Comparing the Effect of Albumin 5% versus Ringer Lactate on Blood Coagulation in Trauma-Induced Coagulopathy during Initial Resuscitation

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Abstract
Background: Trauma-induced coagulopathy (TIC) denotes abnormal blood clotting that occurs as a result of a physical injury. During the initial stages of trauma-induced coagulopathy development, there is usually a condition of reduced blood clotting ability, leading to bleeding.
Objectives: This study aimed to ascertain the difference between using albumin and ringer lactate in resuscitation of traumatized patients and their impact on blood coagulation.
Patients and methods: This prospective comparative study was carried out on 80 patients aged above 18 years old, both sexes, trauma induced coagulopathy clinical score over 10. Patients were divided into two equal groups: Group A: received ringer lactate, and group B: received albumin.
Results: Coagulation test at day 1, 2 and 3 of initial resuscitation were insignificantly different between both groups. Regarding coagulation tests in Group A, B were insignificantly different amongst coagulation tests at days 1 and 3 of initial resuscitation. However, there was improvement of the coagulation test results during day 3 of initial resuscitation. Changes in platelet count and hemoglobin at different intervals of time were insignificantly different between both groups.
Conclusion: The effect of administration of albumin solution with Ringer's lactate on blood coagulation in TIC during initial resuscitation showed no difference as regard effect on coagulation profile between two groups, but patients received albumin showed better improvement in resuscitation parameters on the second day in comparison to the patients received Ringer's lactate**.**

Keywords: Trauma-Induced Coagulopathy; Initial Resuscitation; Albumin; Ringer Lactate; Coagulation.
DOI: 10.21608/SVUIJM.2024.306891.1941
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Received: 24 July,2024.
Revised: 23 September,2024.
Accepted: 25 September,2024.
Published: 27 September, 2024
Cite this article as: Yahya Abdel Tawab Mohammed Meky. (2024). Comparing the Effect of Albumin 5% versus Ringer Lactate on Blood Coagulation in Trauma-Induced Coagulopathy during Initial Resuscitation. *SVU-International Journal of Medical Sciences*. Vol.7, Issue 2, pp: 508-516.

Introduction

Trauma is the third most prevalent reason of mortality; it accounts for 10% of deaths worldwide. One-fourth of trauma cases have laboratory-based evidence of trauma-induced coagulopathy (TIC), which is linked to worse results, including a higher mortality rate **Chang et al.,(2016)**.

TIC means abnormal blood clotting that results from a physical injury. During the initial stages of TIC development, there is usually a decreased ability of the blood to clot, leading to bleeding **Erdoes et al.,(2023)**. TIC is described or defined by a hypercoagulable state that is linked with venous thromboembolism and multiple organ failure. Tissue injury and stress lead to the activation of endothelial cells, the immune system, platelets, and coagulation. This activation is further enhanced by the "lethal triad," which is one of numerous pathophysiological pathways that contribute to TIC. The deadly triad consists of hypothermia, coagulopathy, and acidosis **Moore et al.,(2021)**.

Fluid resuscitation remains a crucial component in the treatment of trauma patients, consistently included in care protocols. In the past, intravenous (IV) fluids were used to bring cases back to a normal state of blood circulation **Kochanek et al.,(2019)**.

Multiple categories of crystalloids have been suggested for the purpose of fluid resuscitation. Studies have been conducted on hypertonic saline, with or without dextran, colloids, and crystalloids, and none of these treatments have shown superiority in preventing death. Various animal and human investigations have shown that administering large amounts of crystalloid fluids during resuscitation can lead to an increased occurrence of metabolic disorders and a decrease in survival rates **Finfer et al.,(2018)**.

The treatment of severe hemorrhagic shock has undergone substantial changes in the past two decades due to the use of damage control resuscitation (DCR). DCR is founded on many key principles.

Crystalloids are the primary approach for boosting volume in cases of acute hemorrhagic shock **Woolley et al.,(2018)**.Albumin has been found to be inferior to other fluid resuscitation products. The Saline versus Albumin Fluid Evaluation (SAFE) trial examined the effects of albumin versus normal saline in critically ill cases **Tseng et al.,(2020)**.

The aim of this work was to investigate the effect of fluid resuscitation and the ideal resuscitation fluid in trauma patients, to find out TIC in traumatized patient after the initial resuscitation with ringer lactate vs. human albumin, and to compare the occurrence of trauma induced coagulopathy in the 1st three days of intensive care unit (ICU) admission in the patient's receiving ringer and patients receiving human albumin.

