Whey protein preloading can alleviate stress adaptation disorder and improve hyperglycemia in women with gestational diabetes mellitus

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Research Article

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Abstract

Aim

To investigate the change of stress hormones, oxidative stress and insulin resistance (IR) in women with gestational diabetes mellitus (GDM) after supplement whey protein, in an attempt to gain insights into the prevention and treatment of GDM.

Methods

60 GDM women were recruited in this study, and 30 women receive a preload drink containing 25 g whey protein as group GDM-W, and the other 30 women receive control flavoring drink as group GDM, and the trial last for 14 days. Plasma epinephrine (E), noradrenaline (NE), and cortisol were detected, we also investigate levels of malondialdehyde (MDA), superoxide dismutase (SOD) and glutathione (GSH). Homeostasismodel assessment of insulin resistance (HOMA-IR) was used to assesse IR.

Results

In GDM-W group, postprandial blood glucose was decreased significantly on 3d, 5d, 7d and 14d ($p < 0.05$), plasma 2h insulin was increased by 7.2%, 8.6% and 20.5% on days 5, 7 and 14 ($p < 0.05$). HOMA-IR was decreased significantly on days 14 ($P < 0.01$). MDA was increased by 20.7% on days 14 ($P < 0.01$), and anti-oxidative enzymes SOD was increased by 13.4% on days 14 ($P < 0.01$) and GSH was increased by 16.7% and 29.1% on days 7 and 14 (both $P < 0.05$). Stress hormones E and cortisol were decreased by 10.8% and 19.8% respectively on days 14 ($p < 0.05$).

Conclusion

Whey protein supplementation may improve hyperglycemia by alleviate stress disorder and oxidative stress injury in GDM women.

This trial was registered at chictr.org.cn/ as **ChiCTR1800020413.**

Introduction

Gestational diabetes mellitus (GDM) is characterized by abnormal glucose tolerance during pregnancy, and it is a common complication of pregnancy, which canincreases the risk of occurrence of type 2 diabetes mellitus (DM2) in both mothers and their offspring, also cause adverse effects on the outcome of mothers and fetus[1, 2]. In recent years, the incidence of global GDM is on the rise. The incidence of GDM in pregnant women in China is as high as 22.94%, while the pathogenesis of GDM is not clear[3]. How to prevent and treat GDM and reduce the risks it brings?

Several studies show that Whey protein preloading can increase insulin sensitivity and have a positive response to the control of hyperglycemia[4, 5]. We previously reported that stress adaptation disorder exists

in GDM women and may beassociated with the pathogenesis of GDM[6, 7]. The purpose of our study is to explore the effect of whey protein supplementation on stress hormones in GDM women, and to observe the effect of whey protein preloading on postprandial blood glucose control in GDM patients, in an attempt to gain insights into the prevention and treatment of GDM.

Materials And Methods

Subjects

60 pregnant women patients with GDM at 24–28 weeks were included in this study.

According to the American Diabetes Association criteria, a 75-g oral glucose tolerance test (OGTT) at 24–28 weeks of pregnancy was used, GDM was diagnosed with the cutoff value being > 5.1 mmol/L at fasting, > 10.0 mmol/L at 1 h, and > 8.5 mmol/L at 2 h[8]. They were diveded into 2 groups consisting of 30 pregnant women each: GDM-W group receive 250ml preload drink containing 20 g whey protein isolate (73Kcal; Agropur inc, Le Sueur MN, America) 30 min before lunch and GDM group receive 250ml preload drink containing 20 g control flavoring (6.5 kcal; Cottee's, Southbank, Australia) 30 min before lunch. Blood samples were collected on days 3, 5, 7 and 14. The experiment lasts for14 days.

Inclusion criteria were 1) single pregnancies; and 2) fasting plasma glucose (FPG) < 6.1mmol/L before pregnancy. Exclusion criteria were 1) pregnant women with previously known medical complications during pregnancy such as DM 1 or 2, polycystic ovary syndrome, hyperthyreosis, hypothyroidism; and 2) women who were treated with hormones or drugs that may affect blood glucose.

