Closed system for blood sampling and transfusion in critically ill patients

Utilização de sistema fechado para coleta de sangue e necessidade de transfusão em pacientes graves

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This trial was conducted at Hospital do Servidor Público Estadual "Francisco Morato de Oliveira" HSPE-FMO - São Paulo (SP), Brazil, Hospital São Francisco - Ribeirão Preto (SP), Brazil and Hospital de Emergência e Trauma Senador Humberto Lucena - João Pessoa (PB), Brazil.

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Edwards Lifesciences (Irvine-CA) supplied the closed systems for blood sampling (VAMP® - Venous Arterial Blood Management Protection). No financial support was involved.

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ABSTRACT

Objective: Anemia is common in severely ill patients, and blood sampling plays a relevant causative role. Consequently, blood transfusions are frequent an related to several complications. Trying to reduce the transfusion-related risk, minimizing blood loss is mandatory. Thus, this work aimed to evaluate a closed blood sampling system as a strategy to spare unnecessary blood losses and transfusions.

Methods: This was a prospective, randomized, controlled, multicenter, 6 months, clinical trial. The patients were assigned to either VAMP (Venous Arterial Blood Management Protection) group, using a closed blood sampling system, or control group. The groups' transfusion rate, as well as hemoglobin (Hb) and Hematocrit (Ht) changes were compared for 14 days.

Results: Were included 127 patients, 65 assigned to the control group, and 62 to VAMP. During the intensive care unit stay, both groups experienced both hemoglobin and hematocrit drops. However, when the final Ht and Hb were compared between the groups, a difference was identified with higher values in the VAMP group (p=0.03; p=0.006, respectively). No statistical difference was found for both groups transfusion rates, although the VAMP group had an absolute 12% blood transfusion reduction.

Conclusion: The use of a closed blood sampling system was able to minimize blood count values changes, however failed to reduce transfusions rate.

Keywords: Anemia; Blood transfusion; Blood specimen collection; Intensive care unit

INTRODUCTION

Blood or blood components transfusion is a frequent procedure in severely ill patients, and its main rationale is to increase tissue oxygen availability.[1] It is however important to bear in mind the hemotherapy-related effect, for sensibly prescribing this therapy. Thus, the blood transfusion decision should be guided by precise diagnosis, based both on low hemoglobin values and on perfusion indicators.[2,3] Transfused patients have increased mortality both in the intensive care unit (ICU) and hospital, increased infection rates, organ failures, and longer ICU stays.[4-6]

Anemia is common in severely ill patients, and several causes contribute for its development and persistence, such as gastrointestinal

bleeding, sepsis, renal failure and red blood cells changes.[7] Frequent blood sampling plays a relevant role in this process.[8] The transfusion threshold is currently around 7 g/dL hemoglobin, with this evidence supported by a study comparing two transfusion strategies (liberal versus restrictive) in severely ill anemic patients.[9]

Attempting to reduce the transfusion-associated risk, blood losses should be minimized, such as phlebotomy losses which mount up to 41 mL/daily.[10] Thus, the use of closed blood sampling systems in ICU looks reasonable, however these devices actual benefits on blood transfusions reduction is so far not clear.

Thus, this trial primary objective was to compare the rates of transfused patients and the number of packed red blood cells units used for the closed blood sampling system group versus control. In addition, to compare the groups' hemoglobin and hematocrit changes.

METHODS

After the institutions' Ethics Committees approval, this multicenter, prospective, randomized by chart clinical trial was conducted in the three hospitals' ICUs for 6 months.

Patients with arterial catheter (MBP) and/or a central venous line (CLV) for blood sampling, ≥ 24 hours mechanic ventilation patients included within the first 48 hours from ICU admission and with a signed informed consent form were included. Were excluded patients younger than 18 years old, moribund or with low 30 days life expectation, and those with no-treating decision by the family; were also excluded patients admitted to the ICU with upper digestive hemorrhage, primary hematological diseases and Jehovah's Witnesses.

