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SCIENTIFIC ARTICLE

Role of acute hemodilution in blood transfusion rate in patients submitted to scoliosis surgery: observational retrospective study

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KEYWORDS
Hemodilution;
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Abstract
Background and objectives: The study assessed the role of acute hemodilution in the blood transfusion rate in patients submitted to surgical treatment of scoliosis.
Methods: Retrospective observational study performed at Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo (HC-FMRP–USP). Medical charts of patients submitted to elective correction of scoliosis between January 1996 and December 2016 were analyzed. Variables assessed were: age, weight, sex, presence of comorbidities, data regarding anesthesia and surgery, lab data, adverse events and blood transfusion rate. The final sample consisted of 33 procedures performed by the same anesthesiologist and same surgeon, divided into two groups: Hemodilution Group (n = 16) and Control Group (n = 17). Indication of acute normovolemic hemodilution was determined by patient refusal of blood transfusion for religious reasons.
Results: The sample was statistically homogeneous and the groups were compared in terms of the attributes analyzed. The volume of homologous blood used by the Hemodilution Group was significantly lower than the Control Group ($p = 0.0016$). The percentage of patients who required transfusion was 12.5% in the Hemodilution Group, while it was 70.69% ($p = 0.0013$) in the Control Group. Upon hospital discharge, mean values of hemoglobin and hematocrit between groups did not present significant differences ($p = 0.0679$; $p = 0.1027$, respectively).

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Conclusions: Acute normovolemic hemodilution, in scoliosis correction surgeries, reduces blood transfusion rates, meeting patient needs without increasing adverse events or infection rates.

PALAVRAS-CHAVE
Hemodiluição;
Artrodese;
Escoliose

Papel da hemodiluição aguda na taxa de transfusão sanguínea em pacientes submetidos a tratamento cirúrgico de escoliose: estudo observacional retrospectivo

Resumo
Justificativa e objetivos: Este estudo avaliou o papel da hemodiluição aguda na taxa de transfusão sanguínea em pacientes submetidos a tratamento cirúrgico de escoliose.
Método: Estudo observacional retrospectivo realizado no Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo (HCFMRP-USP). Analisados prontuários de pacientes submetidos à correção de escoliose no período entre janeiro de 1996 a dezembro de 2016, em regime eletivo. As variáveis avaliadas foram: idade, peso, sexo, presença de doenças concomitantes, dados referentes à anestesia e à cirurgia, dados laboratoriais, eventos adversos e taxa de transfusão sanguínea. A amostra final foi composta por 33 procedimentos realizados pelo mesmo médico anestesiologista e pelo mesmo cirurgião, divididos em dois grupos: Grupo Hemodiluição (n = 16) e Grupo Controle (n = 17). A indicação de hemodiluição normovolêmica aguda foi determinada pela recusa à transfusão sanguínea pelos pacientes, por motivos religiosos.
Resultados: A amostra foi estatisticamente homogênea e os grupos foram comparados considerando os atributos analisados. O volume de sangue homólogo utilizado pelo Grupo Hemodiluição foi significativamente menor que no Grupo Controle ($p = 0{,}0016$). A porcentagem de pacientes que necessitou transfusão foi de 12,5% no Grupo Hemodiluição, enquanto no Grupo Controle foi de 70,69% ($p = 0{,}0013$). Na alta hospitalar, os valores médios de hemoglobina e hematócrito entre os grupos não apresentaram diferenças significantes ($p = 0{,}0679$; $p = 0{,}1027$, respectivamente).
Conclusões: A hemodiluição normovolêmica aguda, em cirurgias para correção de escoliose, reduz a taxa de transfusão sanguínea, satisfazendo as necessidades dos pacientes sem aumentar as taxas de eventos adversos e de infecção.

