

Original Article

Sodium bicarbonated Ringer's solution effectively improves coagulation function and lactic acid metabolism in patients with severe multiple injuries and traumatic shock

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Abstract: Objective: To explore the effect of sodium bicarbonated Ringer's solution on the coagulation function and the lactic acid metabolism in patients with severe multiple injuries and traumatic shock. Methods: A prospective, randomized controlled study was designed to enroll 50 patients with severe multiple injuries and traumatic shock. The enrolled patients were randomly assigned into a Test group (n=25) or a Control group (n=25), which received restrictive fluid resuscitation with sodium bicarbonated Ringer's solution or sodium lactated Ringer's solution, respectively. The success rate of rescue, the changes in coagulation function indices, lactic acid level, arterial blood pH level, hemorheological indices, blood pressure and heart rate before and after resuscitation, as well as the shock-related complications were observed. Results: The coagulation function of the Test group was significantly improved after resuscitation as compared with the Control group ($P<0.05$). After resuscitation, the Test group had significantly lower lactic acid level and significantly higher pH level than those of the Control group (both $P<0.05$). The hemorheological indices of the Test group were improved more significantly after resuscitation as compared with those of the Control group ($P<0.05$). There was no significant difference in the success rate of rescue between the Test group and the Control group (92.0% vs. 80.0%; $P>0.05$), but the total incidence of complications in the Test group was significantly lower than that in the Control group (16.0% vs. 56.0%; $P<0.01$). Conclusion: Sodium bicarbonated Ringer's solution is effective in early resuscitation for patients with severe multiple injuries and traumatic shock through improving the coagulation function and lactic acid metabolism, reducing the risk of related complications and improving the clinical outcome in patients.

Keywords: Sodium bicarbonated Ringer's solution, multiple injuries with traumatic shock, lactic acid, coagulation function

Introduction

Trauma from traffic accidents, mechanical accidents, and fall injuries has now become the main cause of death among young and middle-aged people under 40 years old [1, 2]. Nearly 50% of the deaths were attributed to hemorrhagic shock from post-traumatic hemorrhage [3]. Patients with severe multiple injuries have a higher rate of hemorrhagic shock, with a median survival time of 2 h (from shock to death) [4, 5]. Therefore, timely antishock treatment is the key to saving lives.

The pathophysiological process of traumatic shock is that bleeding at the trauma site sharp-

ly decreases the effective blood volume in the body, resulting in insufficient perfusion for tissues and organs, which leads to a series of complications such as microcirculation disorders, inflammations, coagulation dysfunction and organ damages [6, 7]. Timely resuscitation of body fluids and supplementation of circulating blood volume are the main clinical antishock treatments. Currently, the restrictive fluid resuscitation has been clinically recognized, showing a significantly better efficacy than adequate fluid resuscitation [8, 9]. However, the choice of resuscitation fluids has always been controversial. Normal saline and sodium lactated Ringer's solution are now the commonly used crystalloids as resuscitation fluids in clini-

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cal practice [10, 11]. But both of them have their limitations. Normal saline has a high chloride ion content, which can cause hyperchloremia and aggravate the disorders of water-electrolyte balance in patients during rapid replenishment, thereby accelerating the disease progression [12]. Although sodium lactated Ringer's solution could avoid this limitation, study showed that sodium lactated Ringer's solution for resuscitation can aggravate the inherent lactic acidosis [13]. Sodium bicarbonated Ringer's solution is a new type of crystalloid solution composed of various electrolytes such as sodium, magnesium, potassium and calcium ions [14]. Studies have shown that sodium bicarbonated Ringer's solution has a promising clinical effect in supplementing circulating blood volume and improving metabolic acidosis [15, 16]. But its effect in patients with severe multiple injuries and traumatic shock is rarely reported. Therefore, we designed a randomized controlled trial to compare the effects of sodium bicarbonated Ringer's solution and sodium lactated Ringer's solution on early fluid resuscitation in patients with severe multiple injuries and traumatic shock, with the aim of providing clinical reference.

