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Iron status among blood donors deferred due to low haemoglobin level

Ispitivanje statusa gvožđa kod davalaca krvi vraćenih zbog niskog nivoa hemoglobina

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Abstract

Background/Aim. Haemoglobin (Hb) determination is a routine part of the blood donor selection process. Previously reported studies have revealed that iron deficiency is common in frequent donors. This prospective investigation was aimed at examining iron status among blood donors with low circulating Hb and evaluating correlation between Hb values determined by capillary methods and those obtained by reference method from venous blood count (BC), as well as ferritin level. **Methods.** Between February 2017 and December 2018, 200 consecutively recruited regular blood donors with low Hb, aged 19 to 64 years (median 39), were included. Hb level was determined using the copper sulphate method, the HemoCue capillary method, and also from venous blood within the complete blood count (CBC) test. Plasma ferritin was determined turbidimetrically. **Results.** In 42.7% of men and 57.3% of women, ferritin concentration was low (p = 0.008). The relative numbers of males and females, with levels < 12 μg/L (p = 0.023) or > 50 μg/L (p = 0.022), differed. Comparison of the values obtained with the capillary methods with reference Hb levels obtained from the CBC test showed that the copper sulphate procedure gave false fails in 10.5% of cases (p < 0.001). Hb values from HemoCue were significantly correlated with Hb values from the CBC test, but no correlation was observed between ferritin levels and Hb levels determined by both capillary method. **Conclusion.** Low ferritin was observed in 51.5% of Serbian blood donors deferred due to low Hb. Based on our results, the determination of the algorithm in the iron deficiency detection is necessary, while the capillary method (HemoCue) represents a more convenient method for Hb testing prior to blood donation.

Key words:
blood donors; hemoglobins; iron; ferritin; clinical laboratory techniques.

Apstrakt

Uvod/Cilj. Određivanje nivoa hemoglobin (Hb) je rutinski deo selekcije dobrovoljnih davalaca krvi. Prethodno publikovane studije pokazale su da se nedostatak gvožđa javlja kod redovnih davalaca krvi. Cilj ove prospektivne studije je bio da se utvrdi status gvožđa kod davalaca kod kojih je pre davanja utvrđen nizak nivo Hb i da se proceni stepen korelacije kapilarnih metoda, sa referentnom metodom određivanja Hb iz venske krvi, kao i sa i nivoom feritina. **Metode.** U periodu od februara 2017. do decembra 2018. godine, bilo je uključeno 200 dobrovoljnih davalaca sa niskim nivoima Hb, starosne dobi 19–64 godine (medijana 39 godina). Hb je određivan primenom metode bakar sulfat, kapilarnom metodom „HemoCue", i iz venske krvi u sklopu određivanja kompletne krvne slike (KKS). Nivo feritina određivan je primenom turbodimetrijske metode. **Rezultati.** Nizak nivo feritina utvrđen je kod 42,7% muškaraca i 57,3% žena (p = 0,008). U odnosu na nivo feritina < 12 μg/L, odnosno > 50 μg/L, zabeležena je značajna razlika između polova (p = 0,023, odnosno p = 0,022). Poređenje vrednosti Hb dobijenih kapilarnim metodama u odnosu na referentne vrednosti Hb, određene iz KKS, pokazalo je da metoda s bakar sulfatom daje lažno niske vrednosti Hb kod 10,5% slučajeva (p < 0,001). Vrednosti Hb dobijene metodom „HemoCue-a" značajno su korelirale sa vrednostima Hb iz KKS, dok korelacija između nivoa feritina i Hb, određenog pomoću obe kapilarne metode, nije uočena. **Zaključak.** Kod 51,5% naših davalaca krvi koji su vraćeni zbog niskih vrednosti Hb utvrđen je snižen nivo feritina. Na osnovu ovih rezultata neophodno je odrediti algoritam za detekciju nedostatka gvožđa, dok je kapilarna metoda (HemoCue) pogodnija metoda za testiranje Hb pre davanja krvi.

Ključne reči:
krv, davaoci; hemoglobini; gvožđe; feritin; laboratorijske tehnike i procedure.

