Nutrition 31 (2015) 733–739

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Basic nutritional investigation

Duodenal-jejunal exclusion improves insulin resistance in type 2 diabetic rats by upregulating the hepatic insulin signaling pathway

Ze-Qiang Ren M.D., Ph.D. [a], Peng-Bo Zhang M.D., Ph.D. [a,*], Xiu-Zhong Zhang M.D. [a], Shou-Kun Chen M.D. [a], Hong Zhang M.D. [b], Dun-Tao Lv M.D. [a], Bu-Qiang Zhuang Ph.D. [a], Yu-Qing Wen Ph.D. [c], Hui-Hui Hu Ph.D. [c], Wei-Chao Ding Ph.D. [a], Chong Zhang M.D. [a]

[a] Department of General Surgery, Affiliated Hospital of Xuzhou Medical College, JiangSu, China
[b] Operating Room, Affiliated Hospital of Xuzhou Medical College, JiangSu, China
[c] College of Nursing, Xuzhou Medical College, JiangSu, China

ARTICLE INFO

Article history:
Received 29 March 2014
Accepted 22 October 2014

Keywords:
Duodenal-jejunal exclusion operation
Type 2 diabetes mellitus
Insulin receptor substrate-2
Glucose transporter-2
Hepatic insulin signaling

ABSTRACT

Objectives: Previous studies have shown duodenal-jejunal exclusion (DJE) results in the rapid resolution of type 2 diabetes; however, the underlying mechanism is unknown. This study aimed to measure the hepatic expression of insulin receptor substrate-2 (IRS-2) and glucose transporter-2 (GLUT-2) in type 2 diabetic rats post-DJE, and to investigate their roles in improved hepatic insulin resistance and glucose intolerance.

Methods: Type 2 diabetic Sprague-Dawley (SD) rats were randomly divided into DJE operation (DO) and control (DC) groups. Normal SD rats were also divided into DJE operation and control groups. Fasting plasma glucose and insulin concentrations were measured, and the quantitative insulin sensitivity check index (QUICKI) and Homeostasis Model Assessment Insulin Resistance (HOMA-IR) were calculated. Eight weeks postoperation, the hepatic IRS-2 and GLUT-2 protein and mRNA levels were measured using western blotting and reverse transcription polymerase chain reaction, respectively.

Results: The fasting blood glucose in the DO group decreased from a preoperative level of 20.21 ± 2.14 mmol/L to 8.50 ± 2.19 mmol/L ($P < 0.05$) 8 wk post-DJE. A change in the QUICKI revealed a dramatic increase, and HOMA-IR showed a significant decrease in the DO group ($P < 0.05$). Additionally, the IRS-2 and GLUT-2 protein and mRNA levels at 8 wk postoperation were significantly increased in the DO group compared with the DC group.

Conclusions: DJE led to upregulated hepatic IRS-2 and GLUT-2 expression in the hepatic insulin signaling pathway and improved insulin sensitivity in type 2 diabetic rats.

© 2015 Elsevier Inc. All rights reserved.

Introduction

The worldwide incidence of obesity is rising at an alarming rate, and 80% of severely obese patients suffer from type 2 diabetes mellitus (T2 DM) [1]. The incidence of this complex glucose metabolism disorder is increasing at an epidemic rate, and it is one of the most serious threats to human health [2]. Complications in the cardiovascular system, brain, kidneys, and other vital organs due to diabetes directly threaten patient health and survival [3]. Insulin resistance is a fundamental pathogenic factor in various metabolic disorders, including obesity and T2 DM [4]. Lifestyle modifications and pharmaceutical treatments aimed at improving insulin sensitivity in T2 DM patients are not always successful.

Bariatric surgery, which is widely used to treat obesity, has recently been recognized as a new, effective, and long-term T2 DM treatment strategy [5–7]. The first one, to our knowledge, to describe glucose control after gastric surgery was Friedman in

This work was supported by the Science and Technology Planning Project of Xuzhou City, Jiangsu province (no. XM12 B028).

Ze-qiang Ren and Xiu-zhong Zhang contributed equally to this work.

