

Two different dosing regimens of human recombinant erythropoietin beta during preoperative autologous blood donation in patients having hip arthroplasty

Buljan, Melita; Nemet, Damir; Golubić-Čepulić, Branka; Bićanić, Goran; Tripković, Branko; Delimar, Domagoj

Source / Izvornik: **International Orthopaedics, 2012, 36, 703 - 709**

Journal article, Accepted version

Rad u časopisu, Završna verzija rukopisa prihvaćena za objavljivanje (postprint)

<https://doi.org/10.1007/s00264-011-1367-7>

Permanent link / Trajna poveznica: <https://um.nsk.hr/um:nbn:hr:105:792126>

Rights / Prava: [In copyright](#)/[Zaštićeno autorskim pravom.](#)

Download date / Datum preuzimanja: **2025-01-28**



Repository / Repozitorij:

[Dr Med - University of Zagreb School of Medicine](#)
[Digital Repository](#)





Središnja medicinska knjižnica

Buljan M., Nemet D., Golubić-Čepulić B., Bićanić G., Tripković B., Delimar D. (2012) *Two different dosing regimens of human recombinant erythropoietin beta during preoperative autologous blood donation in patients having hip arthroplasty*. International Orthopaedics, 36 (4). pp. 703-9. ISSN 0341-2695

<http://www.springer.com/journal/264/>

<http://www.springerlink.com/content/0341-2695/>

<http://dx.doi.org/10.1007/s00264-011-1367-7>

<http://medlib.mef.hr/1657>

University of Zagreb Medical School Repository

<http://medlib.mef.hr/>

Two different dosing regimen of human recombinant erythropoietin beta during preoperative autologous blood donation in patients having hip arthroplasty

Melita Buljan MD¹, Damir Nemet MD, PhD², Branka Golubic-Cepulic MD³, Goran Bicanic MD, PhD¹, Branko Tripkovic MD PhD¹, Domagoj Delimar MD, PhD¹

1. Department of Orthopaedic Surgery, University Hospital Centre Zagreb, University of Zagreb School of Medicine, Zagreb, Croatia
2. Department of Internal Medicine, Division of Hematology, Zagreb, University Hospital Centre Zagreb, Zagreb, Croatia
3. Department of Clinical Transfusiology, University Hospital Centre Zagreb, Zagreb, Croatia

Corresponding author

Goran Bicanic, MD, PhD

Dpt. of Orthopaedic Surgery, University Hospital Centre Zagreb

Salata 6-7, 10000 Zagreb

Croatia

email:gbic@mef.hr

phone +38512368911

fax +38512379913

ABSTRACT

Purpose: Aim is to evaluate the effectiveness of two different dosing regimen of human recombinant erythropoietin (rHuEpo) for preoperative autologous blood collection in patients undergoing hip arthroplasty.

Methods: Prospective randomized trial where erythropoietin was administered intravenously;15000IU twice a week or 30000IU once a week (total of 90000IU)), combined with fero II sulfat peroraly and compared to administration of only fero II sulfat.

Results: Although different dosing regimen of the same rHuEpo administration during preoperative autologous blood donation have similar effect on collecting of two units of autologous blood, preoperative haemoglobin level and perioperative allogenic blood transfusion, once weekly dose regimen of rHuEpo was more convenient (although not statistically significant) for patients.

Conclusion: We suggest more practical and comfortable but still very effective therapeutic regimen with single weekly intravenous administration of recombinant human erythropoietin (for patients scheduled for THA).

Key words: autologous blood donation, hip arthroplasty, human recombinant erythropoietin, dose regimen, blood transfusion, erythropoietin

INTRODUCTION

Patients undergoing total hip arthroplasty (THA) with baseline haemoglobin level of ≤ 130 g/L are usually unable to donate sufficient autologous blood volume to satisfy their transfusion requirements during and after the surgery. More than 50% of such patients require additional allogenic blood transfusions [1,2]. The goal of preoperative administration of recombinant human erythropoietin (rHuEpo) is to increase erythropoiesis in patients who are donating blood for autologous use and therefore decrease the need for allogenic transfusions [3,4]. Previous reports found that the pharmacological response to erythropoietin therapy is a function of dose and administration regimen and that repeated administration of rHuEpo is more effective in stimulating reticulocyte response than single-dose administration of the same total amount of rHuEpo[5]. Several studies suggest that if rHuEpo is administered subcutaneously rather than intravenously, a lower dose may be sufficient to maintain the haematocrit at a given level [6]. But, over the last twenty years researches recorded cases where patients developed neutralizing anti-erythropoietin antibodies, a rare complication after usage of rHuEpo to increase red-cell production, in patients with the anaemia because of chronic renal failure. Such antibodies can cause pure red-cell aplasia [7]. The occurrence of antibody-mediated pure red-cell aplasia was mostly related to the subcutaneous administration of human recombinant erythropoietin [8,9]. The optimal dose, interval and route of administration for rHuEpo are yet to be established.

The aim of this study is to evaluate the effectiveness of two different dosing regimen of rHuEpo administered intravenously to avoid all possible complications of subcutaneous administration (15000 IU of rHuEpo intravenously twice a week (total of 90000IU) or 30000 IU of rHuEpo intravenously once a week (total of 90000 IU)), combined with fero II sulfat peroraly and compared to administration of only fero II sulfat peroraly, for collecting of two units of preoperative autologous blood and therefore reducing the need for allogenic blood transfusions after primary THA.

