Resuscitation fluid practices in Brazilian intensive care units: a secondary analysis of Fluid-TRIPS

Práticas de ressuscitação volêmica em unidades de terapia intensiva brasileiras: uma análise secundária do estudo Fluid-TRIPS

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ABSTRACT

Objective: To describe fluid resuscitation practices in Brazilian intensive care units and to compare them with those of other countries participating in the Fluid-TRIPS.

Methods: This was a prospective, international, cross-sectional, observational study in a convenience sample of intensive care units in 27 countries (including Brazil) using the Fluid-TRIPS database compiled in 2014. We described the patterns of fluid resuscitation use in Brazil compared with those in other countries and identified the factors associated with fluid choice.

Results: On the study day, 3,214 patients in Brazil and 3,493 patients in other countries were included, of whom 16.1% and 26.8% ($p < 0.001$) received fluids, respectively. The main indication for fluid resuscitation was impaired perfusion and/or low cardiac output (Brazil: 71.7% *versus* other countries: 56.4%, $p < 0.001$). In Brazil, the percentage of patients receiving crystalloid solutions was higher (97.7% *versus* 76.8%, $p < 0.001$), and 0.9% sodium chloride was the most commonly used crystalloid (62.5% *versus* 27.1%, $p < 0.001$). The multivariable analysis suggested that the albumin levels were associated with the use of both crystalloids and colloids, whereas the type of fluid prescriber was associated with crystalloid use only.

Conclusion: Our results suggest that crystalloids are more frequently used than colloids for fluid resuscitation in Brazil, and this discrepancy in frequencies is higher than that in other countries. Sodium chloride (0.9%) was the crystalloid most commonly prescribed. Serum albumin levels and the type of fluid prescriber were the factors associated with the choice of crystalloids or colloids for fluid resuscitation.

Keywords: Fluid therapy; Critical care; Colloids; Crystalloid solutions; Hemodynamics; Shock

Clinical Trials register: Clinicaltrials.gov: Fluid-Translation of research into practice study (Fluid-TRIPS) - NCT02002013.

INTRODUCTION

Fluid resuscitation is defined as intravenous fluid administration with the aim of improving tissue perfusion in shock states. It is one of the most common interventions in critically ill patients. Despite being a frequent intervention, fluid resuscitation lacks a clear definition. The choice of fluid to be administered as well as the dose and speed are not well determined, leading to differences in bedside practices.[1,2]

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In the last 15 years, multiple randomized controlled trials and subsequent meta-analyses have shown that the type of fluid used for resuscitation, particularly hydroxyethyl starch (HES), may negatively affect outcomes.[3-12] Even with recent published guidelines including new evidences,[13,14] delays and failures with translating recommendations into practice are common, leading to variability in care.[15,16] The Saline versus Albumin Fluid Evaluation - Translation of Research Into Practice Study (SAFE-TRIPS), a cross-sectional study conducted in 2007 including 391 intensive care units (ICUs) across 25 countries, reported that resuscitation practices varied significantly. Although colloid solutions were more expensive and may possibly be harmful in some patients, they were administered to more patients and during more resuscitation episodes than crystalloids.[17]

Recently, the same group conducted a similar observational study in a convenience sample of ICUs: the Fluid-TRIPS.[18] This study demonstrated an important change in clinical practice, with a preferential use of crystalloids, specifically buffered salt solutions, over colloids. Another interesting finding of this study was that fluid choice was determined by local practice rather than by any identifiable patient characteristic.

The number of contributing ICUs from Brazil in the Fluid-TRIPS was just over half of all participating units, allowing the unique opportunity to separately analyze Brazilian data. Our hypothesis was that Brazilian ICUs would have different standards for fluid resuscitation, mainly regarding the choice of crystalloids.

Thus, the objective of this study was to describe current practices on fluid resuscitation in Brazilian ICUs and to compare Brazil with the other countries participating in the study.

METHODS

This secondary analysis of a prospective, international, cross-sectional, observational study was carried out in a convenience sample of ICUs in 27 countries using the Fluid-TRIPS database, compiled in 2014.[18]

In Brazil, we recruited participating sites at critical care meetings through the Brazilian Research in Critical Care network (BRICNet) website and contacts and personal contacts with key opinion leaders. Participation was voluntary, and any hospital willing to join the study was considered eligible, with no exclusion criteria. The coordinating center was the *Universidade Federal de São Paulo,* and the institution's Ethics and Research Committee approved the study protocol under the number CAAE 36093314.4.1001.5505 with a waiver for Informed Consent considering the observational nature of the study.

Participants and data collection

In Brazil, the sites collected data on any single day between December 9th and 11th 2014. Methodological details were previously published.[18] Briefly, the study day was defined as a 24-hour period. The investigators included all patients over 16 years old who required one or more fluid resuscitation episodes during the study period. There were no exclusion criteria. The total number of patients being treated in the ICUs on the study day was also recorded. We defined a fluid resuscitation episode as an

