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Effects of starch nanospheres solution on hemodynamic values in rats with hemorrhagic shock: A preliminary study in hemorrhagic shock resuscitation

Yuan Li, MD,[a,1] *Xiao-Miao Li, MD,*[b,1] *and Li-xian Xu, MD*[a,*]

[a] *Department of Anesthesiology, Fourth Military Medical University School of Stomatology, Xi'an, China*
[b] *Department of Endocrinology, Xijing Hospital, Fourth Military Medical University, Xi'an, China*

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ABSTRACT

Background: The objective of the present study was to explore the resuscitation effects of starch nanospheres solution on hemodynamics in rats with hemorrhagic shock.
Methods: A total of 20 Sprague-Dawley rats were randomly divided into 2 groups: resuscitation group 1 (infusion with Ringer's solution) and resuscitation group 2 (infusion with starch nanospheres solution) with 10 rats per group. The rats in resuscitation groups 1 and 2 were subjected to hemorrhagic shock, and resuscitation was performed with Ringer's solution and starch nanospheres solution. The changes in the hemodynamic values of the rats in both groups were observed and recorded.
Results: The hemodynamic values included the systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, heart rate, and respiratory rate. After resuscitation, the systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate in resuscitation group 2 had reverted back to the base values ($P > 0.05$). The systolic blood pressure, diastolic blood pressure, and mean arterial pressure were lower at all points in resuscitation group 1 than in resuscitation group 2 ($P < 0.05$). The respiratory rate was more rapid after resuscitation at 30 and 60 min in resuscitation group 1 than in resuscitation group 2 ($P < 0.05$).
Conclusions: Starch nanospheres solution expands the circulating blood volume and improves the hemodynamics. It also increases the effective circulating blood volume and improves the shock symptoms of effective hypovolemia.

1. Introduction

Hemorrhagic shock is the most common type of shock. It is a state of inadequate organ perfusion for normal aerobic metabolism resulting from a loss of circulating blood. The lack of organ perfusion disrupts normal cellular metabolism and, if not reversed, will ultimately lead to multiple organ dysfunction syndrome or, worse, multiple organ failure [1,2]. At present, the treatment methods for hemorrhagic shock mainly include the rectification of acidosis, expansion of the

* *Corresponding author*. Fourth Military Medical University School of Stomatology, Xi'an 710032 China. Tel.: +86 29 8477 6119; fax: +86 29 8477 6115.
E-mail address: xiaomiao@fmmu.edu.cn (L.-x. Xu).
[1] These authors contributed equally to this report and should be regarded as co-first authors.
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plasma volume, and the use of vasoactive drugs. In the recovery of shock, we have found that transfusion therapy is the most effective treatment method [3]. For treatment of hemorrhagic traumatic shock to be effective, most have contended that the rapid transfusion of considerable fluid before completely controlling the massive hemorrhage is required to return the blood pressure to a normal level to ensure blood perfusion of the major visceral organs. However, this vastly neglects the input of much crystalloid solution, which does not contain hemoglobin and cannot directly and effectively increase the blood and oxygen supply to the major visceral organs. In contrast, it will accelerate deterioration of the body environment and seriously disrupt the protective mechanism of the body. For early fluid resuscitation, it has been reported that if the fluid is transfused at a low level and slow speed, the blood pressure can be controlled at a stable level and might cause less disruption to the body environment and reduce the occurrence of the various complications of shock, effectively reducing the death rate at a later period. As a drug carrier, the cross-linked starch nanospheres with N,N′-methylenebisacrylamide are biologically compatible and biodegradable. Additionally, they are nonpoisonous, immunogenic free, stable in storage, and low in cost because starch is an abundant and inexpensive natural biopolymer compared with to blood products and can be degraded by enzymes within the body. The cross-linked nanospheres are changeable, expand in water, and can keep a relatively long period during delivery [4–6]. Therefore, on the basis of the swelling property of dry nanospheres in liquid medicine, we designed a new type of resuscitation solution (i.e., the starch nanospheres Ringer's solution). Similar to the electrolytes of extracellular fluid, this solution can result in the required blood pressure at a low volume to help normalize the blood circulation and protect the vital organs. In addition, without much disturbance to the body environment, it is able to create favorable conditions and gain precious time for subsequent rescue and treatment. The present experiment compared the starch nanospheres Ringer's solution and common crystalloid Ringer's solution to observe whether the starch nanospheres Ringer's solution had a better effect on resisting hemorrhagic shock.

