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Does a Single Low Dose Preoperative Intravenous Erythropoietin Affect Postoperative Blood Loss and Transfusion in Elderly Hip Fracture Patients Receiving Intravenous Iron Therapy: A Randomized Controlled Trial

Chavarat Jarungvittayakon[1], Paphon Sa-ngasoongsong[1], Kitchai Luksameearunothai[2], Norachart Sirisreetreerux[1], Noratep Kulachote[1], Thumanoon Ruangchaijatuporn[3], Sasivimol Rattanasiri[4], Suporn Chuncharunee[5], Patarawan Woratanarat[1], Pongsthorn Chanplakorn[1]

[1] Department of Orthopedics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

[2] Department of Orthopaedics, Faculty of Medicine Vajira Hospital, Navamindrahiraj University, Bangkok, Thailand

[3] Department of Diagnostic and Therapeutic Radiology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

[4] Section of Clinical Epidemiology and Biostatistics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

[5] Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Background: Combined recombinant human erythropoietin (rHuEPO) and iron therapy significantly reduced postoperative blood loss (PBL) and allogeneic blood transfusion (ABT) in elderly hip fracture (HF) patients. However, the minimum effective rHuEPO dosage and route had not been studied before.

Objective: To evaluate the efficacy of single low dose preoperative intravenous rHuEPO on PBL and ABT in elderly HF.

Methods: A randomized controlled trial (RCT) in 32 elderly HF underwent surgical intervention was conducted. The patients were randomly assigned to receive a single dose of 10 000 IU rHuEPO (EPO group, n = 16) or placebo (control group, n = 16) on admission. All patients were given 200-mg iron sucrose intravenously for 3 days after admission. Perioperative data, outcome related to PBL, ABT, rHuEPO adverse effects, and functional outcome during 1-year period were collected and analyzed.

Results: There was no significant difference in demographic data, postoperative complication, and functional outcome between both groups ($P < .05$). Total hemoglobin loss (THL) and the number of patients receiving ABT in EPO group (2.1 ± 1.0 g/dL and 12 patients) did not significant differ from those in control group (2.2 ± 0.8 g/dL and 10 patients) ($P = .81$ and $P = .44$, respectively). However, EPO group demonstrated a nonsignificant greater in hemoglobin recovery ($P = .07$) and increase in reticulocyte count ($P = .10$).

Conclusions: Combined single low dose preoperative intravenous rHuEPO with iron therapy does not significantly reduce PBL and ABT in elderly HF compared to who received intravenous iron therapy alone. However, this adjunct rHuEPO may hasten the hemoglobin recovery and helpful for the patients' outcome.

Keywords: Recombinant human erythropoietin, Elderly hip fracture, Allogeneic blood transfusion, Postoperative blood loss

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Corresponding Author:
Paphon Sa-ngasoongsong
Department of Orthopedics,
Faculty of Medicine
Ramathibodi Hospital,
Mahidol University,
270 Rama VI Road, Ratchathewi,
Bangkok 10400, Thailand.
Telephone: +66 2201 1589,
Fax: +66 2201 1599
E-mail: paphonortho@gmail.com

Introduction

Perioperative anemia is one of the most common problems in elderly hip fractures (HF)[1] due to their preexisting comorbidities and a large amount of perioperative blood loss from HF surgery, resulting in a significant demand of blood transfusion.[2] Elderly HF patients with postoperative anemia requiring allogeneic blood transfusion (ABT) also have a significant association with mortality and readmission rates, ambulatory recovery, and poorer functional outcome.[3, 4] Moreover, ABT also increases the risk of postoperative infection, length of hospital stay, and transfusion-related morbidity.[5, 6] In addition to the blood loss from fracture and surgical bleeding, postoperative anemia could be aggravated by inflammatory effect from the surgery, which affects the iron metabolism and then inhibit postoperative erythropoiesis.[7] As a result, the recovery of hemoglobin (Hb) concentration would be slow and requires longer time up to 4 weeks after surgery to return to preinjury level.[8]