* Corresponding author. Tel.: +86 15895202125; fax: +86 51685601527.
E-mail address: zpb_ok@126.com (P.-B. Zhang).

http://dx.doi.org/10.1016/j.nut.2014.10.012
0899-9007/© 2015 Elsevier Inc. All rights reserved.

Table 1
Comparisons of preoperative weights, food rations, and fasting plasma glucose and quantitative insulin sensitivity check index and Homeostasis Model Assessment Insulin Resistance values ($\bar{x}\pm s$)

Index	DO group	DC group	NC group	NO group
Weight (g)	406.3 ± 44.7*	402.1 ± 37.8*	334.7 ± 21.3	321.6 ± 17.2
Food ration (g/d)	212	205	205	201
FPG (mmol/L)	20.21 ± 2.14*	21.06 ± 2.09*	6.61 ± 0.64	6.18 ± 0.65
QUICKI	0.43 ± 0.02*	0.43 ± 0.01*	0.60 ± 0.02	0.59 ± 0.02
HOMA-IR	9.72 ± 1.39*	9.83 ± 1.65*	2.13 ± 0.83	2.19 ± 0.81

DC group, T2 DM-control group; DO group, T2 DM-DJE operation group; HOMA-IR, Homeostasis Model Assessment Insulin Resistance (HOMA-IR); NC group, normal-control group; NO group, normal-DJE operation group; QUICKI, quantitative insulin sensitivity check index (QUICKI)
Comparison of the DO and DC groups and the NC and NO groups; *$P < 0.05$

1955 [8]. Pories et al. reported an 83% remission rate in 146 T2 DM patients after 14 y of follow-up [9]. Subsequently, Buchwald et al. confirmed a remission rate exceeding 80% [10]. Duodenal-jejunal exclusion (DJE) surgery is a surgical procedure commonly used in research, to study the effect of duodenal exclusion from nutrient transit in isolation of gastric manipulation [11–15]. Common explanations for this response involve changes in the release of gastrointestinal hormones, and particularly glucagon-like peptide-1, which occurs because of anatomic alterations in the gastrointestinal tract [16]. However, the underlying mechanisms of the antidiabetic effects of DJE remain poorly understood.

T2 DM pathogenesis is characterized by peripheral insulin resistance and impaired insulin secretion by pancreatic β-cells. Insulin resistance in the liver (an insulin target tissue) contributes significantly to the development of T2 DM [17]. Previous studies have demonstrated that hepatic insulin resistance may be caused by changes in the hepatic insulin signaling pathway [18,19].

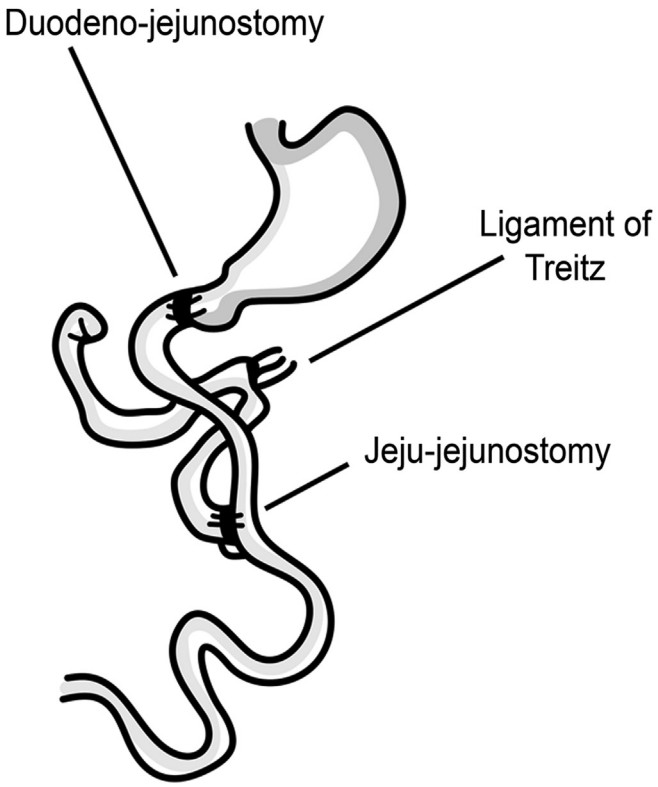

Fig. 1. Duodenal-jejunal exclusion (DJE). The DJE bypassed the entire duodenum and 8 cm of the proximal jejunum.

