

Comparative analysis of the effects of dalteparin and reviparin on perioperative blood loss in patients with extracapsular hip fractures treated with intramedullary nailing

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ABSTRACT

Aim To determine differences between reviparin and dalteparin treatment in patients with extracapsular hip fractures treated with intramedullary nailing and their effects on perioperative blood loss and early postoperative recovery.

Methods Retrospective comparative study included 68 patients with extracapsular hip fracture who were divided into dalteparin and reviparin group. Medical records were used to obtain demographic data, laboratory parameters, haemoglobin and haematocrit levels, platelet count, mortality rate and medical complications.

Results Out of total 68 patients, 31 were in reviparin and 37 in dalteparin group. Mean age of patients was 70.5 (± 14.4) and 76.8 (± 8.4) years in reviparin and dalteparin group, respectively ($p=0.071$). Median values of haemoglobin levels on the first postoperative day were lower in dalteparin group compared to reviparin group ($p=0.012$). On the first postoperative day haematocrit values were also lower in dalteparin than in reviparin group ($p=0.015$). Both groups showed an increase in platelet count on the first postoperative day, but without significant difference ($p=0.084$). There was no statistically significant difference in intrahospital mortality between the groups (6.4% vs. 2.7%; $p=0.588$). One case of pulmonary embolism was detected in the dalteparin group.

Conclusion Low-molecular-weight heparin is the drug of choice in patients with hip fractures for thromboprophylaxis. Due to non-antithrombin-mediated actions, reviparin and dalteparin could have different effects on perioperative blood loss. Both dalteparin and reviparin are safe and effective agents for thromboprophylaxis in patients with proximal femur fractures.

Key words: anticoagulants, femur, haemorrhage

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INTRODUCTION

Proximal femur fractures are the most frequently operated fracture type in orthopaedic surgery. Due to high cost of care and postoperative fatality rate they have raised intense interest globally (1). Mortality rate in the first year after the hip fracture is 30% and has been unchanged throughout the years (2). It is estimated that the number of hip fractures occurring worldwide will double to 2.6 million by the year 2025, and 4.5 million by the year 2050, because of the increase in life expectancy (3).

Extracapsular hip fractures are associated with low-energy trauma in older age patients and high-energy trauma in young patients, resulting in similar fracture patterns. For pertrochanteric fractures minimally invasive osteosynthesis with short intramedullary nail is the treatment of choice and may be associated with shorter operation time and less blood loss (4). This method allows early post-operative weight bearing, which is associated with shorter hospital stay and fewer medical complications (5).

Fractures of the hip and lower extremity have been noted to increase the risk of thrombosis (1). Low-molecular-weight heparin (LMWH) is the drug of choice for thromboprophylaxis in patients with hip fracture. It has not been shown that dose adjustment has influence on anticoagulation effectiveness, but different LMWHs can have pharmacokinetic and pharmacodynamic differences due to molecular structures, half-lives, antithrombin- and non-antithrombin-mediated actions, anti-factor Xa:anti-factor IIa ratio (6). Thus, they can have different effects on perioperative blood loss, especially in patients who are treated with intramedullary implants, since surgeons do not have much influence on haemostasis (7). Reviparin sodium is a LMWH with a mean peak molecular weight of 3900 daltons. It is characterised by a narrow molecular weight distribution profile, with an anti-factor Xa:anti-factor IIa ratio of ≥ 3.6 (8). Dalteparin sodium has the mean molecular weight of 6000 daltons, the antifactor Xa to anti-factor IIa ratio for dalteparin is about 2.7 (6).

Anaemia is a strong negative prognostic factor in patients with hip fracture (7). It is associated with increased postoperative mortality, poor physical performance, increased length of hospitalisation

(9). In order to decrease blood loss in patients with intertrochanteric fractures, effects of tranexamic acid were investigated (10,11). Different factors that can affect perioperative blood loss were analysed such as wound drainage (12) and fracture fixation methods (13,14).

According to available data most studies which analyse different LMWHs are focused on the frequency of venous thromboembolism (VTE) (15,16). Very few studies compare the effects of different LMWHs on blood loss (17).

The aim of this study was to determine differences between reviparin and dalteparin in patients with extracapsular hip fracture treated with intramedullary nailing and their effects on perioperative blood loss and early postoperative recovery.

PATIENTS AND METHODS

Patients and study design

A retrospective comparative study including 68 patients with extracapsular hip fractures who were treated operatively at the Department of Orthopaedics and Traumatology in Canton Hospital Zenica during the years 2019 and 2021 was conducted. Before 2020 at our department LMWH reviparin was used for thromboprophylaxis of hospitalised patients with hip fractures. During the Covid 19 pandemic in 2020 our institution switched to dalteparin.

