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Kardiyak Cerrahi Geçiren Hastalarda Preoperatif Aneminin Etkisi

The Impact of Preoperative Anemia in Patients Undergoing Cardiac Surgery

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ÖZ

GİRİŞ ve AMAÇ: *Kalp cerrahisi hastalarında preoperatif anemi insidansı ortalama %26 olup maksimum %30'a ulaşmaktadır. Bu çalışmada kalp cerrahisi geçiren hastalarda preoperatif anemi insidansının, mortalite ve perioperatif komplikasyonlar ile ilişkisini değerlendirmeyi amaçladık.*

YÖNTEM ve GEREÇLER: *İskemik kalp hastalığı nedeniyle koroner bypass ameliyatı geçiren erişkin hastalar çalışmaya dahil edildi. Hastaların demografik özellikleri, kardiyak rezervleri, ameliyat öncesi ve sonrası Hemotokrit değerleri, transfüzyon hacmi, komplikasyonlar ve mortalite oranları kaydedildi. Diğer laboratuvar testleri, yapılan cerrahi ameliyat, re-eksplorasyon sıklığı, yoğun bakım ve hastanede kalış süresi kaydedildi.*

BULGULAR: *Bu çalışmada 333 hastanın verileri değerlendirildi. Anemi insidansı %43 idi. Hastaların %80'i kan transfüzyonu aldı ve transfüzyonların %75'i anemik gruptaydı. Perioperatif kanama miktarı 715,7 ± 452,3 mL idi ve ortalama kanama miktarı anemik grupta anlamlı derecede yüksekti (p = 0,000). Dokuz hasta re-eksplorasyon geçirdi. Anemik grupta Taze Donmuş Plazma kullanımı daha yüksekti (p=0,019). Gruplar arasında mortalite, drenaj, hastanede kalış ve mortalite bakımından fark yoktu.*

TARTIŞMA ve SONUÇ: *Çalışmamızda preoperatif dönemde anemi insidansı yüksek bulundu. Komplikasyonlarda artış olmamasına rağmen, kan transfüzyonu ile ilişkili riskler mevcuttur. Sonuç olarak preoperatif anemi konusunda farkındalığın artırılması gerektiğine inanmaktayız.*

Anahtar Kelimeler: *anemi, kardiyak cerrahi, mortalite*

ABSTRACT

INTRODUCTION: *The incidence of preoperative anemia in cardiac surgery patients was found to be 26% on average, up to a maximum of 30%. In this study, we aimed to evaluate the relationship between preoperative anemia incidence, mortality and perioperative complications in patients undergoing cardiac surgery.*

METHODS: *Adult patients undergoing coronary bypass surgery due to ischemic heart disease were included. Patient demographics, cardiac reserves, preoperative and postoperative Hemotocrit values, transfusion volume, complications and mortality rates were recorded. Other laboratory tests, type of surgery, re-exploration frequency, intensive care and hospital stay were recorded.*

RESULTS: *The data of 333 patients were evaluated in this study. The incidence of anemia was 43%. Eighty percent of patients received transfusion and 75% of blood transfusions were in anemic group. Perioperative bleeding amount was 715.7±452.3 mL, and the mean amount of bleeding was significantly higher in anemic group (p=0.000). Nine patients were reexplored. The use of Fresh Frozen Plasm in anemic group was higher (p=0.019). There was no difference between groups in terms of mortality, drainage, hospital stay and mortality.*

DISCUSSION AND CONCLUSION: *The incidence of anemia in the preoperative period was found high. Although our study did not lead to an increase in complications, the risks associated with blood transfusion exists. We believe that the awareness of preoperative anemia should be increased.*

