European Journal of Internal Medicine xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

European Journal of Internal Medicine

journal homepage: www.elsevier.com/locate/ejim

Original Article

Could lung function be modified by repeated blood donations?

Maurizio Rizzi *, Andrea Cristiano, Francesca Frassanito, Claudio Macaluso, Andrea Airoldi, Silvia Vanni, Delfino Legnani

Pulmonary Departement, "Luigi Sacco" University Hospital, Milan, Italy

ARTICLE INFO

Article history:
Received 20 January 2016
Received in revised form 6 April 2016
Accepted 10 May 2016
Available online xxxx

Keywords:
Blood donation
DLCO
Sympathetic nervous system

ABSTRACT

Background: Whole blood donation consists in the removal of 10% of total blood volume (500 ml). In this situation several compensatory mechanisms occur, involving sympathetic nervous system, renin–angiotensin–aldosterone system and the release of erythropoietin. Aim of this study is to evaluate whether a periodic stimulation of sympathetic nervous system, such as in blood donors in the period following the donation, may affect lung function.

Methods: 100 consecutive Caucasian male blood donors were compared with 50 healthy male subjects, recruited from the general population. Respiratory tests, including lung transfer factor (DLCO) and its components, alveolar-capillary membrane (Dm) and pulmonary capillary blood volume (Vc) were performed in each subject enrolled and in blood donors, before and after donation.

Results: At baseline DLCO ($p < 0.0001$), and Dm ($p < 0.0001$) were significantly reduced in the blood donors' group. A blood donation reduced DLCO ($p < 0.01$) due to decreased Vc ($p < 0.05$). There is a progressive reduction of DLCO related to years of blood donation, due to a greater impairment of the alveolar–capillary membrane diffusion. The correlation between reduction of DLCO, Dm and years of blood donation is statistically significant ($p < 0.001$).

Conclusions: In blood donors DLCO reduction is related to the total number of years of donation. It may be indicated to evaluate DLCO in donors who made blood donations for many years, to possibly reduce donations frequency.

Moreover particular attention should be paid to blood donors with a smoking habit in which frequent donations may increase the impairment of DLCO due to exposure to cigarette smoke.

1. Background

Nowadays blood donation is very important for public health. The total amount of blood in human circulatory system is about five litres [1]. Red blood cells contain a protein called haemoglobin which carries oxygen to organs and muscles and has a role in carbon dioxide removal. Haemoglobin contains heme groups, to which iron is bound. Iron portion is the binding site for oxygen [2]. Circulation of blood throughout the body is maintained by heart rate, cardiac output and blood pressure. Cardiac output and blood pressure are controlled and regulated by baroreceptors in the aortic arch and carotid arteries. Baroreceptors detect volume and pressure of blood flowing through aorta and carotid arteries at each heart pulse [3]. Baroreceptors are also responsible for adjusting heart rate in response to changes in blood pressure [4].

Whole blood donation consists in the removal of 500 ml of blood; this volume corresponds to a reduction of 10% of total blood volume [1]. Due to this reduction of blood volume, approximately 225–250 mg of heme is removed [5]. Consequently, concentration of oxygen in the body is reduced [6]. The reduction of oxygen delivery to organs could decrease tissue perfusion, and a great reduction could possibly lead to cellular hypoxia, organ damage, and death [7].

When blood loss is around 10%, such as in one blood donation, several compensatory mechanisms occur [8]. These compensatory mechanisms involve the sympathetic nervous system, the renin–angiotensin–aldosterone hormone system and the release of erythropoietin [5,9].