Patients and methods

This prospective comparative study was carried out on 80 patients aged above 18 years old, both sexes, trauma-induced coagulopathy clinical score over 10. The study was done from August 2023 to April 2024 after approval from the Ethical Committee Armed forces College of Medicine. An informed written consent was obtained from the patients.

Exclusion criteria were cases with Glasgow Coma Scale (GCS) 3/15, disseminated intravascular coagulopathy (DIC) diagnosed patients, patients with a history of bleeding disorder or heart failure, and patients on anticoagulant medication. The participants were allocated using simple randomization by a random number generator into two equal groups. Predetermined fixed rates were infused such that normotension was not achieved in both groups: Group A: received ringer lactate only for resuscitation, fluid resuscitation was achieved based on fluid loss and daily maintenance requirements guided by goal-

directed resuscitation goal-directed resuscitation aiming to maintain a systolic blood pressure of 80–90 mmHg and a mean arterial blood pressure of 50–60 mmHg and serum lactate < 2 mmol/L. [Systolic blood pressure (SBP)/ mean arterial blood pressure (MAP) was targeted based on patient physiology or controlled resuscitation] and group B: received 1-2 ml human albumin 5% per minute every 6 hours combined with normal saline 0.9% for resuscitation, fluid resuscitation was achieved based on fluid loss and daily maintenance requirements guided by goal-directed resuscitation goal-directed resuscitation aiming to maintain a systolic blood pressure of 80–90 mmHg and a mean arterial blood pressure of 50–60 mmHg and serum lactate < 2 mmol/L. [SBP/MAP was targeted based on patient physiology or controlled resuscitation].

All patients were subjected to complete history taking, physical examinations and laboratory investigations [Complete blood count (CBC), international normalized ratio (INR), prothrombin time (PT), fibrin degradation products (FDPs), activated partial thromboplastin time (aPTT), bleeding time, clotting time, D-dimer, serum fibrinogen concentration and serum lactate and arterial blood gas (ABG) on admission and on a daily basis for 3 days during ICU admission].

The Trauma Induced Coagulopathy Clinical Score

It is a clinical evaluation tool used to evaluate patients with severe trauma. It consists of three items: blood pressure, general severity and amount of bodily injury. The score ranges from zero to eighteen & is calculated by paramedics on-site.

Glasgow Coma Scale (GCS)

The degree of consciousness was evaluated using GCS while the patient remained in the intensive care unit. The Glasgow Coma Scale was employed to provide an objective assessment of the level of impaired awareness in patients with acute medical conditions or trauma. The scale evaluated cases based on three dimensions of responsiveness: motor, ocular, & vocal responses. Providing distinct reports for each of these elements allowed for a clear and easily understandable depiction of the patient. The Glasgow Coma Scale is comprised of three parameters: the most optimal eye response (E), the most optimal verbal response (V), and the most optimal motor response (M). The GCS measures the levels of reaction in its components. These levels are graded on a scale ranging from 1, indicating no response, to normal values of 4 for eye-opening response, 5 for verbal response, & 6 for motor response. The overall Coma Score ranged from three to 15, with three being the most severe state and 15 indicating the maximum level. The score was the aggregate of the scores in addition to the individual components. As an illustration, a score of 10 may be represented as GCS10 = E3V4M3.

Blood and blood products transfusion were performed according to transfusion guidelines and transfusion triggers.

The primary outcomes were clinical bleeding, changes in PT, aPTT, INR, D-dimer, serum fibrinogen concentration, FDPs, bleeding time, clotting time, and changes in Hb and platelet count.

Sample Size Calculation

A sample size of total 80 cases (40 patients in each group) would provide 80 % statistical power with a 2-sided alpha level of 0.05 for detecting if there was a variance in the coagulation profile between the two groups of patients where One of the groups were resuscitated with albumin 5% and the other group was resuscitated with ringer lactate, based on prior data from Madinah, H., Shabaniyan, G. and Hadadzadeh, M. **Madinah et al.,(2020)** as the mean(±SD) of their PTT was 28.76(± 2.25) and 30.66(± 2.98) respectively. Taking into consideration a 10% dropout

rate was added to the sample size calculated.