Keywords: *anemia, cardiac surgery, mortality*

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INTRODUCTION

Preoperative anemia is a risk factor for transfusion of blood and blood products in patients undergoing cardiac surgery. There are three major risk factors for development of preoperative anemia in cardiac surgery patients: hospital-acquired anemia, iron deficiency anemia, and anemia of chronic disease (1). All these factors are preventable and treatable causes. A multi-center cohort study showed the mean incidence of preoperative anemia in cardiac surgery patients to be 26%, upper limit being 30% (2). In another study of elective vascular surgery patients, preoperative anemia incidence was reported to be 47% while the risk for mortality and cardiac events was 2.4% in these patients (3). The number of studies carried out on cardiac surgery patients in this regard are limited and were performed with small populations (4-6). Patients, who have coronary artery bypass graft (CABG) surgery, generally have severely limited cardiac reserves. For this reason, such patients are relatively sensitive to low hemoglobin levels. Our hypothesis in this study is that the incidence of preoperative anemia may be high in patients undergoing cardiac surgery and that such a high incidence rate may be associated with mortality and perioperative complications. In the light of the results of this study, we believe that awareness on preoperative anemia can be increased; elective patients can be taken under surgery after preoperative anemia treatment; and thus, the requirement for blood and blood product transfusion and transfusion-related complications can be reduced. We aimed to evaluate the association of preoperative anemia incidence with mortality and perioperative complications in patients undergoing cardiac surgery.

MATERIAL AND METHODS

Following the approval of the ethics committee, patients over 18 years of age, who underwent open heart surgery with Cardiopulmonary Bypass (CPB) at our center between 2014 and 2017 because of ischemic heart disease (IHD) and/or heart valve disease, were included in the study. Patients' demographic data, cardiac reserves, preoperative and postoperative complete blood count (CBC), anticoagulant drug use, rate of blood and blood product transfusions and complications, and mortality rates were recorded. Additionally, other laboratory tests, surgery type, re-exploration, length of stay at hospital and intensive care unit (ICU), and causes of death were determined and noted.

We divided patients into two groups: patients with anemia (n=100) and patients without anemia (n=233). According to the World Health Organization (WHO), anemia is defined as a hemoglobin level less than 12 g/dL in women and less than 13.0 g/dL in men (7). We took these reference levels into consideration for diagnosis of preoperative anemia in our study.

If a patient had a history of multiple surgeries, only the data of the first surgery was taken into consideration. Exclusion criteria were as follows: emergency surgery, age under 18 years, known bleeding disorder(s), renal insufficiency, liver insufficiency or congestive heart failure, history of heart transplantation, presence of a left ventricle assist device system, and surgeries, such as congenital heart defect corrective surgery. Deep vein thrombosis (DVT), stroke, and re-operation were considered as postoperative complications.

Statistical Analysis

The SPSS 22.0 program was used for the analysis of the study data. The descriptive statistics employed in the study were mean, standard deviation, median, minimum, maximum, frequency, and ratio. The Kolmogorov-Smirnov test was used to measure the distribution of variables. The Mann-Whitney U test was used to analyze quantitative independent data while the Chi-square test was used to assess the qualitative independent data. In cases where the Chi-square conditions were not met, the Fisher test was used for the qualitative data. A value of $P<0.05$ was considered statistically significant.

RESULTS

In total the data of 333 patients were evaluated. The incidence of anemia was 43%. There was no significant difference between the two groups in terms of demographics, duration and type of surgery, CPB time, mortality, hospital and ICU stay, drainage, reexploration and mortality rate ($P>0.05$, Table 1). There were 100 patients with anemia and 233 patients without anemia (Table 1).

There was no significant difference between anemic and non-anemic patients regarding the amount of red blood cell (RBC), platelet (PLT) and cryoprecipitate transfusions ($P>0.05$, Table 2). 265

patients received RBC transfusions (79.6%) and 75% of blood transfusions were found in the anemic group compared to the RBC transfusions in the non anemic group and 89% in the anemia group (P=0.005, Table 1,2). The use of fresh frozen plasma (FFP) in the anemic group was higher than in nonanemic patients (60.0%, 45.9%, respectively, P=0.019, Table 2).