Among the current methods for correction of the perioperative anemia and reduction of the postoperative blood loss (PBL) and ABT requirement in elderly HF, iron supplement therapy and recombinant human erythropoietin (rHuEPO) injection are ones of the interesting options. Previous studies on the combined subcutaneous (SC) rHuEPO injection and intravenous (IV) iron therapy had revealed the ability to stimulate postoperative erythropoiesis and significantly reduce the ABT.[9-12] However, the dosage for SC rHuEPO injection in these studies was very high, as 500 - 600 IU/kg, due to the poor drug absorption from SC route, which raised the concern of severe drug-related adverse effects, such as severe hypertension and venous thromboembolism (VTE), especially in the high surgical risk elderly HF patients. Moreover, the mean time to surgery in the previous studies was up to 4 days,[11-12] which was not suitable for the geriatric patients who need urgent surgical intervention. Through our knowledge, the minimum effective rHuEPO dosage to reduce ABT in elderly HF patients is unknown[13] and the efficacy of combined low dose IV rHuEPO (150 - 300 IU/kg) and IV iron therapy in these patients had not been investigated before. Therefore, this aim of this study was to evaluate the effect of a single low dose preoperative IV rHuEPO in the elderly HF patients who already received IV iron therapy.

Methods

Participants, Inclusion/Exclusion Criteria, and Randomization

This study was a randomized controlled trial (RCT) in a medical university hospital, between 2013 and 2014. Prior approval was obtained from our institutional review board (No. MURA2013/522). Informed consent was obtained from all patients before the surgery was scheduled, in accordance with the Declaration of Helsinki. The manuscript was prepared according to the Consolidated Standards of Reporting Trials (CONSORT) 2010 guideline.[14]

Eligible participants were patients diagnosed as either intertrochanteric fracture or femoral neck fracture undergoing HF surgery during 2013 - 2014 period. The inclusion criteria were the patients who were 1) aged over 60 years; 2) having low-energy trauma; 3) having no contraindication for HF surgery, and 4) willing to participate into this study. The exclusion criteria were the patients who were 1) delayed presentation more than 5 days after injury; 2) having too high preoperative Hb as more than 14.5 g/dL; 3) having no contraindication of rHuEPO or iron therapy (myeloproliferative disorder, uncontrolled hypertension, previous acute myocardial infarction or stroke, unstable angina, hemochromatosis, inflammatory arthritis, and allergic to rHuEPO or intravenous iron sucrose); 4) having serum creatinine > 2.0 mg/dL; and 5) having coagulopathy or taking anticoagulant therapy.

Patients were randomized by using the computer-generated randomization table with blocks of 4 to receive either an IV injection of 10 000 IU of rHuEPO (Hema-Plus®, Apexcela, Zuellig Pharma Ltd, Bangkok, Thailand) once on admission or placebo (1 mL of normal saline solution). Randomization was concealed with sealed envelopes in sequentially numbered container. On admission, the envelope was opened and the study medication was prepared under sterile conditions by a nurse who was not involved in the care of the patients. All patients were received 3 consequent doses of IV 200-mg iron sucrose (Venofer®, Vifor Pharma, Glattbrugg, Switzerland) on the time of admission, 24 hours and 48 hours from the first dose.

Data Collection

Demographic data such as age, gender, fracture diagnosis, American Society of Anesthesiologist (ASA) physical status, history of taking antiplatelet agents, the time to surgery (the time between admission and operation), preoperative Hb and reticulocyte count (RC) were collected preoperatively by one orthopaedic surgeon (K.L.).

Surgical Procedure and Postoperative Care

HF surgery was performed by the orthopaedic trauma surgeons (P.S., N.K., and N.S.), as soon as the medical condition was stable. The surgical options depended on the fracture type. Femoral neck fractures were treated with bipolar hip replacement using the anterolateral approach with anterior hemimyotomy of the gluteus medius. The decision of femoral stem, either cemented or cementless, depended on the proximal femoral geometry. Intertrochanteric fractures were treated with closed reduction and internal fixation with proximal femoral nail antirotation (PFNA) without cement augmentation.