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Shapiro-Wilks test and histograms were used to evaluate the normality of the distribution of data. Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t-test. Qualitative variables were presented as frequency and percentage (%) and analyzed using the Chi-square test when appropriate. A two-tailed P value < 0.05 was considered statistically significant.

Results

Age, BMI, sex, TICCS score and hemodynamic parameters during resuscitation were insignificantly different between the studied groups, **(Table.1).** MAP and lactate at day 1, 2, 3 were insignificantly different between the studied groups, (**Table.2**).

Table 1. Demographic data and hemodynamic parameter during resuscitation in the studied groups

Variables (mean ± SD)		Group A (n=40)	Group B (n=40)	P-value
Age (years)		32.1±10.07	33.2±10.03	0.62#
BMI (Kg/m^2)		28.16± 3.46	28.47±2.92	0.66#
Sex N (%)	Male N (%)	25 (62.5%)	22 (55%)	0.49##
	Female N (%)	15 (37.5%)	18 (45%)	
TICCS score		12.99±1.76	13.05±1.96	0.88#
Hemodynamic parameter	HR	127.5±8.8	127.7±7.67	0.914#
	RR	23.65 ± 5.65	23.1 ± 5.16	0.650#
	MAP	93.07 ± 10.03	95.1 ± 8.77	0.338#
	Temperature	37.27 ± 0.28	37.27 ± 0.26	1#

BMI: Body mass index; TICCS: Trauma Induced Coagulopathy Clinical Score; HR: heart rate, RR: respiratory rate; MAP: mean arterial blood pressure. #: unpaired Student's t-test, ##: Chi-square

Table 2. MAP and Lactate level at day 1, 2,3 of initial in the studied groups

Variables (mean ± SD)	Group A (n=40)	Group B (n=40)	P-value
Day 1 of initial resuscitation			
MAP (mmHg)	47.56± 3.29	48.21± 3.26	0.37#
Lactate (mmol/L)	3.74± 0.79	3.51± 0.80	0.199#
Day 2 of initial resuscitation			
MAP (mmHg)	48.83±2.26	49.41±2.95	0.326#
Lactate (mmol/L)	1.89±0.53	1.62±0.90	0.106#
Day 3 of initial resuscitation			
MAP (mmHg)	73.87±2.83	74.36±2.47	0.41#
Lactate (mmol/L)	0.904±0.147	0.825±0.28	0.11#

MAP: mean arterial blood pressure. #: unpaired Student's t-test,

Laboratory investigations were insignificantly different between both groups, (**Table.3).** Coagulation test at day 1, 2,3 of initial resuscitation were insignificantly different between both groups, (**Table 4).**

Table 3. Laboratory investigations on in the studied groups

Variables (mean ± SD)	Group A (n=40)	Group B (n=40)	P-value
Platelets count (10^3)	161.27±46.2	144.67± 37.7	0.08#
Hb(gm/dl)	10.06±0.45	9.99±0.45	0.48#
Fibrinogen mg/dl	352.8±3.24	353.7±8.23	0.56#

PT (seconds)	12.52±0.22	12.44±0.32	0.19#
aPPT(seconds)	29.9±0.73	29.9±0.66	1#
INR	1.05±0.069	1.03±0.069	0.198#
D. Dimer (mg/L FEU)	0.36±0.12	0.36±0.13	1#
FDPs(ug/ml)	8.67±1.7	8.57±1.7	0.79#

Hb: hemoglobin; PT: prothrombin time; aPPT: activated partial thromboplastin time; INR: international normalised ratio; FDPs: Fibrin degradation products. #: unpaired Student's t-test