Materials and methods

Patients

The study included 50 patients with severe multiple injuries and traumatic shock who were admitted to our hospital from June 2019 to June 2020. Patients were eligible if they had multiple and severe damages in tissues or organs; had traumatic hemorrhagic shock meeting the diagnosis criteria for shock caused by medium or low blood volume in the Guidelines for Resuscitation of Hypovolemic Shock [17]; were rescued within 6 h after injury; and had injury severity score >16 points. Patients were excluded if they received fluid resuscitation before admission; had serious chronic diseases of heart, lung, kidney or other organs; had a history of blood system diseases such as coagulation dysfunction; died within 1 h after admission; or could not reach the target blood pressure after 30 min of resuscitation.

Ethics statement

This study was conducted in accordance with the Declaration of Helsinki and approved by the

ethics committee of our hospital. All patients and their families were informed of the study protocol and signed an informed consent form.

Assessment of shock degree

Shock index (SI) was used to assess the degree of shock in patients [18]. $1.0 \leq SI < 1.5$ indicated mild shock; $1.5 \leq SI < 2.0$ indicated moderate shock; $SI \geq 2.0$ indicated severe shock.

Treatment

Patients in both groups were immediately rescued after admission by keeping respiratory tract clear (applying tracheal intubation and mechanical ventilation if necessary), establishing large venous access, giving invasive blood pressure monitoring through arterial puncture and catheterization, indwelling catheter, correcting acid-base imbalance, as well as giving oxygen inhalation, analgesia and sedation, etc. Restricted fluid resuscitation was conducted within 1 h by using sodium lactated Ringer's solution (H20065323, specification 500 mL; Sichuan Pacific Pharmaceutical, China) in the Control group and sodium bicarbonated Ringer's solution (H20190021, specification 500 mL; Jiangsu Hengrui Pharmaceutical, China) in the Test group. The patients' mean arterial pressure (MAP) was controlled to reach 60-70 mmHg within half an hour and maintained for another 30 min by adjusting the amount and the speed of fluid input [19]. Then the infusion rate was reduced, and the ratio of crystalloids to colloids was 2:1.

Both groups underwent targeted surgical treatments according to their injured site and type of injury. Patients with fractures were given bone fixation. Patients with open trauma were treated with debridement, hemostasis and suture. For those who had visceral injury, open abdomen exploration was firstly performed to clarify the location and the condition of the injury, then corresponding surgical treatment was carried out.

Outcome measures

There were 3 primary outcome measures. First, the coagulation function before and after resuscitation was evaluated, including prothrombin time (PT), activated partial thromboplastin time (APTT) and thrombin time (TT). Cubital

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Table 1. Baseline data of the two groups

Item	Test group (n=25)	Control group (n=25)	t/ χ^2	P
Sex (n, %)			0.857	0.355
Male	16 (64.0)	19 (76.0)		
Female	9 (36.0)	6 (24.0)		
Age (year, $\bar{x} \pm sd$)	36.6 \pm 4.6	38.0 \pm 4.2	1.124	0.267
Injury severity score (point, $\bar{x} \pm sd$)	18.3 \pm 1.3	18.0 \pm 1.5	0.756	0.454
Time from injury to rescue (h, $\bar{x} \pm sd$)	3.7 \pm 0.9	3.5 \pm 1.0	0.743	0.461
Cause of injury (n, %)			1.192	0.755
Traffic accident	13 (52.0)	12 (48.0)		
Fall injury	6 (24.0)	8 (32.0)		
Crush injury	4 (16.0)	2 (8.0)		
Others	2 (8.0)	3 (12.0)		
Degree of shock (n, %)			0.486	0.784
Mild	8 (32.0)	8 (32.0)		
Moderate	11 (44.0)	9 (36.0)		
Severe	6 (24.0)	8 (32.0)		

