

Blood Transfusion Practice in a Referral Cardiovascular Center in Tehran, Iran: A Critical Point of View

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Received: July 5, 2014; Revised: August 25, 2014; Accepted: September 4, 2014

Background: Unnecessary perioperative transfusions are likely to be related to increased morbidity and additional costs in cardiac surgery.

Objectives: The aim of this study was to evaluate the blood transfusion practice during and after adult cardiac surgery in a referral university hospital in Iran.

Patients and Methods: In a descriptive study, we collected data from 153 adult patients underwent cardiac surgery at Rajaie Cardiovascular Medical and Research Center, Tehran, Iran from January to March 2013. The variables were patients' demographic, operative and post-operative data and the numbers of transfused packed red blood cell (PC) units and fresh frozen plasma (FFP) during and after cardiac surgery. Then we evaluated patients' and physicians' related causes of relatively increased transfusion rate in our patients and compared them with literature.

Results: Of 153 patients, 96.8% received PC and 54.9% transfused FFP during or after surgery. Most of the transfusions were done after operation in intensive care unit (ICU). Also, 20% and 17% of the patients underwent transfusion of more than 6 units of PC and FFP, respectively. The mean left ventricular ejection fraction of the patients was $42.5 \pm 10.9\%$. A significant number of patients had anemia (especially women) or received anticoagulants or antiplatelet agents preoperatively. Thirteen percent of the patients underwent emergency operations and 12.3% had re-exploration.

Conclusions: The results of this study demonstrate that the cardiac surgery patients receive a relatively greater number of PC or FFP units during and after the operation in our center. This finding may be explained to some extent by the fact that the sicker and more co-morbid patients referred to our center and such patients are more anemic and undergoing more emergent and complex procedures. Moreover, Transfusion strategy or protocol should be updated, especially after the operation in ICU.

Keywords: Blood Transfusion; Fresh Frozen Plasma; Cardiac Surgical Procedures; Practice Guideline

1. Background

Transfusion of red blood cells is an essential part of medical care, which if it is used correctly can be life-saving (1). Correct use of blood transfusions means using red blood cells only for the prevention of mortality in patients who cannot be saved with other methods except with blood transfusion (1). About 85 million red blood cell units are transfused annually worldwide, and 10-20% of total units are transferred during cardiac surgeries (2, 3). Anemia is less-tolerated in older patients and in cases with coronary artery disease undergoing the coronary artery bypass graft surgery (CABG) (4). Transfusion of red blood cells may increase tissue oxygenation in patients with coronary artery disease (5). However, unnecessary transfusions are likely to be related to unnecessary morbidity and additional indirect hospitalization costs (6). Blood transfusion can be associated with a risk for infection and transfusion reactions such as fever, anaphylactic

shock, acute pulmonary edema, viral and bacterial infections, which may occur during transfusion, 24 hours or even years after transfusion (7, 8). Therefore, whether the benefits are greater than the risks associated with transfusion of red blood cells in anemic stable patients during vascular surgery is not known (6). Many guidelines tried to provide uniform insight and approaches to maximize benefits and minimize risks of blood and plasma transfusion practice (9-11). However, according to different population characteristics and referral pattern of high-risk patients to tertiary-university based-hospitals in developing countries such as Iran; the "blood transfusion practice" and statistics of transfused blood products may be somehow different from developed countries.

2. Objectives

The aim of this study was to critically *appraise* the blood

and plasma transfusion practice in adult patients undergoing cardiac surgery at a referral university cardiovascular hospital.

