Klinik Araştırma

Hypoalbuminemia is A Predictor for Severity of Acute Non-Variceal Upper Gastrointestinal Bleeding

Hipoalbuminemi Akut Varis Dışı Üst Gastrointestinal Sistem Kanamasının Şiddetini Gösteren Bir Belirteçtir

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SUMMARY

Objective: *To evaluate the significance of hypoalbuminemia in red blood cell transfusion requirement in patients with acute non-variceal upper gastrointestinal bleeding (UGIB).*

Methods: *In this retrospective study data from consecutive patients admitted and hospitalized with UGIB during the period from January 2007 to January 2009 were collected. The data of total 353 (265 men, 88 women, mean age of 55.44±19.62 years; range from 15 to 97) patients eligible for the study were analyzed. Existence of chronic hepatic disease, variceal bleeding, chronic renal failure, malignancy and hematological disease were exclusion criteria. Hypoalbuminemia is defined as serum albumin < 3.5 g/dL. The outcome assessments in the hypoalbuminemia and normal albumin groups were compared.*

Results: *Hypoalbuminemia was seen in 174 (49.29 %) patients. Compared to patients with normal albumin, patients in the hypoalbuminemia group were older (57.69±20.08 vs 53.27±18.96 years, p=0.035; had more red cell transfusion (RBC) requirement (3.55±2.28 vs 1.57±1.65 unit, p<0.0001), longer hospital stay (6.61±3.12 vs 5.83±2.24 days, p=0.007), lower hemoglobin level (8.57±2.49 vs 10.36± 2.43 g/dL, p<0.0001), and had higher blood urea nitrogen (BUN) level (38.53±21.55 vs 30.99±16.83 mg/dL, p<0.0001) and BUN/creatinine ratio (40.47±18.46 vs 34.05±15.33, p=0.001) at admission. RBC transfusion requirement was correlated negatively with serum albumin (r= -0.498, p<0.0001) and hemoglobin levels (r=-0.480, p<0.0001), positively with BUN level (r=0.243, p<0.0001), age (r=0.123, p=0.021), hospital stay (r=0.283, p<0.0001) and white blood cell count (r=0.161, p=0.001).*

Conclusion: *Hypoalbuminemia can be an indicator for the severity of non-variceal UGIB.*

Key words: *Hypoalbuminemia, red blood cell transfusion, upper gastrointestinal bleeding.*

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ÖZET

Hipoalbüminemi Akut Non-Varisiyel Üst Gastrointestinal Kanamanın Ciddiyeti İçin Bir Prediktördür.

Amaç: *Akut non-varisiyel üst gastrointestinal kanaması olan hastalarda eritrosit transfüzyonu gereksiniminde hipoalbümineminin önemini değerlendirmek.*

Metod: *Bu retrospektif çalışmada ocak 2007-2009 tarihleri arasında üst gastrointestinal kanama ile müracaat eden ve hastaneye yatırılan hastaların verileri toplandı. Çalışma için uygun toplam 353 hastanın (265 erkek, 88 kadın, ortalama yaş: 55.44±19.62 yıl, en genç 15-en yaşlı 97) verileri analiz edildi. Kronik karaciğer hastalığı, varis kanaması, kronik renal yetmezlik, malignite ve hematolojik hastalık varlığı çalışma dışında bırakılma kriterleri idi. Hipoalbüminemi <3.5 g/dL serum albumin olarak tarif edildi. Hipoalbüminemi ve normal serum albumini olan grupların sonuçları karşılaştırıldı.*

Bulgular: *Hipoalbüminemi 174 (%49.29) hastada görüldü. Müracaatta normal serum albumini olan hastalara kıyasla hipoalbüminemik gruptaki hastalar daha yaşlı (57.69±20.08 vs 53.27±18.96 yıl, p=0.035;) idi ve daha çok eritrosit süspansiyonu transfüzyonuna (3.55±2.28 vs 1.57±1.65 ünite, p<0.0001), daha uzun yatış süresine ((6.61±3.12 vs 5.83±2.24 gün, p=0.007), daha düşük hemoglobin seviyesine (8.57±2.49 vs 10.36± 2.43 g/dL, p<0.0001), daha yüksek kan üre nitrojen seviyesine (BUN) (38.53±21.55 vs 30.99±16.83 mg/dL, p<0.0001) ve daha yüksek BUN/kreatinin oranına (40.47±18.46 vs 34.05±15.33, p=0.001) sahipti. Eritrosit transfüzyonu serum albümini (r= -0.498, p<0.0001) ve hemoglobin seviyesi (r=-0.480, p<0.0001) ile negatif; BUN (r=0.243, p<0.0001), yaş (r=0.123, p=0.021), yatış süresi (r=0.283, p<0.0001) ve lökosit sayısı ile (r=0.161, p=0.001) pozitif olarak korele bulundu.*