venous blood (2 mL) was collected before and 1 h after resuscitation to test PT, APTT and TT using XN-9000 automatic blood coagulation analyzer (Sysmex, Japan). Second, the levels of lactic acid and pH before and after resuscitation were compared between the two groups. Third, the hemorheological indices were compared, including plasma viscosity (PV), red blood cell aggregation index (AI), erythrocyte sedimentation rate (ESR) and hematocrit (HCT). To determine the hemorheological indices, 4 mL of cubital venous blood was collected before and 1 h after the resuscitation and then heparinized to determine the hemorheological indices using MVIS-2015 automatic hemorheology analyzer (Chongqing Tianhai, China).

There were 2 secondary outcome measures. First, hemodynamic indicators, MAP and heart rate were compared before and after the resuscitation between the two groups. Second, the rescue results and the complications were compared between the two groups. Success rate of rescue = (number of surviving patients after rescue/total number of patients) \times 100%. Total incidence of complications = (number of patients with complications/total number of patients) \times 100%.

Statistical methods

SPSS 23.0 software (SPSS, Inc., Chicago, IL, USA) was used for statistical analyses. Count data were expressed as number of cases (n, %), and processed by χ^2 test (test level: two-

sided $\alpha=0.05$). The measurement data in this study conformed to normal distribution and were expressed as mean \pm standard deviation ($\bar{x} \pm sd$). Independent sample t-test was used for the comparison between groups, and paired t-test was used for comparison before and after resuscitation within the same group (test level: two-sided $\alpha=0.05$). $P<0.05$ indicates a statistically significant difference.

Results

Baseline data

A total of 50 patients with severe multiple injuries and traumatic shock were included in this study and randomly assigned into a Test group (n=25) and a Control group (n=25) using a random number table. The baseline clinical data of the two groups are shown in **Table 1**. Both the Test group and the Control group showed a majority of male patients (64.0% and 76.0%, respectively) and a main cause of injury as traffic accident (52.0% and 48.0%, respectively). There was no significant difference between the two groups in gender, age, injury severity score, time from injury to rescue and other baseline data (all $P>0.05$), so the two groups were comparable.

Coagulation function before and after resuscitation

Before resuscitation, there was no significant difference in coagulation function indices between the two groups (all $P>0.05$). After resus-

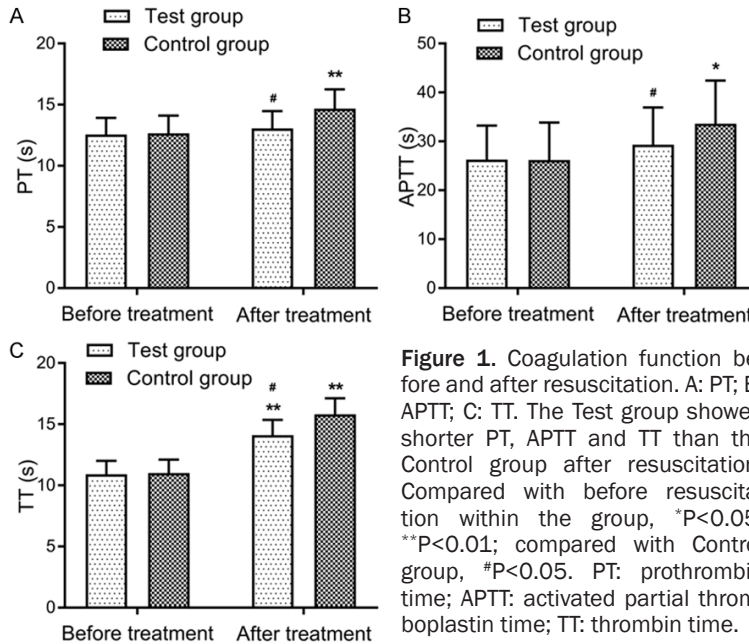


Figure 1. Coagulation function before and after resuscitation. A: PT; B: APTT; C: TT. The Test group showed shorter PT, APTT and TT than the Control group after resuscitation. Compared with before resuscitation within the group, ^{*}P<0.05, ^{**}P<0.01; compared with Control group, [#]P<0.05. PT: prothrombin time; APTT: activated partial thromboplastin time; TT: thrombin time.