Table 1: The Analysis of Demographics, Duration and Type of Surgery, Cardiopulmonary Bypass Time, Cross Clamp Time, Hospital and Intensive Care Unit Stay, Drainage, Reexploration, Complication and Mortality Rate

		min-max			median	mean±sd/n(%)		
Age (years)		37.0	-	89.0	64.0	64.3	±	10.0
Gender	Female					57		17.1%
	Male					276		82.9%
BMI		22.5	-	31.6	26.0	26.6	±	1.9
Duration of surgery (min)		25.0	-	300.0	210.0	217.1	±	35.0
CPB time		25.0	-	220.0	80.0	84.7	±	21.8
CX time		10.0	-	135.0	65.0	64.8	±	18.6
Drainage in ICU (mL)		150.0	-	2500.0	450.0	446.1	±	254.7
Stay in ICU	1 day					271		81.4%
	≥ 2 days					62		18.6%
Stay in hospital	7 days					259		77.8%
	8 days					72		21.6%
Mortality rate	(-)					331		99.4%
	(+)					2		0.6%
RBC		1.0	-	10.0	2.0	2.9	±	1.7
RBC	Not transfused					43		12.9%
	Transfused					290		87.1%
FFP		1.0	-	56.0	2.0	3,7	±	5.9
FFP	Not transfused					166		49.8%
	Transfused					167		50.2%
Platelet		2.0	-	124.0	16.0	29.3	±	30.0
Platelet	Not transfused					285		85.6%
	Transfused					48		14.4%
Cryopresipitate	Not transfused					327		98.2%
	Transfused					6		1.8%
Perioperative bleeding (mL)		100.0	-	3400.0	600.0	715.7	±	452.3
EF (%)		38.0	-	60.0	50.0	50.7	±	5.1
Postoperative DVT	(-)					333		100.0%
	(+)					0		0.0%
Postoperative stroke	(-)					333		100.0%
	(+)					0		0.0%
Reexploration	(-)					324		97.3%
	(+)					9		2.7%

BMI: Body Mass Index, CPB: Cardiopulmonary Bypass, CX: Cross clamp, ICU: Intensive Care Unit, RBC: Red Blood Cell, FFP: Fresh Frozen Plasm, EF: Ejection Fraction, DVT: Deep Vein Thrombosis

Table 2: The Comparison of Anemic and Non-Anemic Patients Undergoing Cardiac Surgery

		Anemia (-)				Anemia(+)				p	
		mean±sd/n-%			Median	mean±sd/n-%			Median		
Age (years)		63,9	±	10,2	64,0	65,2	±	9,6	64,5	0,251	m
Gender	Female	44		18,9%		13		13,0%		0,191	x^2
	Male	189		81,1%		87		87,0%			
BMI		26,6	±	1,9	26,0	26,6	±	1,7	26,0	0,914	m
Duration of surgery		215,6	±	36,0	210,0	220,5	±	32,6	210,0	0,464	m
CPB time		84,6	±	20,5	80,0	84,9	±	24,7	80,0	0,892	m
CX time		64,9	±	18,8	65,0	64,7	±	18,4	67,5	0,993	m
Drainage in ICU (mL)		442,1	±	272,4	450,0	455,6	±	208,6	450,0	0,166	m
Stay in ICU (days)	1 day	186		79,8%		85		85,0%		0,266	x^2
	≥ 2 days	47		20,2%		15		15,0%			
Stay in hospital (days)	7 days	181		77,7%		78		78,0%		0,943	x^2
	8 days	50		21,5%		22		22,0%			
Mortality rate	(-)	231		99,1%		100		100,0%		1,000	x^2
	(+)	2		0,9%		0		0,0%			
RBC		2,9	±	1,8	2,0	2,9	±	1,7	2,0	0,593	m
RBC	-	32		13,7%		11		11,0%		0,495	x^2
	+	201		86,3%		89		89,0%			
FFP		3,9	±	6,5	2,0	3,3	±	4,8	2,0	0,056	m
FFP	-	126		54,1%		40		40,0%		***0,019***	x^2
	+	107		45,9%		60		60,0%			
Platelet		28,5	±	29,4	16,0	31,1	±	32,1	16,0	0,991	m
Platelet	-	200		85,8%		85		85,0%		0,842	x^2
	+	33		14,2%		15		15,0%			
CRYO	-	229		98,3%		98		98,0%		1,000	x^2
	+	4		1,7%		2		2,0%			
Perioperative bleeding (mL)		766,7	±	456,7	680,0	596,8	±	420,7	500,0	***0,000***	m
EF (%)		50,7	±	5,1	50,0	50,9	±	5,3	50,0	0,766	m
Postoperative DVT	(-)	233		100,0%		100		100,0%		-	
	(+)	0		0,0%		0		0,0%			
Postoperative stroke	(-)	233		100,0%		100		100,0%		-	
	(+)	0		0,0%		0		0,0%			
Reexploration	(-)	226		97,0%		98		98,0%		0,604	x^2
	(+)	7		3,0%		2		2,0%			

