JOURNAL OF SURGICAL RESEARCH 191 (2014) 344–349

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Ginsenoside Rb1 improves energy metabolism in the skeletal muscle of an animal model of postoperative fatigue syndrome

Shan-Jun Tan, MD,[a] *Ning Li, MD,*[a,*] *Feng Zhou, MD,*[b] *Qian-Tong Dong, MD,*[b] *Xiao-Dong Zhang, MD,*[b] *Bi-Cheng Chen, MD,*[c] *and Zhen Yu, MD*[d,**]

[a] *Research Institute of General Surgery, Jinling Hospital, Medical School of Nanjing University, Nanjing, Jiangsu Province, China*
[b] *Department of Gastrointestinal Surgery, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China*
[c] *Wenzhou Key Laboratory of Surgery, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China*
[d] *Department of General Surgery, Shanghai Tenth People's Hospital Affiliated to Tongji University, Shanghai, China*

ARTICLE INFO

Article history:
Received 28 January 2014
Received in revised form
11 April 2014
Accepted 24 April 2014
Available online 2 May 2014

Keywords:
Ginsenoside Rb1
Postoperative fatigue syndrome
Energy metabolism
Animal experiment

ABSTRACT

Background: Postoperative fatigue syndrome (POFS) is a common clinical complication followed by almost every major abdominal surgery. Ginsenoside Rb1 (GRb1), a principle ginsenoside in *ginseng*, could exert a potent anti-fatigue effect on POFS. However, the mechanism is still unknown. Previous studies revealed that alterations in the energy metabolism in the skeletal muscle may play a vital role in the development and progression of fatigue. In the present study, we investigate the effect of GRb1 on energy metabolism in the skeletal muscle of a rat model of POFS induced by major small intestinal resection.

Methods: GRb1 (10 mg/kg) was intraperitoneally administrated once daily for 1, 3, 7, and 10 d from the operation day, respectively. The locomotor activity was recorded every day, and total food intake was calculated starting from 24 h after surgery. After GRb1 treatment was completed, blood and skeletal muscle were sampled. The level of blood glucose was determined by an automatic biochemical analyzer. The content of adenosine triphosphate (ATP) in skeletal muscle was determined by high-performance liquid chromatography. The activity of energy metabolic enzymes Na^+-K^+-ATPase, pyruvate kinase, and succinate dehydrogenase (SDH) was assessed by commercially available kits.

Results: The results revealed that GRb1 could increase locomotor activity of POFS rats and significantly increase their total food intake postoperatively ($P < 0.05$). Furthermore, GRb1 also significantly increased ATP content in the skeletal muscle of POFS rats ($P < 0.05$). Meanwhile, the activity of Na^+-K^+-ATPase and SDH in the skeletal muscle of POFS rats was enhanced by GRb1 ($P < 0.05$). However, no significant differences in blood glucose and pyruvate kinase were found between the POFS and GRb1 treatment rats ($P > 0.05$).

* *Corresponding author*. Research Institute of General Surgery, Jinling Hospital, Medical School of Nanjing University, 305 East Zhongshan Road, Nanjing 210002, Jiangsu Province, China. Tel.: +86 25 80860037; fax: +86 25 80860220.
** *Corresponding author*. Department of General Surgery, Shanghai Tenth People's Hospital Affiliated to Tongji University, 301 Middle Yanchang Road, Shanghai 200072, China. Tel.: +86 21 66307132; fax: +86 21 66301035.
E-mail addresses: liningnju@163.com (N. Li), yuzhen0577@gmail.com (Z. Yu).
0022-4804/$ – see front matter
http://dx.doi.org/10.1016/j.jss.2014.04.042

Conclusions: These results suggest that GRb1 may improve skeletal muscle energy metabolism in POFS, and the underlying mechanism may be associated with an increase in the content of ATP and an enhancement in the activity of energy metabolic enzymes such as Na^+-K^+-ATPase ATPase and SDH in the skeletal muscle.

1. Introduction

Postoperative fatigue syndrome (POFS) is a common clinical complication followed by almost every major abdominal surgery [1]. Patients who suffer from this syndrome have a feeling of lethargy, malaise, concentration difficulties, loss of energy, and debilitating fatigue. POFS seriously affects postoperative rehabilitation and increases health-service costs [2–4]. Interest in the application of various methods for attenuation of POFS has recently increased in modern surgery [5–7].