Introduction

Acute Normovolemic Hemodilution (ANH) is performed to reduce the rate of blood transfusion and consists in blood volume withdrawal and its replacement with acellular fluids. It is essential that volemia be preserved and the method be performed before major blood loss. The blood withdrawn is kept in the operating room up to eight hours and re-infused at the end of the surgical procedure or earlier, according to patient requirements.[1] The cardiovascular system is fundamental for oxygen delivery regulation.[2] Tissue delivery of oxygen is sustained by decrease in blood viscosity and increase in cardiac output. Increase in the extraction rate compensating low oxygen delivery works during normovolemia only.[3–5] ANH is indicated for anticipated blood loss estimate of over 1,000 mL or 20% of the blood volume.[5,6] As surgical repair of spine deformities are associated with large intraoperative blood loss,[7] ANH is more frequently used during these procedures.

Although ANH is recommended by the National Health Institute for avoiding transfusions,[8] there is still disbelief in its efficacy.[9] Few studies have assessed ANH and scoliosis surgery, and results are discordant. The present study aimed to assess the role of ANH in the reduction in allogenic transfusion rates in patients submitted to surgical repair of scoliosis at the Ribeirão Preto School of Medicine Hospital (HC-FMRP-USP, from *Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto*, in Portuguese).

Methods

The retrospective observational study was performed by assessing medical charts of patients submitted to surgical repair of scoliosis at HC-FMRP-USP between January 1996 and December 2016. After approval of the Research Ethics Committee (CAAE: 68525317.8.0000.5440), data was collected by the researcher. The sample included medical charts of patients over one year of age submitted to elective scoliosis surgery, with anesthetic care performed by

$$V = VSE \times \frac{[\,(Ht_i - Ht_f)\,]}{[\,\frac{Ht_i + Ht_f}{2}\,]}$$

Figure 1 Gross formula. V, Withdrawn Volume; EBV, Estimate Blood Volume (70 mL.Kg^{-1}); Ht_i, Initial Hematocrit and Ht_f, Final Hematocrit.

the same anesthesiologist (one of the authors of the study) and the surgical procedure performed by the same surgeon. All patients included were submitted to general anesthesia with mechanical ventilation. Monitoring comprised ECG, pulse oximetry, non-invasive arterial blood pressure, urinary output via indwelling catheter, radial artery catheterization and central venous access. Patients were divided into two groups: Hemodilution Group (ANH performed) and Control Group (no ANH). ANH was performed after blood transfusion refusal by the patient due to religious conviction. Hemodilution was performed by determining the blood volume to be withdrawn in order to achieve target hematocrit (there was no single hematocrit goal for all patients), based on the GROSS formula[10] (Fig. 1).

Blood was withdrawn via a previously punctured radial artery, by spontaneous gravity drainage, into a bag containing anticoagulant. The volume withdrawn was checked by weighing the bag. We collected a maximum of 450 grams per bag. Before disconnecting the arterial catheter, the bag was connected, via blood infusion set, to the central venous catheter. Bags were kept at room temperature in the operating room connected to patients up to a maximum of eight hours. All bags were reinfused back to patients before the eight-hour period elapsed. Hemodynamic parameters were followed during the entire ANH procedure. Volemia was maintained by concomitant infusion of crystalloid and colloid solutions. The following regimen was employed: the first 1,000 mL of blood withdrawn were replaced by the same volume of colloid solution, and the remaining replaced until completing the volume estimated by the Gross formula, by 2 mL of crystalloid solution for each 1 mL of blood collected. All withdrawn blood was reinfused to the patient at the end of the anesthesia or before, whenever required. At the conclusion of the surgical procedure, the autologous blood was reinfused, preceded by 0.5–1 mg.Kg^{-1} of furosemide infusion.

The primary outcome was to assess the blood transfusion rate. Additional variables assessed were: age, weight, sex, co-morbidities, data related to anesthesia and surgery, laboratory tests and adverse events.

Data were treated by the GraphPad Prism version 5.0 software. Normality of data distribution was analyzed by the Kolmogorov-Smirnov test. Variables with normal distribution were compared using the Student *t*-test for independent samples. When normal distribution was absent, we used the Mann-Whitney test as the non-parametric alternative. Proportions were compared with Fisher's exact test. Significance probability level (*p*-values) presented are the bilateral type, and values below 0.05 were considered statistically significant.

