Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

Available online at http://aacc.tums.ac.ir

Research Article

Determination of Allogeneic Transfusion after Injection of Injectable Iron in Patient's Candidates for Intertrochanteric Fracture Surgery

Faranak Behnaz[1], Rahmatollah Mohammadzadeh Namaghi[1], Gholmreza Mohseni[1]*, Meisam Jafari Kafiabadi[2]

[1]*Department of Anesthesiology, Anesthesiology Research Center, Shohada -e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

[2]*Department of Orthopedic Surgery, Clinical Research Center Development Unit of Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

ARTICLE INFO

Article history:
Received 23 September 2023
Revised 15 October 2023
Accepted 29 October 2023

Keywords:
Allogeneic transfusion;
Intertrochanteric fracture;
Iron

ABSTRACT

Background: The purpose of this study is to investigate the rate of allogeneic transfusion after the administration of intravenous iron in patients who are candidates for intertrochanteric fracture surgery.

Methods: Patients who were candidates for intertrochanteric surgery referred to the orthopedic surgery and trauma department of Shahada Tajrish Hospital were included in the study after providing full explanations and obtaining written consent. The 80 patients were randomly divided into control group (No: 40) and intervention (No: 40). Patients in the intervention group were prescribed 600 mg of Venofer drug by ViforCo. This is while patients in the control group were not injected with Venofer before surgery. The results were evaluated using t-test and SPSS21 software.

Results: Based on the results, the 1 hour after surgery, three indicators of systolic blood pressure, pulse rate, breathing rate, RBC showed a significant decrease in patients undergoing intervention ($P<0.05$). However, the oxygenation index showed a significant increase in the patients of this group ($P>0.05$). Meanwhile, in the period of 1 week after the surgery, we also see a significant decrease in the two indices of average hemoglobin and PTT time in the mentioned patients compared to the control subjects ($P=0.030$, $P=0.037$). The amount of blood consumed significantly lower in the patients of the intervention group than in the control group.

Conclusion: The administration of injectable iron in patients with intertrochanteric fracture surgery candidates can improve some of the patients' clinical indicators in addition to a significant reduction in allogeneic blood transfusion.

Introduction

Many patients undergoing orthopedic surgery need red blood cell transfusion for reasons such as severe bleeding during surgery or a history of anemia [1]. Among the orthopedic surgeries that are usually associated with severe bleeding, knee and hip joint surgery can be mentioned [2]. Anemia in patients known as Iron Deficiency Anemia (IDA) usually occurs due to functional defects or lack of iron reserves in the body [3]. Investigations have shown that inflammation during surgery causes a decrease in the speed of erythropoiesis and, as a result, functional defects lead to iron deficiency [3]. During the process of inflammation, the level of hepcidin hormone increases

The authors declare no conflicts of interest.
*Corresponding author.
E-mail address: mohsen85ir@yahoo.com

due to inflammatory cytokines, and the function of macrophages to recover iron is weakened [4].

Hepcidin is known as a regulator of iron erythropoiesis, which prevents the recycling of iron in food by red blood cells in the duodenum, inhibits iron storage in the liver, and prevents iron absorption by red blood cells [5].

One of the methods used to compensate for anemia in patients undergoing surgery is the use of allogeneic injection to the surgical areas. This method is associated with the risk of allergic reactions, infection, transmission of various diseases, aggravation of cancer, and failures caused by immune system defects [6]. Another way to compensate for anemia in patients undergoing surgery is to administer iron, which can reduce the need for blood transfusions and control side effects [7-8]. The use of iron is done in two ways, oral and intravenous.

Oral iron is cheap and available, but its continuous use may cause digestive problems in patients [9]. Studies conducted on the role of oral iron in controlling anemia in patients undergoing knee or hip surgery did not confirm the positive effect of this treatment method [9-10]. On the other hand, the effectiveness of intravenous iron (IVIT) in reducing the need for blood transfusion and increasing hemoglobin in patients undergoing anemia surgery has been confirmed in various studies [11-13]. However, this method was associated with different results in different patients. Therefore, in the present study, the effect of intravenous iron on allogeneic transfusion in patients undergoing intertrochanteric orthopedic surgery has been investigated.