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18. Hospital Santa Lúcia - Divinópolis (MG), Brazil.
19. Hospital Evangélico de Sorocaba - Sorocaba (SP), Brazil.
20. Hospital PIO XII - São José dos Campos (SP), Brazil.
21. Hospital São Camilo Pompéia - São Paulo (SP), Brazil.
22. Hospital Alvorada Brasília - Brasília (DF), Brazil.
23. Hospital Ecoville - Curitiba (PR), Brazil.
24. Hospital do Trabalhador - Curitiba (PR), Brazil.
25. Hospital Vita Batel - Curitiba (PR), Brazil.
26. Hospital das Clínicas, Faculdade de Medicina de Botucatu, Universidade Estadual "Júlio de Mesquita Filho" - Botucatu (SP), Brazil.
27. Hospital Geral Dr. César Cals - Fortaleza (CE), Brazil.
28. Hospital Copa D'Or - Rio de Janeiro (RJ), Brazil.
29. Associação Beneficente Hospital Unimar - Marília (SP), Brazil.
30. Hospital Casa de Saúde de Santos - Santos (SP), Brazil.
31. Hospital Estadual Getúlio Vargas - Rio de Janeiro (RJ), Brazil.
32. Hospital e Maternidade Otaviano Neves - Belo Horizonte (MG), Brazil.
33. Instituto Estadual do Cérebro Paulo Niemeyer- Rio de Janeiro (RJ), Brazil.
34. Hospital Universitário, Universidade Federal de Juiz de Fora- Juiz de Fora (MG), Brazil.
35. Lifecenter - Belo Horizonte (MG), Brazil.
36. Hospital Geral de Fortaleza - Fortaleza (CE), Brazil.
37. Hospital Municipal Dr. Moysés Deutsch (M'Boi Mirim) - São Paulo (SP), Brazil.
38. Santa Casa de Misericórdia de Presidente Prudente - Presidente Prudente (SP), Brazil.
39. Hospital 9 de julho - São Paulo (SP), Brazil.
40. Hospital Estadual Rocha Faria - Rio de Janeiro (RJ), Brazil.
41. Hospital Municipal Santa Isabel - João Pessoa (PA), Brazil.
42. Hospital e Maternidade Municipal Dr. Odelmo Leão Carneiro - Uberlândia (MG), Brazil.
43. Hospital Evangélico de Londrina - Londrina (PR), Brazil.
44. Universidade Estadual de Londrina - Londrina (SC), Brazil.
45. Hospital Samaritano João Pessoa - João Pessoa (PB), Brazil.
46. Hospital de Caridade Astrogildo de Azevedo - Santa Maria (RS), Brazil.
47. Vitória Apart Hospital - Vitória (ES), Brazil.
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hour during which a patient received a specifically prescribed intravenous fluid bolus of any crystalloid or colloid solution, a continuous infusion of 5mL/kg/hour or greater of crystalloid and/or any dose of colloid by continuous infusion.[18]

We recorded information on fluid availability in the participating ICUs as well as data related to patients, including demographic data, illness severity scores, admission diagnosis, laboratory test data, clinical data on the study day, predefined subgroup characteristics (trauma, traumatic brain injury - TBI, sepsis, and acute respiratory distress syndrome - ARDS), and information on the type and volume of fluids for resuscitation. The reason for fluid resuscitation and the prescriber characteristics were also recorded. We defined specialist or assistant physician as the board-certified intensivist or the physician responsible for the ICU on the study day. We defined senior resident or fellow as graduated students or residents in the last years of their residency, and we defined residents as those in the first years of their residency regardless of the specialty as it is usual in Brazil to have residents of different specialties in training.

We collected all data using an electronic data capture system (REDCap, Vanderbilt University, Tennessee, USA), hosted at *Instituto D'Or de Ensino e Pesquisa*, Rio de Janeiro, Brazil.

Statistical analysis

Continuous variables are expressed as the mean ± standard deviation - SD or the median [interquartile range]. Categorical variables are expressed as counts (percentages). The comparison of the data between Brazil and other countries and between the administration of colloids and crystalloids in Brazilian patients were performed using a t-test or Wilcoxon rank-sum test for continuous data or Pearson's chi-squared test for categorical data, as appropriate. Differences in the proportions of crystalloid and colloid episodes were tested using generalized estimating equations (GEEs), accounting for clustering at the patient level.

As in the main study,[18] multivariable analyses using GEEs accounting for clustering at the patient level were conducted to determine associations between patient demographics, clinical characteristics and the type of fluid administered. We used 2 binary outcomes in the analysis: 1) crystalloid episode Yes *versus* crystalloid episode No, and 2) colloid episode Yes *versus* colloid episode No. The denominators of these two outcomes were the total number of fluid episodes; thus, as a given patient could have received crystalloids as well as colloids within the same hour (the same fluid episode), the total number of fluid episodes was higher than the sum of crystalloid episodes and colloid episodes. As these outcomes were analyzed separately, two different sets of odds ratios (ORs) were generated for each variable. Variables meeting a predetermined level of statistical significance ($p < 0.1$) with the administration of crystalloids or colloids in univariate models were included in the final multivariable model. Associations were considered statistically significant if $p < 0.01$. The results of the multivariable analysis are presented as adjusted ORs and 95% confidence intervals (95%CI). Details regarding the handling of missing data are provided in the main paper.[18] All analyses were carried out using the R statistical software package, version 3.1.0 (2014-04-10).