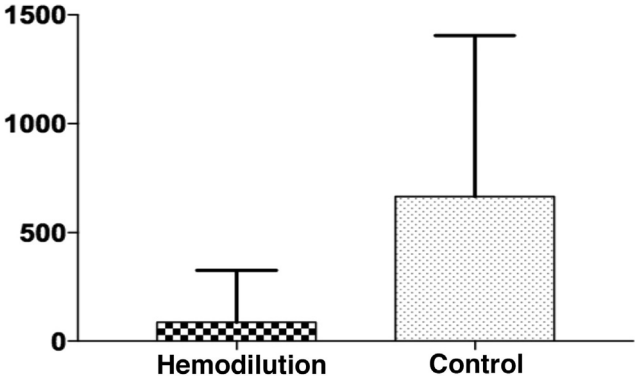

Figure 2 Perioperative volume of packed blood red cells transfused. Mann-Whitney test; $p = 0.0016$ (significant). Source: Author.

Results

During the study period 183 scoliosis surgeries were performed. The final selection included 33 scoliosis surgery procedures that met inclusion criteria. Of the latter, 16 procedures comprised the Hemodilution Group and 17 the Control Group.

Analysis of patient and procedure-related data did not show any significant differences between groups (Table 1).

The frequency of neuromuscular scoliosis, precisely associated with the most severe bleeding, was comparable in both groups. In the Hemodilution Group, the percentage of neuromuscular scoliosis was 18.75% (3 of 16 patients), while it was 17.64% (3 of 17 patients) for the Control Group. Although 7 of 16 patients of the Hemodilution Group were treated preoperatively with erythropoietin and/or iron, we did not find a statistically significant preoperative difference between groups regarding mean values of hemoglobin and hematocrit. Preoperatively, the Hemodilution Group showed mean values for hemoglobin (13.53 ± 1.29 g.dL^{-1}) and hematocrit (40.33% ± 3.25%) higher than the Control Group, that showed mean values for hemoglobin and hematocrit of 12.95 ± 1.72 g.dL^{-1} and 38.04% ± 4.78%, respectively. In the Hemodilution Group, the percentage of procedures performed via posterior approach was 81.25% (13 of 16 patients), while in the Control Group the percentage was 76.47% (13 of 17 patients).

The volume of blood transfused (Fig. 2) and the blood transfusion rate during the perioperative period were statistically higher in the Control Group when compared to the Hemodilution Group ($p = 0.0016$; $p = 0.0013$, respectively). At hospital discharge, mean hemoglobin and hematocrit values did not present a statistically significant difference between the groups ($p = 0.0679$; $p = 0.1027$, respectively). Although Control Group patients seemed to present shorter hospital length of stay, the difference between groups was not significant ($p = 0.6081$). The percentage of adverse events and infection during the postoperative period up to hospital discharge did not show a significant difference between groups ($p = 0.4646$; $p > 0.9999$, respectively) (Table 2).

The Hemodilution Group showed the following adverse events during the postoperative period until hospital dis-

Table 1 Patient and surgical procedure features.

	Hemodilution Group (n = 16)	Control Group (n = 17)	*p*
Age (years)[a]	18.19 ± 6.06	14.59 ± 4.55	0.1172
Weight (kg)[b]	46.46 ± 5.40	41.38 ± 15.03	0.2186
Female gender[c]	13 (81.25%)	12 (70.59%)	0.688
Co-morbidity[c]	3 (18.75%)	7 (41.18%)	0.2587
Number of levels approached[b]	10.79 ± 4.56	11.12 ± 4.22	0.8351
Duration of anesthesia (min)[b]	451.90 ± 123.40	432.60 ± 164.30	0.7069
Duration of surgery (min)[b]	352.2 ± 111.1	365.3 ± 144.9	0.7736
Pre-operative hemoglobin ($g.dL^{-1}$)[b]	13.53 ± 1.29	12.95 ± 1.72	0.2951
Pre-operative hematocrit (%)[b]	40.33 ± 3.25	38.04 ± 4.78	0.1299

Values in mean ± SD; number of patients and percentages (between parenthesis).
[a] Mann-Whitney test.
[b] Student *t*-test.
[c] Fisher's exact test.

