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Pyruvate in reduced osmolarity oral rehydration salt corrected lactic acidosis in sever scald rats

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ARTICLE INFO

Article history:
Received 23 May 2017
Received in revised form
10 December 2017
Accepted 12 January 2018
Available online xxx

Keywords:
Burn
Lactic acidosis
Oral rehydration salt
Pyruvate
Shock

ABSTRACT

Background: A novel pyruvate-based oral rehydration salt (Pyr-ORS) was demonstrated of superiority over bicarbonate- or citrate-based one to preserve organ function and correct lactic acidosis in rehydration of lethal shock in animals. This study further compared these effects between low-osmolar Pyr-ORS and equimolar citrate-based counterpart.

Methods: Eighty rats, using a fatal burn shock model, were randomized into four groups (two subgroups per group: $n = 10$): the sham group (group SR), Pyr-ORS group (group PR), WHO-ORS III group (group CR), and no rehydration group. ORS was delivered by manual gavage during 24 h following burns. Oral administration consisted of half of counted volume in the initial 8 h plus the rest in the later 16 h. Systemic hemodynamics, visceral organ surface blood flow, organ function, and metabolic acidosis were determined at 8 h and 24 h after burn. Another set of rats with identical surgical procedures without tests was observed for survival.

Results: Survival was markedly improved in the groups PR and CR; the former showed a higher survival rate than the latter at 24 h (40% *versus* 20%, $P < 0.05$). Systemic hemodynamics, visceral blood flow, and function of heart, liver, and kidney were greatly restored in group PR, compared with group CR (all $P < 0.05$). Hypoxic lactic acidosis was efficiently reversed in group PR, instead of group CR, (pH 7.36 *versus* 7.11, base excess 2.1 *versus* −9.1 mmol/L, lactate 4.28 *versus* 8.18 mmol/L; all $P < 0.05$) at 24 h after injury.

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Conclusions: Pyruvate was advantageous over citrate in low-osmolar ORS for protection of organs and survival; pyruvate, but not citrate, in the ORS corrected hypoxic lactic acidosis in rats subjected to lethal burn shock in 24 h.

Introduction

Early and appropriate fluid resuscitation is an essential treatment in patients subjected to burn shock. Oral rehydration solution (ORS), either alone or in combination with intravenous (IV) fluids, has shown its benefits in burn treatment and is encouraged in the guidance on resuscitation of moderately sized burns by the American Burn Association.[1,2] The WHO-guided ORS consists of a base, alkalizer, which is bicarbonate or citrate. Compared with them, pyruvate has multifactorial benefits because of its favorable properties associated with cellular function: enhancement of anoxia and/or hypoxia tolerance, antioxidative stress and anti-inflammation, and prevention of apoptosis in severe pathogenic insults.[3-8]

Recently, compared with the bicarbonate-based ORS (WHO-ORS I, 331 mOsm/L), a novel pyruvate-based ORS (Pyr-ORS, pyruvate replaces equimolar bicarbonate in WHO-ORS I, 335 mOsm/L) showed its advantages. It enhanced intestinal absorption of sodium and water, improved visceral blood flow, and preserved multiple organs in rehydration of lethal shock in rodents.[9,10] The Pyr-ORS was also more protective than citrate-based ORS (WHO-ORS II, Cit-ORS, equimolar citrate substitutes bicarbonate in WHO-ORS I, 311 mOsm/L) in improvement of hemodynamics, vascular permeability, multiorgan function, and survival rate in burn shock of dogs.[11] Notably, oral pyruvate, instead of bicarbonate or citrate, in ORS effectively corrected hypoxic lactic acidosis (type A) complicated with lethal shock and profoundly prolonged survival in these severe shock models.[10,11] Type A lactic acidosis is a life-threatening symptom that occurred in critically ill patients with high incidence and mortality in both children and adults in intensive care units. However, there is still no ideal medical therapy available for its treatment in clinical scenarios.[12] Thus, this innovative finding concerning lactic acidosis correction by Pyr-ORS may be of clinical importance.

Since 2003, the WHO has formally recommended and promoted reduced osmolarity Cit-ORS (WHO-ORS III, low-osmolar ORS, 245 mOsm/L) with equimolar citrate and less glucose and sodium in WHO-ORS II for pediatric diarrhea (noncholera) worldwide.[13] The low-osmolar ORS increases intestinal absorption of water and salts and reduces stool output and the need for IV fluids in children with diarrhea.[13] Recently, a substitute of WHO-ORS III (CeraLyte 90) was effectively used with IV solutions in resuscitation of adults subjected to burn shock, but lactic acidosis correction was not investigated.[1] Therefore, to verify the impact of pyruvate and citrate in ORS on lactic acidosis, this study focused on the lactic acidosis correction in comparison of the new reduced osmolarity Pyr- ORS (247 mOsm/L) to the low-osmolar Cit-ORS (WHO-ORS III, 245 mOsm/L) in simple oral rehydration of rats with severe scald injury.

Materials and methods

Animals and surgical procedures

Animal experiments were conducted following Guidelines for the Care and Use of Animals, China, and the protocol was allowed by the Scientific Research Committee of General Hospital of PLA, Beijing, China.

Male Sprague–Dawley rats, aging 8-10 wk and weighing 260-300 g (obtained from Beijing Hua-Fu-Kang (HFK) Bioscience Co, Beijing, China) were used in the experiment. After acclimating for 1 wk, rats were fed the standard laboratory diet. Animals were fasted but still free to water until 4 h before the experiment.

Pentobarbital sodium was injected to rats for anesthesia (50 mg/kg, IM). After shaving the back, abdomen, and legs, approximately 50% total body surface area of III-degree scald was imposed by a stickers jigsaw method with near boiling water (96°C) on the back for 15 s, legs for 15 s, and abdomen for 8 s, as recently described.[11] The water temperature was 37°C in the scald sham group as a control. Following burns, the rat obtained 500 μL buprenorphine (Sigma–Aldrich, St. Louis, MO) in 0.5 mL normal saline via subcutaneous injection per 6-8 h for the pain control. Using a heating lamp, the rectal temperature was kept at 37°C. The third degree burn injury was verified by pathological examinations.

At 8 h and 24 h postscald, the following surgery was performed in each live rat to determine experimental parameters. With aseptic technique, the right femoral artery and femoral vein were exposed. With the PICCO-PLUS monitor, a pressure fibrotic sensor was inserted into the femoral artery up to the aorta, and a temperature fibrotic sensor was introduced into the femoral vein up to the superior vena cava to measure hemodynamic variables (Pulsion Co, Germany): cardiac output, maximal rate of ventricular contractility assessment of left ventricle pressure, systemic vascular resistance, and mean arterial pressure. Both sensors were fixed to the skin exit in each rat, as reported previously.[11] Thereafter, the visceral blood perfusion, which indicated the blood flow of organ surfaces, was determined by surgically inserting a fine laser rheophore in the flexible probe into the abdomen to monitor blood flow on right lobe of liver, upper pole of left kidney, and mucosa of intestine (through a tiny enterotomy 10 cm from the Treitz ligament). The visceral blood perfusion was documented with a laser Doppler flow monitor of Peri Flux 5000 (Perimed AB, Jarfalla, Sweden) continuously for 30 s and taken from a 10-s stable signal as the average flow at the two time points. The signals were inputted into the computer to plot curves; data were expressed as blood perfusion units (PBU), as previously described.[14]