PATIENTS AND METHODS

Patients

The study included 93 patients between 60 and 80 years of age who were scheduled for primary THA due to osteoarthritis. All patients who were able to donate autologous blood preoperatively with haemoglobin level between 105 and 130 g/L were suitable for the study. Patients were enrolled in the study after giving informed consent in accordance with the ethical committee of the hospital. Exclusion criteria were: history of bleeding disorder, history of seizures or uncontrolled hypertension, history of deep vein thrombosis, gastrointestinal

bleeding within 6 month before the surgery, malignancy, acute or chronic infection and consumption of cytostatic or immunosuppressant drugs. Iron was given orally in all patients as ferrous-II sulphate (3x 65 mg elementary iron) during the study, starting one week before the first autologous blood donation. THA in all patients was performed by senior authors using direct lateral approach. The human recombinant erythropoietin beta (Recormon[®]) used in the study was provided by F Hofmann - La Roche, Basel, Switzerland. For all patients routine premedication included midazolam per os (0,1 mg/kg) 1 hour before the induction of anaesthesia and 500mL of Ringer's solution before they were positioned upright for the induction of spinal anaesthesia at level of either L3/L4 or L2/L3 via midline approach. An isobaric solution of levobupivacain (3,0 – 3,5 mL) were administered with 25 or 27G pencil-point needle.

Study design

Patients were randomly assigned in three groups: 30 patients received 15000 IU (average 200IU/kg) of rHuEpo intravenously twice a week (on 17th, 13th, 10th, 6th, 3rd day preoperatively, and 2nd day postoperatively), and iron perorally (group I); 31 patient received 30000 IU IU (average 400IU/kg) of rHuEpo intravenously once a week (on 17th, 10th and 3rd day preoperatively), and iron perorally (group II); 32 patients received only iron perorally (group III). Donation of 12% of total blood volume was performed at 10th and 3rd preoperative day. The minimum haemoglobin level (Hb) for donation was 110 g/L, according to current European guidelines for preoperative autologous donation[10]. The pre-study evaluation included thorough medical history and physical examination. Pre-study laboratory tests included complete blood count, reticulocyte count, serum chemistry studies, urin analysis, serum iron, TIBC, transferin saturation, and serum ferritin. At the time of each injection of rHuEpo, (17th, 13th, 10th, 6th and 3rd preoperative day, for group I, and 17th, 10th, and 3rd preoperative day, for group II and group III, respectively, vital signs, hematologic values (including reticulocytes) and serum chemistry (potassium) were assessed. If the Hb level was greater than 150 g/L erythropoietin beta was not administered, if the Hb level was less than 110 g/L, autologous blood was not donated. Adverse events, blood loss and transfusion data were collected for all patients by anaesthesiologist. The criteria for perioperative transfusion (both autologous and allogenic) included haemoglobin level ≤ 80 g/L, and/or clinical symptoms of anaemia (increased heart rate or lower blood pressures despite an intravenous fluid bolus). All patients received the same protocol for deep venous thrombosis prophylaxis with low-molecular-weight heparin, and cefazolin (1g iv) was administered 60min before procedure for perioperative infection prophylaxis. In all patients reinfusion drains were used. The reinfusion drains (for cell salvage) were used in the immediate postoperative period in the

recovery room (first 6 hours), and were later converted to standard Hemovac drains. All drains were removed 48 hours after arthroplasty.

Laboratory studies

Samples were obtained on 17th, 13th, 10th, and 3rd day preoperatively, in group I and II before each injection of rHuEpo, and in group III immediately before donation of autologous blood. Blood was taken on the day of surgery: 2 hours preoperatively and 6 hours postoperatively, and on several postoperative days (1st, 2nd, 3rd, 10th, and 35th) from all patients. Ferro-kinetic studies (serum iron, serum ferritin, TIBC and transferrin saturation) were measured before and at the end of the study. Three groups were similar in terms of male/female ratio, age, height, weight, total blood volume, ASA classification, and baseline haemoglobin level. Group I included 5 male and 25 female patients, with mean age 68.43. Group II included 3 male and 28 female patients with mean age 67.71. Group III included three male and 29 female patients with mean age 66.31. The primary variable which measured efficiency was the percentage of patients in each group requiring allogenic blood and the mean number of units given to each patient who received a transfusion. The secondary variable which measured efficiency was percentage of patients in each group who collected planned two units of autologous blood, the mean number of units collected per patients, and a change in haematological parameters.

Statistical methods

Demographic and analytical values were presented using descriptive statistics and expressed as mean±SD; medians, minimal and maximal observed values or percentage. The paired Student t-test was used to determine the significant differences within the group, and Wilcox test was used for data which values cannot be assumed to be normally distributed. The unpaired Student t-test and MannWhitney test were used to determine the statistical significance between the groups. A p value of less than 0.05 was considered as statistically significant.

RESULTS

Patients in Group I were able to collect 58 of the requested 60 units of autologous blood. Forty-nine of the 58 units were transfused, and nine units were discarded. Patients in Group II were able to collect 61 of the requested 62 units of autologous blood. Forty-three of the 61 unit were transfused, and eighteen units were discarded. Patients in Group III were able to collect 58 of the requested 64 units of autologous blood. Fifty of the 58 units transfused, and eight units were discarded. The effect of erythropoietic activity on haemoglobin level and reticulocytes count over time is shown in Figures 1 and 2. Only one patient in group II had haemoglobin level at

baseline less than, for autologous donation recommended 110 g/L (105. g/L), but because of effective stimulation of erythropoiesis, patient was able to donate one unit of autologous blood (at the time of first autologous blood donation haemoglobin level was 110 g/L). There were no significant differences among groups between postoperative haemoglobin levels. Mean reticulocyte count was not significantly different at initial assessment between all the groups. From 10th preoperative day to the day of surgery, there was significant increase in reticulocyte count in both erythropoietin-treated groups. The reticulocyte count returned to baseline levels 5 weeks after surgery in all three groups. Six hours after surgery, and at the first postoperative day, patients who received erythropoietin (group I and II) had significantly higher values than did those in no-erythropoietin group (III), $p < 0.001$, t-test. Difference between reticulocytes count in Group I and II didn't reach significance during study period at any time. Intraoperative blood loss, postoperative reinfusion blood, blood loss in drains, and total blood loss are shown in Figure 3. The perioperative blood loss was similar among all groups.