Table 4. Coagulation test at day 1,2,3 of initial in the studied groups

Variables (mean ± SD)	Group A (n=40)	Group B (n=40)	P-value
Coagulation test at day 1 of initial resuscitation			
Fibrinogen mg/dl	351.2± 4.55	352.4± 8.56	0.315#
PT (seconds)	12.14± 0.54	12.65± 0.43	0.31#
aPPT(seconds)	30.06± 1.12	30.25± 0.61	0.450#
INR	1.07±0.07	2.05±0.02	0.086#
D. Dimer (mg/L FEU)	0.35±0.13	0.4±0.1	0.063#
FDPs(ug/ml)	8.67±3.06	9.4±1.46	0.17#
Coagulation test at day 2 of initial resuscitation			
Fibrinogen (mg/dl)	350.07± 4.95	350.8± 8.3	0.63#
PT (seconds)	12.8±0.32	12.68±0.43	0.16#
aPPT(seconds)	32.01±3.17	30.88±2.98	0.10#
INR	1.34±0.58	1.18±0.54	0.20#
D-dimer (mcg/mL)	0.37±0.16	0.4±0.09	0.30#
FDPs(ug/ml)	8.03±2.65	9.1±2.59	0.07#
Coagulation test at day 3 of initial resuscitation			
Fibrinogen mg/dl	349.4±4.5	348.3± 9.9	0.524#
PT (seconds)	12.31±0.49	13.49±3.12	0.067#
aPPT(seconds)	30.41±1.07	35.38±19.4	0.058#
INR	1.14±0.23	2.2±2.02	0.632#
D. Dimer (mg/L FEU)	0.4±0.1	0.45±0.2	0.582#
FDPs(ug/ml)	7.8±2.45	9.8±1.2	0.232#

PT: prothrombin time, aPPT: activated partial thromboplastin time, INR: international normalised ratio, FDPs: Fibrin degradation products. #: unpaired Student's t-test

Regarding coagulation tests in Group A, B were insignificantly different amongst coagulation tests at day1 and day3 of initial resuscitation. However, there was improvement of the coagulation tests result during the day 3 of initial resuscitation (**Table .5).**

Table 5. Comparison between coagulation tests at day1 and day 3 of initial resuscitation within Group A and B

Variables (mean ± SD)	Day 1	Day 3	P-value
Group A			
Fibrinogen mg/dl	351.2± 4.55	349.4± 4.5	0.079#
PT (seconds)	12.14± 0.54	12.31±0.49	0.144#
aPPT(seconds)	30.06± 1.12	30.41±1.07	0.157#
INR	1.07±0.07	1.14±0.23	0.07#
D. Dimer (mg/L FEU)	0.35±0.13	0.4±0.1	0.06#
FDPs(ug/ml)	7±2.7	7.8±2.45	0.17#
Group B			

Fibrinogen mg/dl	352.4± 8.56	348.3± 9.9	0.05#
PT (seconds)	12.65± 0.43	13.49±3.12	0.09#
aPPT(seconds)	30.25± 0.61	35.38±19.4	0.17#
INR	2.05±0.02	2.2±2.02	0.63#
D. Dimer (mg/L FEU)	0.4±0.1	0.45±0.2	0.2#
FDPs(ug/ml)	9.4±1.46	9.8±1.2	0.18#

PT: prothrombin time; aPPT: activated partial thromboplastin time; INR: international normalized ratio; FDPs: Fibrin degradation products. #: unpaired Student's t-test

Changes in platelets count and Hb at different interval time were insignificantly different between both groups (**Table.6).**

Table 6. Comparison between group A and group B as regard changes in platelets count and Hb at concentration at day 1,2,3 of initial resuscitation

Variables (mean ± SD	Group A (n=40)	Group B (n=40)	P-value
At day 1			
Platelets count (10^3)	160.62±42.3	142.71± 38.1	0.07#
Hb(gm/dl)	10.1±0.51	9.69±0.5	0.71#
At day 2			
Platelets count (10^3)	162.45±40.1	143.52±38.02	0.06#
Hb(gm/dl)	10.72±0.54	9.82±0.46	0.68#
At day 3			
Platelets count (10^3)	163.07±40.02	143.91±38.08	0.12#
Hb(gm/dl)	10.87±0.61	10.12±0.52	0.05#

Hb: hemoglobin. #: unpaired Student's t-test

Discussion

Haemorrhage is the primary avoidable factor resulting in mortality. Approximately 25% of people who experience severe trauma develop a clotting disease known as TIC, which has a fatality rate ranging from thirty percent to fifty percent. Gaining a comprehensive understanding of TBI pathophysiology is crucial in order to decrease death rates associated with trauma **Kleinveld et al.,(2022)**.

Our investigation revealed no significant variance among the analyzed groups in terms of fibrinogen levels, aPPT, INR, D Dimer, PT, and FDPs on day 1. In contrast with our results, **Madinah et al. (2020)** who stated that the five percent albumin group had a considerably lower INR on day 1, as well as a different blood coagulation status (PT and PTT) compared to the other group, based on results from the Mann-Whitney U and analysis of variance tests.

In our study we found that regarding coagulation test at day 2, when looking at PT, aPTT, as well as INR, the groups that were tested did not show any statistically significant variations.