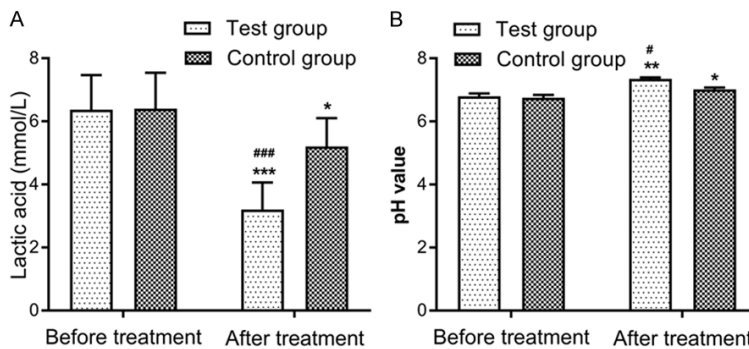


Figure 2. Levels of lactic acid (A) and pH (B) before and after resuscitation. (A) Lactic acid; (B) pH. Compared with before resuscitation within the group, ^{*}P<0.05, ^{**}P<0.01, ^{###}P<0.001; compared with Control group, [#]P<0.05, ^{**}P<0.01, ^{###}P<0.001.

citation, the Control group showed significant increase in PT, APTT and TT as compared with those before resuscitation (all P<0.05), while the Test group only showed significant increase in TT (P<0.05). The Test group showed shorter PT, APTT and TT than the Control group after the resuscitation, with statistically significant differences (all P<0.05). See **Figure 1**.

Levels of lactic acid and pH before and after resuscitation

Before resuscitation, there was no significant difference in the level of blood lactic acid and pH value between the two groups (both P>

0.05). After resuscitation, the level of blood lactic acid was significantly reduced, while the pH value was significantly increased in both groups (all P<0.05). The Test group showed lower level of blood lactic acid and higher pH value (closer to the normal level) than the Control group after resuscitation (P<0.001 and P<0.05). See **Figure 2**.

Hemorheological indices before and after resuscitation

Before resuscitation, there was no significant difference in the hemorheological indices between the two groups (all P>0.05). After resuscitation, the PV, AI, ESR and HCT of the two groups were significantly lower than those before resuscitation (all P<0.05), and the PV, AI, ESR and HCT of the Test group were observed to be further reduced (nearly to the normal level) as compared with the Control group, with significant differences (all P<0.05). See **Figure 3**.

Hemodynamic indices before and after resuscitation

There was no significant difference in MAP and heart rate between the two groups before resuscitation (both P>0.05). After resuscitation, both groups had significantly higher MAP and significantly lower heart rate than before (all P<0.001). But differences in MAP and heart rate after resuscitation were not significant between the two groups (both P>0.05). See **Table 2**.

Success rate of rescue and incidence of complications

In terms of success rate of rescue, the difference was not significant between the two groups (92.0% vs. 80.0%; P>0.05). But the overall incidence of complications in the Test