The patients were assigned to one of two groups, either VAMP or control. In the VAMP group, patients received a closed system for blood sampling (VAMP®-Venous Arterial Blood Management Protection, Edwards Lifesciences, Irvine, USA), adapted to the arterial or central venous lines. All laboratory tests blood samples were collected from the VAMP® closed system, which avoids discarding blood before laboratory sampling.

The control group patients remained without the closed blood sampling system. All laboratory samples were collected from the arterial and/or central venous catheter, and thus an initial volume was discarded in the sampling process.

Exceptionally for both groups, blood culture samples were collected by venous puncture. Daily hematocrit and hemoglobin values (morning) were recorded. Eventually needed packed red blood cells transfusion units were recorded.

The professionals involved in the laboratory tests were blinded for the groups. The daily blood samplings were performed by trained personnel, in an attempt to minimize the initial volume loss in the control group. These intensive care units medical teams did already comply with a blood transfusion protocol. This trial had no interference with hemotherapy procedures.

Statistical analysis

The physiological variables were measured twice before the study enrollment. These variables mean was created for an inter-groups comparison. The entry and final Hb comparison was performed considering the last Hb value (discharge or death).

The physiological groups' variables were compared with the T Student test. Chronic diseases were analyzed as multiple responses, as one single patient could have more than one illness. The pairwise T Student test was used for pairwise Hb and Ht samples comparison between entry and final values. The 5% significance level was adopted a priori.

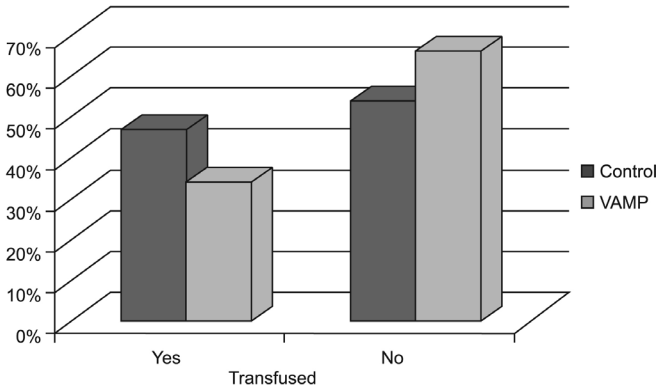
RESULTS

Were included 127 patients, 66 (52%) males and 61 (48%) females. The ICU stay length was 13.6 ± 10.54 days. Among comorbidities, the most frequent was cardiovascular disease, in 48.8% patients. Nineteen patients (15%) had single-lumen central line catheter, 85 (66.9%) had double-lumen center line catheter, and 110 (87%) had MBP catheter.

Regarding patients' demographics, comorbidities and physiological variables, both groups were similar, with no mean or median differences, nor on each variable patients' rates (Table 1).

Both groups had statistically significant Hb drops during their ICU stay (10.5 ± 2.24 to 9.1 ± 1.80, p=0.002 and VAMP group 10.4 ± 2.37 to 9.7 ± 1.3, p=0.012). However, the final Hb and Hb intergroups comparisons showed a difference, with higher Hb and Ht values for the VAMP group (Table 1).

The total blood transfusions were observed for 14 days. The sum of all transfusions and mean transfusions per patient in each transfusion day were compared, with no significant inter-groups difference (Table 2). A dichotomized variable was created to evaluate at least one transfusion versus none, considering all transfusions during the observation period. The inter-groups transfusions frequency was compared with the Chi-Square test. There was no difference regarding transfusion rate between the groups (p=0.158), although the VAMP group had an absolute 12% transfusions reduction (Figure 1).



Number of patients (%). [A] – Chi-square test (p = 0.158).

Figure 1 – Transfused patients rate.