Blood loss, anaemia and a frequent sympathetic activation may result in a reduction of transfer lung factor (DLCO) [10,11,12,13], which is defined by Hughes as a "window on the pulmonary microcirculation" [14]. This process can be simplified in two stages, as proposed by Roughton and Foster: the first stage is the diffusion of CO from the alveolus to the red cell interior, described as the membrane component (Dm), the second stage is the uptake of CO by binding with Hb in the red cells per mm Hg CO tension (θ) and the blood volume of the pulmonary capillary bed (Vc) [15]. The basic equation for DLCO is a flow divided by pressure change ($V / \Delta P$) which is a conductance. The

* Corresponding author at: Ospedale "Luigi Sacco" Azienda Ospedaliera, Polo Universitario, Via GB Grassi, 74, 20157 Milano, Italy. Tel.: +39 0239042277; fax: +39 0239042613.

E-mail addresses: rizzi.maurizio@hsacco.it, rizzi.maurizio@asst-fbf-sacco.it (M. Rizzi), andrea.cristiano@unimi.it (A. Cristiano), francesca.frassanito@unimi.it (F. Frassanito), claudio.macaluso@unimi.it (C. Macaluso), airoldi.andrea@asst-fbf-sacco.it (A. Airoldi), vanni.silvia@asst-fbf-sacco.it (S. Vanni), legnani.delfino@asst-fbf-sacco.it (D. Legnani).

http://dx.doi.org/10.1016/j.ejim.2016.05.007
0953-6205/

reciprocal of conductance is resistance, and resistances can be added in series. Roughton and Foster proposed the following equation to describe the diffusion of CO in the lung.

$$1/DLCO = 1/Dm + 1/\theta Vc$$

Using different O_2 concentrations, the importance of each component can be determined by measuring DLCO: increasing partial pressure of O_2, it competes with CO for Hb binding, reducing the θVc component. This equation is important in determining the pathophysiologic mechanism for reduced DLCO in various conditions.

The aim of this study is to evaluate whether a periodic stimulation of the sympathetic nervous system, such as that in blood donors in the period following the donation, may affect lung transfer factor.

2. Methods

2.1. Subjects

Between April 2014 and April 2015, 100 consecutive Caucasian male blood donors aged 48 ± 10 years were compared with 50 healthy male subjects, recruited from the general population, well matched in terms of age, body mass index (BMI), who voluntarily participated the study. All the subjects were enrolled by the physicians of the haematology Department of L. Sacco University Hospital in Milan, Italy.

The study was approved by the local ethics committee and conducted according to the Declaration of Helsinki. All study visits occurred at the L. Sacco Hospital.

Subjects enrolled met these criteria: absence of medical, neurological or psychiatric disorders and no tobacco or alcohol consumption or drug abuse.

Respiratory tests were performed in each subject enrolled and in blood donors before and after the donation. Moreover haemoglobin level was assessed for each patient immediately before and immediately after blood donation.

2.2. Pulmonary function tests

Lung volumes and spirometry dynamic parameters were assessed by plethysmography (VMAX227 Autobox V6200; Sensor Medics; Yorba Linda, CA), performed in accordance with European Respiratory Society criteria [16]. Lung transfer factor (DLCO) was measured with the single breath technique (Transfer Test; Morgan Kent, UK), according to the recommendations from the European Respiratory Society [16]. DLCO was measured using low oxygen concentration (CO 0.25%; He 14%; O_2 20%); breath-holding time was at least 10 s, and washout volume was 0.75 L. To evaluate Dm and Vc according to the Roughton and Foster equation we performed measurements of DLCO using a high oxygen concentration (CO 25%; He 14%; O_2 85–75%). Double measurements were accepted when estimates of DLCO and effective alveolar volume differed by 5%; the good reproducibility of the measurements allowed the use of only two gas mixtures of different concentrations of O_2.

Time interval between measurements was 5 min, and the tests were performed in sitting position [17].

The flow sensor was calibrated before each test using a three-litre syringe.

The carbon monoxide transfer factor coefficient (Kco) was derived from the following equation:

$$Kco = DLCO/alveolar\ \ volume$$

The two components of lung transfer: alveolar–capillary membrane (Dm) and pulmonary capillary blood volume (Vc) were calculated using the Roughton and Foster equation [15].

