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Effect of hypertonic saline in the pretreatment of lung donors with hemorrhagic shock

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ARTICLE INFO

Article history:
Received 3 May 2017
Received in revised form
4 December 2017
Accepted 28 December 2017
Available online 21 February 2018

Keywords:
Hemorrhagic shock
Donor
Lungs
Hypertonic
Experimental study

ABSTRACT

Background: Hemorrhagic shock–induced lung edema and inflammation are two of the main reasons for the rejection of lungs donated for transplantation. Hypertonic saline (HS) induces intravascular volume expansion and has considerable immunomodulating effects that might minimize edema. Our hypothesis is based on the use of a hypertonic solution for treatment of donors who are in shock in an attempt to increase the supply of lungs for transplantation.

Methods: A total of 80 rats were allocated to four groups: one group was given an infusion of normal saline (NS; $n = 20$), one group received HS; $n = 20$, a sham group ($n = 20$), and a Shock group ($n = 20$). Half of the lungs from each group were evaluated in an *ex vivo* perfusion system, and the other half was used for measurements of cytokine levels and neutrophil counts.

Results: In the *ex vivo* perfusion assessment, the pulmonary artery pressures of the animals in the NS and HS groups did not exhibit significant differences compared with those in the sham group ($P > 0.05$) but were lower than those in the Shock group ($P < 0.01$). Furthermore, the tumor necrosis factor-α levels and neutrophil counts were lower in the HS group than those in the Shock group ($P < 0.01$) and did not exhibit significant differences compared with those in either the NS and Sham groups ($P > 0.05$).

Conclusions: We showed that HS was equivalent to isotonic saline and contributed to the treatment of lungs subjected to hemorrhagic shock.

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0022-4804/$ – see front matter
https://doi.org/10.1016/j.jss.2017.12.041

Introduction

Lung transplantation is an effective treatment for severe lung diseases.[1] Due to technological advances and improvements in surgical techniques and organ preservation, the number of lung transplants has increased considerably to more than 3200 cases in 2009.[2] Despite this increase, the number of patients on the waiting list continues to increase significantly. In an attempt to increase the number of donors, strategies such as the use of reconditioned lungs, non-beating-heart organ donation, and the extension of the clinical criteria for selection (nonideal donors) have been disseminated and employed by various transplant centers.[3-7]

Brain-dead potential organ donors often exhibit hemodynamic instability, such as hypovolemia, which might lead to progressive organ deterioration.[8] The lungs are highly vulnerable to hemorrhagic shock, which impairs the perfusion of tissues due to insufficient intracellular volume. Uncontrolled bleeding causes early lung injury associated with increased capillary permeability and edema. One of the clinical strategies to induce recovery from hemorrhagic shock consists of early administration of fluids and blood products. Normal saline (NS) is widely used as a standard for fluid resuscitation of lungs in shock; however, high volumes of such solutions are required to achieve this purpose. Treatment with three- to four-fold smaller amounts of hypertonic saline (HS) suffices to promote blood volume restoration. HS induces intravascular volume expansion due to the osmotic gradient,[9,10] thus restoring the mean arterial pressure (MAP). In addition, HS has a considerable immunomodulating effect that might minimize edema.[9-11] Few studies in the literature have investigated the use of HS in lung donors with hemorrhagic shock. To increase the availability of lungs from donors subjected to hemorrhagic shock, we studied the administration of 7.5% HS in an experimental model of lung donors with hemorrhagic shock. In the present study, we evaluated the respiratory mechanics in an *ex vivo* system and compared the results with normal 0.9% saline (traditional fluid resuscitation therapy).

Methods

This research was approved by the ethics committee of our institution. All animals were treated in agreement with the Brazilian regulations for the use of animals in scientific research.

Experimental design

A total of 80 adult male Sprague Dawley rats with an average weight between 250 and 350 g were used. The number of animals needed for each group was established in a pilot study. The animals were randomly allocated to the following experimental groups: Sham—20 animals subjected to catheterization without shock induction nor any type of fluid resuscitation; Shock—20 animals subjected to vascular catheterization and shock induction; NS (shock + NS treatment)—20 animals subjected to vascular catheterization shock induction and treatment with 33 mL/kg of 0.9% saline solution; and HS (shock + HS treatment)—20 animals subjected to vascular catheterization, shock induction, and treatment with 4 mL/kg of 7.5% HS (Fig. 1).

Experimental protocol

The animals were anesthetized with an intraperitoneal injection of pentobarbital sodium (50 mg/kg), weighed, and immobilized on a thermal board (36°C). The cervical trachea was exposed for tracheostomy, followed by mechanical ventilation using a small animal ventilator (Harvard Apparatus model 683, Holliston, MA) with a tidal volume of 10 mL/kg and a frequency of 80 cycles per minute in O_2 (FiO_2 21%). With the animals immobilized on the board, the right and left

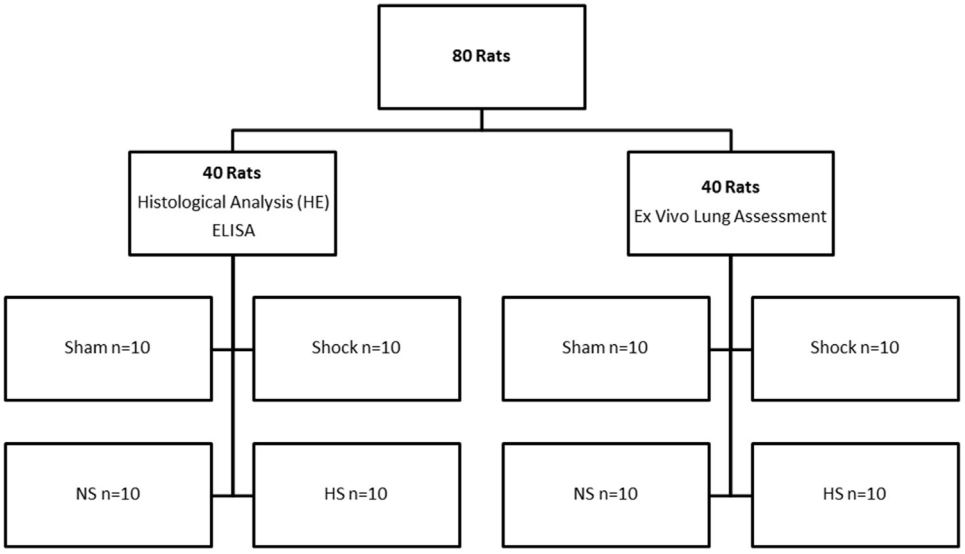

Fig. 1 – Flow diagram of study design showing how the rats were divided.