Perioperative IV fluid maintenance and correction of the third space fluid loss were replaced with balanced crystalloid solutions. Daily Hb level was measured postoperatively until the patients were discharged. Blood transfusion was considered, according to ASA guideline, when Hb level was below than 8 g/dL or the patients had anemic symptoms (dyspnea, tachypnea, and hypoxemia).[15] Postoperative deep vein thrombosis (DVT) prophylaxis protocol, as using mechanical pneumatic pumps early active ankle motion and early ambulation, were applied in all patients. All patients were daily examined postoperatively for clinical signs and symptoms of DVT and pulmonary embolism (PE) until discharge. If DVT or PE were suspected, they were sent for diagnosis by using Doppler ultrasonography or computerized tomogram angiography.

After discharge, all patients were followed at 2 weeks postoperatively for clinical evaluation and laboratory tests (Hb level and RC percentage). Follow-up visit, either outpatient clinic or telephone interview, was scheduled at 3 months, 6 months, and 1 year postoperatively for collecting the postoperative complications.

Outcome Measurement

PBL was defined by using intraoperative blood loss (IBL) and total hemoglobin loss (THL). IBL was quantified by measuring irrigation fluid and weighing surgical sponges used for blood and fluid collection during surgery. THL was calculated from Hb levels at preoperative period, postoperative day 3, and the amount of Postoperative packed red cell (PRC) unit used by using the formula.[16]

$$\text{THL [g/dL]} = \text{Pre-op Hb [g/dL]} + \text{Total blood in [unit]} - \text{Hb post op day 3 [g/dL]}$$

THL was calculated by the formula based on the assumptions that the blood volume would be the same on admission and on postoperative day 3. To minimize the effect of hemodilution or hemoconcentration the postoperative Hb was measured on the third postoperative day, when the effect of fluid retention may be less prominent than in the earlier postoperative period.

Hb recovery was defined by the difference of Hb values between preoperative period and postoperative 2 weeks. RC difference at 2 weeks was defined by the difference of RC percentage between postoperative 2 weeks and preoperative period. PRC transfusion was recorded as the number of patients requiring transfusion and the number of PRC unit used. Adverse reactions known to be associated with rHuEPO, such as hypertension, tachycardia, arrhythmia, myalgia, urticarial, thromboembolism, fever, nausea and vomiting, edema, diarrhea or constipation were evaluated during the first 48 hours after operation. Postoperative mortality and morbidity such as cardiac complication (myocardial infarction, cardiac arrhythmia, and congestive heart failure), pulmonary complication (atelectasis, and pneumonia), urinary tract infection, pressure ulcer, and VTE complication (DVT or PE) were collected. Functional outcome, as cumulated ambulatory score (CAS), was used to assess the ambulatory ability at the time of discharge and 2 weeks postoperatively.[17] These data were all collected by one orthopaedic surgeon (K.L.) who was blinded to the treatment allocation.

Sample Size Calculation

The sample size was estimated using Power & Sample Size (PS) version 3.0.0002 (Vanderbilt University, Tennessee, USA) and data from review of 100 elderly HF patients underwent surgical intervention in our hospital before this study which showed the average THL was 2.8 ± 1.2 g/dL. It was assumed that the effect of significant PBL reduction should be 50% with pre-study power of test (β) was set as 0.8 and significant difference (α) as 0.05, the required sample size in each group of the study was 12 patients. Then the sample size was increased by 20% to compensate for expected dropouts, resulting in 16 patients per group.

Statistical Analysis

STATA program version 13.1 (StataCorp. Version 13.1. College Station, TX: StataCorp LP; 2013) was used for statistical analysis. An intention-to-treat analysis was applied to compare the study groups. Normality of the data was tested by Kolmogorov-Smirnov test. Continuous variables were presented as mean and standard deviation (SD), and compared with unpaired *t* test. Categorical variables were presented as proportion and compared with Fisher exact test or chi-square test. A *P* value of < .05 was considered significant.