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52. Hospital Municipal Irmã Dulce - Praia Grande (SP), Brazil.
53. Hospital Universitário Júlio Müller, Universidade Federal do Mato Grosso - Cuiabá (MT), Brazil.
54. Hospital de Urgência - Goiânia (GO), Brazil.
55. Hospital Geral de Goiânia - Goiânia (GO), Brazil.
56. Fundação Doutor Amaral Carvalho - Jaú (SP), Brazil.
57. Hospital Adventista de Belém - Belém (PA), Brazil.
58. Hospital Santa Juliana - Rio Branco (AC), Brazil.
59. Hospital Dom Vicente Scherer - Porto Alegre (RS), Brazil.
60. Hospital Primavera - Aracaju (SE), Brazil.
61. Hospital Carlos da Silva Lacaz - Francisco Morato (SP), Brazil.
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64. Hospital Professor Edmundo Vasconcelos - São Paulo (SP), Brazil.
65. Hospital Paulo Sacramento - Jundiaí (SP), Brazil.
66. Clínica Dom Rodrigo - João Pessoa (PA), Brazil.
67. Complexo Hospitalar Ortotrauma de Mangabeira - Fortaleza (CE), Brazil.
68. Hospital Nossa Senhora da Conceição - Tubarão (SC), Brazil.
69. Hospital Regional de Samambaia - Brasília (DF), Brazil.
70. Hospital São Camilo Ipiranga - São Paulo (SP), Brazil.
71. Hospital da Restauração - Recife (PE), Brazil.
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73. Hospital Santa Rita - São Paulo (SP), Brazil.
74. Hospital Estadual Jayme Santos Neves - Recife (PE), Brazil.
75. Hospital SOS Cárdio - Florianópolis (SC), Brazil.
76. Hospital da Luz Vila Mariana - São Paulo (SP), Brazil.
77. Hospital Maternidade e Pronto-Socorro Santa Luci - Poços de Caldas (MG), Brazil.
78. Santa Casa de Misericórdia de Vitória da Conquista - Vitória da Conquista (BA), Brazil.
79. Santa Casa de Misericórdia de Porto Alegre - Porto Alegre (RS), Brazil.
80. Hospital São Francisco de Assis - Porto Real (RJ), Brazil.
81. Hospital Memorial São José - Recife (PE), Brazil.
82. Hospital Regional de Jundiaí - Jundiaí (SP), Brazil.
83. Hospital Universitário, Faculdade de Medicina de Jundiaí - Jundiaí (SP), Brazil.
84. Hospital Regional de Presidente Prudente - Presidente Prudente (SP), Brazil.
85. Santa Casa de Misericórdia de Assis - Assis (SP), Brazil.
86. Hospital de Clínicas Gaspar Vianna - Belém (PA), Brazil.
87. Hospital do Coração do Brasil - Brasília (DF), Brazil.
88. Hospital Hélio Anjos Ortiz - Curitibanos (SC), Brazil.
89. Hospital Vila da Serra - Belo Horizonte (MG), Brazil.
90. Hospital Nereu Ramos - Florianópolis (SC), Brazil.
91. Hospital Santa Maria Intensibarra - Barra Mansa (RJ), Brazil.
92. Santa Casa de Misericórdia de Santo Amaro - São Paulo (SP), Brazil.

RESULTS

In Brazil, 217 ICUs participated in the study (participating centers are listed at the end of this manuscript). The overall summary of FLUID-TRIPS data is shown in table 1. Data on the participation of other countries can be found in detail in the main study.[18] During the 24-hour study period, 3,214 patients were included in Brazil, of whom 519 (16.1%) received fluids. Almost half of the patients received fluids within the first two days of ICU admission (46%). The baseline characteristics of patients in Brazil and those of patients in the other countries are shown in table 2.

In 880 fluid resuscitation episodes in Brazil, a specialist was the main fluid prescriber (82.3%), and the main indication for fluid resuscitation was impaired perfusion and/or low cardiac output (71.7%) (Table 3 and Table 1S in Supplementary material). The total volume of resuscitation fluid received and net fluid balance on the survey day were higher in Brazil than in other countries (Table 4).

Compared to other countries, crystalloid solutions were more frequently used than colloid solutions in Brazil (Figure 1). In Brazil, 0.9% sodium chloride was significantly more commonly used than in other countries (62.5% *versus* 27.1%, $p < 0.0001$) (Table 1S - Supplementary material), despite the availability of different fluids at the participating ICUs (Table 2S - Supplementary material). In Brazil and other countries, the most commonly used balanced crystalloid solution was Ringer's lactate. Plasma Lyte was used more frequently in other countries than in Brazil (Table 1S - Supplementary material). The percentage of patients receiving crystalloid or colloid solutions or the number of crystalloid or colloid episodes were not modified in the presence of trauma, TBI, sepsis or ARDS. These conditions did not lead to significant changes in the total volume of resuscitation fluid received on the survey day. However, patients with sepsis and ARDS had a higher net fluid balance on the survey day (Table 3S to Table 6S - Supplementary material).

We analyzed the factors associated with the choice of crystalloids or colloids for fluid resuscitation episodes. The multivariable analysis (Table 5) suggested that, in Brazil, lower albumin levels (i.e., < 27g/dL, ≥ 27g/dL, or missing), in general, were associated with both the use of crystalloids and colloids ($p = 0.001$ and < 0.0001, respectively).

Table 1 - Overall summary of Fluid-TRIPS

Variable	Brazil	Other countries	Total
Total number of participating ICU sites	217	209	426
Total number of ICU sites recruiting FLUID patients*	176	195	371
Total number of ICU patients	3,214	3,493	6,707
Total number of FLUID patients*	519	937	1,456
FLUID patients* among total ICU patients† (%)	16.1	26.8	21.7
Total number of fluid episodes	880	1,836	2,716

ICU - intensive care unit. *FLUID patients: patients who required one or more fluid resuscitation episodes during the study period; †$p < 0.001$ for difference between Brazil and other countries (p-values of Pearson's Chi-squared test). Results expressed as n or %.

