Effects of blood transfusion in patients with upper gastrointestinal bleeding

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Abstract

Aim: Acute upper gastrointestinal bleeding (AUGB) could pose numerous threats to patient's health and life. Blood transfusion strategy is still controversial whereas its effectiveness draws considerable scientific interest. Our aim was to evaluate the effectiveness of blood transfusion in AUGB patients in Albania.
Methods: This cross-sectional study was carried out in Tirana during January 2014-December 2014 among 92 patients experiencing AUGB (66% males, average age 51 years old). Laboratory (number of erythrocytes, haemoglobin (Hb) and haematocrit (Hct) level) and clinical parameters (cardiac frequency, respiratory frequency and arterial pressure) were measured before and 12 hours after blood transfusion. Patients were divided into three groups based on number of blood units being transfused.
Results: After the transfusion, mean values of clinical parameters across study groups were significantly different. Mean number of erythrocytes and mean values of Hb and Hct increased significantly with the number of blood units being transfused. Transfusion of one blood unit was almost as effective as the supply of two blood units in terms of clinical parameters. After transfusion, the laboratory parameters significantly improved in all study groups but differences across groups remained not significant.
Conclusion: Transfusion of one unit of blood in patients experiencing acute upper gastrointestinal bleeding might significantly improve their clinical and laboratory parameters. The transfusion of more than one unit of blood could result in further improvements of these parameters, but in this case the financial costs should be considered as well.

Keywords: Acute upper gastrointestinal bleeding, Albania, blood transfusion, haematocrit, haemoglobin.

Introduction

Acute upper gastrointestinal bleeding represents a serious emergency condition that requires prompt intervention to avoid potential complications and save patient's life (1,2). The clinical manifestations of patients with acute gastrointestinal bleeding might include hematemesis, melena, and hematochezia (3-5). Because of the potential for life threatening blood loss, severe acute gastrointestinal bleeding might require the transfusion of red blood cells (RBC) (6). There is a debate regarding the optimal threshold of haemoglobin (Hb) for starting the transfusion of red blood cells in patients with acute GI bleeding (6). The two prevailing modalities are the restrictive and liberal transfusion strategies. In restrictive transfusion strategy the Hb threshold for initiation of red blood transfusion is $\leq$7 g/dL whereas in liberal transfusion strategy the Hb threshold is $\leq$9 g/dL (6,7), even though the thresholds of Hb, haematocrit (hCT) or other parameters used to decide upon red blood transfusion vary quite a lot (8-10). The decision whether restrictive or liberal strategy is best depends on the patient's conditions (7). However, restrictive transfusion strategy seems to be safe in most clinical settings (11) and, in patients with acute gastrointestinal bleeding it significantly improves outcomes such as reducing the risk of further bleeding and length of hospital stay, reducing other serious adverse events and improving the probability of survival 6 weeks after the transfusion (6,12). Regardless of patients' conditions, in general the number of red blood units transfused is lower with restrictive transfusion strategy (11). The thresholds of Hb for indicating blood transfusions in patients without active bleeding are published by the American Association of Blood Banks (AABB) (13).

A recent cluster randomised feasibility trial comparing restrictive versus liberal blood transfusion for acute upper gastrointestinal bleeding suggested that mean levels of haemoglobin concentration after the transfusion did not differ significantly between the study groups (116 g/L for the restrictive strategy group and 118 g/L for the liberal strategy group) and also no significant differences in red blood cell units transfused (14). However, the haemoglobin threshold for the initiation of blood transfusion in the restrictive group was <80 g/L whereas for the liberal group was <100 g/L (14). In this perspective, the increase of Hb level after the transfusion was higher (in absolute number) in the restrictive than in liberal group (a mean increase of 36 units vs. 18 units, respectively) (14). Usually, transfusion of red blood cells aims to reach a Hb level of at least 100 g/L or a haematocrit level of at least 30% (15).

The improvement of Hb and Hct levels is expected to occur after the administration of RBC units, as this is the main objective of such a procedure. For example, a study reported that 24 hours after the administration of two units of RBCs there was an increase in Hb level of 22.4 g/L whereas the level of Hct increased by 6.4% percentage points (16).

In Albania the change in Hb and Hct levels after the administration of RBCs units in patients suffering from upper gastrointestinal bleeding is not documented. In this context, the aim of this study was to evaluate the effectiveness of blood transfusion in patient with upper gastrointestinal bleeding based on the selected clinical and laboratory parameters.

Methods

This was a cross-sectional study carried during January 2014 - December 2014 at the University Hospital Center "Mother Theresa" in Tirana, Albania.

Study population

The study involved 92 patients: 61 males (66%) and 31 females (34%) with acute anaemia due to acute upper gastrointestinal bleeding. The age of the patients varied from 28 years to 62 years old, with a mean age of 51 years old. All patients were diagnosed with upper gastro-intestinal bleeding. No patient complained of pre-existing cardiovascular or pulmonary diseases.