Table 2 Volume and blood transfusion rate; hospital length of stay; rate of adverse events and infection; hemoglobin and hematocrit at hospital discharge.

	Hemodilution Group (n = 16)	Control Group (n = 17)	*p*
Packed red blood cells transfused – perioperative (mL)[a]	86.38 ± 240.6	630.8 ± 676.8	0.0016
Homologous blood transfused – perioperative (mL)[c]	2 (12.5%)	12 (70.59%)	0.0013
Hospital length of stay (days)[a]	16 (23.26)	12.76 (10.76)	0.6480
Postoperative adverse events (up to hospital discharge)[c]	10 (62.50%)	13 (76.47%)	0.4646
Postoperative infection (up to hospital discharge)[c]	4 (25.00%)	4 (23.53%)	> 0.999
Hemoglobin at hospital discharge ($g.dL^{-1}$)[b]	8.82 ± 1.72	10.42 ± 1.90	0.0679
Hematocrit at hospital discharge (%)[b]	27.09 ± 5.06	31.28 ± 5.69	0.1027

Values in mean ± SD; number of patients and percentages (between parenthesis).
[a] Mann-Whitney test.
[b] Student *t*-test.
[c] Fisher's exact test.

charge: nausea and/or vomiting (4 of 16 patients), upper gastrointestinal bleeding (1 of 16 patients), surgical wound bleeding (1 of 16 patients), gynecological bleeding (1 of 16 patients), surgical wound bleeding with severe anemia and need for orotracheal intubation (1 of 16 patients). In the Control Group the following adverse events were observed during the postoperative period until hospital discharge: febrile peak (5 of 17 patients), surgical wound dehiscence (2 of 17 patients), acute lung edema with cardiogenic shock progressing to death (1 of 17 patients), deep venous thrombosis (1 of 17 patients), isolated thrombocytopenia (1 of 17 patients).

We reported surgical wound infection in two patients in the Control Group and in three patients in the Hemodilution Group. In the Hemodilution Group we reported one patient with ventilator-associated respiratory infection, while in the Control Group we observed one patient with urinary tract infection and one with ventilator-associated respiratory infection.

Discussion

In the present study ANH for scoliosis surgery decreased blood transfusion requirement. Patients submitted to hemodilution, nevertheless, presented low hematocrit intraoperative values and recovery of the hematocrit level after reinfusion of the blood collected at the end of surgery. Thus, upon hospital discharge, the ANH procedure proved efficacy in decreasing blood transfusions and meeting patient needs, assuring hemoglobin and hematocrit levels, both clinically safe and comparable to those presented by the Control Group. ANH was not associated with significant increase in duration of anesthesia and hospital length of stay, or increase in the percentage of adverse events and infection. We were not able to impute ANH for any of the severe adverse events observed.

Despite the bias related to the patient selection method, the sample was statistically homogeneous and groups were comparable regarding features such as age, weight, sex, surgery duration, etiology of scoliosis, presence of comorbidities, number of levels approached and preoperative hemoglobin and hematocrit values, differing only in relation to performing ANH. In addition, procedures performed by the same anesthesiologist were selected, minimizing differences in subjective transfusion criteria. Similarly, all procedures were performed by the same surgeon. We can then suggest that the differences found in the results may be statistically due to the action of the variable: performing ANH or not.