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94. Santa Casa de Misericórdia de Santana do Livramento - Santana do Livramento (RS), Brazil.
95. Hospital Unimed de Macaé - Macaé (RJ), Brazil.
96. Hospital Municipal Pedro II - Rio de Janeiro (RJ), Brazil.
97. Hospital Federal dos Servidores do Estado - Rio de Janeiro (RJ), Brazil.
98. Hospital São Mateus - Fortaleza (CE), Brazil.
99. Hospital IBR - Vitória da Conquista (BA), Brazil.
100. Hospital Uniclinic - Fortaleza (CE), Brazil.
101. Santa Casa de Misericórdia de Paraguaçu Paulista - Paraguaçu Paulista (SP), Brazil.
102. Associação Hospitalar Beneficente São Vicente de Paulo - Passo Fundo (RS), Brazil.
103. Hospital do Servidor Público Municipal de São Paulo - São Paulo (SP), Brazil.
104. Hospital Santa Isabel - Blumenau (SC), Brazil.
105. Hospital Municipal Dr Jose Soares Hungria - São Paulo (SP), Brazil.
106. Hospital Fernandes Távora - Fortaleza (CE), Brazil.
107. Hospital Distrital Evandro Ayres de Moura - Fortaleza (CE), Brazil.
108. Hospital Saúde da Mulher - Belém (PA), Brazil.
109. Hospital Estadual de Urgência e Emergência de Vitória - Vitória (ES), Brazil.
110. Samur - Vitória da Conquista (BA), Brazil.
111. Hospital e Pronto-Socorro 28 de Agosto - Manaus (AM), Brazil.
112. Hospital Assunção - São Bernardo do Campo (SP), Brazil.
113. Hospital Universitário de Santa Maria - Santa Maria (RS), Brazil.
114. Hospital Universitário Cajuru - Curitiba (PR), Brazil.
115. Instituto do Câncer do Estado de São Paulo - São Paulo (SP), Brazil.
116. Hospital Unimed de Limeira - Limeira (SP), Brazil.
117. Hospital Amecor - Cuiabá (MT), Brazil.
118. Santa Casa de Caridade de Diamantina - Diamantina (MG), Brazil.
119. Hospital das Clínicas, Faculdade Ribeirão Preto, Universidade de São Paulo - Ribeirão Preto (SP), Brazil.
120. HCor - Hospital do Coração - São Paulo (SP), Brazil.
121. Hospital Goiânia Leste - Goiânia (GO), Brazil.
122. Hospital Ortopédico - Goiânia (GO), Brazil.
123. Hospital Santa Maria - Goiânia (GO), Brazil.
124. Hospital Municipal Dr. Munir Rafful - Volta Redonda (RJ), Brazil.
125. Hospital Jardim Amália - Volta Redonda (RJ), Brazil.
126. Hospital Madre Regina Prottman - Santa Tereza (ES), Brazil.
127. Hospital Universitário São Francisco de Paula, Universidade Católica de Pelotas - Pelotas (RS), Brazil.
128. Hospital São Joao de Deus - Divinópolis (MG), Brazil.
129. Hospital Nossa Senhora Monte Serrat - Salto (SP), Brazil.
130. Hospital Unimed Salto - Salto (SP), Brazil.
131. Hospital Moinhos de Vento - Porto Alegre (RS), Brazil.
132. Hospital Geral de Vitória da Conquista - Vitória da Conquista (BA), Brazil.

Table 2 - Baseline characteristics of patients in Brazil and other countries

Variables	Brazil (n = 519)	Other countries (n = 937)	p value
Age (year)	63.0 (46.0 - 75.0)	64.0 (53.0 - 74.0)	0.061
Sex, male	296 (57.0)	582 (62.1)	0.058
APACHE II in 24 hours prior to survey day	18.0 (12.0 - 25.0)	18.0 (12.0 - 25.0)	0.910
Number of days in ICU	2.0 (1.0 - 6.0)	1.0 (0.0 - 7.0)	0.007
Patients receiving fluid resuscitation according to the number of days in the ICU at the study day			
Day 0	119/519 (22.9)	327/936 (34.9)	< 0.0001
Day 1	120/519 (23.1)	172/936 (18.4)	
Day 2	68/519 (13.1)	87/936 (9.3)	
Days 3 - 7	101/519 (19.5)	135/936 (14.4)	
Days 8 - 14	53/519 (10.2)	99/936 (10.6)	
Days 15 - 21	25/519 (4.8)	42/936 (4.5)	
Days 22 - 28	7/519 (1.3)	25/936 (2.7)	
Days 29 - 59	16/519 (3.1)	35/936 (3.7)	
Day ≥ 60	10/519 (1.9)	14/936 (1.5)	
Admission characteristics			
Operating room after elective surgery	137/519 (26.4)	243/936 (26.0)	0.185
Emergency room	132/519 (25.4)	198/936 (21.2)	
Hospital floor	83/519 (16.0)	169/936 (18.1)	
Operating room after emergency surgery	69/519 (13.3)	135/936 (14.4)	
Transferred from other ICU or hospital	49/519 (9.4)	117/936 (12.5)	
Hospital floor after previous ICU stay	49/519 (9.4)	74/936 (7.9)	
Admission diagnosis			
Nonsurgical	298/519 (57.4)	512/936 (54.7)	0.318
Surgical	221/519 (42.6)	424/936 (45.3)	
Trauma category at hospital admission			
No trauma	468/518 (90.3)	843/935 (90.2)	0.921
Trauma with TBI	14/518 (2.7)	23/935 (2.5)	
Trauma without TBI	36/518 (6.9)	69/935 (7.4)	
ARDS in 24 hours prior to survey day	32 (6.2)	83 (8.9)	0.070
Sepsis in 24 hours prior to survey day	205 (39.7)	345 (36.9)	0.293
APACHE II chronic health points criteria			
Chronic health points liver criteria	14/508 (2.8)	42/927 (4.5)	0.097
Chronic health points renal criteria	15/509 (2.9)	18/928 (1.9)	0.223
Chronic health points cardiac criteria	30/508 (5.9)	58/928 (6.2)	0.795
Chronic health points respiratory criteria	27/509 (5.3)	65/932 (7.0)	0.215
Chronic health points immunocompromised	66/511 (12.9)	91/929 (9.8)	0.069

APACHE - Acute Physiology and Chronic Health Evaluation; ICU - intensive care unit; TBI - traumatic brain injury; ARDS - acute respiratory distress syndrome. Summary statistics of continuous variables are presented as the median (interquartile range), with p-values based on the nonparametric test (i.e., Wilcoxon rank-sum test). Summary statistics of categorical variables are presented as percentages, with p-values based on Pearson's Chi-squared test.

