Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/burns

Pyruvate in oral rehydration salt improves hemodynamics, vasopermeability and survival after burns in dogs☆,☆☆

Rui Liu[a], Xiao-Hang Hu[b,c], Shu-Ming Wang[d], Si-Jia Guo[e], Zong-Yu Li[a], Xiao-Dong Bai[f,**], Fang-Qiang Zhou[g,**], Sen Hu[b,*]

[a] Department of Burns, the Fifth Hospital of Harbin, Harbin, 150040, China
[b] Laboratory for Shock and Multiple Organ Dysfunction of Burns Institute, Key Research Laboratory of Tissue Repair and Regeneration of PLA, and Beijing Key Research Laboratory of Skin Injury and Repair Regeneration, First Hospital Affiliated to the Chinese PLA General Hospital, Beijing 100048, China
[c] School of Medical Science, Faculty of Science Office, Level 2, Carslaw Building (F07), University of Sydney, NSW 2006, Australia
[d] Department of Emergency Medicine, First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin 150040, China
[e] Department of Human Resources, the First Hospital of Harbin, Harbin 150010, China
[f] Department of Burn Surgery, the General Hospital of Armed Police Forces, Beijing 100039, China
[g] Shanghai Sandai Pharmaceutical R&D Co., Pudong, Shanghai 201203, China

ARTICLE INFO

Article history:
Accepted 5 January 2016

Keywords:
Burn
Oral rehydration salt
Organ function
Pyruvate
Shock
Vasopermeability

ABSTRACT

Background: To investigate whether pyruvate-enriched oral rehydration solution (Pyr-ORS), compared with citrate-enriched ORS (Cit-ORS), improves hemodynamics and organ function by alleviating vasopermeability and plasma volume loss during intra-gastric fluid rehydration in dogs with severe burn.

Methods: Forty dogs subjected to severe burn were randomly divided into four groups ($n = 10$): two oral rehydrated groups with Pyr-ORS and Cit-ORS (group PR and group CR), respectively, according to the Parkland formula during the first 24 h after burns. Other two groups were the intravenous (IV) resuscitation (group VR) with lactated Ringer's solution with the same dosage and no fluid rehydration (group NR). During the next 24 h, all groups received the same IV infusion. The hemodynamics, plasma volume, vasopermeability and water contents and function of various organs were determined. Plasma levels of vascular endothelial growth factor (VEGF) and platelet activating factor (PAF) were detected by ELISA.

Results: Hemodynamics parameters were significantly improved in group PR superior to group CR after burns. Levels of VEGF and PAF were significantly lower in group PR than in group CR. Organ function parameters were also greatly preserved in group PR, relative to groups CR and NR. Lactic acidosis was fully corrected and survival increased in group PR (50.0%), compared to group CR (20.0%).

☆ Supported by the special foundation of the 11 five-year plan for military medical project, No. 06Z055.
☆☆ Supported by the youth science fund of Heilongjiang province, No. QC2016101.
* *Corresponding author*. Tel.: +86 1066867397.
** *Corresponding authors*.
E-mail addresses: 2237978564@qq.com (X.-D. Bai), fqzh60130@yahoo.com (F.-Q. Zhou), bs0425@163.com (S. Hu).
http://dx.doi.org/10.1016/j.burns.2016.01.012

Conclusion: Pyr-ORS was more effective than Cit-ORS in improving hemodynamics, visceral blood perfusion and organ function by alleviating vasopermeability-induced visceral edema and plasma volume loss in dogs with severe burn.

