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Original Research Article

Efficacy of Erythropoietin in treatment of anemia in patients hospitalized in the ICU of Ardabil city hospital

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ABSTRACT

Background: Several studies have shown that approximately 95% of patients who have been admitted to the ICU are anemic. Anemia in acute patients leads to significant transfusion. Transfusion can lead to significant complications. Because of the risks of transfusion an alternative therapy for anemia in patients seems be a necessary need for its. The aim of this study was to investigate the efficacy of Erythropoietin in treatment of anemia in patients hospitalized in the ICU of Ardabil city hospital.
Methods: This study is a clinical trial. In this study after selection of patients based on inclusion and exclusion criteria, their data were entered in a check list. Patients were divided into two groups of 35 persons randomly. For first group, erythropoietin was administrated in addition of iron and in second group only iron was administrated. All patients were administrated 100 mg of iron. Hematological indexes and clinical status of patients was evaluated and results were analyzed by statistical methods in SPSS version 19.
Results: In this study, in cases 65.7% and in controls 71.4% were male. The average age of patients in cases was 61.6±20.8 and controls were 61.02±22.5 years. The mean duration of hospitalization in internal ICU was 37.73 days and in surgical ICU was 21.35 days and was observed that at baseline the hemoglobin levels in internal patients was lower than surgical patients (p=0.023). 80% of patients in case group (5.8 units) and 88.57% of patients in controls (6.3 units) required blood transfusion. The hemoglobin level in erythropoietin receiving group increased significantly compared to the control group.
Conclusions: The results of this study showed that erythropoietin is an effective drug to increase hemoglobin level and can provide a significant increase in hemoglobin level compared to placebo.

Keywords: Anemia, Erythropoietin, Intensive Care Unit

INTRODUCTION

Anemia define as a reduction in red blood cell mass, hemoglobin (Hb)<12g/dL and hematocrit less than 36% in women and Hb<14 g/dL and hematocrit less than 41% in men and its clinical manifestations vary according to etiology, severity and starting speed. Other disorders such as cardiopulmonary diseases may be effective in the severity of anemia symptoms. Severe anemia can be tolerated if it is gradually developed, but usually patients with Hb<7g/dL show hypoxic tissue symptoms such as fatigue, headache, asthma, light-headedness and angina. Wannes, visual disturbance, Syncop and tachycardia may be an indication of hypovolemic anemia that needs to immediate attention.[1]

According to Prakash idea in 2012, anemia was common in the intensive care unit (ICU) and increases morbidity and mortality; its etiology is multi-factorial but anemia due to inflammation is the most important cause and is exactly like anemia of iron deficiency. Transfusion and the use of erythropoietin are two methods that are used to correct anemia in sick patients.[2] A great part of these patients have

anemia during hospitalization and a great part of them undergoing anemia during their stay in the ICU that anemia increases with the duration of hospitalization in the ICU. Sekhon and et al, stated that the average of Hb on day seventh is less than 9 g /dL in hospitalized patients with severe brain trauma which admitted to ICU with high mortality risk.[3] In various studies it has been shown that 95% of patients suffered to anemia in the third day of hospitalization in ICU.[4] This event may be due to the fact that patients with severe illness who need to be admitted to the ICU, in 90% of cases it has low of iron and total connection capacity (TIBC) and had normal or slightly higher than normal ferritin.[5-6]

Herbert and et al in a study showed that the effect of maintaining Hb in ICU patients at 8-9g/dL is at least equal to the effect of maintaining this level at 10g/dL by helping transfusion. Also, transfusion to be widely used for anemia patients.[7] 50% of all anemia patients during their hospitalization in the ICU and 85% of patients with more than one week hospitalization in ICU undergoing blood transfusion at least once.[8-9] Transfusion is not a safe process and can have many problems including infection, immune response, pulmonary edema and pulmonary injury to the recipient, especially when this person has other problems that led to his hospitalization in the ICU.[10,11] Due to the dangers of transfusion, there is emergency need for alternative treatment for anemia in severe patients. Erythropoietin treatment in severe patients increases erythropoietin and results in high levels of hemoglobin and finally reduced transfusion.[12-15] The aim of this study was to evaluate the efficacy of erythropoietin in the treatment of anemia in ICU patients in Ardabil.