133. Hospital Marcelino Champagnat - Curitiba (PR), Brazil.
134. Hospital São Lucas, Pontifícia Universidade Católica do Rio Grande do Sul - Porto Alegre (RS), Brazil.
135. Hospital Universitário, Universidade Federal da Grande Dourados - Dourados (GO), Brazil.
136. Hospital Português - Salvador (BA), Brazil.
137. Hospital Brigadeiro - São Paulo (SP), Brazil.
138. Hospital Regional de Sousa - Sousa (PB), Brazil.
139. Hospital das Clínicas, Universidade Federal do Espírito Santo - Vitória (ES), Brazil.
140. Santa Casa de Misericórdia de Ribeirão Preto - Ribeirão Preto (SP), Brazil.
141. Hospital Universitário Lauro Wanderley - João Pessoa (PB), Brazil.
142. Santa Casa de Belo Horizonte - Belo Horizonte (MG), Brazil.
143. Hospital Adventista de Manaus - Manaus (AM), Brazil.
144. Santa Casa Maringá, Universidade Estadual Maringá - Maringá (PR), Brazil.
145. Hospital Total Cor - Rio de Janeiro (RJ), Brazil.
146. Hospital Universitário, Universidade de Santa Cruz do Sul - Santa Cruz do Sul (RS), Brazil.
147. Hospital Dom Hélder - Cabo (PE), Brazil.
148. Hospital das Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul - Porto Alegre (RS), Brazil.
149. Hospital Anis Rassi - Goiânia (GO), Brazil.
150. Instituto de Infectologia Emílio Ribas II - São Paulo (SP), Brazil.
151. Hospital Unimed Rio de Janeiro - Rio de Janeiro (RJ), Brazil.
152. Hospital Alemão Oswaldo Cruz - São Paulo (SP), Brazil.
153. Hospital Samaritano Rio de Janeiro - Rio de Janeiro (RJ), Brazil.
154. São Bernardo Apart Hospital - Colatina (ES), Brazil.
155. Hospital Nossa Senhora dos Prazeres - Lages (SC), Brazil.
156. Hospital Unimed ABC - São Bernardo do Campo (SP), Brazil.
157. Hospital Municipal de Paracatu - Paracatu (MG), Brazil.
158. Hospital Municipal Padre Germano Lauck - Foz do Iguaçu (RS), Brazil.
159. Hospital Santa Helena - São Paulo (SP), Brazil.
160. Hospital Santa Izabel - São Paulo (SP), Brazil.
161. Santa Casa de Misericórdia de São Paulo - São Paulo (SP), Brazil.
162. Hospital Tereza Ramos - Lages (SC), Brazil.
163. Hospital Alvorada Taguatinga - Brasília (DF), Brazil.
164. Hospital Maternidade São José - Colatina (ES), Brazil.
165. Hospital Universitário Ciências Médicas, Fundação Educacional Lucas Machado - Belo Horizonte (MG), Brazil.
166. Santa Casa de Belém do Pará - Belém (PA), Brazil.
167. Instituto Nacional de Cardiologia - Rio de Janeiro (RJ), Brazil.

Table 3 - Indications for fluid resuscitation in Brazil and in other countries

Variables	Brazil	Other countries	p value‡
Indication for fluid in each fluid resuscitation episode	n = 877*	n = 1,820†	p < 0.0001
Impaired perfusion/low cardiac output	629 (71.7)	1,026 (56.4)	
Ongoing bleeding	25 (2.9)	38 (2.1)	
Other fluid losses	24 (2.7)	84 (4.6)	
Unit protocol	15 (1.7)	119 (6.5)	
Abnormal vital signs	175 (20.0)	518 (28.5)	
Other	9 (1.0)	35 (1.9)	
Fluid prescriber	n = 880	n = 1.836	p < 0.0001
Specialist/assistant physician	724 (82.3)	597 (32.5)	
Senior resident/fellow	92 (10.5)	706 (38.5)	
Resident	42 (4.8)	455 (24.8)	
Nurse	1 (0.1)	42 (2.3)	
Other	21 (2.4)	36 (2.0)	

Missing data: 0.3%; † missing data: 0.9%; ‡ generalized estimating equation model adjusted for the patient-level clustering effect. Results expressed as n (%).

Table 4 - Characteristics of fluids received per patient in Brazil and other countries

Variable	Brazil (n = 519)	Other countries (n = 937)	p value
Patients received crystalloid	507 (97.7)	720 (76.8)	< 0.0001
Patients received colloid	38 (7.3)	356 (38.0)	< 0.0001
Total volume of resuscitation fluid received on survey day (mL)	1,000.0 (500.0 – 1,500.0)	550.0 (400.0 - 1,460.0)	< 0.0001
Total volume of crystalloid received on survey day (mL)	1,000.0 (500.0 – 1,500.0)	835.0 (500.0 – 1,500.0)	0.018
Total volume of colloid received on survey day (mL)	275.0 (100.0 - 500.0)	250.0 (100.0 - 500.0)	0.688
Total volume of fluid input on the survey day (mL)	3,059,0 (2,015.0 – 4,165.5)	3,343.0 (2,436.0 – 4,537.5)	< 0.0001
Total volume of fluid output on the survey day (mL)	1,385.0 (750.0 – 2,325.0)	2,050.0 (1,152.0 – 3,310.0)	< 0.0001
Net fluid balance on the survey day (mL)	1,310.0 (500.0 – 2,517.0)	1,018.0 (150.0 – 2,350.0)	0.002

Summary statistics of continuous variables are presented as the median (interquartile range), with p-values based on the nonparametric test (i.e., Wilcoxon rank-sum test) and categorical variables are presented as percentages, with p-values based on the Chi-squared test.