Results

Between 2013 and 2014, 50 elderly HF patients who met the inclusion criteria were enrolled into this study. Eighteen patients were excluded due to refusal to participate (10), serum creatinine more than 2.0 mg% (4) and abnormal coagulation time (4). Therefore, a total of 32 HF patients (3 males and 29 females) were recruited and randomly assigned into 2 groups; 1) EPO group (n = 16), and 2) Control group (n = 16). All patients in both groups were followed our protocol and completed follow-up at one year (Figure 1). The average patients' age was 80 years (range, 63 - 96 years). There were 21 intertrochanteric fractures (67%) and 11 femoral neck fractures (33%). Nine patients (28%) had received antiplatelet agents before injury. The average time to surgery was 2.5 days (range, 1 - 6 days). The average time between rHuEPO administration and operation was 44 hours (range, 1 - 115 hours). The average preoperative Hb was 10.9 g/dL (range, 8.8 - 14.0 g/dL).

There was no statistically significant difference in preoperative data, in terms of age, gender, fracture type, ASA status, the number of patients receiving antiplatelet therapy, the time from admission to operation, preoperative Hb and preoperative RC percentage between both groups (Table 1)

There was no significant difference in the mean THL (2.1 ± 1.0 g/dL vs 2.2 ± 0.8 g/dL, *P* = .81), the number of patients receiving PRC transfusion (12 patients vs 10 patients, *P* = .44), and the mean transfused PRC (0.9 ± 0.7 unit vs 0.9 ± 0.9 unit, *P* = 1.00) between

Figure 1. Flow Diagram of This Study

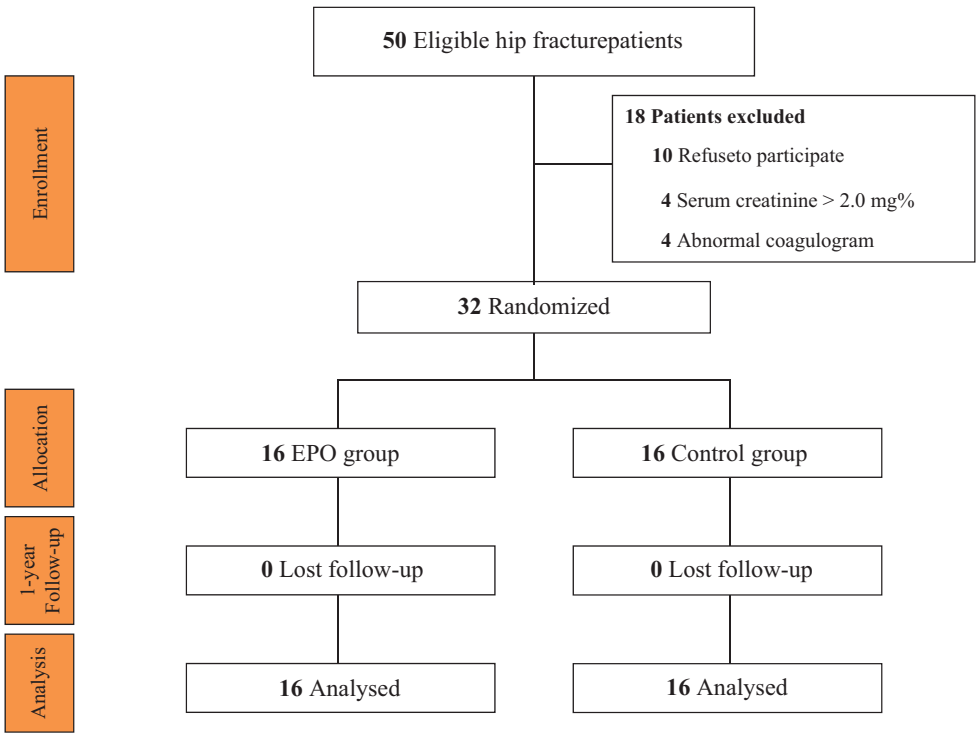

Table 1. General Characteristics of Study Population

Characteristic	EPO Group (n = 16)	Control Group (n = 16)	*P* Value
Age, mean ± SD, y	79.0 ± 9.0	81.0 ± 8.0	.47
Male : Female, No.	1 : 15	2 : 14	1.00
Intertrochanteric fracture : Femoral neck fracture, No.	12 : 4	9 : 7	.45
ASA status, mean ± SD	3.0 ± 0.6	3.1 ± 0.5	.54
Receiving antiplatelet agents, No. (%)	5 (31)	4 (25)	1.00
Day from admission to operation, mean ± SD, d	2.9 ± 1.5	2.1 ± 1.4	.10
Preoperative Hb, mean ± SD, g/dL	10.8 ± 1.4	11.0 ± 1.3	.67
Preoperative RC, mean ± SD, %	1.3 ± 0.4	1.5 ± 0.7	.32

Abbreviations: ASA, American Society of Anesthesiologist; Hb, hemoglobin; RC, reticulocyte count; SD, standard deviation.