Data collection and procedures

All included patients suffering from upper gastro-

intestinal bleeding were subjected to sclerotherapy. The procedure resulted successful in all of them. Every patient was catheterized by a central venous catheter in order to give the proper amount of crystalloid and colloid solutions and on the other hand to measure the central venous pressure (CVP). Every patient had oxygen supply given by a nasal catheter (4-5l/min).

The following laboratory parameters were evaluated: number of erythrocytes (Er), haemoglobin (Hb), haematocrit (HCt). The following clinical parameters were evaluated: cardiac frequency (fC) and respiratory frequency (fR), mean arterial pressure (MAP).

All clinical and laboratory parameters were measured in the moment of admission and again 12 hours after blood transfusion.

After sclerotherapy the patients did not have active haemorrhage. Patients were treated with crystalloid, colloid solutions and blood transfusion. After the treatment patients were normovolemic.

Based on the number of blood units being received, patients were divided into three groups:

- Group I = 66 patients: 44 males (66%) and 22 females (34%) = one unit transfused;
- Group II = 18 patients: 12 males (65%) and 6 females (35%) = two units transfused;
- Group III = 8 patients: 5 males (62%) and 3 (38%) female = three units transfused.

Statistical analysis

For describing the continuous variables included in the study the measures of central tendency (mean values) and measures of dispersion (respective standard deviations) were calculated and reported.

For comparing continuous variables across patients' groups the ANOVA procedure was used.

A p-value of ≤ 0.05 was considered as statistically significant. All analysis was carried out through the Statistical Package for Social Sciences (SPSS), version 20.

Results

Table 1 presents the mean values and standard deviations of laboratory parameters under study according to study group, before and after the transfusion of RBCs units.

Mean values of number of erythrocytes, percentage of Hct and level of Hgb before transfusion were not statistically different across the three study groups but after the transfusion these differences were significant (Table 1). In general, the higher the number of RBCs units transfused the higher the mean value of erythrocytes, Hct and Hgb after transfusion.

Table 1. Changes in the laboratory parameters before and after transfusion

Time of measurement	Laboratory parameter	Study group			P-value
		Group 1	Group 2	Group 3	
Before transfusion	Erythrocytes (in millions)	2.47 ± 0.48 *	2.16 ± 0.42	2.30 ± 0.20	>0.05 †
	Haematocrit (in %)	23.0 ± 4.3	20.6 ± 3.9	22.0 ± 2.2	>0.05
	Haemoglobin (in g/dL)	6.44 ± 0.67	6.34 ± 0.33	6.45 ± 0.45	>0.05
After transfusion	Erythrocytes (in millions)	2.80 ± 0.45	2.84 ± 0.38	3.32 ± 0.35	<0.05
	Haematocrit (in %)	27.0 ± 4.3	27.9 ± 2.8	34.0 ± 2.1	<0.05
	Haemoglobin (in g/dL)	7.40 ± 0.07	7.76 ± 0.40	9.20 ± 1.1	<0.05

* Mean value and standard deviation (in parenthesis).

† P-value according to the ANOVA procedure.

Table 2 presents the mean values and standard deviations of clinical parameters under study according to study group, before and after the transfusion of RBCs units.

It can be noted that the mean values of cardiac frequency, respiratory frequency and mean arterial pressure were not significantly different across study groups both before and after the transfusion of RBC units (Table 2).

Table 2. Changes in the clinical parameters before and after transfusion

Time of measurement	Clinical parameter	Study group			P-value
		Group 1	Group 2	Group 3	
Before transfusion	Cardiac Frequency	120 ±4.6 *	122.5 ± 7.5	124.7 ± 4.4	>0.05 †
	Respiratory frequency	29.9 ± 2.5	31.4 ± 1.7	31.4 ± 1.8	>0.05
	Mean Arterial Pressure	82.4 ± 6.3	83.2 ± 8.2	82.1 ± 5.6	>0.05
After transfusion	Cardiac Frequency	98.7 ± 4.2	96.8 ± 8.1	94.0 ± 4.3	>0.05
	Respiratory frequency	17.5 ± 1.5	18.6 ± 1.1	19.3 ± 0.5	>0.05
	Mean Arterial Pressure	83.1 ± 6.4	85.0 ± 5.7	85.0 ± 7.8	>0.05

* Mean value and standard deviation (in parenthesis).
† P-value according to the ANOVA procedure

Mortality in the three groups of patients included in this study was zero.