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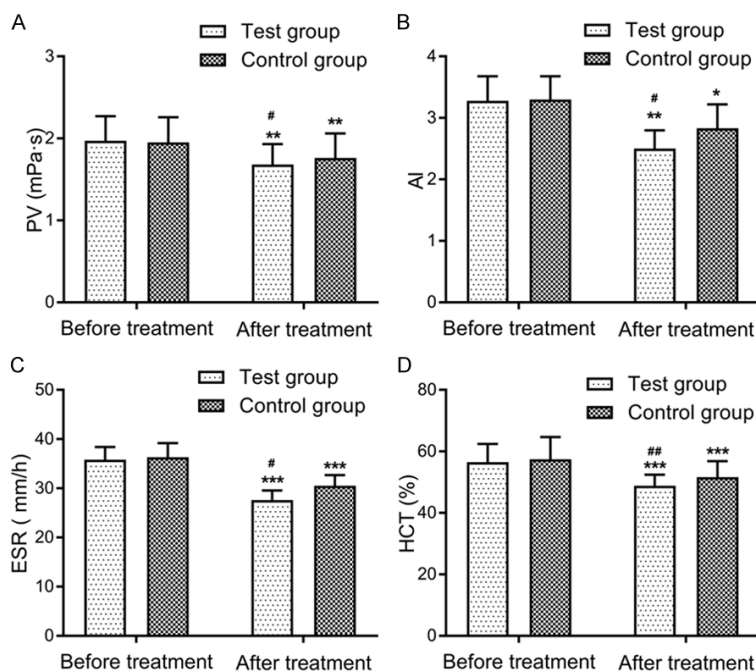


Figure 3. Hemorheological indices before and after resuscitation. A: PV; B: AI; C: ESR; D: HCT. The PV, AI, ESR and HCT after resuscitation were improved more significant in the Test group than in the Control group. Compared with before treatment within the group, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; compared with Control group, # $P < 0.05$, ## $P < 0.01$. PV: plasma viscosity; AI: red blood cell aggregation index; ESR: erythrocyte sedimentation rate; HCT: hematocrit.

group was significantly lower than that in the Control group (16.0% vs. 56.0%; $P < 0.01$). See **Table 3**.

Discussion

Timely body fluid resuscitation can quickly restore the effective circulating blood volume of patients, increase blood pressure, and ensure blood perfusion of tissues and organs [19]. The current restrictive fluid resuscitation method reduces the excessive dilution of blood as compared to the traditional adequate fluid resuscitation which may aggravate the coagulation dysfunction in shock patients [20]. However, the therapeutic effect of restrictive fluid resuscitation still needs to be improved. The use of better resuscitation fluids is the key to further improvement.

In this study, we compared the effects of sodium bicarbonated Ringer's solution and sodium lactated Ringer's solution for early fluid resuscitation in patients with severe multiple injuries and traumatic shock. Our results showed

higher PT, APTT and TT values in both groups after resuscitation than those before resuscitation, indicating that resuscitation has a diluting effect on patient's blood, which is consistent with the finding of previous studies [21, 22]. Furthermore, the coagulation function was significantly improved, and the PT, APTT and TT were significantly shorter in the Test group than those in the Control group after resuscitation, indicating that sodium bicarbonated Ringer's solution can inhibit the aggravation of coagulation dysfunction to a certain extent during resuscitation. The reasons could be that sodium bicarbonated Ringer's solution contains various electrolyte components such as Mg^{2+} , K^+ and Ca^{2+} , and its properties are closer to human extracellular fluid, which makes it more effective for

restoring the water and electrolyte balance and reducing the tissue edema in patients. This speculation was confirmed by a previous research [23]. In addition, study also showed that the metabolic rate of sodium bicarbonate is 6 times more than that of lactic acid, so sodium bicarbonate gives less metabolic burden to the liver [24]. Tissue edema and liver metabolism are closely related to human coagulation function [25]. So, we further compared the lactic acid metabolism of the two groups, and the results showed that the blood lactic acid level and pH value of the Test group were improved more significantly than those of the Control group after resuscitation. This may be related to the HCO_3^- buffer system in the sodium bicarbonated Ringer's solution that can neutralize acidity without increasing extra lactic acid. An animal experiment in Japan also confirmed that sodium bicarbonated Ringer's solution could effectively improve metabolic acidosis in dogs with hemorrhagic shock, and its effect was significantly better than that of sodium lactated Ringer's solution and sodium