EPO group and control groups. Also, no significant difference in the IBL, length of hospital stay, in-hospital postoperative complications, and CAS score at discharge had been found between both groups ($P > .05$ all). However, at 2 weeks postoperatively, EPO group demonstrated a nonsignificant better in Hb recovery and a nonsignificant increase in RC difference (0.9 ± 1.4 g/dL and 1.1 ± 0.5%) compared to those in control group (1.8 ± 1.3 g/dL and 0.8 ± 0.7%) ($P = .07$ and $P = .10$, respectively) (Table 2).

There were 2 patients (1 patient in each group) experienced adverse effects, as anaphylactoid reactions

Table 2. Comparison of Postoperative Blood Loss and Transfusion, and Postoperative Outcomes

Outcome	EPO Group (n = 16)	Control Group (n = 16)	*P* Value
In-hospital outcomes			
Intraoperative blood loss, mean ± SD, mL	198 ± 168	238 ± 249	.60
Patients require blood transfusion, No. (%)	12 (75%)	10 (62.5%)	.44
PRC transfusion, mean ± SD, unit	0.9 ± 0.7	0.9 ± 0.9	1.00
Total Hb loss, mean ± SD, g/dL	2.1 ± 1.0	2.2 ± 0.8	.81
Length of stay, mean (range), d	7 (4 - 29)	7.5 (4 - 25)	.39
Anaphylactoid reactions, No. (%)	1 (6)	1 (6)	1.00
Postoperative complications, No. (%)			
Overall	3 (19)	4 (25)	.68
Pneumonia	1 (6)	0 (0)	.45
UTI	1 (6)	2 (13)	
Pressure ulcer	1 (6)	2 (13)	
CAS at discharge, mean ± SD	2.9 ± 1.3	2.8 ± 1.3	.78
Postoperative 2 weeks outcomes			
Hb, mean ± SD, g/dL	10.8 ± 1.2	10.1 ± 1.2	.11
Hb recovery, mean ± SD, g/dL	0.9 ± 1.4	1.8 ± 1.3	.07
RC, mean ± SD, %	2.44 ± 0.73	2.22 ± 0.50	.33
RC difference, mean ± SD, %	1.12 ± 0.47	0.75 ± 0.73	.10
CAS, mean ± SD	4.7 ± 1.4	4.5 ± 1.5	.71

Abbreviations: CAS, cumulative ambulatory score; Hb, hemoglobin; PRC, packed red cell; RC, reticulocyte count; SD, standard deviation; UTI, urinary tract infection.

(itching and generalized rash), after IV iron sucrose administration. However, the symptoms were relieved after discontinuation of the drug infusion. None of the patients had the uncontrolled hypertension after the drug administration. None of patients had postoperative symptomatic DVT during the admission period. There was no symptomatic VTE during the one-year follow-up period.

Discussion

Elderly HF and their surgical interventions usually result in a significant amount of blood loss and the need of blood transfusion which can lead to perioperative anemia and its complications, transfusion-related morbidity or even mortality. Recent studies had demonstrated the efficacy of the combined administration of IV iron and SC rHuEPO for erythropoiesis stimulation and reducing postoperative ABT in elderly HF patients.[9-12] However, to the best of our knowledge, the information on using IV iron therapy and low dose preoperative IV rHuEPO in elderly HF did not exist in the literature. This study aimed to evaluate the PBL and ABT requirement between the elderly HF patients undergoing the surgical intervention and receiving IV iron sucrose alone and those receiving combine IV iron sucrose and a single shot low dose preoperative IV rHuEPO.

