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Hemoglobin Trend in Critically Ill Patients with Long ICU Stay

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Abstract

Introduction: Critically ill patients develop anemia due to several reasons: bleeding prior or during intensive care unit (ICU) stay, frequent flebotomies, hemodilution and inflammatory status with altered erythropoiesis. The aim of this study was to assess the trend of hemoglobin (Hb) level during long ICU stay (more than 7 days) in transfused and nontransfused patients.

Materials and Methods: We conducted a prospective observational study that included all patients with long ICU length of stay (LOS) admitted during 1 year in a 19-beds mixed ICU of a tertiary care university hospital. Patients were divided into two groups: never transfused (NT) and ever transfused (ET) according to their transfusional status during ICU stay. Collected data: demographic data, severity scores, Hb values during ICU stay transfusion status and outcome. Statistical analysis was conducted with SPSS 15.0.

Results: 132 patients (54 NT, 78 ET) were enrolled in the study. On ICU admission, overall mean Hb level was 9.2 g% (95%CI 8.72-9.72) with a significant difference between NT and ET group (10.1 g% versus 8.5 g%; p<0.01). By the day 7 there was little change in overall mean Hb value (9.1 g%; 95%CI 8.85-9.43) as in NT group the Hb values continued to drop while in ET group raised as a result of transfusions. However, at two weeks after ICU admission there was a significant decrease in mean Hb value, from 9.2 g% in day 1 to 8.1 g% (95%CI 7.71-8.49) in day 14. The variance also had a significant decrease over time (8.94 in day 1; 1.58 in day 14) indicating a convergence of Hb values in studied patients, regardless of their transfusion status.

Conclusions: Despite the fact that Hb values on ICU admission may vary widely, after 14 days of ICU stay the Hb values tend to converge. The Hb level in critically ill patients with long ICU stays decreases stadly over time no matter the transfused or non-transfused status.

Keywords: Critical Ill Patients; Anemia; Transfusion; Hemoglobin; Intensive Care

Introduction

Anemia, highly prevalent (75-98%) in critically ill patients, is associated with increased health care resource use and may be associated with poor patient outcomes [1]. Hemoglobin levels continue to drop during ICU stay [2].

Critically ill patients develop anemia due to several reasons: bleeding prior or during Intensive Care Unit (ICU) stay, frequent phlebotomies, inflammatory status with altered erythropoiesis, hemodilution [3-7]. The most common treatment of anemia in critically ill patients is blood transfusions. Taking into account the benefits and risks of transfusion, the decision to transfuse or not is a matter of continuous debate [3,4,7-9]. Despite the fact that hemoglobin (Hb) levels and transfusion practices have been the aim of many studies, most of them characterize the ICU patients with short-to-moderate Length of Stay (LOS) or particular groups of ICU patients [4,7,9,10]. For critically ill patients with prolonged ICU stay such data are still needed. Moreover, evidences suggest that a greater Hb variability overtime is independently associated with a higher mortality rate in end stage renal disease patients [11]. The aim of our study was to assess the trend of hemoglobin value in critically ill patients with long ICU LOS (more than 7 days) with respect to transfusion status.

Material and Methods

We conducted a prospective, single center observational study in a 19-beds mixed ICU of an adult tertiary care hospital, over one year. Patients admitted to ICU were critically ill, surgical, medical or trauma patients. All patients admitted to ICU during a 12 months period, with a continuous length-of-stay (LOS) of more than 7 days were enrolled in the study (132 patients). For each patient demographic data (age, gender, admission type), Acute Physiology and Chronic Health Evaluation (APACHE) II scores, Sequential Organ Failure Assessment (SOFA) scores, daily hemoglobin values and transfusion status were recorded. For all transfused patients, further information regarding transfusion trigger, number of red blood cells (RBC) units during each transfusion event and ICU LOS before first transfusion were collected. Outcome variables including ICU LOS and mortality were recorded.

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Patients were divided into two groups: never transfused (NT - 54 patients; 40.9%) and ever transfused (ET-78 patients, 59.1%).

