Course of Hemoglobin and Hematocrit during and after Preparatory Plasmaphereses without and with Infusion of NaCl 0.9% 500 ml

Josef Evers Norbert Ehren Tanja Engelen Michael Hansen Kerstin Luethje Uwe Taborski

Deutsche Gesellschaft für Humanplasma (DGH), Plasmazentrum Aachen, Germany

Keywords

Apheresis · Hemoglobin · Hematocrit ·
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Summary

Background: The aim of this study was to evaluate the course of hemoglobin (HGB) concentration and hematocrit (HCT) in donor blood during and after preparatory plasmaphereses (PP) without NaCl and with an infusion of 500 ml 0.9% NaCl during PP. **Methods:** After informed consent 32 plasma donors were studied in a crossover design. They underwent PP once without NaCl infusion and once, on a different day, with infusion of 500 ml 0.9% NaCl. HGB concentration and HCT values in donor blood were analyzed using a Sysmex KX-21N analyzer. The values of HGB concentration and HCT before PP were set to 100%. Changes in HGB concentration and HCT were calculated in percent directly after PP, and after 24 and 72 h. **Results:** During PP, there was a notable change in HGB concentration ($11.2 \pm 4.0\%$) and HCT ($11.6 \pm 3.9\%$) in donor blood. The difference between the 2 samples without and with NaCl was highly significant ($p < 0.001$). After 24 and 72 h, all differences were reduced. **Conclusion:** We observed significant changes in HGB concentration and HCT in donor blood during PP. We recommend a concomitant infusion of 500 ml 0.9% NaCl during PP to all donors.

the changes in hemoglobin (HGB) concentration and hematocrit (HCT) values in donor blood during and after PP without or with an infusion of saline solution. Increases of HGB concentration and HCT might be the cause of the diminished blood flow that is sometimes seen at the end of plasma donations, and could be dangerous for donors who have a risk for venous thromboses or ischemic infarction. Infusion of 500 ml 0.9% NaCl is a commonly accepted practice to prevent hypotensive events during PP or apheresis. The disadvantage may be a dilution effect of infused saline solution on the separated plasma by 5% [1]. However, the benefits to donor safety and satisfaction are compelling reasons to implement saline infusion during plasmapheresis [2].

In a preliminary surveillance of 12 different donors, we found a marginally significant increase of HGB concentration and HCT ($p = 0.04$) in donors without saline infusion compared to donors with an infusion of 500 ml 0.9% NaCl during PP immediately after PP using a Haemonetics® Plasma Collecting System 2 (PCS2) [3]. We undertook this study as we could not find sufficient data in the literature on changes in HGB concentration or HCT during and after PP performed with modern automated collecting systems in humans. The aim or primary endpoint of the present study was to determine the course of HGB concentration and HCT during and after PP performed using the Haemonetics® PCS2 without saline infusion and in PP with an infusion of 500 ml 0.9% NaCl.

Introduction

Although the influence of an infusion of 500 ml 0.9% NaCl during preparatory plasmapheresis (PP) on separated plasma has been studied recently [1, 2], there are only limited data on

Participants and Methods

Participants

In the study we enrolled 32 donors of plasma who did not usually receive a saline infusion during apheresis. Donors who regularly received an infusion of 500 ml 0.9% NaCl during PP were excluded. The details of the participants are given in table 1. All donors were in good health on the basis of medical history, physical examination and hematological

Table 1. Clinical data (32 patients, 17 male, 15 female)

	Mean	SD	Max	Min
Age, years	30	11	49	18
Weight, kg	70.4	8.9	97	59
Volume of separated plasma, ml/kg	11.7	1.1	13.4	8.9

screening. They had no laboratory evidence of hepatitis B, hepatitis C, human immunodeficiency virus infection, or syphilis. Volunteers were excluded if they had any contraindication for donating plasma according to the regulations of the German Medical Association [4] or the Guide of Preparation and Quality Assurance of Blood Components of the Council of Europe [5].