m Mann-whitney u test / x^2 Ki-kare test

BMI: Body Mass Index, CPB: Cardiopulmonary Bypass, CX: Cross clamp, ICU: Intensive Care Unit, RBC: Red Blood Cell, FFP: Fresh Frozen Plasm, EF: Ejection Fraction, DVT: Deep Vein Thrombosis

Perioperative bleeding ranged from 100 mL to 3400 mL with a mean of 715.7±452.3 mL, and the mean amount of bleeding was significantly higher in the anemic group than in the non-anemic group (P=0.000). Postoperative Hb, Htc and platelet values decreased at the end of the surgery compared to preoperative values in all patients. Statistically significant increase in creatinine values was detected (P<0.005, Table 3). Nine patients were reexplored.

Table 3: Comparison of anemic and non-anemic patients in terms of Hemoglobin, Hematocrit, creatinine and platelet count.

	Anemia (-)				Anemia (+)				p	
	mean±sd			Median	mean±sd			Median		
Hemoglobin (g/dL)										
Preoperative	14,3	±	1,1	14,3	11,5	±	1,0	11,6	***0,000***	m
Postoperative	10,5	±	1,1	10,4	10,6	±	1,2	10,4	0,781	m
Pre/Post Change rate (p)		***0,000***		w		***0,000***		w		
Hematocrit (%)										
Preoperative	41,2	±	3,0	40,8	34,1	±	3,1	34,6	***0,000***	m
Postoperative	30,4	±	3,0	30,2	30,9	±	3,3	30,9	0,223	m
Pre/Post Change rate (p)		***0,000***		w		***0,000***		w		
Creatinine (mg/dL)										
Preoperative	1,0	±	0,5	0,9	1,6	±	3,5	1,0	***0,042***	m
Postoperative	1,1	±	0,3	1,0	1,3	±	0,9	1,1	***0,002***	m
Pre/Post Change rate (p)		***0,000***		w		***0,000***		w		
Platelet count (x10^9/L)										
Preoperative	237,3	±	63,4	229,0	260,0	±	97,5	245,0	0,121	m
Postoperative	186,9	±	65,0	179,0	203,4	±	74,3	192,0	0,055	m
Pre/Post Change rate (p)		***0,000***		w		***0,000***		w		

m Mann-whitney u test / w Wilcoxon test

DISCUSSION

In this study, we retrospectively analyzed patients undergoing coronary artery bypass grafting with CPB and detected preoperative anemia in 43% of the patients. A significant rise was observed in the amount of intraoperative bleeding among this relatively higher number of patients with anemia, and they showed increased need for FFP transfusion.