Discussion

The current study is an effort to contribute to the definition of transfusion effects based on the certain clinical and laboratory indicators. The clinical and laboratory evaluation was carried out 12 hours after the transfusion in order to acquire the most real values for the effectiveness of the treatment. Our study showed that the mean increase of the number of red cells after this interval in the patients belonging to the first group was about 430.000, the increase of haematocrit level was about 4 percentage points and the increase of haemoglobin level in this group was approximately 0.9 g/dl (Table 1).

Failure to achieve the expected laboratory parameters after transfusion of one unit of RBCs should orient us toward the possibility of an unidentified haemorrhage. These situations demand a change in the treatment strategy for these patients, and the identification and domination of the haemorrhage source becomes a priority, since it can be a threat to the life of the patient and make the transfusion therapy ineffective.

After the transfusion the laboratory parameters of the second and third group of patients showed statistically significant increases in comparison with the patients of the first group. This might be an indication that the transfusion of two or more units of blood could be more effective and helpful to the patients. Meanwhile, clinical parameters improve in all the three groups of patients after the transfusion of RBC units compared to before-transfusion values (Table 2) but no significant differences were observed between groups before and after transfusion. As a result, the clinical effects are similar, independently of the number of the blood units transfused.

Patients suffering from acute anaemia face a high life-risk. Therefore the substitute treatment with

blood and liquids should be very accurate and decided upon in a very short time. The consensus conferences on the blood transfusion problem have set the laboratory parameters which serve as limits for starting transfusion. The current guideline for red blood cell transfusion derives from recommendations of the WHO published in 2003 (17) and AABB published in 2012 (13). ABB guidelines strongly recommend adhering to a restrictive transfusion strategy when the Hb level is 7-8 g/dl in hospitalized, stable patients (13). In patients with pre-existing cardiovascular disease, the transfusion should be considered for patients with symptoms and Hb level $\leq$8 g/dl (13). The AABB does not make recommendations for or against liberal or restrictive transfusion threshold for hospitalized, hemodynamically stable patients with an acute coronary syndrome, but it suggests that transfusion decisions be influenced by symptoms as well as Hb concentration (13).

There is still a controversy regarding the safest and most cost-efficient strategy for treating patients suffering from acute anaemia (6). In this perspective two issues might be of interest: the optimal number of RBCs units to be transfused and the cost of blood transfusion compared to alternative therapy.

Is one unit of blood always sufficient?

Results of the current study showed that transfusion of one unit of blood was sufficient to improve both the laboratory parameters and the clinical ones, and 92.5% of them didn't need a second transfusion. For the five patients (7.5%) whose clinical improvement was not satisfactory, the transfusion of one unit of blood provided time to evaluate the need for a second transfusion. Therefore, the transfusion of one unit of blood does not always optimize the clinical situation of the patients, but in most of the cases it is sufficient.

This might come as a result of the high tolerance that the human organism has towards low levels of haemoglobin (18). Blood transfusions aim to improve oxygen supply to tissues (19). All the patients included in our study experienced profound anaemia or circulatory shock, implying a critical impairment of tissue oxygenation. If the patient is normovolemic a normal Hb concentration is not critical for adequate tissue oxygenation (19). In our study all patients were firstly treated with crystalloid and colloid solutions and blood transfusion until CVP was in normal ranges. This engaged compensatory mechanisms such as the increase of cardiac input and oxygen extraction, decrease of haematocrit and reduction of blood viscosity (19). As a consequence, venous return to the heart and left ventricular preload increase, while systemic vascular resistance and thus left ventricular afterload decrease, resulting again in increase of left ventricular performance and cardiac output (20). The decrease of haematocrit will ultimately lead to a decrease of oxygen delivery to tissues but body's oxygen demand can still be met (19) since oxygen transporting capacity is several times greater than the demand in calm conditions (17). This can explain the similar clinical effects achieved after blood transfusion in the three groups of patients. Also this could be due to the restoration of the plasma volume through liquids, which not only improves the cardiac debit and increases the amount of oxygen dissolved in plasma, but at the same time lowers the blood viscosity, resulting in considerable improvement of perfusion and tissue oxygenation (20).

Mortality in three groups of the patients included in this study was 0. It may be result of the small number and the young age of patients included in the study. A literature review suggested that transfusion strategy does not affect mortality measures (21).

The cost of blood transfusion

According to the data given by the National Centre of Blood Transfusion in Tirana, one unit of blood costs $75, a figure that is much higher if compared to the therapy with solutions. Obviously the

increase of the number of RBC units transfused is accompanied by a considerable increase of costs and therefore the most cost-effective strategy to treat acute anaemia patients is by transfusing one unit of blood.

The decision for transfusion is taken after a precise evaluation of both laboratory and especially the clinical parameters (17). After the transfusion of the first unit of blood, the parameters are evaluated again. Only then the decision for a second possible transfusion is taken. However this procedure has not been always followed in the patients included of our study. Often the decision for blood transfusion, or about the number of RBCs to be transfused, is taken without evaluating the clinical parameters or without re-evaluating these parameters after the transfusion of the first unit of blood.