Sonuç: *Hipoalbüminemi non-varisiyel üst gastrointestinal kanamanın ciddiyetinin bir göstergesi olabilir.*

Anahtar Kelimeler: *Hipoalbüminemi, eritrosit transfüzyonu, üst gastrointestinal kanama.*

INTRODUCTION

Variceal and non-variceal upper gastrointestinal bleeding (UGIB) are urgent medical conditions that have significant morbidity, mortality and health care resource use. Both severity of UGIB and existence of comorbidities are important predictors of mortality and morbidity in patients with UGIB. Clinical findings such as low blood pressure, postural hypotension and tachycardia can help to differentiate severe UGIB from non-severe. However, these clinical findings are not always reliable, especially in elderly population with multiple comorbidities necessitating many medications that may alter vital signs. In addition, the initial hemoglobin (Hb) level and, in particular, the hematocrit (Hct) level may not reflect a patient's true erythrocyte level, because they may be falsely elevated as a result of hemoconcentration or may be affected by a chronic anemic state in addition to the acute bleeding event (1, 2). Blood transfusion requirement within 24 h of presentation to the emergency service, need for intensive care unit admission because of hemodynamic parameters and findings of high risk endoscopic lesions on emergency endoscopy are important indicators of severe UGIB. High blood urea nitrogen (BUN) level or BUN/creatinine ratio has been suggested as an indicator of severe UGIB in some studies (3-5). In addition, association of hypoalbuminemia and high white blood cell (WBC) count with severe UGIB has been reported in a few studies (6, 7). In this retrospective study, in which red blood cell (RBC) transfusion requirement is accepted as an indicator of severe UGIB, we investigated the relation of low admission serum albumin level with RBC transfusion requirement, hospital stay duration as well as values of some biochemical and hematological parameters including BUN, WBC and Hb.

METHODS

In this retrospective study data from consecutive patients admitted and hospitalized with UGIB during the period from January 2007 to January 2009 were collected. The data of total 353 (265 men, mean age of 52.64±18.10 years; and 88 women, mean age of 63.86±21.58 years) patients eligible for the study were analyzed. Existence of a chronic hepatic disease, variceal bleeding, chronic renal failure, malignancy or hematological disease was exclusion criteria. RBC transfusion requirement was accepted as indicator of severity of UGIB. Hypoalbuminemia is defined as serum albumin < 3.5 g/dL. In addition to demographic features, admission values of serum albumin, BUN, creatinine, BUN/creatinine ratio, WBC count and Hb/Hct levels were recorded from patient cards in all eligible patients. Statistical analysis was conducted by using SPSS (Statistical Package for Social Sciences) for windows 10.0 program. Results were expressed as mean +/- SD (standard deviation). Quantitative data with normal distributions were compared in both groups using Student t test and data with other distributions were analyzed with Mann Whitney U test and Spearman correlation method. The parameters affecting the number of RBC transfusions were analyzed by stepwise regression analysis. Chi square test was used in comparison of qualitative data. Results were analyzed with 95% confidence interval and probability levels less than 0.05 were considered significant.

RESULTS

Mean age of patients were 55.44±19.62 years (range from 15 to 97). The age of 132 patients was equal to or greater than 65 years. In 272 (77.05 %) patients a total of 898 U (mean of 3.30±2.38) RBC transfusions were performed. RBC transfusion requirement of elderly patients (≥65 years) was significantly higher than those who were younger (3.05±2.57 vs. 2.21±2.39 unit, p=0.002, respectively). Compared to patients with normal serum albumin, more patients in hypoalbuminea group (89.08 % vs 65.36 %, p<0.0001) received RBC transfusions. Compared to patients with normal serum albumin, the hypoalbuminemia group were older (57.69±20.08 vs 53.27±18.96 years, p=0.035; had more RBC red cell transfusion (3.55±2.28 vs 1.57±1.65 unit, p<0.0001), longer hospital stay (6.61±3.12 vs 5.83±2.24 days, p=0.007), lower hemoglobin level (8.57±2.49 vs 10.36± 2.43 g/dL, p<0.0001), and had higher blood urea nitrogen (BUN) level (38.53±21.55 vs 30.99±16.83 mg/dL, p<0.0001) and BUN/creatinine ratio (40.47±18.46 vs 34.05±15.33, p=0.001) on admission **(Table 1)**.

	Serum Albumin <3.5 g/dL	Serum Albumin ≥3.5 g/dL	p
Age (year)	57.80 ±19.82	53.27 ±18.96	0.032
Hospitalization Duration (day)	6.66 ±2.93	5.83 ±2.24	0.003
Mean Blood Transfusion (U)	3.60 ±2.86	1.57 ±1.65	<0.0001
Hb (g/dL)	8.58 ±2.49	10.36 ± 2.43	<0.0001
Hct (%)	25.39 ±7.18	30.74 ±6.89	<0.0001
WBC (µL)	10185.19 ±3796.21	9650.28 ±3362.74	0.169
Total Protein (g/dL)	5.12 ±0.65	6.02±0.55	<0.0001
BUN (mg/dL)	38.33 ±20.34	30.99 ±16.83	<0.0001
Creatinine (mg/dL)	1.00 ±0.43	0.94 ±0.40	0.174
BUN/ Creatinine	40.38 ±18.26	34.05 ±15.33	0.001

Table 1: Various parameters of patients with low (<3.5 g/dL) and normal (≥3.5 g/dL) serum albumin.