1. Introduction

The most effective resuscitation of patients subjected to massive burn shock is timely sufficient fluid resuscitation. The later fluid resuscitation is initiated, the higher mortality will be [1]. Unfortunately, in mass thermal casualty events, such as wars, natural disasters, or terrorist attacks, the blood volume decreases suddenly in numerous victims and intravenous (IV) fluid delivery is limited to implement in a short time at source-poor settings. In particular, there have been multiple nuclear conflicts where treatment of burns is more of a challenge than a problem in contemporary medicine [2]. Most burned and wounded patients would miss the best treatment time for IV fluid resuscitation, leading to a huge initial loss of life. Oral fluid resuscitation is a simple way to rehydrate hypovolemic patients with no sterilized medical supply. It was reported to be a successful alternative in early clinical studies of burn care and has been encouraged by the American Burn Association in the guidance of burn resuscitation [3,4]. One of the World Health Organization-guided oral rehydration salt (WHO-ORS) formula, which was initially developed for treatment of diarrhea and cholera worldwide for decades, citrate-enriched oral rehydration salts with low osmolarity (Cit-ORS, CeraLyte 90) has been recently recommended and appreciated in the burn treatment of adults [5]. The ORS may play a critical role in the prevention of gut-origin sepsis and multiple organ dysfunction syndrome (MODS) in burn care, as indicated in recent findings with novel pyruvate-ORS (Pyr-ORS) relative to the standard bicarbonate-based WHO-ORS [6,7].

The exogenous pyruvate has been reported to hold superior pleiotropic biological properties in cell/organ protection, including enhancement of hypoxia tolerance, improvement of glucose metabolic pathways, correction of hypoxic lactic acidosis and anti-oxidative stress and anti-inflammation [7–9]. More recently, discoveries in burn rats demonstrated that Pyr-ORS was also superior to Cit-ORS in the activation of hypoxia-inducible factor-1 (HIF-1α)–erythropoietin (EPO) signaling pathway to protect barrier function in the burn-injured intestine [10]. It was recently also evidenced that enteral pyruvate was advantageous over intraluminal citrate to stimulate enteric glial cells in preservation of intestinal barrier integrity and function in an intestinal ischemia–reperfusion model (submitted for publication).

Further, previous studies have shown that the vascular endothelial growth factor (VEGF) and the platelet activating factor (PAF) are two important indices, which modulate vascular permeability [11–14]. It is also known that burn triggers significantly high vasopermeability and tissue edema by systemic inflammatory reactions, leading to blood volume loss, hemodynamic deterioration and poor prognosis [15]. However, a little is effective to combat vascular hyperpermeability and tissue edema in burn care [16]. In this respect, pyruvate has shown to protect endothelial cells against metabolic disturbance and oxidative stress [17,18]. Therefore, the present study, as a continuation of previous investigations, compared effects of Pyr-ORS with Cit-ORS on hemodynamics, vasopermeability and vascular endothelial function and tissue edema in dogs subjected to severe burn shock. A hypothesis was tested that Pyr-ORS would be also an ideal option, relative to Cit-ORS, in the preservation of hemodynamics, vasopermeability and organ function and in the improvement of metabolic disturbances in the dogs with burn.

2. Materials and methods

2.1. Ethics approval

The Committee of Scientific Research of the First Hospital Affiliated to the General Hospital of PLA, China, approved all the research protocols. The study was conducted in compliance with the Guide for Care and Use of Laboratory Animals of the National Research Council, China.

2.2. Animals

Forty pure bred Beagle dogs, aged 16–20 months, weighing 10.2 ± 0.5 kg, with a body length of 73.8 ± 4.2 cm (purchased from Marshall Bio Resources Co., Ltd., Beijing, China (License of qualification SCX 2014-0005)) were used. They were acclimatized in the animal quarter of our laboratory for two weeks. The animals were fasted for 16 h and water was withheld for 4 h before surgery.

2.3. Surgical procedures

Following anesthesia with an intramuscular injection of ketamine (8 mg/kg, purchased from Gu-Tian Pharmacy, Fujian Province, China), the right carotid artery and jugular vein were exposed using aseptic techniques. A pressure and temperature fibrotic sensor of the PICCO-PLUS monitor (Pulsion Co., Germany) was introduced into the carotid artery down to the aorta to measure hemodynamic variables. A sensor to determine temperature was inserted into the jugular vein down to the superior vena cava. Both sensors were led out through a subcutaneous tunnel and fixed to the skin exit. A midline abdominal incision was made and a gastric catheter was introduced into gastric fundus through a stoma. The gastric catheter was fixed with double purse-string suture. The abdominal area was closed. The outside end of catheter was fixed on the abdominal wall and clamped for infusion of ORS. After the surgical procedure, the dogs in a conscious state were returned to their cages and they were given with 5% glucose solution (20 ml/kg) intravenously to supplement physiological needs.