3. Patients and Methods

After approval of the study protocol by the institutional review board, this descriptive study was conducted at Rajaie Cardiovascular Medical and Research center- a referral university hospital- in Tehran, Iran. This hospital is the largest cardiovascular center in the Middle East region in which up to 4500 cardiac operations performed annually. One hundred fifty-three adult patients who underwent CABG, or valvular surgery or both from January to March 2012 and admitted to one of the ICUs afterwards were enrolled. The patients who died 6 hours after ICU admission were excluded from the study. The clinical data of the patients were reviewed and the required data including demographic data (age, gender, history of hypertension, diabetes mellitus (DM), renal disease, chronic obstructive pulmonary disease, liver disease, history of smoking, drug history (such as: aspirin, warfarin, heparin or clopidogrel), and ejection fraction, pre-operative laboratory data such as hemoglobin (Hb), hematocrit (Hct), prothrombin time, partial thromboplastin time, blood urea nitrogen, serum creatinine, platelets count, operation data, post-operative laboratory data including Hb, Hct, PT, PTT, Plt, BUN, creatinine, the amount of blood loss after surgery and duration of ICU stay were collected and the correlation of the above-mentioned variables with the independent variable of blood transfusion requirement during and after the surgery was also evaluated. We recorded the number of transfused units of packed cell (PC) and fresh frozen plasma (FFP) during and after cardiac operations, separately.

The collected data were entered into SPSS for Windows v. 22 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were used to explain what's going on in our data. Clinical data are expressed as mean \pm SD for the quantitative and number (percentage) for qualitative values.

4. Results

In this study, 153 patients (86 male patients, 56.2% and 67 female cases, 43.8%) with mean age of 56.3 ± 14.9 years were enrolled. Of 153 patients, 84 (54.9%) underwent CABG, 53 (34.6%) valve surgery and 16 (10.5%) patients had CABG plus valve operation. The patients background characteristics and clinical data were summarized in Table 1. As showed in Table 1, our patients are mainly middle-aged (56.3 ± 14.9 years old), partially anemic, especially in women (Hb = 11.6 ± 2.0 mg/dL) and have moderately reduced left ventricular function (LVEF = $42.5 \pm 10.9\%$).

Nearly one third of our patients had the cardiovascular risk factors such as DM and hypertension and one fourth of them underwent emergency operations. Our patients experienced a relatively higher frequency of re-exploration (12.3%) mainly secondary to excessive post-operative bleeding or unexplained hypotension in early postoperative

period. Hematologic profile and coagulation related drug history of the patients presented in Table 2. Nearly all of patients scheduled for CABG surgery taking aspirin and 11.3% of all patients received Clopidogrel before transferring to operating room (OR). In Table 3 the number of transfused PC units during and after the surgery and also the total number of transfused PCs were illustrated. Nearly half of the patients didn't receive any blood in OR, but most of them underwent PC transfusion in ICU, and finally, only 3.2% of the patients remained un-transfused. Only two patients (0.13%) received more than 6 units of PC during operation while 22 patients (14.4%) had transfusion ≥ 6 units in post-op. period. Table 3 also shows the pattern of FFP transfusion during and after cardiac surgery and demonstrates that most of FFP transfusion was done in ICU.

Table 1. Background and Clinical Characteristics of Patients According to Sex Distribution (n = 153)

Variables	Descriptive Index ^a
Age, y	56.3 \pm 14.9
Weight, kg	69.3 \pm 10.4
Body surface area, m ²	1.78 \pm 0.15
Diabetes mellitus	42 (27.1)
Hypertension	52 (33.3)
Cigarette smoking	37 (23.9)
Emergency operation	20 (13.1)
Left Ventricular Ejection Fraction	42.5 \pm 10.9
Renal disease	13 (8.4)
Blood urea nitrogen, mg/dL	20.6 \pm 12.2
Creatinine, mg/dL	1.16 \pm 0.41
Re-exploration	19 (12.3)

^a Data are presented as mean \pm SD or No. (%).

Table 2. Hematologic and Coagulation Parameters of the Patients (n=153)

Variables	Descriptive Index ^a
Hemoglobin, mg/dL	12.8 \pm 1.8
Hematocrit, %	37.3 \pm 4.7
Platelet, 1000/mL	228 \pm 66
Prothrombin time, s	13.8 \pm 1.5
Partial thromboplastin time, s	30.1 \pm 6.9
Bleeding time, s	103 \pm 51
Clotting time, s	60 \pm 35
Heparin	3 (1.9)
Warfarin	18 (11.6)
Aspirin	74 (47.7)
Clopidogrel	17 (11.3)
Postoperative Bleeding, mL	786 \pm 681
Postoperative Hemoglobin, mg/dL	9.2 \pm 1.3
Postoperative Hematocrit, %	27.3 \pm 4.6
Postoperative Platelet, 1000/mL	158 \pm 47.0

^a Data are presented as mean \pm SD or No. (%).