Table 2
Comparisons of weights and food rations 8 wk postoperation ($\bar{x}\pm s$)

Index	DO group	DC group	NC group	NO group
Weight (g)	399.5 ± 36.8*	408.1 ± 47.5*	351.2 ± 28.7	342.6 ± 20.2
Food ration (g/d)	202	208	209	201

DC group, T2 DM-control group; DO group, T2 DM-DJE operation group; NC group, normal-control group; NO group, normal-DJE operation group Comparison of the DO and DC groups and the NC and NO groups; *$P < 0.05$

Insulin sensitivity studies focus on insulin signaling, and the hepatic pathway plays an important role in insulin resistance (IR) and T2 DM [20]. Obstructions in insulin signaling at this site are the primary cause of IR [21]. Consistent with these findings, key proteins in the insulin signaling pathway, such as the insulin receptors (IRs) and insulin receptor substrates (IRSs), are down-regulated in diabetic rodent and human livers [22–24]. IRSs, the key mediators of insulin signaling, play a central role in maintaining glucose metabolism [25]. The metabolic actions of insulin depend on IRS protein tyrosine phosphorylation [26], which induces a signaling cascade by activating phosphatidylinositol 3-phosphate kinase (PI3 K) and the serine/threonine kinase Akt/PKB. These events translocate glucose transporter (GLUT)-containing vesicles from the cytoplasm to the plasma membrane. Four members of the IRS protein family have been identified: IRS-1, IRS-2, IRS-3, and IRS-4. IRS-2 is especially important for hepatic nutrient homeostasis because it mediates the anabolic effects of insulin through the PI3 K-Akt cascade [27,28] and suppresses gluconeogenesis and apoptosis [29,30], while maintaining hepatic glucokinase activity [31]. Mice lacking IRS-2 develop diabetes because of peripheral insulin resistance, failed hypothalamic appetite regulation, and β-cell insufficiency [32]. Furthermore, studies of IRS-2(−/−) mice have confirmed that insulin signaling defects in the liver, but not in the skeletal muscle or adipose tissue, play a major role in the development of diabetes, particularly when combined with pancreatic β-cell dysfunction [23,32]. IRS-2 specifically regulates the hepatic insulin response [33], and reduced IRS-2 expression has been correlated with type 2 diabetes, and especially insulin resistance [34–36].

This study measured hepatic IRS-2 and GLUT-2 expression in type 2 diabetic rats post-DJE and explored the influences underlying improved insulin resistance. This study aimed to clarify the mechanisms of improved glycemic control after DJE. A greater understanding of these mechanisms is essential for the development of non-invasive interventions for severe obesity, which often contributes to diabetes. To accomplish our aim, we performed DJE on Sprague-Dawley (SD) rats with diet-induced obesity and analyzed tissue-specific changes in IRS-2 and

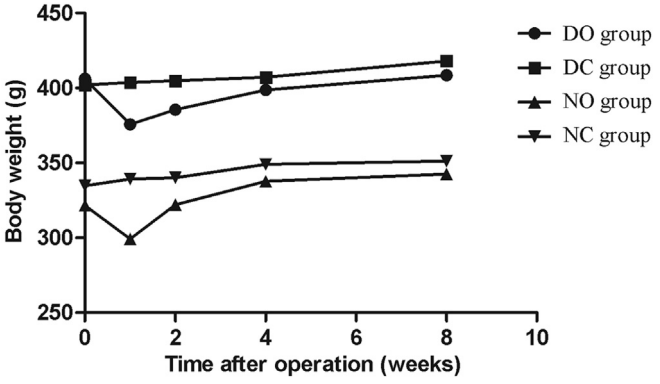

Fig. 2. Body weight of rats in the four groups before and after surgery.

Download English Version:

https://daneshyari.com/en/article/6089079

Download Persian Version:

https://daneshyari.com/article/6089079

Daneshyari.com