Among the patients who received crystalloids, the odds of having an albumin level ≥ 2g/dL were 9.4 times (OR = 8.6 [0.8 - 89.8]) that of having an albumin level < 27g/dL.

There was also a higher chance of having unknown/missing values for albumin (OR = 7.2, 95%CI = 2.5 - 20.7) than having an albumin level < 27g/dL. Similarly, among those who received colloids, the odds of having an albumin level ≥ 27g/dL was one-fiftieth (OR = 0.2 [0.0 - 0.9]) that of having levels < 27g/dL. In addition, for patients receiving crystalloids, the odds of them being prescribed by a senior resident/fellow was 9.9 times

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169. BP - A Beneficência Portuguesa de São Paulo - São Paulo (SP), Brazil.
170. Hospital Universitário Maria Aparecida Pedrossian, Universidade Federal de Mato Grosso do Sul - Campo Grande (MS), Brazil.
171. Hospital do Servidor Público Estadual "Francisco Morato de Oliveira" - São Paulo (SP), Brazil.
172. Hospital Norte D'Or - Rio de Janeiro (RJ), Brazil.
173. Hospital Estadual Ipiranga - São Paulo (SP), Brazil.
174. Hospital Universitário de Maringá, Universidade Estadual de Maringá - Maringá (PR), Brazil.
175. Albert Sabin Hospital e Maternidade - Juiz de Fora (MG), Brazil.
176. Casa de Caridade de Carangola - Carangola (MG), Brazil.
177. Irmandade de Misericórdia de Guaxupé - Guaxupé (MG), Brazil.
178. Disciplina de Emergências Clínicas, Universidade Estadual de Campinas - Campinas (SP), Brazil.
179. Hospital São Lucas - Aracaju (SE), Brazil.
180. Fundação Pio XII- Hospital de Câncer de Barretos - Barretos (SP), Brazil.
181. Clínica Campo Grande - Campo Grande (MS), Brazil.
182. Hospital das Clínicas, Universidade Federal de Minas Gerais - Belo Horizonte (MG), Brazil.
183. Casa de Saúde Santa Lúcia - Rio de Janeiro (RJ), Brazil.
184. Hospital Regional de Itapetininga São Camilo - São Paulo (SP), Brazil.
185. Santa Casa de Angra dos Reis - Angra dos Reis (RJ), Brazil.
186. Grupo Hospitalar Nossa Senhora da Conceição - Porto Alegre (RS), Brazil.
187. Irmandade Misericórdia Hospital Santa Casa de Monte Alto - Monte Alto (SP), Brazil.
188. Hospital São Marcos - Recife (PE), Brazil.
189. Hospital Unimed de Manaus - Manaus (AM), Brazil.
190. Hospital Universitário Getúlio Vargas, Universidade Federal do Amazonas - Manaus (AM), Brazil.
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Conflicts of interest: None.

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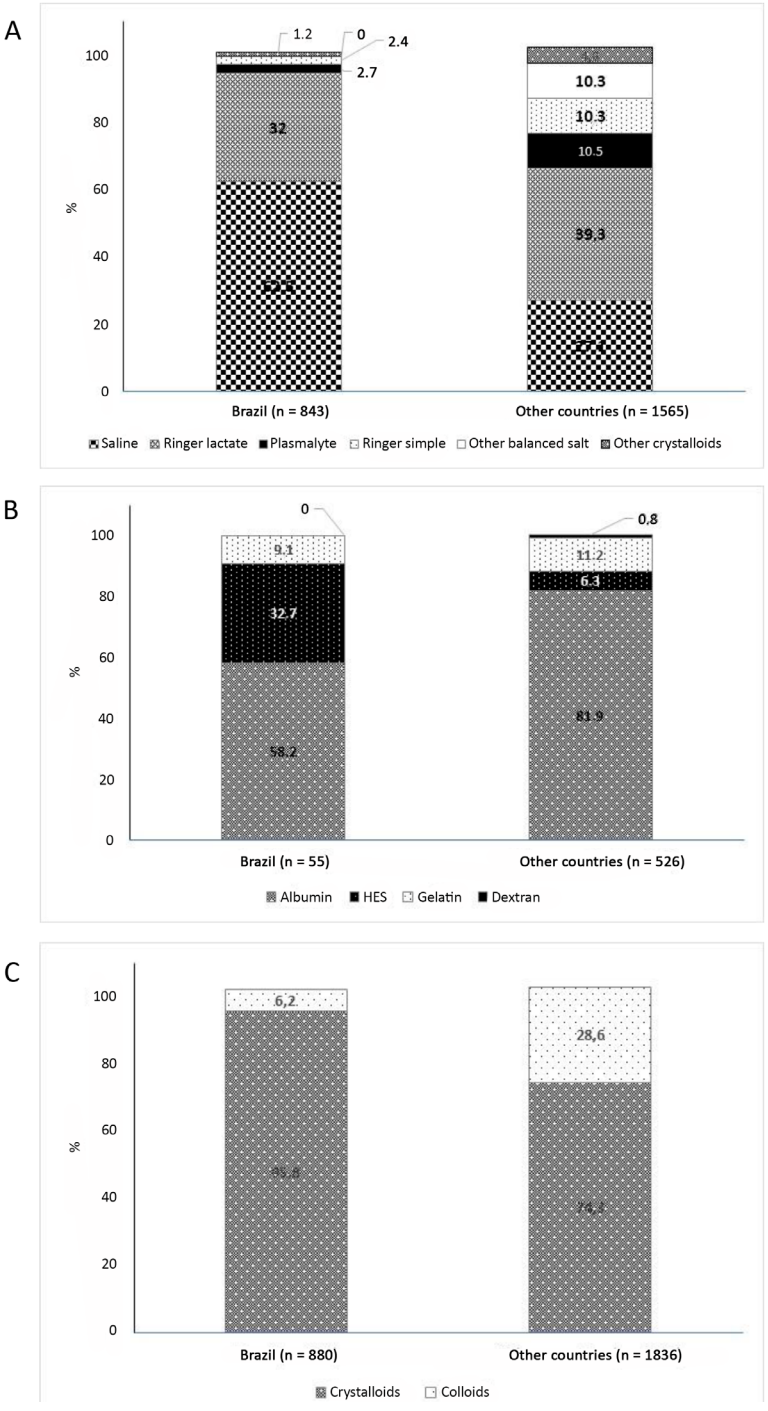