Table 3. Number of Transfused Blood and Fresh Frozen Plasma Units in Operating Room and After Cardiac Operation in Intensive Care Unit ^a

Location of transfusion	Units, No. (%)						
	0	1	2	3	4	5	≥ 6
Blood							
Operating room	58 (37.4)	28 (18.1)	40 (25.8)	21 (13.5)	6 (3.9)	0	2 (0.13)
ICU	25 (16.1)	46 (29.7)	33 (21.3)	16 (10.3)	5 (3.2)	8 (5.2)	22 (14.4)
Total	5 (3.2)	29 (18.9)	33 (21.5)	22 (14.4)	21 (13.7)	14 (9.2)	31 (20.3)
FFP							
Operating room	110 (71.9)	10 (6.5)	11 (7.2)	17 (11.1)	1 (0.7)	1 (0.7)	3 (2.1)
Total	87 (56.1)	1 (0.7)	18 (11.6)	10 (6.5)	11 (7.1)	8 (5.2)	20 (13.0)
FFP	69 (45.1)	3 (2)	19 (12.4)	18 (11.8)	7 (4.6)	11 (7.2)	26 (17.1)

^a Abbreviations: FFP, fresh frozen plasma; ICU, intensive care unit.

5. Discussion

In this study we found that a high percent of cardiac surgery patients in our hospital received blood products such as PC and FFP; therefore, only 3.2% of our patients didn't take blood and 45% of those didn't receive FFP in peri-operative period. Also, a significant number of patients underwent a transfusion of more than 6 units of PC (20% of patients) or FFP (17% of patients). We transfused more PCs in our patients in comparison with Ferrari's study (9) and partially fewer FFPs compared with Mustafa's study in Turkey.

The referral pattern of our patients may be partially different from other studies because our center is a tertiary university-based governmental hospital that admits mainly the sophisticated and high risk patients with various co-morbidities from other centers or cities across the country. For example in Warwick et al. study (12), only 31.4% of the patients have the moderate left ventricular systolic dysfunction, while in our study mean LVEF of our patients was $42.5 \pm 10.9\%$ (i.e. half of patients have $LVEF \leq 42.5\%$).

Another reason for the elevated transfusion rate in our patients may be the higher rate of anemia in our patients (mean Hb levels were 13.3 ± 1.7 mg/dL in men, 11.6 ± 2.0 mg/dL in women and 12.8 ± 1.8 mg/dL in all patients). Alizadehasl et al. reported that 24.2% of the Iranian cardiovascular patients are anemic according to the WHO criteria (13). The lower preoperative Hct increases the probability of transfusion, for example Williams and colleagues reported that 88.5% of patients who have $Hct < 33\%$ received peri-operative blood transfusion (14). The mean Hct in our patients was $37.3 \pm 4.7\%$ and 96.5% of the patients had peri-operative PC transfusion that is relatively higher than Williams' study. In a study in the USA, Shaw and co-workers in 2013 reported the incidence of $Hct < 36\%$ in about one third of CABG patients; of $Hct < 36\%$ patients, 79.1% received blood transfusion (15).

In evaluating of the relatively higher transfusion rate in our hospital, other causes are related to physicians' practice including cardiologist, surgeon and anesthesiologist.

We have not any pre-donation protocol in our center. Preoperative visit with surgeon or anesthesiologist (16) can detect and correct preoperative anemia with iron tablets (17) or erythropoietin (18). Also we didn't use an acute normo-volumic dilution (ANH) technique during operation. Some studies showed a reduction of allogeneic blood and FFP transfusion in cardiac surgery patients by the ANH method (19, 20). We usually use the cell saver when it is available.