Conflicts of interest: None declared.

Conclusions

Based on the findings of this study, the transfusion of one unit of blood in the patients suffering from acute anaemia results in improvement of clinical parameters (mean number of RBCs, mean level of Hb and Hct), as well as decrease of cardiac and respiratory frequency. On the other hand, the transfusion of two or three units of blood in these patients is accompanied by considerable further improvement of laboratory parameters (as well as financial costs) compared to the transfusion of one unit of blood. Finally, no significant differences were observed between study groups before and after transfusion regarding clinical parameters. However, the transfusion of two or more blood units implies considerable economic costs and should be carefully assessed against potential additional benefits.

References

1. Gralnek IM, Barkun AN, Bardou M. Management of acute bleeding from a peptic ulcer. N Engl J Med 2008;359: 928-37.
2. Nable JV, Graham AC2. Gastrointestinal Bleeding. Emerg Med Clin North Am 2016;34:309-25.
3. Cleveland K, Ahmad N, Bishop P, Nowicki M. Upper gastrointestinal bleeding in children: an 11-year retrospective endoscopic investigation. World J Pediatr 2012;8:123-8.
4. Cappell MS, Friedel D. Initial management of acute upper gastrointestinal bleeding: from initial evaluation up to gastrointestinal endoscopy. Med Clin North Am 2008;92:491.
5. Jensen DM, Machicado GA. Diagnosis and treatment of severe hematochezia. The role of urgent colonoscopy after purge. Gastroenterology 1988;95:1569.
6. Villanueva C, Colomo A, Bosch A, Concepción M, Hernandez-Gea V, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med 2013;368:11-21.
7. Docherty AB, O'Donnell R, Brunskill S, Trivella M, Doree C, et al. Effect of restrictive versus liberal transfusion strategies on outcomes in patients with cardiovascular disease in a non-cardiac surgery setting: systematic review and meta-analysis. BMJ 2016;352:i1351.
8. Hébert, PC, Wells G, Blajchman MA, Marshall J, Martin C et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group. N Engl J Med 1999;340:409-17.
9. Hajjar LA, Vincent JL, Galas FR, Nakamura RE, Silva CM, et al. Transfusion requirements after cardiac surgery: the TRACS randomised controlled trial. JAMA - Journal of the American Medical Association 2010;304:1559-67.
10. Carson JL, Terrin ML, Noveck H, Sanders DW, Chaitman BR, et al., for the FOCUS Investigators. Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery. N Engl J Med 2011;365:2453-62.
11. Holst LB, Petersen MW, Haase N, Perner A, Wetterslev J. Restrictive versus liberal transfusion strategy for red blood cell transfusion: systematic review of randomised trials with meta-analysis and trial sequential analysis. BMJ 2015;350:h1354.
12. Rudler M, Thabut D. Transfusion strategy in gastrointestinal bleeding: less is best? J Hepatol 2014;60:453-4.
13. Carson JL, Grossman BJ, Kleinman S, Tinmouth AT, Marques MB, et al. Red blood cell transfusion: a clinical practice guideline from the AABB. Ann Intern Med 2012;157:49-58.
14. Jairath V, Kahan BC, Gray A, Doré CJ, Mora A, et al. Restrictive versus liberal blood transfusion for acute upper gastrointestinal bleeding (TRIGGER): a pragmatic, open-label, cluster randomised feasibility trial. Lancet 2015;386:137-44.
15. Balderas V, Bhore R, Lara LF, Spesivtseva J, Rockey DC. The

hematocrit level in upper gastrointestinal hemorrhage: safety of endoscopy and outcomes. Am J Med 2011;124:970-6.

16. Elizalde JI, Clemente J, Marín JL, Panés J, Aragón B, et al. Early changes in hemoglobin and hematocrit levels after packed red cell transfusion in patients with acute anemia. Transfusion 1997;37:573-6.

17. World Health Organization. The clinical use of blood. World Health Organization. Blood Transfusion Safety. Geneva; 2002.

18. Habler OP, Messmer KF. The physiology of oxygen transport. Transfus Sci 1997;18:425-35.

19. Pape A, Stein P, Horn O, Habler O. Clinical evidence of blood transfusion effectiveness. Blood Transfus 2009;7:250-8.

20. Habler OP, Kleen MS, Podtschaske AH, Hutter JW, Tiede M, et al. The effect of acute normovolemic hemodilution (ANH) on myocardial contractility in anesthetized dogs. Anesth Analg 1996;83:451-8.

21. Carson JL, Hill S, Carless P, Hébert P, Henry D. Transfusion triggers: a systematic review of the literature. Transfus Med Rev 2002;16:187-99.