METHODS

This is a clinical trial study conducted at ICU in Ardabil hospitals. A total of 70 patients hospitalized in the ICU were selected and randomly divided into two similar groups. To the first group in addition to iron, erythropoietin was also prescribed, and only iron was given to the second group (control group). 100mg iron was prescribed for all patients. For the case group in the state of a decrease in Hb levels less than 12g/dL for three times 40,000 units of erythropoietin were injected weekly. In the case of hemoglobin less than 8mg/dL in non-cardiac patients and hemoglobin less than 10mg/dL in patients with heart disease (ischemic) blood were also prescribed for patients. At the end of study, blood indices and clinical status of the patient were evaluated at the end of the study. Required information including demographic information, cause and duration of hospitalization in ICU, history of transfusion, cause of need for blood transfusion, time and dose of receiving erythropoietin, blood parameters before and after receiving erythropoietin and patient's clinical condition after receiving erythropoietin was extracted through a checklist. Data were analyzed by statistical methods in SPSS version 19. In all tests the level of significance was less than 0.05.

Inclusion and exclusion criteria

Patients aged 18 years and above, Hematocrit less than 38% and hospitalization in ICU for more than 7 days were enrolled in the study. Patients with uncontrolled hypertension, uncontrolled seizures, burn grade 3 and higher, pregnancy or lactation, dialysis patients, pulmonary embolism, DVT and chronic hypercoagulopathy were excluded from the study. The study was conducted after approval at the university's ethics committee.

RESULTS

In this study, 65.7% of the case group and 71.4% of the control group were male and the rest of them were female. The mean age of the patients in the case group was 61.62±20.8 and in the control group was 61.02±22.5 years (Table 1).

Table 1: Clinical characteristics of patients in two study group.

Groups / Variables		Case		Control	
		n	%	n	%
sex	m	23	65.7	25	71.4
	f	12	34.3	10	28.6
Age	>70	19	54.3	17	48.6
	<=70	16	45.7	18	51.4
Mean of age		61.62±20.8		61.02±22.5	
Mean of hospitalization		32.2±21.7		30.2±21.5	
RH+	+	29	82.9	27	77.1
	-	6	17.1	8	22.9
History of heart disease	+	24	68.6	21	60
	-	11	31.4	14	40
Blood type o	+	14	40	15	42.9
	-	21	60	20	57.1
History of transfusion	+	9	25.7	7	20
	-	26	74.3	28	80
Need for transfusion	+	28	80	31	88.6
	-	7	20	4	11.4

The mean of injected blood in patients receiving blood in the case group was 5.8±1.8 and 6.3±2.9 in the control group.13 patients in the case group were between 3 to 6 units and 15 patients in the control group received 7-9 blood units. The most common cause of blood transfusion was acute anemia in both groups. In the case group, 24 patients (68.6%) and in the control group, 25 patients (71.4%) survived until the ICU discharged and the end of the study. In term of complications of erythropoietin injection, we observed that none of the patients in the case group hadn't complications. The results showed no significant difference in the experimental results of the patients at the beginning of the study (Table 2).

Table 2: The results of experimental finding in patients in baseline.