Design

The study was undertaken according to national law in Germany and met the standards of the Declaration of Helsinki. A validation plan was established that described how validation and documentation was to be conducted. Written informed consent was obtained from each participant. The study was done prospectively, at a single center, and in a crossover design [6]. 32 participants were studied on 2 days. The 2 days of study (A) and (B) were at least 7 days apart. 16 subjects were first treated without NaCl infusion during PP on day (A). On day (B) an infusion of 500 ml 0.9% NaCl (free flex® Fresenius) was gradually given during PP in divided doses after each cycle through the harness set of the Haemonetics® PCS2. The other 16 participants were first treated with an infusion of 500 ml 0.9% NaCl (B) and subsequently without NaCl (A).

On the days of study, participants had to take a light meal and at least 1.5 l fluid intake within 4 h before PP. They were interviewed and screened within 10 min before apheresis. After venipuncture, samples of 2 ml EDTA blood were taken from the tube of the fistula needle, first for whole blood counts (WBC₁), including HGB concentration and HCT before PP. Aphereses were performed with the Haemonetics PCS2. 4% sodium citrate anticoagulant solution (Haemonetics®) was added to venous blood during the draw phase in a ratio of 1:16. Immediately after apheresis, a second 2-ml EDTA blood sample was taken from a vein of the opposite arm of the donor for WBC in blood (WBC₂). Plasma donors were told to drink at least 2.5–3 l fluid each day after PP. Further 2-ml EDTA blood samples were taken for WBC after 24 and 72 h.

Analysis

WBC, including HGB and HCT, were analyzed on a Sysmex KX-21N automated hematology autoanalyzer within 2–15 min of withdrawal [7].

Statistical Analysis

Details of the participants and results of HGB concentrations and HCT were documented in a protocol and in an excel table (Microsoft® Office Excel® 2007). HGB concentrations and HCT in blood before PP were set to 100%. The changes in HGB concentrations and HCT in blood were calculated at the end of PP, and after 24 and 72 h as the ratio (in %) of values before PP. The difference (ΔHGB) of HGB at the end of PP was calculated as: $\Delta\text{HGB}_{\text{PP}} (\%) = (\text{HGB}_2 - \text{HGB}_1) \times 100 / \text{HGB}_1$. ΔHCT at the end of PP was: $\Delta\text{HCT}_{\text{PP}} (\%) = (\text{HCT}_2 - \text{HCT}_1) \times 100 / \text{HCT}_1$.

With regard to the crossover test layout, statistical analysis was performed as described in up-to-date statistical literature [6]. A pre-test clarified whether carryover effects can be ruled out. A Shapiro-Wilk test was performed to check if the relevant values to calculate carryover and treatment effects were normal distributed [8]. Based on these results a *t*-test or, as non-parametric alternative, a Wilcoxon rank-sum test was used for the decision on the significance of the effects [6]. Paired *t*-tests were carried out for comparison of data before PP compared to immediately after, and 24 and 72 h after PP. Mean values, standard deviation, *t*-tests, and

Table 2. Results of HGB^a

	Without NaCl	With NaCl
HGB before PP, g%	14.3 ± 1.2	14.4 ± 1.0
HGB after PP, g%	15.9 ± 1.3	15.1 ± 0.9
HGB after 24 h, g%	14.9 ± 1.1	14.8 ± 1.1
HGB after 72 h, g%	14.2 ± 1.1	14.2 ± 1.1

^aData are reported as mean ± SD. PP was performed once without NaCl infusion and once, on a different day, with infusion of 500 ml 0.9% NaCl.

Table 3. Results of HCT

	Without NaCl	With NaCl
HCT before PP, %	42.9 ± 3.2	42.9 ± 2.8
HCT after PP, %	47.8 ± 3.8	45.1 ± 2.7
HCT after 24 h, %	44.5 ± 2.7	43.8 ± 2.9
HCT after 72 h, %	42.4 ± 3.1	42.3 ± 2.9

^aData are reported as mean ± SD. PP was performed once without NaCl infusion and once, on a different day, with infusion of 500 ml 0.9% NaCl.

maximal and minimal values were derived from excel calculation. Shapiro-Wilk tests and Wilcoxon rank-sum tests were carried out using Analyse-it®, V.2.3, (Analyse-it Software, Ltd., Leeds, UK).

Results

All 32 included donors completed the study. The results are summarized in tables 2 and 3. The values in the tables are given as mean ± standard deviation. The relevant values to calculate carryover and treatment effects were normally distributed, so *t*-tests were carried out to check the significance of the measured effects [6].