Much of the published research reveals that the pathophysiology of POFS involves many factors including biological, psychological, and social factors [2,8–11]. Among these factors, musculoskeletal changes after surgery such as muscle weakness and muscle fatigue are responsible for the development and progression of POFS [10]. It is well accepted that the shortage of energy supply can lead to a reduction in muscle performance [12,13]. Under the stress of major abdominal operation, energy metabolism is increased and followed by high-energy consumption, which can significantly influence the metabolic status of skeletal muscle. In our previous study, in the rat model of POFS, we found that the maximum grip strength was reduced and it maybe associated with the decrease in the stores of muscle and hepatic glycogen [5]. These findings suggest that poor energy supply provided by energy metabolism in the skeletal muscle may directly affect the function of skeletal muscle and then delay rehabilitation after surgery.

Panax ginseng has been frequently used as a tonic to treat many disorders in Chinese traditional medicine [14,15]. It is a well-known herbal since the earliest Chinese pharmaceutical monograph "*Shen Nong Ben Cao Jing*" [16]. Ginsenosides are the major biological active ingredients of *ginseng*. They can enhance energy metabolism in various diseases [17–19]. Ginsenoside Rb1 (GRb1), a principle ginsenoside in *ginseng*, belongs to the protopanaxadiol group of steroidal saponins. In our previous study, in the rat model of POFS, we also found that GRb1 could increase the stores of muscle and hepatic glycogen and further enhance the maximum grip strength [5]. These findings suggest that the potent anti-fatigue effect of GRb1 on POFS might be achieved through improvement of energy metabolism in the skeletal muscle. However, the detail mechanism is still unknown.

Therefore, in the present study, we used typical parameters of energy metabolism to further study the improvement effect of GRb1 on energy metabolism in the skeletal muscle of a rat model of POFS induced by major small intestinal resection.

2. Materials and methods

2.1. Animals

The protocol for the animal experiment was approved by the Institutional Animal Committee of Wenzhou Medical University. Adult specific pathogen-free male Sprague–Dawley rats (weighing 220 ± 10 g) were obtained from Shanghai SLAC Laboratory Animal Co., Ltd. in China. All rats received human care throughout the experiment in accordance with "Guide for the Care and Use of Laboratory Animals." The rats were maintained under specific pathogen-free conditions, controlled temperatures (20°C–22°C), humidity (45%–55%), and light (12 h light–dark cycle) conditions with a standard rat chow and water made available *ad libitum*, except for 1 d of fasting before and after the operation.

According to the results of our previous studies [5,20], the sample size was determined and calculated using Power And Precision V4 software (Biostat Inc., Englewood): $\alpha = 0.05$, two-tailed confidence level = 95%, power = 80%, and large effect size used based on Cohen's conventions [21]. Eight animals were used in each group.

2.2. Drugs

GRb1 (purity >98%) was purchased from Shanghai Tauto Biotech Co., Ltd., Shanghai, China. The standard substance of adenosine triphosphate (ATP; import subpack) was purchased from Shanghai Boyun Biotech Co., Ltd., Shanghai, China. Other chemicals and reagents were procured from local suppliers and were of analytical grade.

2.3. Animal grouping and administration

After an adaptation period for 1 wk, 96 rats were randomly divided into three groups: a control group (CG), a POFS model group (MG), and a GRb1-treated POFS model group (GG), with 32 in each. The rat model of POFS was induced by major small intestinal resection as described in the previous study [20]. Briefly, rats in the MG and the GG groups had 70% of the length of small intestine removed, which was defined by the length of the small intestinal mesentery starting from 10 cm below the ligament of treitz. The CG group went through the same procedure but without any small intestinal resection. The rats were then maintained separately in cages after surgery. Within the first 24 h postoperatively, animals had only access to water, after which standard chow was reintroduced. The locomotor activity was objectively assessed every day by recording total journey over the course of 10 min in the open field test as described in our previous study [20]. In addition, total food intake was also calculated starting from 24 h after surgery.

Given that the intestinal surgery may affect the intestinal absorption of GRb1, the route of intraperitoneal administration of GRb1 was applied in the present study. Furthermore, in the preliminary experiment, through this administration route, we investigated the effect of GRb1 on POFS at doses of 5, 10, and 15 mg/kg, separately. We found that different doses of GRb1 all improved energy metabolism, and there was a dose-response