promote postoperative rehabilitation receives more and more attention from the medical field.

Tranexamic acid has been widely used for the perioperative period treatment in orthopedics, obstetrics, cardiothoracic surgery and gastroenterology in recent years, and especially knee, hip and pelvic surgery is most widely used<sup>(13)</sup>. Domestic and overseas literature fails to form a consensus on tranexamic acid timing, dose and method. The half-life period of tranexamic acid dripped intravenously is 2h, and the time for reaching the peak concentration is 1h. In most reports, intravenous drip of tranexamic acid was given 10min before skin incision in the operation, with the dose ranging from 10 to 20mg/kg. It has shown good advantages in terms of reducing blood

loss volume and blood transfusion rate in the perioperative period, without the increase of risks of deep venous thrombosis and pulmonary embolism<sup>(14)</sup>. In another study, 2g tranexamic acid injection through medullary space in PFNA could significantly lower postoperative hidden blood loss volume, with good safety<sup>(15)</sup>. In addition, foreign scholars considered that, no bleeding was observed after local administration of tranexamic acid in the blood, and the increase of fibrinogen was not obvious. At the same time, local drug administration could minimize drug concentration in the fracture region<sup>(16)</sup>.

In the study, the blood loss volume of Group B and Group C in the perioperative period was significantly lower than that of Group A ( $P < 0.05$ ). Group A was not given tranexamic acid, but the total blood loss volume and explicit blood loss volume in the perioperative period were more than those reported before. The reason for such difference may be the cases in the study suffered unstable fracture, and the operation time and the quantity of incision opening and reduction increased. Meanwhile, the blood transfusion rate of Group B and Group C was significantly lower than that of Group A ( $P < 0.05$ ). The levels of Hb and Hct of Group B and Group C in 1d, 3d and 5d after operation were significantly higher than those of Group A ( $P < 0.05$ ), proving that intravenous administration of tranexamic acid and local administration of tranexamic acid through medullary space could effectively reduce the blood loss volume and blood transfusion rate of patients with unstable intertrochanteric fracture in the perioperative period. Moreover, no thrombotic complications such as deep venous thrombosis, pulmonary embolism, ACS and stroke were observed in all patients, which complies with the results in the previous reports<sup>(17)</sup>. It is necessary to note that, intravenous administration of tranexamic acid is forbidden for those with thromboembolism, acute myocardial infarction or ischemic retinopathy<sup>(18)</sup>. Local injection of tranexamic acid could effectively increase drug concentration at the potential bleeding site and avoid potential adverse events caused by systemic drug absorption. Therefore, the author considers local administration shall be given to the patients with tranexamic acid contraindications. The study also has some limitations: as a small-sample and monocentric retrospective report, the conclusions of the study could not completely eliminate the influence of mixed factors; the time for follow-up visit was insufficient, and there was lack of long-term efficacy assessment, so a further study is required.

In conclusion, Intravenous injection and intramedullary administration of tranexamic acid in the treatment of elderly patients with AO2.2~3 intertrochanteric fracture in internal fixation can effectively decrease the total blood loss volume and hidden blood loss volume in the perioperative period, reduce the blood transfusion rate, without the increase of the risks of thrombosis related complications.

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### Funding disclosure:

Clinical effect of tranexamic acid on invisible blood loss after PFNA internal fixation for intertrochanteric fracture (Huzhou public welfare research 2017GYB48).

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