2. Methods

2.1. Rats

Male Sprague-Dawley rats (specific pathogen-free grade, age 10–12 weeks, weight 230–250 g) were obtained from the Experimental Animal Centre of the Fourth Military Medical University (Xi'an, China). The rats were housed with free access to food and water at a constant temperature of 22 ± 2°C at 55% ± 5% humidity, with a 12-h light/12-h dark cycle. The ethics committee of the Xijing Hospital of Fourth Military Medical University (Xi'an, China) reviewed and approved the study protocol. The animal handling was in accordance with the guidelines for the capture, handling, and care of mammals, as approved by the American Society of Mammalogists.

2.2. Experimental groups and methods

The rats were randomly divided into 2 groups, with each containing an equal quantity ($n = 10$). Resuscitation group 1 received Ringer's solution, and resuscitation group 2 received starch nanospheres Ringer's solution. Before the experiment, food was withheld so the rats would fast, but water was given freely. All rats were anesthetized with 10% chloral hydrate (0.3 mL/100 g) by intraperitoneal injection. The tubes were inserted into the femoral artery and femoral vein on the right side and into the right carotid artery. The tube in the femoral artery was used to observe the blood pressure and occurrence of bleeding. Through the tube in the femoral artery, physiologic saline with heparin (500 U/kg) was injected for anticoagulation. The tube in the femoral vein was for drug administration. The tube placed in the right carotid artery through left ventricle was to measure the hemodynamics indexes, including the systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and respiratory rate (RR). Acute hemorrhage shock was induced by withdrawing blood through the carotid artery catheter to cause the MAP to decrease to 40 ± 5 mm Hg within 5 min and was stabilized in 10 min. The shock model was successfully copied. Later, Ringer's solution was infused at 3 times the volume of hemorrhage in resuscitation group 1, and starch nanospheres Ringer's solution were infused at an equal ratio to the volume of hemorrhage in resuscitation group 2. The whole solution amount was transfused within 30 min. We recorded the changes in the hemodynamic values for all experimental rats every 30 min. The starch nanospheres Ringer's solution was created using antiphase suspension polymeric nanometer technology, with soluble starch as the material and K2S2O8-Na2S03 as the initiating agent. Finally, it compounds the starch nanospheres cross-linked with N,N′-methylenebisacrylamide, which is then converted into the starch nanospheres antishock fluid (2% concentration) by dissolving in Ringer's solution.

2.3. Statistical analysis

The mean ± standard deviation of the data was calculated, and statistical analyses were performed using SAS, version 9.0 (SAS Institute, Cary, NC). The data were analyzed using 1-way analysis of variance with *post hoc* comparisons and Bonferroni's correction. To assess the effect of starch nanospheres solution *versus* Ringer's solution, the paired-sample *t*-test was used to compare normally distributed data. The results were plotted using SPSS for Windows, version 15.0 (SPSS, Chicago, IL). $P < 0.05$ was considered statistically significant.

3. Results

The changes in hemodynamics before and after resuscitation. After hemorrhagic shock had been induced into both groups of rats, the SBP, DBP, and MAP were obviously lower than the base values and the heart rate (HR) was clearly faster than the base value ($P < 0.05$). For resuscitation group 2, after resuscitation, the HR, SBP, DBP, and MAP at each point had returned to (or was closer to) the base values ($P > 0.05$). However, for