RBC transfusion was correlated negatively with serum albumin (r= -0.498, p<0.0001) and hemoglobin level (r=-0.480,

p<0.0001), positively with BUN (r=0.243, p<0.0001), age (r=0.123, p=0.021), hospital stay (r=0.283, p<0.0001) and white blood cell count levels (r=0.161, p=0.001). At baseline, there was a significant negative correlation of serum albumin level with BUN (r= -0.248, p<0.0001), BUN/creatinine ratio (r=-0.255, p<0.0001), age (r=-0.178, p=0.001), hospital stay (r=-0.176, p=0.001), WBC (r=-0.173, p=0.001), RBC transfusion (r=-0.498, p<0.0001), but a positive correlation with Hb (r=0.370, p<0.0001). Regression analysis revealed that effective factors on the amount of RBC transfusions are serum albumin, Hb levels and WBC (r2=373).

DISCUSSION

RBC transfusion requirement in patients with UGIB is an important parameter indicating the severity of bleeding. The results of this study show that some hematological and biochemical parameters determined at admission on emergency department, particularly serum albumin, can be useful markers for estimation of the severity of UGIB and RBC transfusion requirement. Elderly age (>65) is an another factor increasing RBC transfusion requirement in patients with UGIB. We use a restrictive transfusion strategy, with a Hb level of <8 gr/dL as the threshold for transfusion, as advocated in guidelines for gastrointestinal bleeding for patients with no comorbities. In patients with comorbidities, we use a more liberal transfusion strategy according to hemodynamic status of the patient. Therefore, RBC transfusion requirement in patients with UGIB can not be always a reliable indicator for severe bleeding. Traditionally, the patients with UGIB are followed up by serial Hb/Hct measurements and hemodynamic parameters including blood pressure and pulse rate. It is well known that these clinical and laboratory findings are not always reliable. Vital signs may be altered, especially in elderly population, by multiple comorbidities and medications. Initial Hb levels and, in particular, the Hct levels may be falsely elevated as a result of hemoconcentration or affected by a chronic anemic state in addition to the acute bleeding event. Serum BUN level is increased in patients with UGIB due to ingested blood protein, secondary to prerenal azotemia or renal failure. Unproportionally elevated BUN level to creatinine is also a helpful parameter to discriminate the UGIB from lower gastrointestinal bleeding (5). In addition, some studies have shown that the degree of elevation in the BUN to creatinine ratio correlates best with transfusion requirements (3,4), whereas others (7-9) have reported that the BUN level did not predict the need for blood transfusion. Moreover, the Blatchford scoring system uses BUN as one of the variables to prognosticate the outcome of a patient with UGIB (10). The results of this study show that a weak association exists between an elevated BUN level or a high BUN/creatinine ratio and transfusion requirements.

Hypoalbuminemia occurs in a variety of diseases (11). Loss of albumin by urinary, intestinal or other ways is an important cause for hypoalbuminemia. Serum albumin is an important component of blood, so the patients with bleeding from any origin lose some albumin. Therefore, reduced serum albumin may be used as an indicator of severe UGIB, particularly in patients who have no hypoalbuminemia history. However, the data concerned with serum albumin in UGIB patients is very limited. Tung et al reported that the hypoalbuminemia is common in patients with non-variceal UGIB, and reflects the severity of the bleeding episode, and is associated with a more complicated course (6). The results of the present study are in agreement with their results. The hypoalbuminemia in patients with non-variceal UGIB is associated with increasing RBC transfusion requirement, longer hospital stay and other well-known prognostic factors such as older age, low Hb and high BUN levels, and high BUN/creatinine ratio. Leucocytosis has long been recognized to occur in patients with hemorrhage. High WBC count can be a consequence of increased sympathetic activation due to a decrease in intravascular volume, and can be an indirect indicator of excessive blood loss. Chalasani et al. called attention to that leucocytosis is common in patients with UGIB, and related with the severity of bleeding episode and a more complicated course (7). Tung et al. also reported that hypoalbuminemic patients with UGIB, at the same time, had higher leucocytosis (6). The results of the present study show that WBC count correlates positively with RBC transfusion requirement and negatively with serum albumin level. Meaning of these relations is that increased WBC count is secondary to excess blood loss.

CONCLUSION

The results of this study where RBC transfusion requirement is accepted as an indicator of severe UGIB showed that hypoalbuminemia in patients with non-variceal UGIB could be a useful marker indicating the severity of the bleeding episode.

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