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Pyruvate-enriched oral rehydration solution improved intestinal absorption of water and sodium during enteral resuscitation in burns



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ABSTRACT

Aim: To investigate alteration in intestinal absorption during enteral resuscitation with pyruvate-enriched oral rehydration solution (Pyr-ORS) in scalded rats.

Methods: To compare pyruvate-enriched oral rehydration solution (Pyr-ORS) with World Health Organisation oral rehydration solution (WHO-ORS), 120 rats were randomly divided into 6 groups and 2 subgroups. At 1.5 and 4.5 h after a 35% TBSA scald, the intestinal absorption rate, mucosal blood flow (IMBF), Na^+ -K⁺-ATPase activity and aquaporin-1 (AQP-1) expression were determined (n=10), respectively.

Results: The intestinal Na⁺-K⁺-ATPase activity, AQP-1 expression and IMBF were markedly decreased in scald groups, but they were profoundly preserved by enteral resuscitation with WHO-ORS and further improved significantly with Pyr-ORS at both time points. Na⁺-K+-ATPase activities remained higher in enteral resuscitation with Pyr-ORS (Group SP) than those with WHO-ORS (Group SW) at 4.5 h. AQP-1 and IMBF were significantly greater in Group SP than in Group SW at both time points. Intestinal absorption rates of water and sodium were obviously inhibited in scald groups; however, rates were also significantly preserved in Group SP than in Group SW with an over 20% increment at both time points. Conclusion: The Pyr-ORS may be superior to the standard WHO-ORS in the promotion of intestinal absorption of water and sodium during enteral resuscitation.

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1. Introduction

Enteral resuscitation may provide a means to resuscitation of burn shock when the intravenous route is not available or applicable in resource-poor settings, such as in a disaster or a war with mass casualties. The World Health Organization (WHO) oral rehydration solution (WHO-ORS) has been recently suggested to be of value as a safe and effective alternative to intravenous resuscitation for burn shock and appreciated in clinical burn resuscitation [1–3]. However, oral resuscitation is challenged because the gastrointestinal ischemia due to severe

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burns and resultant hypovolemic shock reduces gastric emptying and impairs the intestinal absorption. Previous studies indicated that the intestinal absorption rates of water and sodium were significantly decreased during enteral feeding or resuscitation for hypovolemic shock, which were attributable to ischemia and/or hypoxia-induced mucosal cell injury [4,5]. Intestinal absorption of water and sodium depends on multi-factors, including the intestinal mucosal blood flow (IMBF), Na⁺-K⁺-ATPase activity and aquaporin-1 (AQP-1) expression. Comparatively, as yet little is known in respect of effective drugs or agents to improve the gastrointestinal blood flow and absorption during burn injury [6,7].

Pyruvate is a metabolic intermediate of the glycolytic pathway and has been explored to be cytoprotective through preservative effects of glucose metabolic pathways, super buffer capabilities and anti-oxidative/nitrosative and antiinflammatory mechanisms [8-10]. Currently, it appears in the nutrition market as a dietary supplement. Thus, in this experiment, a novel oral rehydration composition, pyruvateenriched ORS (Pyr-ORS), was developed, in which equimolar sodium pyruvate replaced sodium bicarbonate in the standard WHO-ORS, and a hypothesis was tested that the Pyr-ORS would improve enteral resuscitation for burn injury. The present investigation was focused on the effects of Pyr-ORS on the intestinal absorption rates of water and sodium, the IMBF, the Na+-K+-ATPase activity and the AQP-1 expression during enteral resuscitation of rats with scald injuries, compared with the bicarbonate-based WHO-ORS.

2. Materials and methods

2.1. Experimental animals

Male Sprague-Dawley rats, age 12 weeks, weighing 288.5 ± 5.7 g, obtained from the Chinese Peking Union Medical College, Beijing, China, were used in the experiments. Rats were acclimatized for one week and fasted overnight but allowed free access to water until 4 h before surgery. All animal experiments were approved by the Committee of Scientific Research of the First Hospital Affiliated to General Hospital of PLA, China and were conducted in accordance with the National Institute of Health Guide for the Care and Use of Laboratory Animals, China.