Medical records in 2019 and 2021 were used to collect data, patients were divided into two groups. A total of 31 and 37 patients met all inclusion criteria in reviparin and dalteparin group, respectively. Inclusion criteria were: fractures of proximal femur type 31.A1 and 31.A2 according to the Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association classification (18), injury less than two weeks old, patients without previous anaemia. Exclusion criteria were previous operations of the ipsilateral hip, associated fractures, pathologic fractures, coagulation disorders, oncologic patients.

Methods

In the preoperative assessment of patients the American Society of Anaesthesiology Scale was used (19). All operations were performed in general or spinal anaesthesia and all patients received 2 g of cefazolin as a prophylactic antibiotic

half an hour before the incision and for two days postoperatively twice daily. In all cases short third generation Gamma-nail was used for osteosynthesis. Patients in the reviparin group received reviparin sodium 0.6 mL or 3436 IU subcutaneously once daily; patients in the dalteparin group received 5000 IU of dalteparin- sodium subcutaneously once daily as thromboprophylactic agent. Perioperatively both agents were administered 12 hours before and 12 hours after the operative procedure.

Medical records from 2019 and 2021 were used to collect preoperative haemoglobin and haematocrit levels and platelet count; the same data were recorded <24 hours after the surgery as the first postoperative day, and on the second postoperative day. Pre-surgical length of hospital days, as well as the duration of postoperative hospitalisation (in days) were also collected.

All patients were evaluated for early complications and mortality rate. A follow-up was done until discharge from the Department. In 15 patients in the reviparin group and 25 in the dalteparin group haemoglobin, haematocrit levels and platelet count were not collected on the second postoperative day due to administration of blood transfusions or because data were missing; however, the number of blood transfusions in neither of the groups was recorded.

Statistical analysis

Demographic characteristics of patients were evaluated using descriptive statistics. χ^2 test or Fisher exact test were used to compare differences between categorical variables. Independent two sided Student t-test was used for continuous variables with normal distribution. Nonparametric Mann-U-Whitney test was used in cases without normal distribution. Statistical significance was set at $p < 0.05$.

RESULTS

Out of 68 patients included in the study, 31 were in reviparin and 37 in the dalteparin group. There were 26 males and 42 females ($p = 0.565$). Mean age of patients was 70.5 (± 14.4) and 76.8 (± 8.4) years in reviparin and dalteparin group, respectively. Patients who received dalteparin were older than patients who received reviparin ($p = 0.071$) (Table 1).

Table 1. Demographic characteristics of patients

Variables	Reviparin (31)	Dalteparin (37)	p
Gender (No)			0.565
Males	13	13	
Females	18	24	
Age (mean \pm SD)	70.5 (± 14.4)	76.8 (± 8.4)	0.071
Hospital stay (days)(CI 95%)			
Time to surgical intervention	8.23 (CI: 7.01 – 9.44)	5.76 (CI: 5.02-6.50)	0.001
Postoperative stay	11.16 (CI: 10.20-12.12)	8.38 (CI: 7.48-9.28)	0.000

Patients in the dalteparin group had shorter time to surgical intervention than patients in the reviparin group, 5.76 (CI: 5.02-6.50) and 8.23 (CI: 7.01–9.44) days, respectively ($p = 0.001$). Duration of postoperative hospitalisation was also shorter in dalteparin than in the reviparin group, 8.38 (CI: 7.48-9.28) and 11.16 (CI: 10.20-12.12) days, respectively ($p = 0.000$).

There were no statistically significant differences in preoperative haemoglobin level between groups ($p = 0.118$). The values of haemoglobin showed a linear decrease on the first and second postoperative day. Median values of haemoglobin level on the first postoperative day were lower in dalteparin compared to the reviparin group, 103.189 (± 12.2901) g/L and 110.861 (± 12.1049) g/L, respectively ($p = 0.012$) (Table 2). The median level of haemoglobin on the second postoperative day in the reviparin group was not statistically different compared to the dalteparin group ($p = 0.871$).

Table 2. Difference between haemoglobin, haematocrit values and platelet counts across groups

Variable	LMWH	No of patients	Mean (SD)	p
Hg (g/L)				
pre-op	Reviparin	31	128.103 (14.1823)	0.118
	Dalteparin	37	122.946 (12.6687)	
post-op day 1	Reviparin	31	110.861 (12.1049)	0.012
	Dalteparin	37	103.189 (12.2901)	
post-op day 2	Reviparin	16	106.000 (8.0944)	0.871
	Dalteparin	12	106.583 (10.7065)	
Hc (L/L)				
pre-op	Reviparin	31	0.3848 (0.04249)	0.091
	Dalteparin	37	0.3676 (0.04030)	
post-op day 1	Reviparin	31	0.3313 (0.03640)	0.015
	Dalteparin	37	0.3086 (67.735)	
post-op day 2	Reviparin	16	0.3156 (0.02607)	0.861
	Dalteparin	12	0.3175 (0.02989)	
Platelet count (x109/L)				
pre-op	Reviparin	31	238.48 (67.735)	0.760
	Dalteparin	37	244.11 (80.890)	
post-op day 1	Reviparin	31	309.32 (99.013)	0.084
	Dalteparin	37	269.30 (88.928)	
post-op day 2	Reviparin	16	307.13 (98.782)	0.177
	Dalteparin	12	259.25 (77.108)	