Transfusion

The incidence of blood transfusion is shown in Figure 4. Only two patients in Group II did not receive blood transfusion. There were no patients who received allogenic blood transfusion intraoperatively. The highest proportion of patients who required blood transfusion intraoperatively (autologous) was in Group III, 16 (50%) patients compared with 7 (23,3%) and 4 (13.3%) patients in Group I and II, respectively, III:I,II $p = 0.0315$, chi-square test. There was no significant difference in postoperative consumption of autologous blood between groups. There were 34.4% of patients in group III exposed to allogenic blood transfusion postoperatively compared with 13.3% , and 6.4% of patients in Group I and II, respectively, III:I,II $p = 0.013$, III:II $p = 0 < 0.001$, chi-square test . The difference in allogenic transfusion rates between Groups I and II (13.3% to 6.4%) did not reach significance ($p = 0.09$, chi-square test). The mean number of blood units is shown in Figure 5. The mean number of units of allogenic blood transfused per patient was 0.23 ± 0.49 (0-3), 0.13 ± 0.51 (0-2), and 0.69 ± 1.23 (0-4) in Group I, II and III, respectively, III:I,II $p = 0.006$, t-test. The mean number of total transfused units (autologous and allogenic) was 1.87 ± 0.86 (0-5), 1.5 ± 0.78 (0-4), and 2.25 ± 1.24 (0-5), in Group I, II, and III, respectively, III: I, II $p = 0.013$, t-test. There was no significant difference among the groups at baseline, as well at the end of study between serum iron, TIBC, ferritin and transferrin saturation. However, serum iron, ferritin and transferrin saturation at the end of study significantly decreased compared with baseline level, $p < 0.05$, t-test for paired samples.

The use of erythropoietin in this study was generally well tolerated, with few adverse reactions which were nausea in four (6.5%), pyrexia in four (6.5%) and headache in three (4.9%) patients. The erythropoietin therapy was not discontinued in any patient because of these reactions. Postoperative complications included five wound hematomas (no operative evacuation was needed).

DISCUSSION

This study suggest that two, here compared, regimens of beta human recombinant erythropoietin intravenously (six-dose regimen vs. three-dose regimen, of the same weekly doses) for three weeks enabled collecting of two units of autologous blood and reduced allogenic blood transfusion in patients having THA. These results are in agreement with studies of Green et al. and Rosencher et al. [11,12]. Both, six-dose and three-dose regimen were associated with better haematological parameters on the day of surgery and lower overall requirement for transfusion of allogenic blood, when compared with no-erythropoietin treated group of patients. Previous major, double-blind, placebo controlled trials with daily regimen of rHuEpo for ten preoperative, and five postoperative days have shown benefit from rHuEpo in orthopaedic surgical patients by increasing total red cell mass of patients and reducing perioperative allogenic blood transfusion[13,14]. The trial by Goldberg et al demonstrated that weekly 600 IU/kg dosing regimen of rHuEpo was similar to the daily 300 IU/kg regimen, with respect to safety and the avoidance of allogenic transfusion in patients scheduled to undergo major orthopaedic arthroplasty[15]. After these trial weekly dose regimen was approved as the standard regimen for orthopaedic surgery. Contrary to this study, several trials demonstrated that more frequent administration could be more effective than less frequent one. Cody et al discussed that initial high peak level from high once weekly dose may be wasted as erythropoietin receptors on progenitor cells in bone marrow may become saturated; when these receptor are again free for binding, the level of serum erythropoietin will fall. Frequent administration of small amounts of rHuEpo could maintain a more constant low level, but effective level of serum erythropoietin[16]. Changes of reticulocytes count is one of powerful predictors of responsiveness to rHuEpo treatment[17,18]. In our study the mean reticulocytes count slightly increases, for several days, after the beginning of erythropoietin treatment, compared to baseline level, in both erythropoietin groups, and this results are consistent with the findings of Ramakrishnan et al.[19] They found that, after repeated erythropoietin administration, reticulocytes count steadily starts to rise until the peak level is reached after 200 to 300 hours. Then reticulocytes count starts declining to reach the baseline level. Non-erythropoietin treated patients received postoperatively allogenic blood transfusion at higher rate (34.4%) than patients who had twice weekly regimen

(13.3%), and once weekly regimen (6.4%). Although there was no significant difference between Groups I and II in percentage of allogenic blood transfusions, there was a slightly lower demand for allogenic blood transfusion in Group II (single weekly dose). The average consumption of transfused, overall blood (autologous and allogenic) were significantly higher (2.25 ± 1.24 units/patient) compared with both erythropoietin treated groups. This results were in agreement with previous studies, which demonstrated that preoperative haemoglobin level was one of the strongest predictors of perioperative allogenic blood transfusion in perisurgical setting[20,21].