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Table 2. MAP and heart rate before and after resuscitation ($\bar{x} \pm sd$)

Item	Test group (n=25)	Control group (n=25)	t	P
MAP (mmHg, $\bar{x} \pm sd$)				
Before resuscitation	51.50±8.02	50.82±7.66	0.307	0.761
After resuscitation	65.85±7.50***	64.56±8.25***	0.579	0.566
Heart rate (times/min, $\bar{x} \pm sd$)				
Before resuscitation	147.52±15.20	148.06±17.65	0.116	0.908
After resuscitation	112.48±12.96***	113.59±13.85***	0.293	0.771

Note: MAP: mean arterial pressure. Compared with before resuscitation within the group, ***P<0.001.

Table 3. Success rate of rescue and incidence of complications (n, %)

Item	Test group (n=25)	Control group (n=25)	χ^2	P
Result of rescue (n, %)				
Survival	23 (92.0)	20 (80.0)	1.495	0.221
Death	2 (8.0)	5 (20.0)		
Complications (n, %)				
DIC	1 (4.0)	3 (12.0)	8.681	0.003
ARDS	2 (8.0)	6 (24.0)		
MODS	1 (8.0)	5 (20.0)		
Total	4 (16.0)	14 (56.0)		

Note: DIC: disseminated intravascular coagulation; ARDS: adult respiratory distress syndrome; MODS: multiple organ dysfunction syndrome.

acetated Ringer's solution [15]. The accumulation of lactic acid can lead to metabolic acidosis and aggravate coagulation dysfunction [26]. Therefore, effectively reducing the lactic acid level and improving the metabolic acidosis may be another evidence for the improvement of coagulation function in patients by sodium bicarbonated Ringer's solution.

The hemorheological changes of patients during resuscitation were also observed in this study. Compared with the Control group, the Test group showed further improvements in PV, AI, ESR and HCT after resuscitation. We believe that sodium bicarbonated Ringer's solution is closer to the extracellular fluid of the human body, so it can be more effective for the blood recovery. Study by Su et al. showed that sodium lactated Ringer's solution can cause granulocyte respiration bursts, releasing a large amount of oxygen free radicals and other inflammatory response mediators to aggravate systemic inflammations [27]. Inflammation response can increase the capillary permeability and plasma extravasation as well as decrease the blood volume, which aggra-

vate the hemorheology. However, our study did not observe whether sodium bicarbonated Ringer's solution can improve the levels of inflammatory response-related factors in patients, which could be a perspective for further studies.

Significant reductions in MAP and heart rate were observed after resuscitation in both groups, but there was no significant difference between the two groups. There were 23 cases in the Test group and 20 cases in the Control group who were successfully rescued. The successful rate of rescue was slightly lower in the Control

group than that in the Test group, but the difference was not statistically significant. The overall incidence of complications in the Test group was significantly lower than that of the Control group (16.0% vs. 56.0%), suggesting that sodium bicarbonated Ringer's solution may be a better choice for early fluid resuscitation in patients with severe multiple injuries and traumatic shock.

There are some limitations in this study. The sample size in this study was small which may lead to statistical bias. Besides, we did not analyze the specific mechanism of sodium bicarbonated Ringer's solution on the improvement of patients' coagulation function. We plan to conduct a larger sample size study to further clarify the specific mechanism of sodium bicarbonated Ringer's solution in patients with severe multiple injuries and traumatic shock.

In conclusions, this study found that sodium bicarbonated Ringer's solution is effective for the early resuscitation in patients with severe multiple injuries and traumatic shock through improving the coagulation function and lactic

acid metabolism as well as reducing the risk of related complications in patients. So, sodium bicarbonated Ringer's solution may be a better choice for resuscitation fluid.

Disclosure of conflict of interest

None.

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