Regarding to the PBL and ABT requirements, the findings from this study showed that an adjunctive single shot low dose preoperative IV rHuEPO did not significantly reduce THL (P = .81), the need of ABT (P = .44), and the number of PRC transfusion (P = 1.00) in the elderly HF patients who already received IV iron therapy during the admission period. However, at postoperative 2 weeks, EPO group demonstrated a nonsignificantly greater ability of the Hb recovery (P = .07) and a nonsignificant increase of the percentage of RC (P = .10) when compared to the preoperative values. It is implied that the clinical efficacy of rHuEPO administration, either SC or IV route, should be dose-dependent. In addition, although the mean time to surgery in the present study (2.9 days) was faster than the previous studies,[11, 12] an add-on single shot low dose preoperative IV rHuEPO with iron therapy should not be clearly seen in a few days postoperatively but able to be detected as early as 2 weeks postoperatively instead. However, the sample size of this study might be too small to detect the difference of these outcomes at 2 weeks postoperatively. Nonetheless, these evidences could support the theoretical advantage of this adjunctive strategy of IV rHuEPO together with IV iron therapy for erythropoiesis stimulation and correction of anemia in the treatment of elderly HF as same as in the previous studies.[9-12]

The results of the present study also demonstrated that the postoperative complications and length of hospital stay, the drug-related adverse effects (anaphylactoid reactions, uncontrolled hypertension, DVT), and the 2-week postoperative functional outcomes, CAS, were not significantly different between both groups (P > .05 all). These findings also support the safety and efficacy of this erythropoiesis stimulation strategy for the elderly HF treatment.

Our study also had some limitations. Firstly, the sample size in this study might be too small for detecting the other interesting outcomes that related to rHuEPO treatment, such as postoperative Hb recovery, RC difference, and the improvement of the functional outcome as we previously mentioned. However, our study was designed as a prospective RCT, which would help for eliminating the confounding factors and selection bias. Secondly, this study did not compare the results between IV with SC rHuEPO. However, the dosage of SC rHuEPO is the previous studies is very high (40 000 unit) and there were only few studies investigating on its safety. Therefore, due to the concerns of our IRB, we decided to perform the study only with a low dose preoperative IV rHuEPO. Lastly, the laboratory investigations related to anemia, such as ferritin level, did not performed.

Conclusions

This study demonstrated that the addition of a single shot low dose preoperative intravenous rHuEPO in elderly HF patients undergoing surgical intervention and receiving intravenous iron therapy was not significantly associated with the reduction of postoperative blood loss or transfusion requirement. However, this adjunct rHuEPO may hasten the Hb recovery and be beneficial for the patients' outcome.

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References

1. Carpintero P, Caeiro JR, Carpintero R, Morales A, Silva S, Mesa M. Complications of hip fractures: a review. *World J Orthop.* 2014;5(4):402-411. doi:10.5312/wjo.v5.i4.402.
2. Foss NB, Kehlet H. Hidden blood loss after surgery for hip fracture. *J Bone Joint Surg Br.* 2006;88(8):1053-1059. doi:10.1302/0301-620X.88B8.17534.