Great proportion of authors have shown the superiority of subcutaneous route over intravenous for more sustained serum levels over time (12-18h) and lesser dose requirements[22-24]. But, subcutaneous injection can be painful and also nearly all patients who had antibody-mediated pure red cell aplasia, received erythropoietin administration by the subcutaneous route[25,26]. For this reason, and for short-term administration, Lee et al.[27] think that treatment by intravenous route is better for patients having autologous blood donation as it allows a more reliable serum level to be achieved and maintained. Several clinical studies[28] analysed the relationship between erythropoietin, iron, and the erythropoietic response to anaemia. In our study relative weak response of erythropoiesis to 90 000 IU rHuEpo (approximately $6 \times 200 \text{ IU/kg}$ or $3 \times 400 \text{ IU}$), could be explained with chosen doses of erythropoietin beta, and iron supplementation. Although all baseline iron parameters (including serum iron, TIBC and saturation of transferrin) were within the normal ranges, with no intergroup differences, iron stores are not sufficient, because the iron requirements exceed the available supply, during rHuEpo administration and accelerated erythropoiesis. Approximately 200 mg/d, (which was used in the current study) is a standard regimen of iron supplementation[17].

Conclusion

Although different dosing regimen of the same rHuEpo administration during preoperative autologous blood donation have had similar effect on the collecting of two units of autologous blood, preoperative haemoglobin level and perioperative allogenic blood transfusion, once weekly dose regimen of rHuEpo was more convenient (although not statistically significant), and probably more comfortable for patients. With assumption that for the great proportion of patients it was more inconvenient, costly and psychologically and physically demanding if they had to visit hospital twice a week. For this reason we suggest more practical and comfortable but still very effective therapeutic regimen with single weekly intravenous administration of recombinant human erythropoietin (for patients scheduled for THA).

The authors declare that they have no conflict of interest.

References:

1. Mercuriali F, Biffi E, Inghilleri G, Vinci A (1989) Low hematocrit: limiting factor in autologous blood predonation program. In: Castelli D, Genetet B, Habibi B (eds) *Transfusion in Europe* Paris ISBT, Paris,
2. Young SW, Marsh DJ, Akhavan MA, Walker CG, Skinner JA (2008) Attitudes to blood transfusion post arthroplasty surgery in the United Kingdom: a national survey. *Int Orthop* 32 (3):325-329. doi:10.1007/s00264-007-0330-0
3. Mercuriali F, Zanella A, Barosi G, Inghilleri G, Biffi E, Vinci A, Colotti MT (1993) Use of erythropoietin to increase the volume of autologous blood donated by orthopedic patients. *Transfusion* 33 (1):55-60
4. Colomina MJ, Bago J, Pellise F, Godet C, Villanueva C (2004) Preoperative erythropoietin in spine surgery. *Eur Spine J* 13 Suppl 1:S40-49. doi:10.1007/s00586-004-0754-9
5. Cheung WK, Goon BL, Guilfoyle MC, Wacholtz MC (1998) Pharmacokinetics and pharmacodynamics of recombinant human erythropoietin after single and multiple subcutaneous doses to healthy subjects. *Clin Pharmacol Ther* 64 (4):412-423. doi:S0009-9236(98)90072-8 [pii] 10.1016/S0009-9236(98)90072-8
6. Kaufman JS, Reda DJ, Fye CL, Goldfarb DS, Henderson WG, Kleinman JG, Vaamonde CA (1998) Subcutaneous compared with intravenous epoetin in patients receiving hemodialysis. Department of Veterans Affairs Cooperative Study Group on Erythropoietin in Hemodialysis Patients. *N Engl J Med* 339 (9):578-583. doi:10.1056/NEJM199808273390902
7. Peces R, de la Torre M, Alcazar R, Urra JM (1996) Antibodies against recombinant human erythropoietin in a patient with erythropoietin-resistant anemia. *N Engl J Med* 335 (7):523-524. doi:10.1056/NEJM199608153350717
8. Eckardt KU, Casadevall N (2003) Pure red-cell aplasia due to anti-erythropoietin antibodies. *Nephrol Dial Transplant* 18 (5):865-869
9. Casadevall N, Nataf J, Viron B, Kolta A, Kiladjian JJ, Martin-Dupont P, Michaud P, Papo T, Ugo V, Teysandier I, Varet B, Mayeux P (2002) Pure red-cell aplasia and antierythropoietin antibodies in patients treated with recombinant erythropoietin. *N Engl J Med* 346 (7):469-475. doi:10.1056/NEJMoa011931 346/7/469 [pii]
10. Europe Co (1997) *Guide to the preparation, use and quality assurance of blood components*. 3rd edn. Council of Europe Press, Strassbourg
11. Green WS, Toy P, Bozic KJ (2010) Cost minimization analysis of preoperative erythropoietin vs autologous and allogeneic blood donation in total joint arthroplasty. *The Journal of arthroplasty* 25 (1):93-96. doi:10.1016/j.arth.2008.10.005
12. Rosencher N, Kerckamp HE, Macheras G, Munuera LM, Menichella G, Barton DM, Cremers S, Abraham IL (2003) Orthopedic Surgery Transfusion Hemoglobin European Overview (OSTHEO) study: blood management in elective knee and hip arthroplasty in Europe. *Transfusion* 43 (4):459-469
13. Laupacis A, Feagan B, Wong C (1993) Effectiveness of perioperative recombinant human erythropoietin in elective hip replacement. COPEs Study Group. *Lancet* 342 (8867):378
14. Faris PM, Ritter MA, Abels RI (1996) The effects of recombinant human erythropoietin on perioperative transfusion requirements in patients having a major orthopaedic operation. The American Erythropoietin Study Group. *J Bone Joint Surg Am* 78 (1):62-72
15. Goldberg MA, McCutchen JW, Jove M, Di Cesare P, Friedman RJ, Poss R, Guilfoyle M, Frei D, Young D (1996) A safety and efficacy comparison study of two dosing regimens of