Statistical analysis was conducted using SPSS version 15.0 for Windows and Microsoft Office Excel. Continuous variables were summarized as mean ± Standard Deviation (SD) for normally and non-normally distributed variables. Comparisons between ET and NT patients were conducted using Student's *t*-test or Wilcoxon's test for normally and non-normally distributed continuous variables, respectively. $\chi 2$ or Fisher's exact test were used to compare categorical variables. 95% reference range (95% RR) and 95% confidence interval (95% CI) were calculated for the mean hemoglobin values on admission and sequentially after (day 7, 14 and 21). Kernel curves for the hemoglobin values on admission and day 14 were drawn and variance was calculated.

Results

During 12 months study period 132 patients with more than 7 days ICU LOS were enrolled. The average age in the study group was 62.8 ± 16.5 years old. The majority of patients were men (59.1%) admitted to the ICU for surgical reasons (82.6%). Mean APACHE II and SOFA scores on admission were 17.2 ± 8.2 and 5.8 ± 2.9 respectively. Overall, mean ICU LOS was 12.9 ± 5.5 days and mortality rate reached 47%. More than half of the critically ill patients with long ICU LOS (78 patients, 59.1%) received one or more red blood cells (RBC) units during their ICU stay.

No statistical differences regarding age, admission type and severity scores on admission were found between the NT and ET groups. However, patients receiving transfusions had higher SOFA scores later on during ICU LOS. Mean "worst" SOFA score was 9.8 ± 4.5 in ET group versus 8.9 ± 3.6 in NT group (P=0.04). Mortality rate was also found to be higher in patients receiving transfusions when compared to non-transfused patients (65.4% versus 20.4%; P=0.04). Baseline information regarding demographics data and outcome variables of patients enrolled in the study are summarized in Table 1.

Table I: Patient's data.

	All Patients	Never Transfused	Ever Transfused	P Value
	132 (100%)	54 (40.9%)	78 (59.1%)	
Age (years) – mean ± SD	62.8 ± 16.5	65.7 ± 14	60.4 ± 17.6	0.07
Gender male - no.(%)	78 (59.1%)	30 (55.6%)	48 (61.5%)	0.48
Admission type - no.(%)				
surgery	109 (82.6%)	49 (90.7%)	60 (76.9)	0.56
emergency	73 (55.3%)	33 (61.1%)	40 (51.3%)	0.88
elective	36 (27.3%)	16 (29.6%)	20 (25.6%)	0.45
medical	18 (13.6%)	5 (9.3%)	13 (16.7%)	-
trauma	5 (3.8%)	0 (0%)	5 (6.4%)	-
Severity of the disease				
APACHE II on admission -mean ± SD	17.2 ± 8.2	16.9 ± 8.3	17.4 ± 8.1	0.36
APACHE II worst - mean ± SD	22.7 ± 9.7	23.3 ± 9.5	22.2 ± 9.8	0.58
SOFA on admission - mean ± SD	5.8 ± 2.9	5.5 ± 3	6.2 ± 2.8	0.83
SOFA worst - mean ± SD	9.4 ± 4.1	8.9 ± 3.6	9.8 ± 4.5	0.04
Outcome				
ICU LOS (days) - mean ± SD	12.9 ± 5.5	12.8 ± 4.6	13 ± 6.1	0.88
ICU mortality - no. (%)	62 (47%)	11 (20.4%)	51 (65.4%)	0.04

The 78 patients of ET group were transfused in 154 different occasions with one or more RBC units. Half of them (51.3%) were transfused in the first 24 hours after ICU admission, and only 6.4% had their first transfusion after one week of ICU stay. Mean transfusion trigger Hb was 7.8 ± 2.3 g%. Most of the patients received 3 units of RBC in 2 different occasions and had a mean Hb increase of 0.9 g% after each transfusion event. Transfusion requirements during ICU LOS were higher in the first 2 days following admission and decreased after this period. The total number of RBC units used during the 12 months study period for critically ill patients with long ICU stay was 228. The informations regarding transfusion policy are summarized in Table 2.

Table II: Transfusion policy.