Methods

The present double-blind clinical trial study has been approved by the ethics committee in biomedical research of Shahid Beheshti university of medical science (Registration number: IRCT20190121042444N4 and code: IR.SBMU.MSP.REC.1400.244). 80 patients who were candidates for intertrochanteric surgery referred to the orthopedic surgery and trauma department of Shahada Tajrish Hospital in a period of 2 years (2020 to 2021) were included in the study if they met the inclusion criteria (all patients should be operated by the same doctor and 65 year<Age< 65) and Excluded factors (Excessive iron disorders, sensitivity to oral or injectable iron drugs, asthma treated with clopidogrel or with acetylsalicylic acid at a dose greater than 150 mg per 24 hours, blood coagulation disorders (Thromboplastin time greater than 1.5), patients Hepatic with impaired liver enzymes, patients with hyperthyroidism or hypothyroidism, chronic kidney failure (Cr> 2 mg/dL), dialysis patients) and after providing full explanations and obtaining written consent.

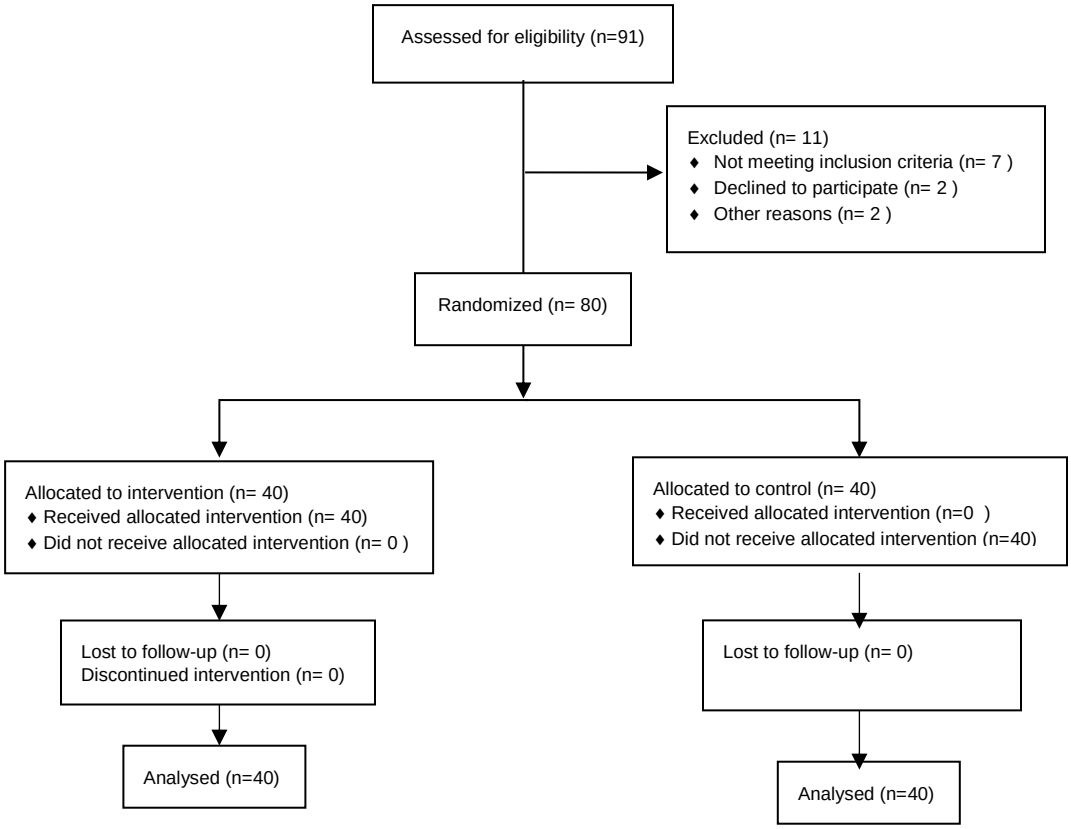

Figure 1- Consort diagram

Patients were divided into two groups using a random number table. The present study was conducted in double-blind conditions so that neither the patient nor the researcher could know which group was studied. All evaluations were done by an independent evaluator. Both groups were subjected to the treatment protocol of intertrochanteric fracture treatment at Shahada Tajrish Hospital trauma center under the supervision of an orthopedic specialist. Blood transfusion criteria were also performed according to the protocol of the blood and anesthesia units of the same hospital and according to national guidelines (Figure1).