Table 1 – Study sample description: demographics and comorbidities

	Total	Control (N = 65)	VAMP (N = 62)	P value
Entry Hb (mg/dL)	10.4±2.29	10.5±2.24	10.4±2.37	0.800[A]
Entry Ht (%)	31.7±7.42	32.0±6.63	31.4±8.21	0.644[A]
Final Hb (mg/dL)	9.4±2.54	9.1±1.80	9.7±1.3	0.033[A]
Final Ht (%)	28.4±6.01	26.5±5.8	29.4±6.0	0.006[A]
Mean blood pressure (mmHg)	84.5±35.24	84.6±36.64	84.4±33.99	0.803[A]
Heart rate (bpm)	118.5±22.41	119.5±20.71	117.4±24.20	0.599[A]
ICU stay (dias)	13.6±10.54	13.1±8.11	14.1±12.61	0.930[A]
Respiratory rate (ipm)	21.0±5.75	20.9±5.55	20.98±6.00	0.872[A]
Males	66 (52)	34 (52.3)	32 (51.6)	0.528[B]
Single-lumen catheter	19 (15)	10 (15.4)	9 (14.5)	0.891[C]
Double-lumen catheter	85 (66.9)	44 (67.7)	41 (66.1)	0.852[C]
IBP use	110 (86.6)	57 (87.7)	53 (85.5)	0.715[C]
Age (years)	62.7 ± 16.04	60.3 ± 18.78	63.0 ± 16.48	0.194[A]
Chronic illness				
Absent	26 (20.8	13 (20.0)	13 (21.7)	
Cardiovascular	61 (48.8)	30 (46.2)	31 (51.7)	0.564[C]
Respiratory	38 (25.2)	19 (29.2)	19 (31.7)	
Renal	11 (8.8)	3 (4.6)	8 (13.3)	
Hepatic	12 (9.6)	8 (12.3)	4 (6.7)	
Immunosuppressed	3 (2.4)	1 (1.5)	2 (3.3)	

VAMP - Venous Arterial Blood Management Protection. Hb – hemoglobin; HT – hematocrit; ICU – intensive care unit; IBP – invasive blood pressure. Results expressed as number (percent), mean ± standard deviation. [A] t –Student test [B]Fisher's exact test by Monte Carlo simulation [C] – Chi-Square test. The type of catheter used, as presented in the questionnaire, do not consider the concomitant use of the different types of catheter, just its use or not. Entry – evaluated by the patients' randomization. Final – evaluated by the patients' discharge or death.

Table 2 – Transfused units – inter-groups comparison

	Total	Control	VAMP	P value
Total transfused units	2.42 ± 1.36	2.52 ± 1.43	2.25 ± 1.24	0.623[A]
Number of days receiving transfusion	1.75 ± 0.91	1.93 ± 0.98	1.48 ± 0.75	0.072[A]
Mean daily transfused units	1.43 ± 0.74	1.30 ± 0.46	1.67 ± 1.05	0.261[A]

VAMP - Venous Arterial Blood Management Protection. Results expressed as mean ± standard deviation; [A] –T Student test.

DISCUSSION

This trial has shown that the use of a closed blood sampling system was not able to prevent blood transfusions, however the hemoglobin and hematocrit values were higher in the closed system group.

Additionally, during the ICU stay the Hb and Ht values were observed to drop, with significant differences between the entry and final values. Several studies have shown increased anemia risk for patients staying longer in the ICU, added to the high disorder prevalence by the admission time.[10-12]

Severely ill patient's anemia is characterized by reduced erythropoetin production, an iron metabolism abnormality identical to the described for chronic illness and excessive loss anemia.[13-14] ICU anemia cause is multifactorial, including excessive phlebotomy for laboratory testing, active bleeding or losses such as hemodyalisis renal failure and erythropoiesis reduction.[15] In turn, these patients' erythropoiesis also involves several causes, including inflammatory, iron and vitamins deficiency and the underlying disease.[16-21]