Figure 1 - Percentage of fluid resuscitation episodes in Brazil and other countries. (A) Comparison of the choice of fluid in each of the fluid episodes. (B) Comparison of the choice of crystalloids in episodes in which crystalloids were used. (C) Comparison of the choice of colloids in episodes in which colloids were used. Percentages may not add to 100%, as patients can be administered more than one type of fluid during resuscitation episodes.
HES - hydroxyethyl starch.

higher (OR = 9.9, 95%CI = 3.6 - 27.7) than that of them being prescribed by a specialist/assistant physician. For patients receiving colloids, there was no clear association with fluid prescriber. The univariate analysis is available in table 7S (Supplementary material).

Table 5 - Multivariate analysis of factors associated with the choice of crystalloid or colloid for fluid resuscitation episodes in Brazilian patients

Variable	Crystalloid given OR (95%CI)	p value	Colloid given OR (95%CI)	p value
Admission characteristics				
Operating room after elective surgery	1.0	0.215	1.0	0.1144
Emergency room	1.0 (0.3 - 2.9)		0.6 (0.2 - 1.5)	
Hospital floor	3.0 (0.3 - 26.8)		0.2 (0.0 - 1.2)	
Transferred from other ICU or hospital	2.5 (0.3 - 22.6)		0.7 (0.2 - 3.1)	
Operating room after emergency surgery	0.6 (0.1 - 2.6)		0.8 (0.2 - 2.7)	
Hospital floor after previous ICU stay	0.3 (0.1 - 1.1)		2.4 (0.8 - 7.5)	
Fluid prescriber				
Specialist/assistant physician	1.0	< 0.0001	1.0	0.1483
Senior resident/fellow	9.9 (3.6 - 27.7)		0.2 (0.0 - 1.1)	
Resident	0.6 (0.1 - 3.9)		1.4 (0.3 - 6.5)	
Metabolic acidosis				
No	1.0	0.241	1.0	0.2207
Yes	0.5 (0.1 - 1.8)		1.3 (0.5 - 3.4)	
Missing	0.3 (0.1 - 1.2)		2.5 (0.9 - 7.1)	
Lactate (mmol/L) categories				
< 2	1.0	0.394	1.0	0.8014
≥ 2	0.9 (0.2 - 3.5)		0.8 (0.3 - 2.1)	
Missing	0.4 (0.1 - 1.8)		1.1 (0.4 - 3.0)	
Mean arterial pressure (per 10mmHg decrease)	1.2 (1.0 - 1.5)	0.012	0.9 (0.7 - 1.0)	0.0669
Albumin (g/L) categories				
< 27	1.0	0.001	1.0	< 0.0001
≥ 27	8.6 (0.8 - 89.8)		0.2 (0.0 - 0.9)	
Missing	7.2 (2.5 - 20.7)		0.2 (0.1 - 0.4)	

OR - odds ratio; 95%CI - 95% confidence interval; ICU - intensive care unit. The results were generated from a generalized estimating equation model with patient ID as a cluster, using two binary outcomes in the analysis: (1) crystalloid episode Yes versus crystalloid episode No, and (2) colloid episode Yes versus colloid episode No. The denominators of these two outcomes were the total number of fluid episodes; thus, a given patient could have received a crystalloid as well as a colloid within the same hour (the same fluid episode). The analysis included 844 episodes from 503 study participants, as data were lost due to missing values that could not be included in the multivariate analysis. This number represents a loss of 4.1% of episodes and 3.1% of study participants.

DISCUSSION

Our results demonstrated that in Brazil, crystalloids were more frequently used than colloids for fluid resuscitation. In other countries, crystalloids were also the fluid of choice, but in Brazil, the proportion was significantly higher. Sodium chloride (0.9%) was the most prescribed crystalloid in Brazil, despite the availability of balanced solutions. In other countries, balanced solutions were the preferred crystalloids. The availability of serum levels and the current albumin level were the factors associated with the choice of crystalloids or colloids for fluid resuscitation. In addition, the type of fluid prescriber was significantly associated with crystalloid use.