ICU LOS before first transfusion - no. of pts (%)	
<1 day	40 (51.3%)

1-7 days	33 (42.3%)
> 7 days	5 (6.4%)
Transfusion trigger Hb (g%) - mean ± SD	7.8 ± 2.3
Transfusion events/pacient - mean ± SD	2 ± 1.2
RBC units transfused/patient - mean ± SD	2.9 ± 2.4
Post transfusion Hb (g%) - mean ± SD	8.3 ± 1.9
Mean Hb increase/transfusion event - g%	0.9
78 ever transfused patients;154 transfusion events – 228 RBC units	

Overall, mean Hb value on admission was 9.2 ± 3 g%. There was a statistically significant difference in mean Hb on admission in NT patients versus ET patients (10.1 g% versus 8.5 g%; P<0.01). However the prevalence of anemia (Hb<12 g%) on ICU admission was high in both groups (74.1% in NT patients, 89.7% in ET patients). Moderate and severe anemia on admission had higher prevalence rates in transfused than in non-transfused patients (moderate anemia 21.8% versus 13%; severe anemia 20.5% versus 7.4%, respectively) without reaching statistical significance (P=0.84 and P=0.93 respectively). Prevalence of anemia on ICU discharge was even higher than on admission (95.4% compared to 83.3%, P<0.01) both in the NT (94.4% versus 74.1%, P<0.01) and ET patients (96.1% versus 89.7, P=0.2). Table III summarizes these data.

Table III: Prevalence of anemia.

	All Patients	Never Transfused	Ever Transfused	P Value
	132 (100%)	54 (40.9%)	78 (59.1%)	
Hb (g%) on ICU admission - mean ± SD	9.2 ± 3	10.1 ± 3.3	8.5 ± 2.8	<0.01
Anemia – on ICU admission - no.(%)	110 (83.3%)	40 (74.1%)	70 (89.7%)	0.11
Hb=12 - 8 g%	66 (50%)	29 (53.7%)	37 (47.4%)	0.14
Hb=7,9 - 6 g%	24 (18.2%)	7 (13%)	17 (21.8%)	0.84
Hb<6 g%	20 (15.1%)	4 (7.4%)	16 (20.5%)	0.93
Hb (g%) on ICU discharge - mean ± SD	8.5 ± 1.9	8.6 ± 1.9	8.4 ± 1.9	0.47
Anemia - at ICU discharge - no.(%)	126 (95.4%)	51 (94.4%)	75 (96.1%)	0.64
Hb=12 - 8 g%	74 (56.1%)	32 (59.2%)	42 (53.8%)	0.82
Hb=7,9 - 6 g%	43 (32.6%)	15 (27.8%)	28 (35.9%)	0.13
Hb<6 g%	9 (6.8%)	4 (7.4%)	5 (6.4%)	0.18

ICU course of Hb levels, according to admission Hb range, as well as the trend of mean Hb value in transfused and non-transfused patients, reveals the tendency of convergence toward a value a little higher than the transfusion trigger (Figures 1 and 2).

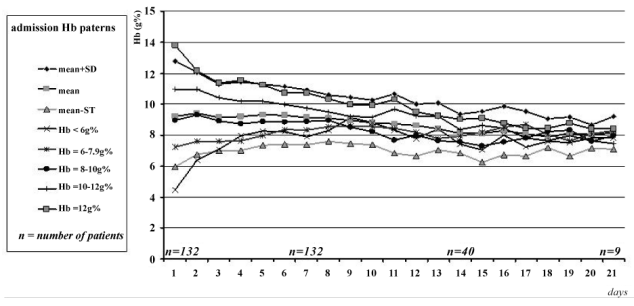

Figure 1: ICU course of Hb levels according to admission Hb range.

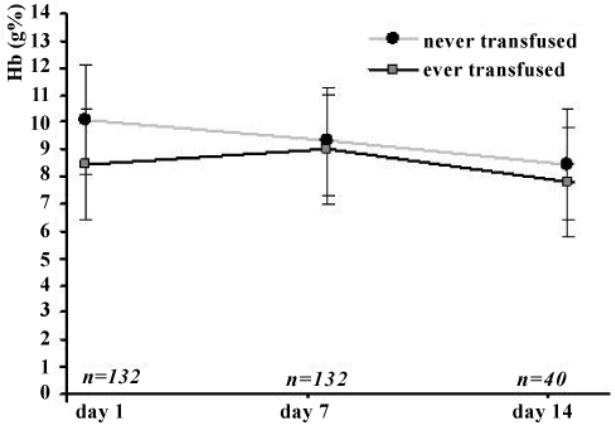

Figure 2: ICU course of mean Hb level in NT and ET groups.