Comparable results were found in a prospective spinal surgery study comparing patients who underwent ANH and intraoperative blood salvage with patients who only were

submitted to intraoperative blood savage. No significant difference was found between the groups for hemoglobin and hematocrit values in the immediate postoperative and late postoperative period (24 hours later). The study's authors concluded that, when all the blood collected during ANH is reinfused to the patient at the end of surgery, it replenishes intravascular plasma, and the proportional redistribution of the erythrocyte fraction between the interstitial compartment and the intravascular compartment occurs after approximately 8 to 12 hours.[11]

Several studies that criticize the benefits of ANH have suggested that the transfusion threshold is reduced, deeper levels of anemia being allowed when the professionals involved know that an effort is being made to avoid blood transfusion.[12] Thus, the use of a restrictive transfusion threshold may be responsible for this outcome and may limit the clinical rationale for ANH.[13] Blood transfusion has been shown to be associated with multiple complications, such as increased mortality, infections, longer hospital length of stay, and increased use of hospital resources.[14] A strategy like ANH, minimizing exposure to blood products, can be useful to reduce costs and morbidity.[15]

Studies have demonstrated the benefits of ANH in spinal and scoliosis surgeries. A study comparing 27 patients who underwent ANH and 24 patients who did not, reported that no patient in the ANH group required transfusion during the intraoperative period. During hospitalization, among those who underwent ANH, 9 did not require homologous blood, 18 required transfusion and, when compared to the control group, these 18 patients received less homologous blood volume.[16] Comparable results were found in a case-control study showing that patients submitted to hemodilution were less transfused (79% vs. 37%).[17] In a study evaluating 25 children, allogeneic blood was required largely in the group that was not submitted to hemodilution (79% vs. 28%). Additionally, children undergoing hemodilution had shorter hospital length of stay than those in the group without hemodilution (7.56 vs. 9.75 days).[18] A study with 40 adult patients showed that, among the 20 patients in the ANH group, only 5 patients (25%) required transfusion, while all 20 patients (100%) required homologous blood in the group without ANH.[7] Another study compared patients who were not submitted to any alternative measures; who were submitted only to ANH; who were submitted to ANH associated with intraoperative blood savage; and who were submitted to a combination of ANH, intraoperative blood savage, erythropoietin treatment and preoperative autologous donation. ANH reduced the use of packed RBC units (a reduction of 2.07 units) and the absolute risk of allogeneic transfusion by 33%.[12] In patients in whom ANH was associated with esmolol-induced hypotension, the number of transfused packed red blood cell units (2.2 ± 0.6 units) was significantly lower ($p < 0.01$) than 4.3 ± 0.4 transfused units in the group in which only controlled hypotension was performed.[19] In the cardiac surgery setting, a meta-analysis showed that ANH reduced the number of transfused allogeneic red blood cells and the rate of allogeneic blood transfusion.[15]

Despite the evidence, there are metanalyses suggesting limited usefulness of ANH regarding outcome. A metanalysis that looked at 24 randomized controlled trials in cardiac and noncardiac surgery reported reduction in homologous transfusions, but with inconclusive results.[20] A metanalysis encompassing 42 studies compared ANH to standard treatment or another method of blood conservation in any surgical scenario and did not prove ANH safety.[21] A meta-analysis of 63 randomized controlled trials suggested that ANH is effective in reducing blood transfusion only when surgical blood loss is one liter or when it exceeds 20% of patients' blood volume. The length of hospital stay and the occurrence of adverse events were comparable and the risk of any infection tended to be lower in the ANH group.[9]

As the present study is retrospective and assessed medical charts, data collected can be subject to reporting bias and the heterogeneity of the characteristics in the sample may not have been completely eliminated. As a single center study, the sample size was restricted, therefore restraining the statistical power of the study to detect small differences in outcomes. Additional factors may have affected the results by limiting the power of the study, such as variations in criteria for blood transfusion and non-random distribution of patients between groups.

ANH has enabled minimizing requirement for blood transfusions in scoliosis surgery, kept hemoglobin and hematocrit values at clinically acceptable and safe levels, and met patient requirements. It was not associated with increase in the duration of surgery and anesthesia time, length of hospital stay, or in the occurrence of severe complications.

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Conflicts of interest

The authors declare no conflicts of interest.

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