Preoperative anemia has been associated with increased morbidity and mortality in major surgical procedures. This is mainly due to the cardiovascular risk factors of this patient population (8). Patients with congestive heart failure were excluded from our study because heart failure is associated with pathological conditions, such as iron deficiency, impaired erythropoietin production, blurred erythropoietin response, and renal insufficiency (9). Additionally, anemia-induced peripheral vasodilatation activates the renin-angiotensin-aldosterone system and further compromises the current state by leading to volume expansion in patients with heart failure (10).

The incidence of preoperative anemia was 43% in this study. Although regarded high in general, this figure is lower than the rates stated in some studies in the literature. Hung et al8. reported the incidence to be 54.4% in their study involving 2,688 patients. They reported increased transfusion rate among patients with anemia and associated anemia with higher mortality and prolonged ICU stay. Another study stated the incidence of anemia as 52% in patients undergoing cardiac surgery for rheumatic heart disease (11). The incidence of mild anemia was 33.15% and of moderate anemia was 18.80% in those patients.

In a study evaluating a total of 182.599 patients, who underwent primary isolated on-pump CABG, associated anemia with a 22% increase in the odds of postoperative renal failure and a 10% increase in the risk of deep sternal wound infection (12). The same

study demonstrated that each 5-point decrease in preoperative Htc was associated with 8% higher odds of death. That study and other previous studies stated preoperative Hb concentration to be is an independent risk factor for mortality (13,14). Contrary to the majority of studies, mortality rates in our study, in which two patients lost their lives, did not differ between anemic and non-anemic groups. However, it is clear that this rate can chance if we increase the patient number. Similarly, another study analyzing 10,025 patients who underwent CABG indicated that preoperative Hb concentration is an independent risk factor for postoperative mortality.

It is still not clear if correcting preoperative anemia in patients undergoing cardiac surgery can improve outcomes and reduce the risk for elevated perioperative transfusion. The recommended method for these patients is early diagnosis and the use of erythropoietin or iron preparations (15-17). However, there is a need for further comparative studies on this matter.

In this study, intraoperative bleeding was observed to be higher in patients with anemia. Nevertheless, although there was no difference between the groups regarding their requirement for RBC or cryoprecipitate transfusion, patients with anemia had higher need for FFP transfusion. The main reason for this higher need is that we applied the strategy of restrictive blood transfusion in our patients. We aimed to maintain the Hb concentration at a level of 7-9 g/dL as recommended by the guidelines (18). One of the main reasons for the increased FFP transfusions was that patients, who underwent CABG surgery in our clinic, were taking high-level vitamin K antagonists, and thus, and it was necessary to use FFP to reserve the effect of these antagonists. Moreover, the absence of increase in blood transfusions other than FFP can explain the reason why there was no rise in mortality.

We observed a significant elevation in creatinine levels of patients with anemia. Acute kidney injury is an important prognostic factor for complications of cardiac surgery (19). This complication, which is seen in 30% of patients, is closely associated with morbidity and mortality both in short- and long-term (20). In our study, preoperative serum creatinine levels were compared between patients with and without anemia, and a significant difference was detected between the groups (1.6±3.5 vs. 1.0±0.5, respectively; P=0.042). Furthermore, the values of the patients with anemia were significantly higher in the postoperative period.

Limitations

One of the major limitations of this study was its retrospective design and limited patient number, resulting from single-center characteristic. For this reason, although we were able to indicate the incidence of anemia in preoperative period among patients, who underwent cardiac surgery, no data could be obtained on the subtypes of anemia. Also, we were not able to analyze the effects of the use of anticoagulants on the need for blood and blood product transfusion.

Conclusion

Despite recommendations of current guidelines and the results of observational studies, the incidence of anemia remains high in cardiac surgery patients. In these major surgeries, patients with anemia are faced with the risk of increased perioperative bleeding, increased requirement for blood product transfusion, and deteriorated renal functions. We, therefore, conclude that it is necessary to optimize preoperative hematocrit values.

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