In contrast with our outcomes, **Patel et al. (2016)** who sought to evaluate ringer lactate, hydroxyethyl starch, & albumin as priming solutions for elective open-heart surgery in children as young as three years old. In this randomized, prospective trial, 105 participants were included. According to their findings, there was a statistically significant disparity in platelet counts among the groups tested on day 2 of the coagulation test.

In our study we found that regarding coagulation test at day 3, there was no statistically significant alteration among the studied groups according to fibrinogen mg/dl, PT (seconds), aPPT,

INR and D Dimer and FDPs. In contrast with our results, **Patel et al. (2016)** who reported that regarding coagulation test at day 3, there was a statistically significant difference between the studied groups according to platelets count.

In our study we found that regarding the coagulation test in Group A, there was highly statistically alteration between coagulation test at day1and coagulation test at day3. Our findings in line with, **Patel et al. (2016)** who found that regarding coagulation test in ringer lactate group, there was highly statistically significant change amongst coagulation test at day1and coagulation test at day3.

Also, our results are consistent with **Madinah et al. (2020)** who reported that regarding the coagulation test in Ringer's lactate group, there was highly statistically significant difference between coagulation test in 6 hours after surgery and coagulation test in 24 hours after surgery.

In our study we found that regarding coagulation test in Group B, there was highly statistically significant distinction between coagulation test at day1and coagulation test at day3. Our results are consistent with **Madinah et al. (2020)** who reported that regarding coagulation test in Albumin group 5%, there was highly significant variance among coagulation test in 6 hours after surgery and coagulation test in 24 hours after surgery.

In addition, **Pesonen et al. (2022)** revealed that there were no significant differences in platelet count, hemoglobin (Hb), and international normalized ratio (INR) among the groups investigated.

Our investigation revealed no significant variance among the analyzed groups in terms of fibrinogen levels (mg/dl), aPPT (seconds), INR, D Dimer, PT (seconds), and FDPs (ug/ml) on day 1.

In the same line,**Patel et al.,(2016)** observed no statistically significant variations among the groups in terms of vital indicators, including HR, SBP, resuscitation rate, metabolic acidosis and temperature.

Our investigation revealed that There was no statistically significant disparity among the investigated groups in terms of mean arterial pressure and lactate levels on day 1, with a p-value greater than 0.05.

The findings of our study align with those of **Arya et al. (2006)**, who sought to compare the hemodynamic alterations resulting from the administration of either Ringer's lactate or albumin. A prospective and randomized investigation was done on a sample of thirty patients. The patients were assigned at random to two groups: group 1 ((Acute normovolemic haemodilution) ANH using Ringer's lactate) or group 2 (ANH using 5%albumin). The researchers discovered that there was no significant change in mean arterial pressure among the groups under study (P>0.05).

Our investigation revealed a statistically significant change among the analyzed groups in terms of Mean Arterial Pressure &Lactate levels on day 2. There was no significant alteration in mean arterial pressure and lactate levels on day 3 between the groups being tested (P>0.05).

Our findings align with those of **Urbano et al. (2015)**, who discovered that controlled bleeding led to a significant reduction in blood pressure, central venous saturation, cardiac index, carotid and peripheral blood flow, brain saturation, in addition to an increase in gastric PCO2, heart rate, and lactate levels. Following the treatment, there were no notable disparities in the majority of hemodynamic (cardiac index, mean arterial pressure) and perfusion parameters (lactate, brain saturation, stomach PCO2, cutaneous blood flow) across the three therapeutic groups.

Limitations of the study included that the sample size was relatively small. The study was in a single center. So, we

recommended performing future investigations utilizing meticulously planned randomized controlled trials or extensive comparative observational studies. Ensure the inclusion of a representative sample of cases who have similar characteristics such as gender, age, and disease severity. Future research should have a sufficiently enough sample size to ensure significant results and to account for confounding factors. In order to obtain precise evaluations of long-term results, it is necessary for studies to have a more extended duration of follow-up. We suggest that future research should incorporate multicenter studies in order to authenticate our findings.

Conclusion

Effect of administering albumin in comparison with Ringer's lactate on Blood Coagulation in TIC during Initial Resuscitation showed no difference as regard effect on coagulation profile between two groups, but patients received albumin showed better improvement in resuscitation parameters on the second day in comparison to the patients received ringer lactate.

Acknowledgments: Nil

Financial support and sponsorship: Nil

Conflict of Interest: Nil

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