- epoetin alfa in patients undergoing major orthopedic surgery. *Am J Orthop (Belle Mead NJ)* 25 (8):544-552
16. Cody J, Daly C, Campbell M, Donaldson C, Khan I, Vale L, Wallace S, Macleod A (2005) Frequency of administration of recombinant human erythropoietin for anaemia of end-stage renal disease in dialysis patients. *Cochrane Database Syst Rev* (3):CD003895. doi:10.1002/14651858.CD003895.pub2
17. Avall A, Hyllner M, Bengtson JP, Carlsson L, Bengtsson A (2003) Recombinant human erythropoietin in preoperative autologous blood donation did not influence the haemoglobin recovery after surgery. *Acta Anaesthesiol Scand* 47 (6):687-692. doi:130 [pii]
18. Perez-Ruixo JJ, Krzyzanski W, Hing J (2008) Pharmacodynamic analysis of recombinant human erythropoietin effect on reticulocyte production rate and age distribution in healthy subjects. *Clin Pharmacokinet* 47 (6):399-415. doi:4764 [pii]
19. Ramakrishnan R, Cheung WK, Wacholtz MC, Minton N, Jusko WJ (2004) Pharmacokinetic and pharmacodynamic modeling of recombinant human erythropoietin after single and multiple doses in healthy volunteers. *Journal of clinical pharmacology* 44 (9):991-1002. doi:10.1177/0091270004268411
20. Salido JA, Marin LA, Gomez LA, Zorrilla P, Martinez C (2002) Preoperative hemoglobin levels and the need for transfusion after prosthetic hip and knee surgery: analysis of predictive factors. *J Bone Joint Surg Am* 84-A (2):216-220
21. Prasad N, Padmanabhan V, Mullaji A (2007) Blood loss in total knee arthroplasty: an analysis of risk factors. *Int Orthop* 31 (1):39-44. doi:10.1007/s00264-006-0096-9
22. Cheung W, Minton N, Gunawardena K (2001) Pharmacokinetics and pharmacodynamics of epoetin alfa once weekly and three times weekly. *Eur J Clin Pharmacol* 57 (5):411-418
23. Goodnough LT, Monk TG, Andriole GL (1997) Erythropoietin therapy. *N Engl J Med* 336 (13):933-938. doi:10.1056/NEJM199703273361307
24. Woo S, Jusko WJ (2007) Interspecies comparisons of pharmacokinetics and pharmacodynamics of recombinant human erythropoietin. *Drug Metab Dispos* 35 (9):1672-1678. doi:dmd.107.015248 [pii] 10.1124/dmd.107.015248
25. Rossert J, Casadevall N, Eckardt KU (2004) Anti-erythropoietin antibodies and pure red cell aplasia. *J Am Soc Nephrol* 15 (2):398-406
26. Bennett CL, Luminari S, Nissenson AR, Tallman MS, Klinge SA, McWilliams N, McKoy JM, Kim B, Lyons EA, Trifilio SM, Raisch DW, Evens AM, Kuzel TM, Schumock GT, Belknap SM, Locatelli F, Rossert J, Casadevall N (2004) Pure red-cell aplasia and epoetin therapy. *N Engl J Med* 351 (14):1403-1408. doi:10.1056/NEJMoa040528 351/14/1403 [pii]
27. Lee JH, Yoon KS, Park JS, Kang SB, Do SH, Kim JY (1999) Recombinant human erythropoietin using preoperative autologous donation in lumbar stenosis operations. *J Korean Soc Spine Surg* 6 (3):5
28. Goodnough LT, Skikne B, Brugnara C (2000) Erythropoietin, iron, and erythropoiesis. *Blood* 96 (3):823-833

Figure 1. Haemoglobin values (means) during the study.

Figure 2. Change in mean reticulocyte count from baseline during the study.

Figure 3. Perioperative blood loss.

Figure 4. The incidence of blood transfusion.

Figure 5. The mean units collected/patient and transfused/patients.

Table 1. The ferrokinetic studies.

Data have shown as mean \pm SD, and (minimal and maximal values)