3. Vochteloo AJ, Borger van der Burg BL, Mertens B, et al. Outcome in hip fracture patients related to anemia at admission and allogeneic blood transfusion: an analysis of 1262 surgically treated patients. *BMC Musculoskelet Disord.* 2011; 12:262. doi:10.1186/1471-2474-12-262.
4. Hagino T, Ochiai S, Sato E, Maekawa S, Wako M, Haro H. The relationship between anemia at admission and outcome in patients older than 60 years with hip fracture. *J Orthop Traumatol.* 2009;10(3): 119-122. doi:10.1007/s10195-009-0060-8.
5. Carson JL, Altman DG, Duff A, et al. Risk of bacterial infection associated with allogeneic blood transfusion among patients undergoing hip fracture repair. *Transfusion.* 1999;39(7):694-700. doi:10.1046/j.1537-2995.1999.39070694.x.
6. Klein HG, Spahn DR, Carson JL. Red blood cell transfusion in clinical practice. *Lancet.* 2007; 370(9585):415-426. doi:10.1016/S0140-6736(07)61197-0.
7. Biesma DH, Van de Wiel A, Beguin Y, Kraaijenhagen RJ, Marx JJ. Post-operative erythropoiesis is limited by the inflammatory effect of surgery on iron metabolism. *Eur J Clin Invest.* 1995;25(6):383-389. doi:10.1111/j.1365-2362.1995.tb01718.x.
8. van Iperen CE, Kraaijenhagen RJ, Biesma DH, Beguin Y, Marx JJ, van de Wiel A. Iron metabolism and erythropoiesis after surgery. *Br J Surg.* 1998;85(1):41-45. doi:10.1046/j.1365-2168.1998.00571.x.
9. Goodnough LT, Merkel K. Parenteral iron and recombinant human erythropoietin therapy to stimulate erythropoiesis in patients undergoing repair of hip fracture. *Hematology.* 1996;1(2):163-166. doi:10.1080/10245332.1996.11746300.
10. Bernabeu-Wittel M, Romero M, Ollero-Baturone M, et al. Ferric carboxymaltose with or without erythropoietin in anemic patients with hip fracture: a randomized clinical trial. *Transfusion.* 2016; 56(9): 2199-2211. doi:10.1111/trf.13624.
11. García-Erce JA, Cuenca J, Muñoz M, et al. Perioperative stimulation of erythropoiesis with intravenous iron and erythropoietin reduces transfusion requirements in patients with hip fracture. A prospective observational study. *Vox Sang.* 2005;88(4):235-243. doi:10.1111/j.1423-0410.2005.00627.x.
12. Garcia-Erce JA, Cuenca J, Haman-Alcober S, Martínez AA, Herrera A, Muñoz M. Efficacy of preoperative recombinant human erythropoietin administration for reducing transfusion requirements in patients undergoing surgery for hip fracture repair. An observational cohort study. *Vox Sang.* 2009;97(3): 260-267.doi:10.1111/j.1423-0410.2009.01200.x.
13. Muñoz M, García-Erce JA, Villar I, Thomas D. Blood conservation strategies in major orthopaedic surgery: efficacy, safety and European regulations. *Vox Sang.* 2009;96(1):1-13. doi:10.1111/j.1423-0410.2008.01108.x.
14. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ.* 2010;340:c332. doi:10.1136/bmj.c332.
15. American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. *Anesthesiology.* 2006;105(1):198-208.
16. Seeber P, Shander A. *Basics of Blood Management*. 1st ed. Massachusetts, USA: Blackwell Publishing; 2007:400.
17. Kristensen MT, Andersen L, Bech-Jensen R, et al. High intertester reliability of the cumulated ambulation score for the evaluation of basic mobility in patients with hip fracture. *Clin Rehabil.* 2009;23(12):1116-1123. doi:10.1177/0269215509342330.

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การศึกษาประสิทธิภาพของการให้ฮอร์โมนกระตุ้นการสร้างเม็ดเลือดสังเคราะห์ทางกระแสเลือดก่อนการผ่าตัดต่อการสูญเสียเลือดระหว่างการผ่าตัดและอัตราการรับเลือดหลังการผ่าตัดในผู้ป่วยสูงอายุที่ได้รับการรักษากระดูกสะโพกหักด้วยการผ่าตัด

ชวรัฐ จรุงวิทยากร[1], ปพน สง่าสูงส่ง[1], กิจชัย ลักษมีอรุโณทัย[2], นรชาติ ศิริศรีตรีรักษ์[1], นรเทพ กุลโชติ[1], ธรรมนูญ เรืองชัยจตุพร[3], ศศิวิมล รัตนสิริ[4], สุภร จันท์จารุณี[5], ภัทรวัณย์ วรธนารัตน์[1], พงศธร ฉันท์พลากร[1]

[1] ภาควิชาออร์โธปิดิกส์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล กรุงเทพฯ ประเทศไทย

[2] ภาควิชาออร์โธปิดิกส์ คณะแพทยศาสตร์วชิรพยาบาล มหาวิทยาลัยนวมินทราธิราช กรุงเทพฯ ประเทศไทย