Without giving an infusion of 0.9% NaCl during apheresis, the average rise in HGB concentration in blood immediately after PP in relation to that in the blood before PP ($\Delta\text{HGB}_{\text{PP}}$) was 11.2 ± 4.0%, and the mean rise in HCT ($\Delta\text{HCT}_{\text{PP}}$) was 11.6 ± 3.9%. The data showed a highly significant ($p < 0.001$) increase in HGB and HCT for values immediately after PP and those after 24 h compared to data before PP, and a very slight decrease after 72 h.

When 500 ml 0.9% NaCl was given during PP, the mean rise in HGB concentrations was 5.4 ± 3.4% and the mean rise in HCT was 5.2 ± 3.8%. With infusion of 500 ml NaCl the data also showed a highly significant ($p < 0.001$) increase in HGB and HCT for values immediately after PP, a significant ($p < 0.05$) increase after 24 h compared to data before PP, and a very slight decrease after 72 h. The differences in $\Delta\text{HGB}_{\text{PP}}$ and $\Delta\text{HCT}_{\text{PP}}$ between the 2 treatment groups without NaCl and with 500 ml 0.9% NaCl at the end of PP were statistically highly significant ($p < 0.001$). After 24 and 72 h the values for ΔHGB and ΔHCT showed no significant treatment effect (with vs. without NaCl). The data showed no evidence for any relevant carryover effect.

Discussion

A slight rise in HGB concentration and HCT in blood was already observed 1964 in a study with 4 blood donors after manual plasmapheresis [9]. To ensure donors' safety, the results of that study of manual plasmaphereses now need to be followed up in larger studies for the modern automated PP systems used today.

Significant differences between pre- and post-donation values for HGB and HCT were found in 112 donors undergoing plateletpheresis using Haemonetics PCS equipment [10]. An initial increase of HCT ($p < 0.001$) with a subsequent overshooting decrease after 24 h ($p < 0.001$) was observed in 19 donors with preparatory combined thrombocytapheresis and plasmapheresis [11]. In 6 clinically healthy horses, the collection of 20 ml plasma/kg body weight via automated plasmapheresis resulted in a mild increase in the HCT, HGB concentration, total erythrocyte, and leukocyte counts ($p < 0.01$), although these appeared of no clinical relevance [12]. Pre- and post-donation hematological values in 457 healthy first-time donors undergoing plateletpheresis with 5 different systems decreased significantly ($p < 0.01$) after each procedure [13]. The volumes of separated plasma in these studies [9–13] are not transferable to modern PP in human donors with automated plasma collecting systems. There have been no studies concerned with the effect of a saline infusion during PP.

In a preliminary study of a small group of 12 different frequent donors, we found an increase of HGB concentrations and HCT at the end of PP with a marginal, but significant, difference ($p = 0.04$) between groups without NaCl and with saline infusion during PP [3]. There have been no similar reports in the literature on changes in HGB concentration and HCT during PP with modern automated PP in humans to confirm the significance of these findings. We performed the cur-

rent study to determine whether the changes in HGB concentration and HCT were significant in larger studies and how long the changes in HGB and HCT persisted after PP.

In summary, this study of PP either without NaCl and with concomitant infusion of 500 ml NaCl showed a significant increase of HGB concentration and HCT for values immediately after PP and those after 24 h compared to data before PP, and a very slight decrease for values after 72 h. However, regarding clinical aspects the latter was small and appeared clinically not important.

Our results imply that infusion of 500 ml 0.9% NaCl during PP avoids excessive changes of HGB concentration and HCT during PP, and that all increases of HGB concentrations and HCT were generally reduced after 24 h if the donors comply to have a fluid intake of 2.5–3 l each day after PP. As the course of HGB concentration and HCT reflect the volume changes during and after PP, we conclude that the volume changes caused by PP in donors are balanced by about 24 h after PP. Therefore, it appears unlikely that adverse events due to volume changes are caused by PP after more than 24 h. It is important to remind donors to have a fluid intake of at least 1.5–2 l before PP and after that 2.5–3 l each day to compensate for volume changes during PP. To improve donor safety, we recommend an infusion of 500 ml 0.9% NaCl during PP to all donors.

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Disclosure Statement

The authors declared no conflict of interest.

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