Variables		Case	Control	p-value
Hb	Case	10/78	1/92	0/558
	Control	11/03	1/71	
Hematocrit	Case	30/80	5/98	0/444
	Control	31/86	5/50	
Platelet	Case	315000	95000	0/318
	Control	285000	84000	
Iron	Case	52/3	32/5	0/337
	Control	48/7	28/5	
Ferritin	Case	668/5	317/5	0/290
	Control	721/4	468/7	
BUN	Case	66/65	43/04	0/853
	Control	68/5	41/6	
Cr	Case	1/54	1/12	0/834
	Control	1/62	1/16	

The results showed that, there was no significant increase in hemoglobin and Hematocrit levels after receiving erythropoietin in the case group compare to control group (Table 3). Hemoglobin levels in the case group at the end of the study was significantly higher than the baseline but in the Hematocrit level the difference wasn't significant (Table 4).

Table 3: Hb and Hematocrit of patients after drug receiving.

Variables		Case	Control	p-value
Hb	Case	11/95	1/50	0/105
	Control	11/40	1/26	
Hematocrit	Case	35/07	4/54	0/074
	Control	33/25	3/79	

Table 4: Compare the Hb of patients in two groups in the end of study compare to base line.

Variables		Case	Control	p-value
Case	Baseline	10/78	1/92	0/006
	End of study	11/95	1/50	
Control	Baseline	11/03	1/71	0/307
	End of study	11/40	1/26	

DISCUSSION

Anemia is a common problem in ICU patients who increase their illness and mortality.[2] In this study, the mean of hospital stay was 37.73 days in ICU and 21.35 days in surgery ICU. Also, it was observed that hemoglobin level in internal patients at the beginning of the study was lower than surgical patients (P=0.023) and the increase in hemoglobin level in internal patients was significantly higher than patients undergoing surgery (P=0.001). In a study by Corwin et al [16] there was no significant correlation between the duration of hospitalization in ICU between traumatic and non traumatic patients after receiving erythropoietin (P=0.43). In Georgopoulos et al study[13], the duration of hospitalization in ICU in the control group was 21.8 days and, in the group, receiving erythropoietin (once daily) was 21 days and in the recipient of erythropoietin (three times a day) was 19.6 days but this difference wasn't significant. In the study of van Iperen and et al, the mean duration of hospitalization in ICU was 37 days in erythropoietin recipients and 58 days in placebo and this difference was statistically significant (P=0.03).[6]

In this study, 80% of patients in the case group and 88.57% in the control group needed to blood transfusion. The mean of need for transfusion in case group was 5.8±1.8 and in the control group was 3.6±2.9 and it was found that erythropoietin could not reduce the number of recipients and the number of P/C units. Studies done elsewhere is in line with the study results.[6,17,18] There were also conflicting studies with our study and had adverse results.[13,19,20]

The reason for the lack of correlation between the numbers of transfusions with erythropoietin injection in this study can be due to: 1) transfusion at higher levels of hemoglobin 2) the most common cause of bleeding and acute anemia among patients and other factors.

In this study, 68.6% of patients in the case group and 71.4% of the patients in the control group survived to the end of the study and discharge from the ICU and there was no difference in the prognosis of the disease between the two groups. The present study showed that there is no correlation between the prognosis of patients admitted to ICU and erythropoietin administration which in line with our study results.[12-14,19,20]

A number of studies have also shown that injectable erythropoietin could improve the prognosis of patients.[19,21] In the following study the prognosis of patients was different for different reasons and authors can't said that erythropoietin can interfere with patient's prognosis which most studies have confirmed.

In this study, there was no significant difference in the level of hemoglobin between two groups at the time of admission and at the end of the study. It was observed that hemoglobin level was significantly increased in the erythropoietin recipient group (P=0.006) that this increase wasn't observed in the control group. The results of this study are in line with other studies[12-14,17,19,21]

In this study, no significant difference was found between the hemoglobin in the case and control groups which can be related to the more transfusion in these patients but in summary erythropoietin could be increase hemoglobin levels in recipients.

CONCLUSION

The results of this study showed that erythropoietin is effective drug for increasing hemoglobin levels and can increase the hemoglobin level in compare to the placebo.

It is suggested that another study has been done to evaluate the level of hemoglobin in patients with chronic underlying illness in the future in a larger population.

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