[3] ภาควิชารังสีวิทยา คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล กรุงเทพฯ ประเทศไทย

[4] กลุ่มสาขาวิชาระบาดวิทยาคลินิกและชีวสถิติ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล กรุงเทพฯ ประเทศไทย

[5] ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล กรุงเทพฯ ประเทศไทย

บทนำ: การให้ฮอร์โมนกระตุ้นการสร้างเม็ดเลือดสังเคราะห์ช่วยลดการสูญเสียเลือดระหว่างผ่าตัดและช่วยลดอัตราการให้เลือดหลังการผ่าตัดกระดูกสะโพกหักในผู้สูงอายุ แต่ยังไม่มีรายงานการศึกษาเกี่ยวกับขนาดและวิธีการให้มาก่อน

วัตถุประสงค์: เพื่อศึกษาการใช้ฮอร์โมนกระตุ้นการสร้างเม็ดเลือดสังเคราะห์ในการลดการสูญเสียเลือดระหว่างการผ่าตัดและลดอัตราการให้เลือดหลังการผ่าตัด

วิธีการศึกษา: ผู้ป่วยจำนวนทั้งหมด 32 คน แบ่งแบบสุ่มเป็น 2 กลุ่มคือ กลุ่มที่ได้รับฮอร์โมนกระตุ้นการสร้างเม็ดเลือดสังเคราะห์ และกลุ่มที่ได้รับยาหลอก โดยทั้งสองกลุ่มจะได้รับธาตุเหล็กในน้ำตาลซูโครสทางหลอดเลือดดำ จากนั้นทำการประเมินผลการลดการสูญเสียเลือดขณะผ่าตัด การลดการรับเลือดหลังผ่าตัด ผลข้างเคียงและเพิ่มคะแนนผลลัพธ์ในการใช้งาน

ผลการศึกษา: ลักษณะพื้นฐานของสองกลุ่มไม่แตกต่างกัน ภาวะแทรกซ้อนหลังผ่าตัดและคะแนนผลลัพธ์ในการใช้งานของสองกลุ่มไม่แตกต่างกัน การได้รับเลือดบริจาคของกลุ่มที่ได้รับฮอร์โมน (2.1 ± 1.0 กรัม/เดซิลิตร) ไม่แตกต่างกันกับกลุ่มที่ได้รับยาหลอก (2.2 ± 0.8 กรัม/เดซิลิตร) อย่างมีนัยสำคัญทางสถิติ อย่างไรก็ตาม ในกลุ่มที่ได้รับฮอร์โมนกระตุ้นการสร้างเม็ดเลือดสังเคราะห์อาจมีผลในการเพิ่มระดับฮีโมโกลบินหลังการผ่าตัด ($P = .07$) และเพิ่มระดับเม็ดเลือดแดงตัวอ่อน ($P = .10$)

สรุป: การให้ฮอร์โมนกระตุ้นการสร้างเม็ดเลือดสังเคราะห์ร่วมกับการให้ธาตุเหล็กในน้ำตาลซูโครสในผู้ป่วยที่ทำการรักษาภาวะกระดูกสะโพกหักด้วยการผ่าตัดไม่มีความแตกต่างกันทั้งในด้านการลดการสูญเสียเลือดหลังการผ่าตัดและอัตราการได้รับเลือด

คำสำคัญ: ฮอร์โมนกระตุ้นการสร้างเม็ดเลือดสังเคราะห์ ภาวะกระดูกสะโพกหักในผู้สูงอายุ อัตราการได้รับเลือดหลังผ่าตัด การสูญเสียเลือดหลังผ่าตัด

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Corresponding Author:
ปพน สง่าสูงส่ง
ภาควิชาออร์โธปิดิกส์
คณะแพทยศาสตร์
โรงพยาบาลรามาธิบดี
มหาวิทยาลัยมหิดล
270 ถนนพระรามที่ 6
แขวงทุ่งพญาไท เขตราชเทวี
กรุงเทพฯ 10400 ประเทศไทย
โทรศัพท์ +66 2201 1589
โทรสาร +66 2201 1599
อีเมล paphonortho@gmail.com