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Introduction

Blood donor selection is one of the most important measures used in blood transfusion centres in order to ensure blood safety [1–5]. Determining haemoglobin (Hb) level is a routine part of the donor selection process in order to ensure high quality of the red cell concentrates collected and, at the same time, protect the health of a potential donor [1, 6]. However, iron deficiency has been found to be common in frequent blood donors, particularly women, while the Hb level measured may not accurately reflect iron stores [7–10]. Determining Hb levels during the donor selection process using capillary methods distinctly saves time and expenditure without endangering blood donors [11]. Data from the forum investigation [12] state that the capillary copper sulphate procedure is used to determine Hb level before donation in three European countries (the United Kingdom, Spain, and Croatia); in one country, both capillary methods are employed, and in the remaining European countries, the capillary photometric method is preferred, most often HemoCue®. In Serbian transfusion centres, we use the capillary copper sulphate method, considering the minimum acceptable Hb level to be > 135 g/L for male and > 125 g/L for female donors.

Low circulating Hb is globally the most common reason for deferral of prospective blood donors [13–16]. During 2017, the total rate of all deferrals in our centre was 14.2%, among which 30.5% were due to low Hb level. Considering the relatively high proportion of deferrals due to low Hb among our voluntary blood donors, we performed a prospective study aimed to determine iron status among such blood donors. In order to indicate the most appropriate procedures in our blood transfusion centre, the second aim was to evaluate the agreement between values for Hb obtained using capillary methods with reference hemoglobin values obtained from the complete blood count (CBC) test and their association with ferritin level.

Methods

Between February 2017 and December 2018, this prospective study included 200 consecutively recruited regular blood donors (102 male and 98 female) with low Hb, aged 19 to 64 years (median 39). The term regular blood donor was defined as someone who had routinely donated blood in the same centre within the previous 2 years, in accordance with minimum time intervals [17]. The total number of previous blood donations in the study group was 3,340, and the median time interval between them was 5.3 months. All study participants were recruited from the Blood Transfusion Institute of Serbia, Belgrade. In the Serbian transfusion service, copper sulphate is used as the standard method for Hb determination in a finger prick sample. This method was applied during the recruitment of the study participants. Another capillary method for a finger prick sample was applied, and Hb was measured photometrically using the HemoCue® Hb 201⁺ System (Mission Viejo, Ca, USA). In addition, Hb was determined in a venous blood sample taken into EDTA tubes, using a haematology analyzer (Horiba Medical ABX Micros ES 60 blood counter, France). Ferritin concentration was determined turbidimetrically in a second venous blood sample collected in plastic tubes for biochemical analysis, using test reagents from Linear Chemicals, Spain. The reference range designated as normal by the manufacturer was 20–250 μg/L for males and 20–200 μg/L for females. In particular, a plasma ferritin level < 12 μg/L is defined as absent iron stores (AIS), and ferritin concentration < 29 μg/L is defined as depletion [18]. These were used in statistical analyses in order to point to the iron status of blood donors deferred due to low Hb.

All study participants were approached with the standard questionnaires for voluntary blood donors. Data related to age, gender, number of previous donations, date of the last donation, dietary regime, and health problems since the last donation, such as haemorrhage, menstrual bleeding, fever, respiratory infection, and stomach problems, were analyzed.

Institutional approval for the study was granted by the Local Research Ethics Committee (EK-number 7767/2016) in accordance with the internationally accepted ethical standards. Each participant signed the informed consent form.

Statistical methods

The Statistical Package for Social Sciences 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis. The Mann-Whitney U-test, Fisher's exact test, and Pearson Chi-squared (χ^2) test were employed to evaluate differences in the demographic and haemoglobin/ferritin test characteristics among the study participants. The probability $p < 0.05$ was considered statistically significant.

Spearman's tests were used for correlation analysis, and $p < 0.01$ was taken as statistically significant.

Results

Referring to their state of health, 25% of our subjects reported fatigue, 6.5% nutrition changes (diets, fasts), 7% bleeding episodes, and 61.5% good health. Considering the lower limit of the reference range to be 20 μg/L, a decreased ferritin level was found in 103/200 (51.5%) subjects (Table 1).

Table 1

Demographic characteristics of the patients

Characteristics	Value
Total number of patients, n (%)	200 (100)
Age (years), median (range)	39 (19–64)
Gender (M/F), n	102/98
Total number of previous donations, n	3,340
Interval from last donation (months), median (range)	5.3 (3.0–9.5)
Condition status, n (%)	
fatigue	50 (25)
diet	13 (6.5)
recently bleeding	14 (7)
good condition	123 (61.5)
Patients with low ferritin level, n (%)	103 (51.5)

M – male; F – female.