The results in Brazil are consistent with more recent studies regarding fluid resuscitation practices. Fluid resuscitation aims at improving tissue perfusion by restoring the perfusion pressure of vital organs and ensuring adequate cardiac output.[13] Aligned with these principles, the main indications for fluid administration in Brazilian ICUs were similar to those found in the main study and in other studies addressing this issue.[18,19] Our results also showed a reduction in the use of colloid solutions.[18-20] The evidence of harm from recent randomized clinical trials (RCTs) with synthetic colloids such as HES (3–12) could explain the preference for crystalloid solutions in Brazil and in other countries. It is interesting to note that the higher proportion of the use of colloids in other countries

is represented by the use of albumin. As albumin is expensive, the costs may have limited its use in Brazil, a middle-income country.[21]

Another aspect that differentiates Brazil from other countries was the use of 0.9% sodium chloride as the crystalloid solution of choice. Although Plasmalyte is a high-cost balanced solution in Brazil, there are low-cost balanced solutions available (e.g., Ringer's lactate). Our study was not designed to assess the potential reasons for this difference between Brazil and other countries. It is possible that this was influenced by the variation in availability among the sites and countries, which would bias any further analysis. The relatively small number of patients and variables in our database might also compromise the reliability of eventual findings. Another possible explanation is a cultural preference derived from years of using saline potentially associated with a reduced awareness of the potential adverse effects of hyperchloremic solutions, as the controversy around balanced vs. unbalanced crystalloids was not as intense as it is currently.[22-24] We believe our findings are potentially useful for hypothesis generation, and further studies are necessary to better evaluate potential factors associated with this choice.

Sepsis, ARDS, trauma and TBI did not influence the choice between colloids and crystalloids. The uncertainty about the ideal fluid for these specific diseases could explain this finding.[25] However, in Brazilian ICUs, albumin serum levels had a clear role in guiding the choice of fluid. This preference is not supported by the available evidence. The results from high-quality RCTs suggest that intravenous albumin administration does not reduce the mortality rate in mixed populations of critically ill patients, including those who have hypoalbuminemia.[26] Even albumin supplementation in addition to crystalloids targeting serum concentrations higher than 30g per liter in septic patients did not improve survival at 28 and 90 days.[27] Thus, we believe that this finding probably reflects local practice patterns rather than solid evidence. It is worth mentioning that senior residents and fellows were more likely to prescribe crystalloid fluids to patients than specialists, probably suggesting that academic exposure to scientific evidence promotes changes in practice behaviors.[28] Another potential explanation is the generation difference. The specialists were previously exposed to a cultural environment in which colloids were heavily used based on their potential better effect on oncotic pressure. In contrast, the new generation, composed of residents and fellows, was exposed to scientific evidence of harm with colloid use. This also suggests that continuous training, even for specialists, is important to ensure better quality of care.

This study has strengths and some limitations, some of which were mentioned in the main study.[18] This is the first study to describe resuscitation fluid practices in a large sample of Brazilian ICUs. The use of standard case report forms and definitions across all countries and detailed information on clinical factors that may potentially influence the choice of fluid for resuscitation at the time of the fluid episode allowed not only comparisons with other countries but also analyses of national practice patterns. Among the limitations of the study, it is important to mention the generalizability of the results. Even with a large sample of ICUs, the use of convenience sampling might have not reflected practices adopted in all Brazilian ICUs. Another limitation is the definition of fluid resuscitation episodes.[18] Finally, the interpretation of fluid administration practices in specific patient populations, such as those with sepsis, requires caution due to relatively small patient numbers.

CONCLUSION

Crystalloids were more frequently used than colloids for fluid resuscitation in Brazilian intensive care units. Sodium chloride (0.9%) was the most prescribed crystalloid in Brazil, despite the availability of balanced solutions. The availability of serum levels and the low albumin level were the factors that influenced the choice between crystalloid or colloid for fluid resuscitation. In addition, senior residents/fellows were more likely to prescribe crystalloid fluids to patients than specialists.

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RESUMO

Objetivo: Descrever as práticas de ressuscitação volêmica em unidades de terapia intensiva brasileiras e compará-las com as de outros países participantes do estudo Fluid-TRIPS.

Métodos: Este foi um estudo observacional transversal, prospectivo e internacional, de uma amostra de conveniência de unidades de terapia intensiva de 27 países (inclusive o Brasil), com utilização da base de dados Fluid-TRIPS compilada em 2014. Descrevemos os padrões de ressuscitação volêmica utilizados no Brasil em comparação com os de outros países e identificamos os fatores associados com a escolha dos fluidos.

Resultados: No dia do estudo, foram incluídos 3.214 pacientes do Brasil e 3.493 pacientes de outros países, dos quais, respectivamente, 16,1% e 26,8% (p < 0,001) receberam fluidos. A principal indicação para ressuscitação volêmica foi comprometimento da perfusão e/ou baixo débito cardíaco (Brasil 71,7% *versus* outros países 56,4%; p < 0,001). No Brasil, a percentagem de pacientes que receberam soluções cristaloides foi mais elevada (97,7% *versus* 76,8%; p < 0,001), e solução de cloreto de sódio a 0,9% foi o cristaloide mais comumente utilizado (62,5% *versus* 27,1%; p < 0,001). A análise multivariada sugeriu que os níveis de albumina se associaram com o uso tanto de cristaloides quanto de coloides, enquanto o tipo de prescritor dos fluidos se associou apenas com o uso de cristaloides.

Conclusão: Nossos resultados sugerem que cristaloides são usados mais frequentemente do que coloides para ressuscitação no Brasil, e essa discrepância, em termos de frequências, é mais elevada do que em outros países. A solução de cloreto de sódio 0,9% foi o cristaloide mais frequentemente prescrito. Os níveis de albumina sérica e o tipo de prescritor de fluidos foram os fatores associados com a escolha de cristaloides ou coloides para a prescrição de fluidos.

Descritores: Hidratação; Cuidados críticos; Coloides; Soluções cristaloides; Hemodinâmica; Choque

Registro Clinical Trials: Clinicaltrials.gov: Fluid-Translation of research into practice study (Fluid-TRIPS) - NCT02002013.

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