On admission mean Hb level was 9.2 g% (95% CI 8.72-9.72) with a significant difference between NT and ET group (10.1 g% versus 8.5 g

%; P<0.01). By the day 7 there was little change in mean Hb value (9.1 g%; 95%CI 8.85-9.43) as in NT group the Hb values continued to drop while in ET group raised as a result of transfusions. However, at two weeks after ICU admission there was a significant decrease in mean Hb value, from 9.2 g% in day 1 to 8.1 g% (95%CI 7.71-8.49) in day 14. The variance also had a significant decrease over time (8.94 in day 1; 1.58 in day 14) indicating a convergence of Hb values in studied patients, regardless of their transfusion status. The convergence of Hb levels over time, no matter the transfusion status or admission Hb level is shown by the Kernel curves of distribution of Hb values in 1st day and 14th day of ICU LOS (Figure 3).

Discussion

Our study evaluated the time course of Hb values in critically ill patients with long ICU LOS. All patients with more than one week of ICU LOS were followed up, no matter the transfusion status. Other studies had already revealed that Hb concentration decreases over time during ICU stay [3,4,7,12]. Most of them concern all ICU patients no matter the duration of ICU LOS.

As other authors, we found a high prevalence of anemia on ICU admission that persisted during ICU LOS [3,7,12-14]. This could be partially explained by the restrictive blood transfusion policy applied in our ICU, mean ± SD transfusion trigger Hb being 7.8 ± 2.3 g%.

Transfusion requirements during ICU LOS were higher in the first 2 days following admission. One reason might be the high proportion of surgical patients included in our study. Another explanation is the necessity of a complete evaluation of a patient on ICU admission which involve placement of invasive devices and frequent phlebotomies.

Time course of Hb levels revealed a tendency of convergence to a value a little higher than the transfusion trigger. This seems to be explainable as the drop in the Hb concentration over time in NT patients was never compensated as they didn't reach the transfusion trigger Hb, while in the ET patients; transfusions were used only when the risk of decreased oxygen carrying capacity was considered to exceed the risk of transfusion. However, this is not the only possible explanation as there was a significant drop in transfusion requirements in the first week of ICU stay. Persisting inflammation in critically ill patients with long ICU LOS might be another cause for sustained anemia [1,15,16]. As the outliers may have a significant influence on the results when analyzing the trend of mean Hb value over time in a group drawn from a population, we tried to overcome this problem by analyzing the variance and the Kernel curves of distribution of Hb concentrations in patients enrolled in the study. Another factor that might influence the data, the unavoidable fall in the number of patients over time, was minimized by choosing the day 14 as a comparing point for the admission Hb variance in studied patients, as after this day there was an unacceptable low number of patients for comparison. The fact that the variance also had a significant decrease over time (8.94 in day 1; 1.58 in day 14) clearly reflects that in critically ill patients with long ICU stay there is a tendency of convergence of Hb levels to a value a little higher than the transfusion trigger Hb no matter the transfusion status.

Recent observational studies do show an important adverse effect of RBC transfusion on mortality, but even the best conducted adjustments for confounding cannot completely eliminate its impact [10,17]. In our study we found no difference on the severity of the disease on admission between groups, as reflected by APACHE II and SOFA scores. However transfused patients had higher SOFA scores during their ICU LOS and a higher mortality rate.

Conclusions

Based on our results, we conclude that despite the fact that Hb values of critically ill patients may vary widely at ICU admission, after 14 days of ICU stay the Hb values tend to converge to a level closed to the transfusion trigger Hb, no matter the transfusion status. The ICU LOS and transfusion policy influence the Hb level of patients at ICU discharge.

Conflict of Interests

Authors have no conflict of interests to disclose.

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