LMWH, low-molecular-weight heparin; Hg, haemoglobin; Hc, haematocrit

Haematocrit values were not statistically different between the groups preoperatively ($p=0.091$). On the first postoperative day haematocrit values were $0.3086 (\pm 0.03824)$ L/L in the dalteparin group and $0.3313 (\pm 0.03640)$ L/L in the reviparin group ($p=0.015$) (Table 2). Haematocrit values were not statistically different between the groups on the second postoperative day ($p=0.861$).

There was no statistically significant difference in the platelet count value between the groups preoperatively ($p=0.760$). Both groups showed an increase in the platelet count on the first postoperative day which was lower in the dalteparin group than in the reviparin group $269.30 (\pm 88.928) \times 10^9/L$ and $309.32 (\pm 99.013) \times 10^9/L$, respectively ($p=0.084$) (Table 2).

Intrahospital mortality rate in the reviparin group of patients was 6.4% and in the dalteparin group 2.7% ($p=0.588$). There were no medical complications in the reviparin group; one case of pulmonary embolism was detected in the dalteparin group.

DISCUSSION

Demographic characteristics of patients in this study are similar to other studies. Proximal femur fractures mostly occur in patients above the age of 70 years (20). The prevalence of this injury is 2–3 times higher in females than in males (21). In our study the mean age of patients was 70.5 (± 14.4) years and 76.8 (± 8.4) years in the reviparin and dalteparin group, respectively; there were 42 females and 26 males. Although males less frequently sustained fractures of proximal femur than females, osteoporosis in males is one of the risk factors that is underestimated, since older males are also affected with hip fracture and state that male osteoporosis is underscreened, underdiagnosed and undertreated, both in primary and secondary prevention of fragility fractures (22,23).

The length of postoperative hospital stay in our study was shorter in the dalteparin group of patients than in the reviparin group; however, shorter postoperative hospital stay in the dalteparin group was probably due to the adaptation of the Department and fewer beds during Covid 19 pandemic in 2021.

Time to surgical intervention was shorter in the dalteparin group, compared to the reviparin group. Ronga et al. state that relation between time-to-surgery and blood loss is poorly studied; they

found that lower blood loss was observed when surgery was performed 24 hours after admission (8). However, another study showed that surgery performed 48 hours after admission can result in a longer hospital stay (24).

Postoperative haemoglobin analysis is essential for monitoring blood loss after surgery in orthopaedic patients. Analysing haemoglobin level preoperatively and five consecutive days postoperatively Nagra et al. found a linear decrease, which was the lowest on the second postoperative day (25). We also found a linear decrease in haemoglobin levels, which were also the lowest on the second postoperative day. However, haemoglobin levels in our study were recorded for only two postoperative days, and data were collected for 16 patients in reviparin and for 12 patients in the dalteparin group on the second postoperative day. Further studies are necessary in order to standardise postoperative haemoglobin monitoring.

In a randomised prospective study of the clinical effectiveness of dalteparin and enoxaparin, Bilawicz et al. did not find statistical difference between haemoglobin level on the first postoperative day, however, more patients in enoxaparin group received more red cell transfusions (26). They also noted a decrease in the platelet count on the first postoperative day. In our study haemoglobin levels on the first postoperative day were lower in dalteparin than in the reviparin group. Also, unlike in the study of Bilawicz et al. we found an increase in the platelet count on the first postoperative day.

Current literature reports one-year mortality rate after hip fracture between 26 to 33% (6). Intrahospital mortality rate in reviparin group of patients was 6.4% and in the dalteparin group 2.7%. A longer follow-up is required to evaluate long-term mortality differences between groups.

We recorded one case of pulmonary embolism which occurred in the dalteparin group on the fifth postoperative day. According to the literature VTE can occur early after injury (27). In a study of Miano et al. most cases of VTE after trauma occurred by the fifth postoperative day (16).

Planès et al. compared the efficacy and safety of reviparin and enoxaparin in patients undergoing total hip replacement. They found that the two treatment groups were clinically equivalent in

efficacy. The reviparin-treated patients had fewer haematomas, bruising and higher red cell counts and lower haemoglobin levels than the enoxaparin-treated patients (28). To our knowledge there are no studies in the literature which compare reviparin and dalteparin in patients with proximal femur fractures.

The limitations of study are retrospective nature and short follow-up of patients.

Based on our results there are some differences in laboratory parameters postoperatively between

the patients who received dalteparin and reviparin, however, both LMWHs remain safe and effective agents for thromboprophylaxis in patients with extracapsular hip fractures. A longer follow-up is required to determine long-term complications and differences between the groups.

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