The rats were anesthetized and instrumented with 3% isoflurane and isoflurane (0.7%) was used to maintain anesthesia during the experiments. Isoflurane (0.7%) was used to maintain anesthesia during the experiments. Rats were allowed to breath spontaneously under a nose cone scavenging system using a veterinary anesthesia delivery system (Kent Scientific TOPO, Torrington, CT, USA). About 35% total body surface area (TBSA) of full-thickness scald was inflicted on the back of rats with boiling water (100 °C, 15 s) in three scald groups. Following the scald injury, the rats received a subcutaneous injection of 0.5 ml normal saline with 500 µL of Buprenorphine for pain control. With aseptic technique, a poly-ethylene catheter (PE-50) was inserted into the proximal duodenum (5 cm distal to pylorus) and distal ileum (5 cm proximal to cecum), respectively, to form an isolated loop of intestine with fluid introduction and collection

stomas in each rat through laparotomy, as previously reported [11]. An ORS was delivered through the infusion catheter during 30 min after scald injuries in rats. The amount of fluid infusion was according to that of Parkland formula (4 ml kg $^{-1}$.1% TBSA $^{-1}$) with half of the total amount infused in the first 8 h, controlled by an infusion pump (Kelifeng Apparatus, Beijing, China) [12].

2.2. Animal grouping and ORS preparations

One hundred and twenty rats with surgical procedures above were randomly assigned to six groups (N = 20, divided to 2 subgroups: n = 10 for 2 time points: 1.5 h and 4.5 h in each group, respectively): scald sham (Group SS), scald with no fluid resuscitation (Group SN), scald sham resuscitation with enteral WHO-ORS (Group W), scald sham resuscitation with enteral Pyr-ORS (Group P), scald resuscitation with enteral WHO-ORS (Group SW), and scald resuscitation with enteral Pyr-ORS (Group SP). One rat was selected and experimented daily in each group by using a random number table. The Pyr-ORS or the WHO-ORS was freshly prepared daily by dissolving sodium pyruvate (NaPyr, Sigma-Aldrich, St. Louis, MO, USA) 3.5 g or bicarbonate (NaHCO₃) 2.5 g, sodium chloride (NaCl) 3.5 g, sodium potassium (KCl) 1.5 g and glucose, anhydrous 20 g with distilled water up to 1000 ml at the laboratory, according to the WHO formula with a high osmolarity [13]. The concentrations of ORS components in mEq/L were Na+ 90, K⁺ 20, Cl⁻ 80, and HCO₃⁻ 30 or Pyr⁻ 32 and glucose 111. The Pyr-ORS had the osmolarity of 335 mOsm L^{-1} with pH 7.35 and the WHO-ORS had 331 mOsm L^{-1} with pH 7.35. Animals were euthanized after experiments at 1.5 h and 4.5 h in two subgroups, respectively.

2.3. Measurement of IMBF

The IMBF was continuously recorded for 5 min with a laser Doppler flow monitor (Peri Flux 5000 Master; Perimed, Järfälla, Sweden) at around 1.5 and 4.5 h after injury in 10 rats each subgroup, respectively, as previously described [11]. Briefly, a flexible probe with 0.25 mm laser rheophore was inserted through a small enterotomy at the proximal end of the jejunum, and it was positioned along the anti-mesenteric border of the jejunum [14]. The measured values were taken as the average flow for a 5-min period and expressed in the blood perfusion unit (BPU).

2.4. Measurement of intestinal absorption rates of water and sodium

Phenol red (Sigma–Aldrich, St. Louis, MO, USA) was added to an ORS (2 μ g/ml) and was administered into the intestine. A standard curve was plotted with absorbance values of different concentrations of phenol red determined by spectrophotometer at 550 nm, according to the modified Cooper's method reported previously [15]. The phenol red concentration in the ORS was measured with the standard curve to reflect the intestinal absorption rates of water and sodium at 1.5 and 4.5 h after the scald injury in 10 rats each subgroup except the no resuscitation groups, respectively, and the values were expressed in a percentage (%). The rates were calculated with a formula, as previously described [11].

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