Table 1

	Blood donors no 100	Controls no 50	p
Age years	48 ± 10	47 ± 11	n.s
BMI hg/h^2	28 ± 3	28 ± 4	n.s.
VC% predicted	108 ± 8	110 ± 7	n.s.
FEV_1% predicted	99 ± 5	101 ± 8	n.s.
RV% predicted	91 ± 5	90 ± 6	n.s.
TLC% predicted	99 ± 8	101 ± 10	n.s
DLCO% predicted	88 ± 6	105 ± 7	<0.0001
Kco% predicted	86 ± 5	99 ± 6	<0.0001
Dm ml/min/mm Hg	17 ± 3	26 ± 4	<0.0001
Vc ml	93 ± 21	96 ± 36	n.s.

Data expressed in mean ± s.d. BMI: body mass index; VC: vital capacity; Fev_1: forced expiratory volume in one second; RV: residual volume; TLC: total lung capacity; DLCO: transfer factor of the lung; Kco: transfer factor coefficient; Dm: diffusing capacity of the alveolar membrane; Vc: pulmonary capillary blood volume.

Reference equations proposed by ATS/ERS task force report were used [16].

All respiratory tests were performed by a single examiner (MR), and their variability and reproducibility were within the range assessed for these parameters, as previously described [16]. As well as haemoglobin level, DLCO was assessed immediately before and immediately after blood donation, with the intent to minimize the influence of haemoglobin reduction on DLCO and its components.

2.3. Statistical analysis

Data were analysed using the Statistical Package SPSS v.6.1 (SPSS; Chicago, IL, USA) and expressed as mean and standard deviation.

Statistical analysis of anthropometric data and pulmonary function tests was performed using unpaired Student's t test. One-way analysis of variance was used to compare data among the groups of subjects considered. The Tukey honestly significant difference test for unequal sample sizes (Spjotvoll and Stoline test) was used to compare differences between groups. The relationships between variables were evaluated using the Pearson product–moment correlation coefficient. The level of significance was $p < 0.05$.

3. Results

The number of years of donation in the 100 blood donors was 12.5 ± 10.3 with a quarterly rate of blood donation. Table 1 shows anthropometric data and pulmonary function tests of blood donors and control subjects; lung volumes did not differ between the two groups, while DLCO (88 ± 6% vs. 105 ± 7% $p < 0.0001$), Kco (86 ± 5% vs. 99 ± 6% $p < 0.0001$) and Dm (17 ± 3 mL/min/mm Hg vs. 26 ± 4 mL/min/mm Hg $p < 0.0001$) were significantly reduced in the blood donors group.

The effect of one blood donation (about 500 ml) on DLCO and its components is summarized in Table 2, where a reduction of

Table 2

	Pre blood donation	Post blood donation	p
VC% predicted	108 ± 8	106 ± 7	n.s.
FEV_1% predicted	99 ± 5	98 ± 6	n.s.
RV% predicted	91 ± 5	92 ± 4	n.s.
TLC% predicted	99 ± 8	97 ± 7	n.s.
DLCO% predicted	89 ± 5	86 ± 4	<0.01
Kco% predicted	88 ± 5	84 ± 6	<0.001
Dm ml/min/mm Hg	17 ± 3	16 ± 5	n.s.
Vc ml	93 ± 21	86 ± 28	<0.05
Hb gr/dl	14.3 ± 0.5	14.2 ± 0.6	n.s.

Data expressed in mean ± s.d. BMI: body mass index; VC: vital capacity; Fev_1: forced expiratory volume in one second; RV: residual volume; TLC: total lung capacity; DLCO: transfer factor of the lung; Kco: transfer factor coefficient; Dm: diffusing capacity of the alveolar membrane; Vc: pulmonary capillary blood volume; Hb: haemoglobin concentration.

Please cite this article as: Rizzi M, et al, Could lung function be modified by repeated blood donations?, Eur J Intern Med (2016), http://dx.doi.org/10.1016/j.ejim.2016.05.007