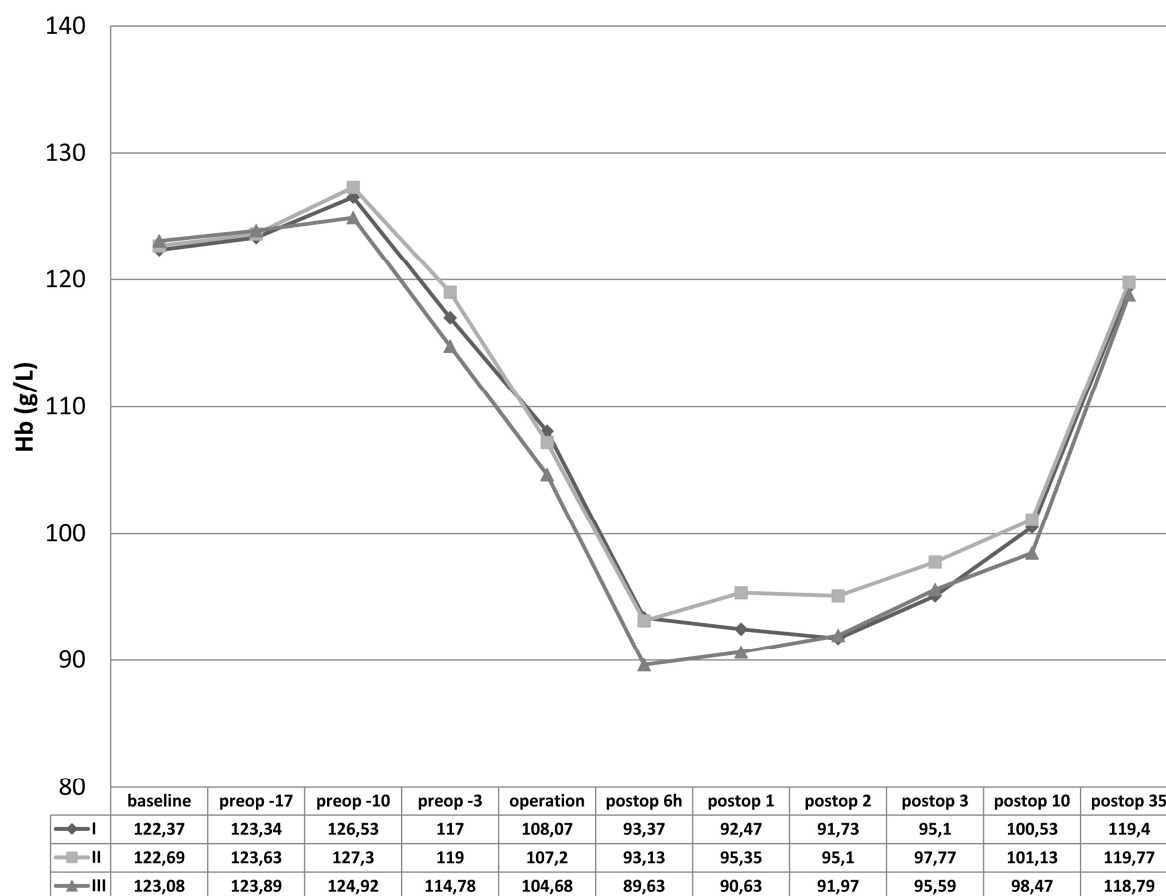


Fig1

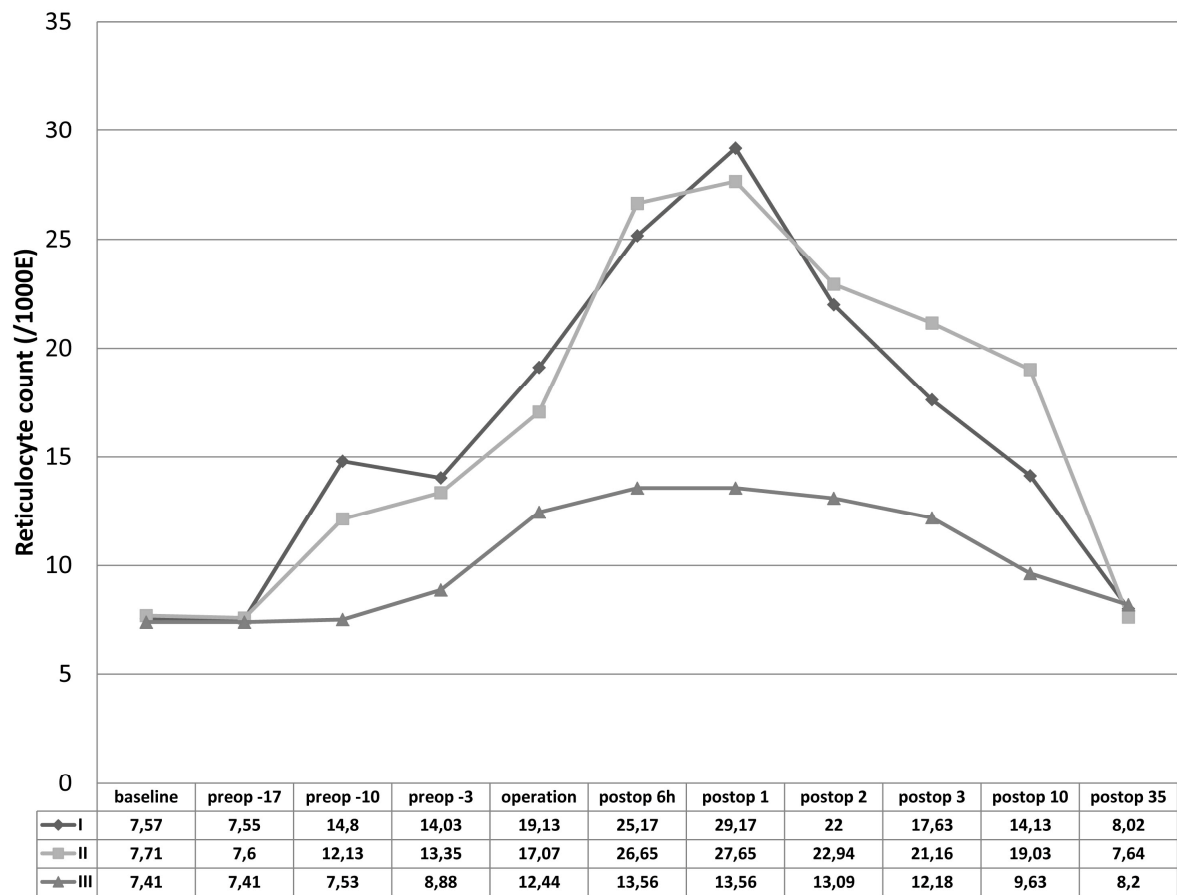


Fig2

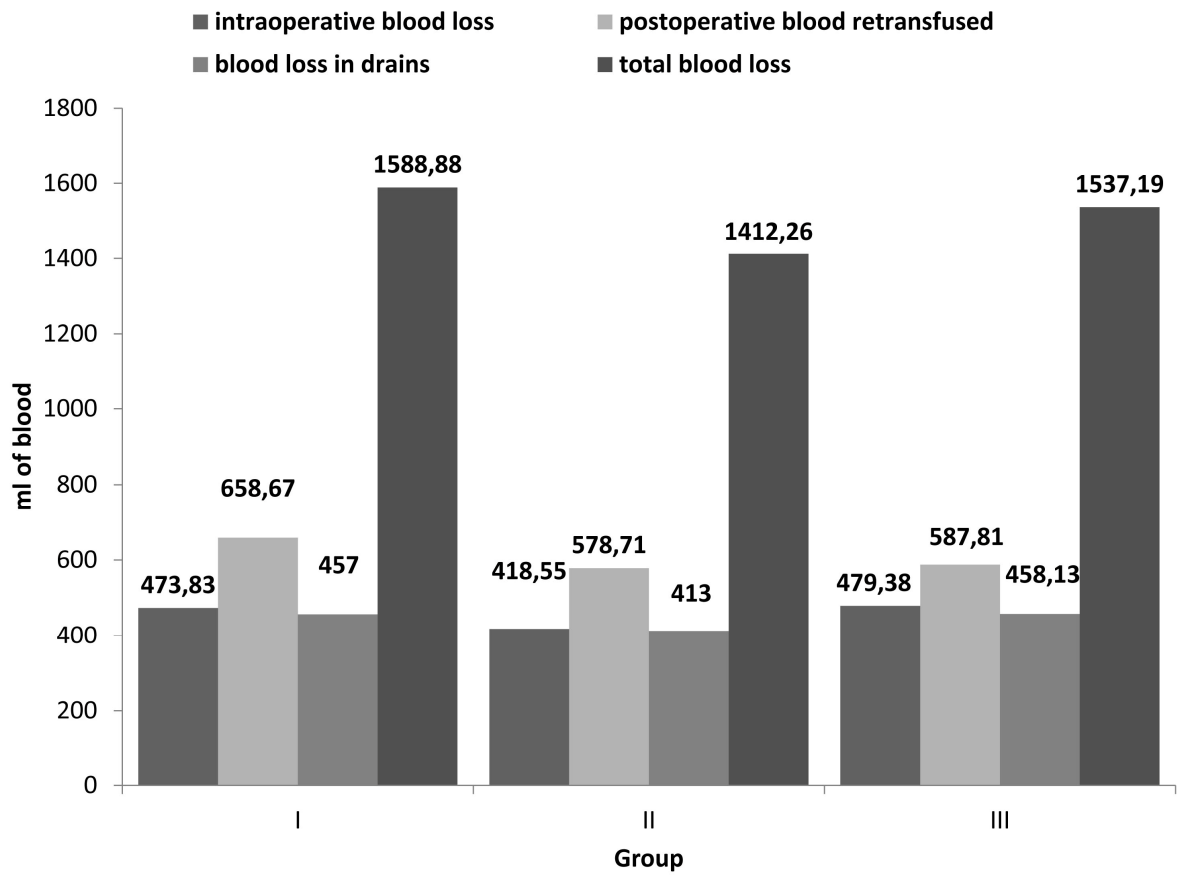


Fig3

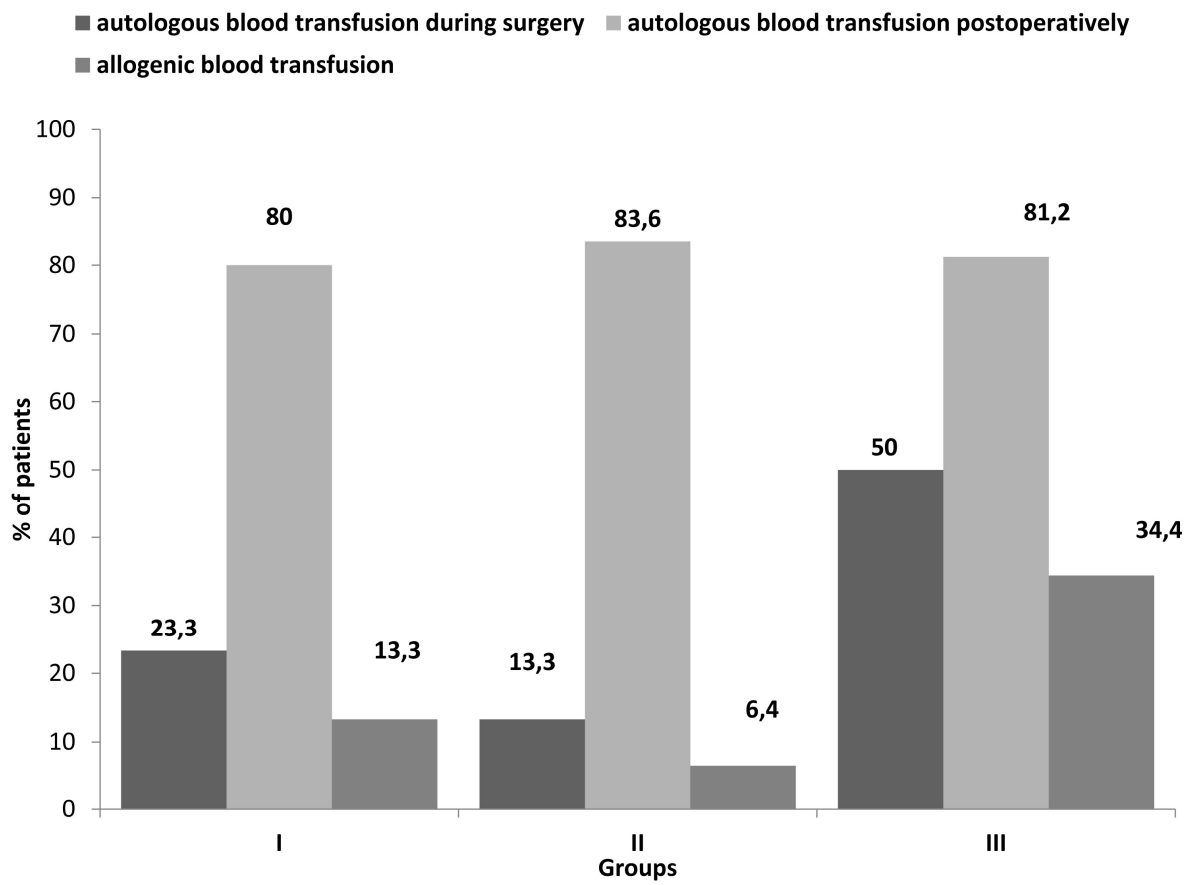


Fig4

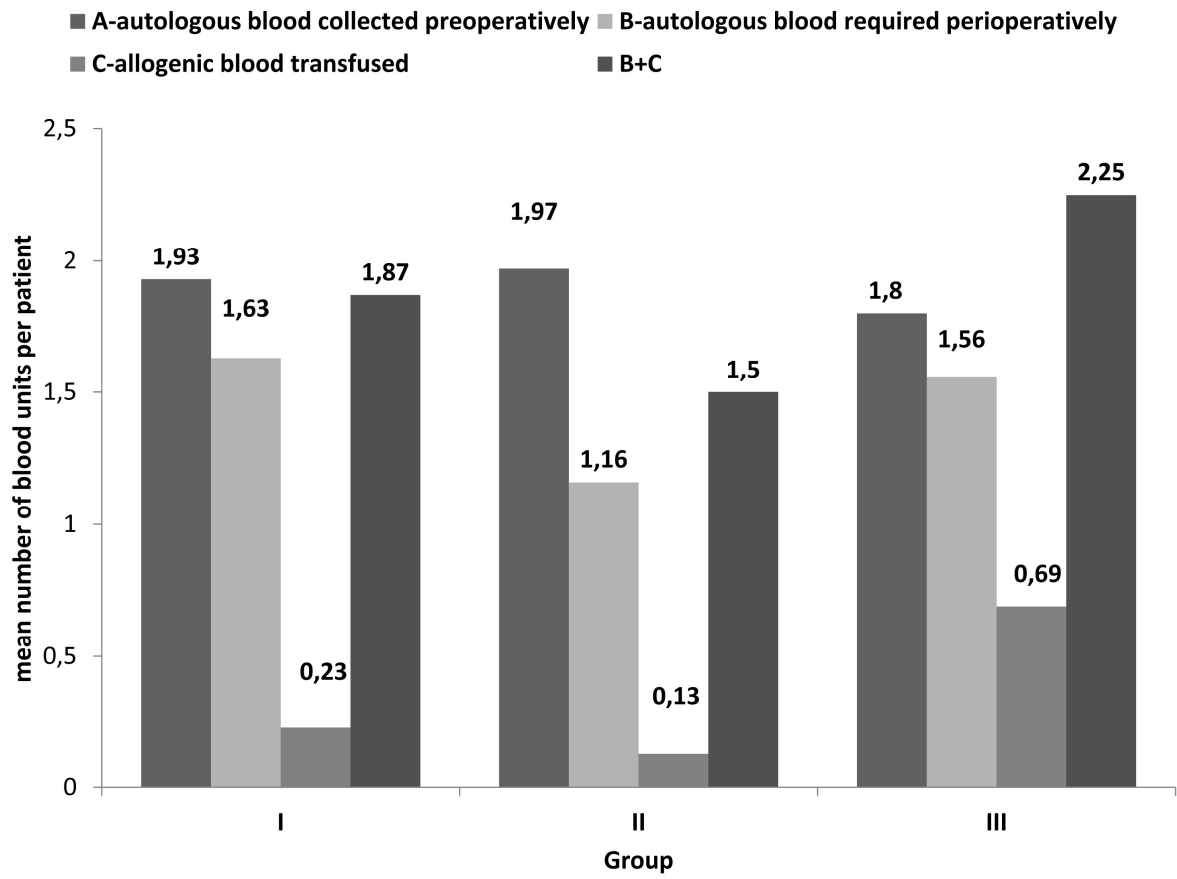


Fig5

		Group I	Group II	Group III	p
Fe (µg/L)	baseline	13.72±3.54 (8.00-23.00)	15.29±4.04 (7.80-23.50)	14.27±3.95 (7.00-25.90)	0,276
	at the end of the study	12.09±4.72 (7.60-32.00)	12.71±4.17 (8.64-31.00)	11.37±2.58 (7.32-28.00)	0,4
TIBC (µg/L)	baseline	53.81±6.16 (40.20-67.00)	56.41±8.22 (44.60-78.00)	56.44±4.26 (49.00-66.00)	0,189
	at the end of the study	52.53±8.39 (40.10-87)	54.15±5.59 (46.50-72.00)	55.42±5.11 (45.60-65.00)	0,22
Feritin (ng/mL)	baseline	78.56±12.6 (45.3-136.8)	81.25±9.8 (52.0-141.80)	76.21±10.2 (50.0-130.6)	0,326
	at the end of the study	62.7±10.2 (40.6-124.8)	58.7±12.8 (46.4-130.80)	70.7±10.8 (59.7-131.8)	0,354
Transferin saturation (%)	baseline	25.72±5.49 (15.00-42.80)	26.94±6.64 (14.90-39.60)	24.96±6.39 (12.10-43.00)	0,5
	at the end of the study	21.72±11.41 (10.90-77.00)	20.17±6.44 (13.30-33.90)	20.53±4.49 (11.60-32.20)	0,239

Table 1