The other possible cause of the increased rate of transfusion in our patients is high rate of re-exploration (12.3%) for bleeding or tamponade after the first main operation. In our hospital, Yazdani et al. (21) in 2013 reported the rate of re-exploration 9.2% in 972 adults undergoing cardiac surgeries (all types). Canadyova et al. in 2012 in Czech Republic showed the rate of 3.4% re-exploration after cardiac surgery (all types) (22); of these patients 72.4% re-operated due to bleeding, 23.7% because of tamponade and 5.9% owing to both of them. Sabzi et al. (23) in 2013 in Kermanshah (Iran) reported the rate of 10.7% re-exploration in 1489 cardiac patients. Our data are similar to Sabzi's finding (23); however, comparing to Canadyova's study (22), the rate of re-exploration is quite high in our center and it mainly related to the fact that: 1) our center is an educational center; and 2) there is higher rate of the emergent cases; 3) there is higher of clopidogrel use.

In present study, 13.1% of the patients underwent emergency operations. Most of these patients took anticoagulant (heparin or warfarin) or antiplatelet (Aspirin, Clopidogrel) agents and these drugs increase the risk of operative bleeding and blood product transfusion. Generally, of 153 studied patients 11.6% received Warfarin and 11.3% used Clopidogrel before the operation. Majority of these patients are at high risk of bleeding followed by blood transfusion. Rahmanian et al. in 2013 reported the rate of emergency surgery 9.29% in 5318 (all types) cardiac surgery patients in the University Hospital Cologne in Germany (24).

In our study, 45.1% of patients didn't take FFP during or after the operation. Gokalp and colleagues (25) in 2011 found that in patients who underwent CABG 24.4% (19/72) didn't receive blood and 61.1% (28/72) didn't take FFP, while in Ulas et al. (26) in 2010 in Turkey only 2% of cardiac surgery patients didn't get FFP. Regarding these studies, our practice in FFP transfusion seems acceptable. Administration of anti-fibrinolytic agents have established an effect on blood product consumption in cardiac operation (27, 28).

The important issue is following "blood conservation guidelines" and determining targets for ordering blood products transfusion. Society of thoracic surgeons guideline suggests to transfuse patients with Hb < 6 g/dL and not to transfuse those with Hb > 10 g/dL (9). Transfusion in Hb between 6 and 10 depends on the patient's conditions. Some institutional variations exist in blood conservation strategies, but it is very important to build up an institutional protocol and all disciplines follow it (9, 11). In our center, most cardiac surgeons consider the 8 g/dL for low-risk patients and 10 g/dL for high risk group, however, some surgeons historically prefer the higher levels of Hg, i.e. 10 and 12 g/dL, respectively.

Finally, in different medical centers some degrees of the inappropriate blood product transfusion are still occur. For example, Faritous et al. reported 33% of platelet, 37% of FFP and 62% of cryoprecipitate transfusions were assessed as inappropriate in 14 general hospitals in Wales in 2003 (29).

The results of this study demonstrated that the cardiac surgery patients receive a relatively greater number of PC or FFP units during and after an operation in our center. This finding is partially related to the fact that the sicker and more co-morbid patients referred to our hospital. In addition, there were higher rate of anemia, emergent surgery, and reexploration in our cases. Finally, this study showed some degree of inappropriate transfusions of blood products especially in ICU.

5.1. Limitations

The major limitation of our study was the small sample size (n = 153) and lack of a comprehensive coverage of all possible pre-, intra- and post-operative related variables that can affect amount of blood product transfusion. However, this study tried to provide a self-assessment of an important clinical practice (blood transfusion) in high risk cardiac surgery patients.

Acknowledgements

With special thanks to operating room and intensive care units staff for their contribution in care of this study patients.

Authors' Contributions

Alireza Alizadeh Ghavidel introduced the study idea and conducted the project and supervised the collecting data and contributed in paper writing. Ziae Totonchi

Conducted the research project and contributed in data collection and final report. Abedin Hoseini contributed in collecting data and analyzing them and contributed in article writing. Mohsen Ziyaeifard conducted the research project and contributed in data collection and paper writing. Rasoul Azarfarin contributed in research project and writing the paper and performed the submission to the journal.

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