Equal frequencies of reduced Hb levels for the genders were indicated with all three methods ($p = 0.323$, $p = 0.796$, and $p = 0.422$, respectively). Statistically significant differences were found between male and female donors regarding age, the total number of donations, and the time interval following the previous donation ($p < 0.001$). Concerning ferritin levels, 44 (42.7%) males and 59 (57.3%) females had low ferritin concentrations, the difference being statistically significant ($p = 0.008$) (Table 2). Moreover, the median plasma ferritin for females (15.0 μg/L) was lower than that for males (22.5 μg/L; $p = 0.002$). For ferritin levels defined as < 12 μg/L or > 50 μg/L, significant differences between male and female donors were also observed ($p = 0.023$ and $p = 0.022$, respectively) (Table 3).

Comparison of the results from the capillary methods with the reference Hb values obtained from BC showed that the copper sulphate method pointed to false fails in 21 (10.5%) donors, 13 male and 8 female ($p < 0.001$). Values for Hb obtained with the capillary HemoCue method were positively correlated with those from BC ($p < 0.001$) (Figure 1) but not with plasma ferritin level ($p = 0.393$) (Figure 2). However, in relation to ferritin level defined as AIS (< 12 μg/L), a significant correlation was observed in the case of the capillary HemoCue method and ferritin level in female donors ($p < 0.001$), but not in male donors ($p = 0.148$). There were no significant correlations when results for Hb levels using the copper sulphate method were compared with those from BC ($p = 0.209$) or ferritin level ($p = 0.855$).

Table 2

Haemoglobin (Hb) and ferritin levels in relation to gender

Parameters	Male n = 102	Female n = 98	*p*
Age (years), median (range)	43 (22–64)	30 (19–64)	< 0.001
Total number of previous donations, median (range)	16 (2–120)	5 (2–48)	< 0.001
Interval from last donation (months), median (range)	4 (3–9.5)	5 (4–17)	0.001
Number with low Hb level by copper sulphate, n <135 g/L M, < 125 g/L F	102 (100)	98 (100)	0.323*
Number of patients with low Hb level by HemoCue, n	90 (88.2)	89 (90.8)	0.796
Number of patients with low Hb from BC, n	89 (87.2)	90 (91.8)	0.422
Hb level (g/L), median (range)			
by HemoCue	128 (92–145)	118 (84–136)	< 0.001
from BC	127 (93–149)	114 (83–136)	< 0.001
Number of patients with low ferritin, n (%)	44 (42.7)	59 (57.3)	0.008
Ferritin level (μg/L), median (range)	22.5 (4–209)	15 (2–349)	0.002

M – male; F – female; BC – blood count; *p* (Mann-Whitney test; *Fisher test). Difference with regard to number with low Hb – copper sulphate vs. BC ($p < 0.001$). The reference ranges for ferritin designated as normal by the manufacturer were 20–250 μg/L for males and 20–200 μg/L for females.

Table 3

Iron status in relation to the different ferritin levels and gender

Ferritin level (μg/L)	Male (n = 102) n (%)	Female (n = 98) n (%)	*p* (Pearson χ^2 test)
<12	30 (29.4)	44 (45)	0.023
< 29	32 (31)	28 (28.5)	0.659
30–50	16 (15.6)	15 (15)	0.942
> 50	24 (23.5)	11 (11.5)	0.022

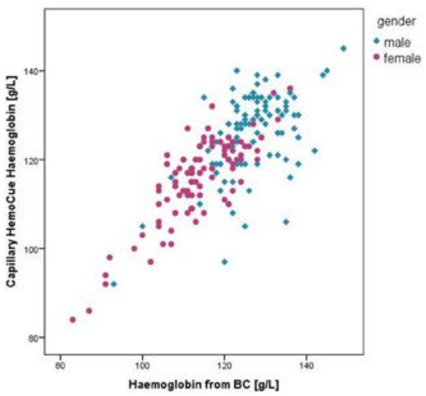

Fig. 1 – Correlation of haemoglobin (Hb) level measured by the HemoCue capillary method with reference Hb from BC (for correlation analysis, Spearman's tests were used, $p < 0.001$).