Patients in the intervention group were prescribed 600 mg of Venofer drug by ViforCo. three doses of 200 mg as a slow infusion (each ampoule of Venofer is infused in 250 cc of 9% diluted saline solution over 90 minutes in the 48 hours before surgery). This is while patients in the control group were not injected with Venofer before surgery.

Then variables were measured during the study period. The results of questionnaire design and its completion were analyzed using t-test and SPSS25 software.

Results

According to the results of this research, the average age of the patients included in the study was 73.55 ±9.18, and this value was 9.48 ± 73.43 in the intervention group and 73.68 ± 7.43 in the control group, and there was no significant difference between the mentioned values. To be examining the gender of the people in the study shows that 55% (44 people) of the patients are men and 45% (36 people) are women. This ratio in the group of patients under intervention was 52.5% (21 people) for men and 47.5% (19 people) for women, while in the control group there were 57.5% (23 people) men and 42.5% (17 people) women that these values are not significantly different in two groups ($p<0.05$) (Table 1). On the other hand, the examination of weight, height and underlying diseases in the patients of the two groups does not show any significant difference.

Based on the results of (Table 2), the respiratory rate index in the period before surgery in the intervention group was significantly lower than the control group patients (P=0.049). This is despite the fact that in the period of 1 hour after surgery, three indicators of systolic blood pressure (P=0.046), pulse rate (P=0.048) and breathing rate (P=0.042) showed a significant decrease in patients undergoing intervention. However, the oxygenation index showed a significant increase in the patients of this group (P=0.041).

Based on the results of (Table 3), which shows the comparative examination of the laboratory and blood parameters of the patients of the two groups, the average number of red blood cells in the patients undergoing intervention has decreased significantly within 1 hour after the surgery (P=0.044). Meanwhile, in the period of 1 week after the surgery, we also see a significant decrease in the two indices of average hemoglobin and PTT time in the mentioned patients compared to the control subjects (P=0.030, P=0.037).

A comparison of the amount of blood consumed in the patients of the two groups shows that this amount was significantly lower in the patients of the intervention group than in the control group (Table 4). On the other hand, the amount of prescription pack for the patients of the two groups does not show a significant difference (Figure 2).

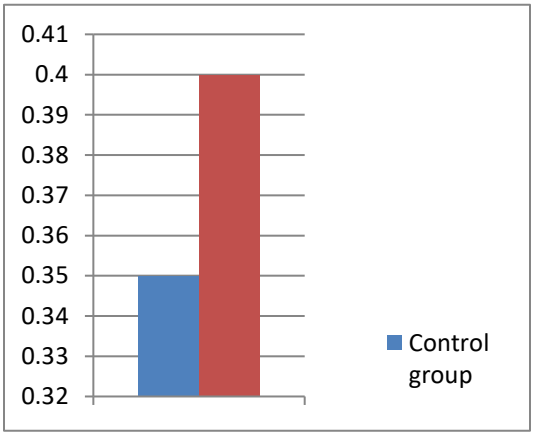

Figure 2- Comparative study of the amount of blood packs received in the patients of the two study groups

Table 1- Comparative study of demographic information between patients of two groups

Indexes		Control group (n=40)	Intervention group (n=40)	P value
Age (year)		73.68±7.43	73.43 ± 9.48	0.123
Gender	Male	23(57.5%)	21 (52.5%)	0.181
	Female	17 (42.5%)	19(47.5%)	0.080
Height (cm)		169.837±26.460	160.670±25.354	0.390
Weight (kg)		74.261±6.738	72.463±5.926	0.283
Underlying disease N (%)		15 (37.5%)	12 (30.0%)	0.631

Table 2- Comparative study of clinical and respiratory indicators of patients of two groups in three time periods before surgery, 1 hour after surgery and 1 week after surgery.