Nevertheless, the final Ht and Hb inter-groups difference was significant, with higher Hb and Ht for the VAMP group. The studies trying this device failed to show this difference, although reducing the iatrogenic blood loss. Peruzzi et al. concluded that the blood discarded in patients not using a closed system is an independent predictor of Hb decline.[22,23]

Hebert et al. (1999) showed that a restrictive transfusion strategy is as effective and possibly superior to a liberal strategy, except for acute myocardial infarction and unstable angina patients. However, more recent studies have shown that about 40% to 50% of the ICU admitted patients receive at least one packed red blood cells transfusion, with a mean 5 units/patient transfused during the ICU stay, and the pre-transfusion hemoglobin around 8.5 g/dL.[10,24-27] Bearing in mind the hemotherapy-related effects and their negative impact on the outcome,[4,5,28-43] measures for minimizing transfusion should be encouraged.

Attention should be given to the phlebotomy, considering this practice as causative of anemia in the severely ill patient. Studies by Smoller and Kruskall identified that about one half of the transfused patients had lost in blood samplings almost the equivalent to one packed blood cells unit, and this was confirmed in other studies documenting 40 to 70 mL daily losses.[10,44-47] Thus, this situation may be minimized with lower blood volume phlebotomies, and with closed sampling systems, measures encouraged by trials proving relevant blood losses spare.[22,23,45,47] This, bearing in mind the importance of bringing the restrictive transfusion strategy to the clinical practice.

In agreement with current literature data, in this trial, when comparing the transfusion need, no reduction was identified with the device.[22-23,47] Perhaps this trial failed to show this reduction because its limitations, such as reduced sample size, insufficiently powered for this. To show a difference in the transfusions amount, at least 400 patients would be needed, which was unfeasible for the institution-determined study time, due to insufficient material availability.

Another limitation was not measuring the amount of patients' spoiled blood during samplings, in addition to measuring transfusions in units and not milliliters, as the bags had different volumes. In addition Hb values were not checked before each transfusion, a possible bias. However we understand that this does not invalidate our findings, as both groups had a single blood transfusions protocol.

CONCLUSION

The use of a closed blood sampling system was able to minimize the blood counts values drops, however failed to reduce transfusions. Larger trials are warranted to better evaluate these data consistency.

RESUMO

Objetivo: A anemia é desordem comum em pacientes graves e as coletas de sangue ocupam papel de destaque como causa. Consequentemente, a transfusão de sangue é freqüente e está relacionada a várias complicações. Na tentativa de reduzir o risco associado à transfusão é necessário minimizar as perdas sanguíneas e para tal, este estudo avaliou o sistema fechado para coleta de sangue como estratégia para diminuir perdas desnecessárias e transfusão sanguínea.

Métodos: Estudo clínico prospectivo, randomizado, controlado, multicêntrico, durante 6 meses. Os pacientes foram alocados em dois grupos, grupo VAMP (*Venous Arterial Blood Management Protection*) que utilizou sistema fechado para coleta de sangue e o grupo controle que não utilizou. O percentual de pacientes transfundidos, assim como a variação da hemoglobina (Hb) e hematócrito (Ht), foram comparados entre os grupos na ao longo de 14 dias.

Resultados: Foram incluídos 127 pacientes, sendo 65 controles e 62 VAMP. Durante a internação na unidade de terapia intensiva , ambos os grupos apresentaram queda nos valores de hemoglobina e hematócrito. Entretanto, quando comparados o Ht final e Hb final entre os grupos houve diferença, com

maiores valores no grupo VAMP (p=0,03; p=0,006). Não houve diferença estatística entre a proporção de pacientes transfundidos nos dois grupos, embora o grupo VAMP tenha apresentado redução absoluta de 12% na transfusão sanguínea.

Conclusão: A utilização de sistema fechado para coleta de sangue conseguiu minimizar a queda nos valores hematimétricos sem, contudo, reduzir o número de transfusões.

Descritores: Anemia; Transfusão de sangue; Coleta de amostras sanguíneas; Unidade de terapia intensiva

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