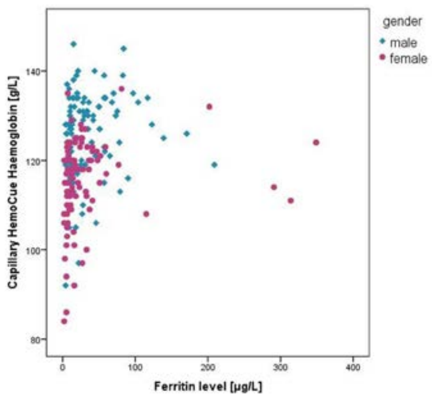

Fig. 2 – Correlation of haemoglobin (Hb) level measured by the HemoCue capillary method with ferritin level (for correlation analysis, Spearman's tests were used, $p = 0.393$).

Discussion

Our evaluation of iron status among blood donors deferred due to low Hb level showed that half of them had decreased plasma ferritin concentrations, while a quarter of them reported fatigue prior to donation. The frequency of low ferritin levels was significantly higher in females, and a greater proportion of women had ferritin levels lower than 12 μg/L, defined as AIS.

A negative correlation between blood donation and the total iron reserve was demonstrated over three decades ago [19, 20] and has been confirmed in recently published studies [7–10]. Our results indicated the same. Based on all these data, additional measures are needed to improve the health of blood donors in order to prevent iron deficiency anemia. Several studies have aimed to determine the best approach for preventing iron deficiency in blood donors [21–27]. Their findings point to a need to re-evaluate current criteria in blood donor selection concerning the interval between donations, optimal testing strategy for measuring iron stores, and the necessity of iron supplementation [28, 29]. A plasma ferritin level below 12 μg/L, defined as AIS, or less than 29 μg/L, defined as depletion, requires deferral of blood donation and confirmation [28]. In Italy, donors with iron deficiency are invited to lengthen the interval between whole blood donations. In Denmark, if plasma ferritin is less than 15 μg/L, the donor is sent 100 iron tablets by post. When the ferritin level is 15–40 μg/L, the donor is given 60 iron tablets for supplementation [12].

In our study, 60% of male and 73.5% of female donors had ferritin values that required deferral of blood donation for three to six months. We should point out that almost half of our low Hb female donors (45%) were observed in the group with ferritin < 12 μg/L, while only 11.5% of them had a ferritin concentration that indicated optimal iron status.

It should be emphasized that donor selection criteria have generally been adopted through health system regulations, but practice according to the current approach in vary among different transfusion centers [30, 31]. Although the demand for blood supplies is decreasing in many countries due to the implementation of Patient Blood Management, in Serbia, this demand is constantly increasing because of the aging of the population and a relatively high incidence of malignant diseases. Another problem of the Serbian society is the emigration of young people during the last few decades for economic reasons. Therefore, defining a rational, evidence-based donor selection process in our transfusion services is crucial in order to minimize unnecessary rejection of voluntary blood donors and to prepare them for future donation so that continuous blood supply is maintained.

Determining Hb levels before donation with two capillary methods and comparing them with the value obtained from BC showed that the copper sulphate method gave false fails in 10.5% of donors. On the other hand, the capillary HemoCue method provided Hb values comparable with those obtained from BC. Moreover, in female donors with ferritin below 12 μg/L, there was a significant association with Hb level obtained with the capillary HemoCue method. Regarding that, every effort should be made to improve the accuracy of Hb screening in our centres. This implies a recommendation that the capillary photometric method should be introduced to replace the copper sulphate procedure for Hb determination. In addition, taking our results for iron status into consideration, determining the algorithm for detecting iron deficiency together with iron supplementation should be included in the Serbian transfusion services.

Our study has limitations that should be considered. Namely, the number of participants was relatively small. Concerning the study design, no selection was made during recruitment; thus, all donors with identified low Hb were included. Therefore, differences among donors regarding age and number of previous donations could have an implication that resulted in recall bias. However, this is the first study conducted among Serbian voluntary donors, and the results obtained need to be confirmed in further investigations involving a larger number of participants.

Conclusion

For determining hemoglobin prior to donation, the HemoCue capillary method is more suitable than the copper sulphate method. A low plasma ferritin concentration was observed in 51.5% of Serbian blood donors deferred due to low hemoglobin. Our findings indicated that determining the algorithm for detecting iron deficiency is necessary. However, in addition to the optimal testing strategy for measuring iron stores, the necessity of iron supplementation and treatment of iron deficiency anemia among blood donors are extremely important.

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