Indexes		Control group (n=40)	Intervention group (n=40)	P value
	SBP1 ()	125.80±12.77	116.44±14.11	0.062
	Pulse count	76.33±7.14	66.75±5.03	0.050

Before	Breathing rate	13.75±1.00	13.18±1.13	0.049*
	Temperatures	36.85±0.31	36.77±0.20	0.164
	Oxygenation	97.13±1.72	96.70±1.96	0.053
	SBP1 ()	125.08±13.61	105.36±11.00	0.046*
	Pulse count	77.45±8.14	66.63±8.48	0.048*
After 1 h	Breathing rate	13.93±1.11	13.18±1.13	0.042*
	Temperatures	37.45±0.35	36.77±0.20	0..097
	Oxygenation	97.13±1.72	99.18±1.83	0.041*
	SBP1 ()	129.40±9.75	119.56±14.76	0.073
After 1 w	Pulse count	73.43±6.69	67.35±4.72	0.060
	Breathing rate	13.23±1.23	13.18±1.13	0.200
	Temperatures	36.78±0.28	36.77±0.20	0.615
	Oxygenation	97.80±1.41	97.15±2.11	0.190

Table 3- Comparative examination of laboratory data between patients of two groups in three time periods

Indexes		**Control group (n=40)**	**Intervention group (n=40)**	**P value**
	Hb	11.43±1.86	11.73±1.24	0.070
	Hct	34.18±5.49	34.90±3.41	0.418
	RBC	3.82±0.62	3.85±0.30	0.066
	WBC	7.64±1.03	6.98±1.08	0.053
	Plt	227.15±49.46	230.28±65.67	0.439
	MCV	86.76±4.86	86.93±5.77	0.337
	MCH	30.60±1.89	29.41±2.49	0.062
	MCHC	32.74±1.92	32.57±2.22	0.080
Before	RDW	12.89±0.87	12.33±1.12	0.055
	RETIC	2.81±0.26	2.91±0.24	0.057
	TIBC	333.70±44.53	284.18±51.84	0.110
	PTT	61.43±2.88	63.38±2.87	0.100
	Ferritin	123.03±15.73	121.23±14.30	0.391
	VB12	279.83±36.245	277.33±53.34	0.637
	Transferrin	303.13±48.93	266.25±59.97	0.090
	Iron	110.73±14.49	90.15±21.39	0.068
	Hb	12.08±1.67	11.02±1.45	0.060
	Hct	34.10±5.45	33.54±3.98	0.167
	RBC	3.87±0.79	3.36±0.46	0.044*
	WBC	7.64±1.03	6.87±1.41	0.082
	Plt	222.63±60.50	220.98±57.61	0.761
	MCV	86.76±4.86	84.14±8.37	0.199
After 1 h	MCH	30.60±1.89	27.89±2.80	0.099
	MCHC	32.74±1.92	31.63±2.20	0.078
	RDW	12.89±0.87	11.73±1.07	0.053
	RETIC	2.73±0.26	2.69±0.34	0.113
	TIBC	333.70±44.53	290.35±54.69	0.138
	PTT	61.43±2.88	63.95±3.54	0.075
	Ferritin	123.02±15.73	118.03±15.37	0.127
	VB12	278.83±36.78	276.38±53.98	0.803
	Transferrin	303.13±48.93	290.63±56.69	0.199
	Iron	107.40±19.410	87.10±24.66	0.051
	Hb	13.33±10.6	11.58±1.10	0.037*
	Hct	32.96±4.12	34.19±3.75	0.085
	RBC	3.80±0.46	3.83±0.29	0.119
	WBC	5.99±0.83	7.02±1.23	0.040
	Plt	227.68±48.55	231.18±62.28	0.816
	MCV	83.33±4.11	86.69±5.35	0.105
	MCH	29.92±1.30	29.18±2.27	0.069
After 1 w	MCHC	32.17±1.56	32.54±2.16	0.188
	RDW	13.30±0.72	12.29±1.17	0.057
	RETIC	2.66±0.31	2.84±0.22	0.062
	TIBC	356.30±42.19	284.33±52.06	0.090

PTT	32.40±9.79	64.58±3.31	0.030*
Ferritin	108.53±13.65	120.68±12.23	0.150
VB12	277.20±33.22	277.43±52.85	0.900
Transferrin	324.63±44.83	267.35±56.98	0.053
Iron	97.43±7.433	90.28±21.06	0.099

Table 4- Comparative examination of the volume of blood consumed in the patients of the two groups examined 1 hour after surgery

Indexes	Control group (n=40)	Intervention group (n=40)	P value
Prescribed blood volume	847.50±322.63	760.00 ± 274.37	0.040

Discussion

One of the most important causes of anemia in patients undergoing orthopedic surgery, especially elderly patients, is the loss of a large volume of blood, which can disrupt hemoglobin production [4]. Hemoglobin levels determine the patient's need for blood transfusion [5]. Many post-surgery events such as reactions of inflammatory cycles inhibit the production and storage of iron by red blood cells and increase anemia [6]. Administration of intravenous iron can be used as a good option to compensate for iron deficiency. Intravenous iron can also moderate severe iron deficiency caused by bleeding by inducing hemoglobin production.

Based on the results obtained from this study, the use of injectable iron plays a positive role in improving iron storage in patients who need intertrochanteric fracture surgery. Our data showed that administration of intravenous iron significantly improves heart rate, systolic blood pressure reduction, increases oxygen supply and respiratory rate in these patients.

Previous studies have shown that intravenous iron administration in the pre-surgery period plays a more effective role in compensating for iron deficiency than oral iron and reduces the need for blood transfusion in the post-surgery period [14]. In addition, the use of intravenous iron also improves the clinical indicators of patients. Despite the promising results of intravenous iron consumption on improving the clinical conditions of patients in the postoperative period, more studies are needed to achieve more reliable results.

In the past years, researchers reported that iron consumption is associated with a decrease in the possibility of blood transfusion [18], while in our results we did not notice the connection between iron injection and cell injections. Among the studies that were consistent with our results, Yang et al. and Shin et al. also reported the results of hip and knee surgery patients [15].

The role of different times before the start of surgery can be an important point in the use of iron supplements. For example, based on the results obtained from a study, better results were obtained in blood transfusion in conditions where iron supplements were not used for more than three days [15]. On the other hand, the patients received iron supplements after being admitted to the hospital, so the number of days of taking iron supplements was not the same in the patients, which can affect the production of hemoglobin and the need for blood transfusion. Also, the way and dose of iron can be considered as one of the effective factors in the effectiveness of iron supplementation in patients.

In many studies, the use of intravenous iron has caused a decrease in the blood transfusion rate of patients undergoing surgery, which indicates the better performance of intravenous iron than oral iron [16-17]. Our study has also been associated with similar results. Despite these findings, the role of dosage in improving the general condition of patients has not received much attention.

Shain et al have shown that the use of lower doses of iron (200-300 mg) in patients undergoing orthopedic surgeries has had successful results in reducing the risk of blood transfusion [18]. There are other studies that confirm Shain's data by confirming the association between iron supplementation and LOS.

By compensating for anemia and reducing the need for blood transfusion, the use of iron supplements can lead to the earlier discharge of older patients undergoing orthopedic surgery. Studies have shown that 3 to 7% of patients with hip fractures die before surgery. Also, 25% of patients who undergo orthopedic surgery for hip fracture can continue living only one year after the surgery [19]. Examining these indicators can help to achieve more useful results in future studies.

Our study was also faced with limitations, including small sample size, single center, defects in patients' records, and some side effects.

Conclusion

In general, based on the results of the present study, it can be said that the administration of injectable iron in patients with intertrochanteric fracture surgery candidates can improve some of the patients' clinical indicators in addition to a significant reduction in allogeneic blood transfusion.

Acknowledgment

The authors express their sincere thanks to the staff of Shohada Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran, for their assistance. Also, we are very grateful to Omid Salemi, Medical Science Liaison from Bersan Daru Company for the necessary arrangements.

References

[1] Bisbe E, Basora M, Colomina MJ. Peri-operative treatment of anaemia in major orthopaedic surgery: a practical approach from Spain. Blood Transfus. 2017; 15(4):296–306.

[2] Gombotz H, Rehak PH, Shander A, Hofmann A. Blood use in elective surgery: the Austrian benchmark study. Transfusion. 2007; 47(8):1468–80.

[3] Goodnough LT. Iron deficiency syndromes and iron-restricted erythropoiesis (CME). Transfusion. 2012; 52(7):1584–92.

[4] Munoz M, Laso-Morales MJ, Gomez-Ramirez S, Cadellas M, Nunez-Matas MJ, Garcia-Erce JA. Pre-operative haemoglobin levels and iron status in a large multicentre cohort of patients undergoing major elective surgery. Anaesthesia. 2017; 72(7):826-834.

[5] Goodnough LT, Nemeth E, Ganz T. Detection, evaluation, and management of iron-restricted erythropoiesis. Blood. 2010; 116(23):4754–61.

[6] Hill GE, Frawley WH, Griffith KE, Forestner JE, Minei JP. Allogeneic blood transfusion increases the risk of postoperative bacterial infection: a meta-analysis. J Trauma. 2003; 54(5):908–14.

[7] Munoz M, Breymann C, Garcia-Erce JA, Gomez-Ramirez S, Comin J, Bisbe E. Efficacy and safety of intravenous iron therapy as an alternative/adjunct to allogeneic blood transfusion. Vox Sang. 2008; 94(3):172–83.

[8] Munoz M, Garcia-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.

[9] Mundy GM, Birtwistle SJ, Power RA. The effect of iron supplementation on the level of haemoglobin after lower limb arthroplasty. J Bone Joint Surg Br. 2005; 87(2):213–7.

[10] Parker MJ. Iron supplementation for anemia after hip fracture surgery: a randomized trial of 300 patients. J Bone Joint Surg Am. 2010; 92(2):265–9.

[11] Litton E, Xiao J, Ho KM. Safety and efficacy of intravenous iron therapy in reducing requirement for allogeneic blood transfusion: systematic review and meta-analysis of randomised clinical trials. Bmj. 2013; 347:f4822.

[12] Auerbach M, Macdougall I. The available intravenous iron formulations: History, efficacy, and toxicology. Hemodial Int. 2017; 21 Suppl 1:S83–s92.

[13] Beris P, Munoz M, Garcia-Erce JA, Thomas D, Maniatis A, Van der Linden P. Perioperative anaemia management: consensus statement on the role of intravenous iron. Br J Anaesth. 2008; 100(5):599–604.

[14] Ionescu A, Sharma A, Kundnani NR, Mihăilescu A, David VL, Bedreag O, et al. Intravenous iron infusion as an alternative to minimize blood transfusion in peri-operative patients. Sci Rep. 2020; 10(1):18403.

[15] Muñoz M, Gómez-Ramírez S, Cuenca J, García-Erce JA, Iglesias-Aparicio D, Haman-Alcober S, et al. Very-short-term perioperative intravenous iron administration and postoperative outcome in major orthopedic surgery: a pooled analysis of observational data from 2547 patients. Transfusion. 2014; 54(2):289-99.

[16] Serrano-Trenas JA, Ugalde PF, Cabello LM, Chofles LC, Lázaro PS, Benítez PC. Role of perioperative intravenous iron therapy in elderly hip fracture patients: a single-center randomized controlled trial. Transfusion. 2011; 51(1):97-104.

[17] Cuenca J, García-Erce JA, Martínez F, Pérez-Serrano L, Herrera A, Muñoz M. Perioperative intravenous iron, with or without erythropoietin, plus restrictive transfusion protocol reduce the need for allogeneic blood after knee replacement surgery. Transfusion. 2006; 46(7):1112-9.

[18] Bisbe E, Rodríguez C, Ruiz A, Sáez M, Castillo J, Santiveri X. Uso preoperatorio de hierro endovenoso, una nueva terapéutica en medicina transfusional [Preoperative use of intravenous iron: a new transfusional therapy]. Rev Esp Anestesiol Reanim. 2005; 52(9):536-40.

[19] Cuenca J, García-Erce JA, Muñoz M, Izuel M, Martínez AA, Herrera A. Patients with pertrochanteric hip fracture may benefit from preoperative intravenous iron therapy: a pilot study. Transfusion. 2004; 44(10):1447-52.