The study protocol was approved by Yantai yuhuangding hospital committee, and informed consents of all participants were obtained.

Characteristics of GDM women

Clinical features including maternal age, pre-gestational body mass index (BMI) and gestational weeks. Pre- BMI = pre-gestational weight (kg)/ height (m^2).

Blood glucose, stress hormones, oxidative stress injury markers and HOMA-IR in GDM women

Roche automatic biochemical analyzer (Roche Diagnostics, Mannheim, Germany) was used to detect blood glucose, and electrochemical luminescence immunoassay (Roche Diagnostics, Mannheim, Germany) was used to test fasting and plasma 2h insulin levels. Insulin resistance (IR) was assessed by homeostatic model assessment of insulin resistance (HOMA-IR) formula[9].

Plasma epinephrine (E), noradrenaline (NE) and cortisol were used as markers of stress hormones. E and NE levels were determined by radioimmunoassay (RIA) (Roche Diagnostics, Mannheim, Germany).

Electrochemical luminescence immunoassay (Roche Diagnostics, Mannheim, Germany) was used to detecte cortisol levels.

Malondialdehyde (MDA), superoxide dismutase (SOD) and glutathione (GSH) were used as markers of oxidative stress. MDA, SOD and GSH were detected by their correspongding assay kits (Jiancheng Bioengineering Institute, Nanjing, China). Results are expressed as umol/L, U/ml and mg/L.

Statistical analysis

Continuous variables of normal distribution data are presented as mean ± standard error. Independent-Samples t test was used to identify between-group differences. Data not normally distributed were log-transformed before analysis. $P < 0.05$ was considered statistically significant. Statistical analyses were performed with SPSS 19.0 (SPSS, Inc., Chicago, IL, USA).

Results

Maternal characteristics

The maternal characteristics including the maternal age, pre-gestational BMI and gestational weeks were similar in GDM and GDM-W groups at entry to the study, there was no significant difference between two groups ($p > 0.05$)(Table 1).

Table 1
Maternal characteristics in GDM and GDM-Whey preload women ($\bar{\chi} \pm s$)

	GDM	GDM-W
Maternal age (years)	26.5 ± 2.3	25.9 ± 3.1
Pre-gestational BMI (Kg/m^2)	23.5 ± 2.7	24.0 ± 3.4
Gestational weeks	26.4 ± 1.8	25.2 ± 2.4

Effects of whey preload on blood glucose related indexes in GDM women

There was no significant difference in fasting blood glucose bewteen two groups during the entire experimental session ($p > 0.05$) (Fig. 2A).

In GDM-W group, postprandial 2h blood glucose was decreased significantly on 3d, 5d, 7d and 14d compared with GDM group ($p < 0.05$) (Fig. 2B).

After whey-perload, plasma 2h insulin was increased by 7.2%, 8.6% and 20.5% on days 5, 7 and 14 in GDM-W group ($p < 0.05$) (Fig. 2C).

Whey-perload decreased HOMA-IR significantly on days 14 in the experimental session ($P < 0.01$) (Fig. 2D).

Effects of whey preload on oxidative stress injury in GDM women

The concentration of MDA in GDM-W group was increased by 20.7% on days 14, and showing significant difference between two groups ($P < 0.01$) (Fig. 2E).

Anti-oxidative enzymes SOD in GDM-W group was increased by 13.4% on days 14 ($P < 0.01$) (Fig. 2F), and same trend was observed in GSH, compared with GDM group, the content of GSH in GDM-W group was increased by 16.7% and 29.1% on days 7 and 14 (both $P < 0.05$) (Fig. 2G).

Effects of whey preload on plasma stress hormones in GDM women

Compared with GDM group, stress hormones E and cortisol were decreased by 10.8% and 19.8% respectively on days 14($p < 0.05$) (Fig. 2H, 2J). However no significant difference between the two groups in NE ($p > 0.05$) (Fig. 2I).

Discussion

Our study showed that whey protein perload can reduce hyperglycemia during 14 days exposure in GDM women. Compared to GDM group, there was no significant difference in fasting blood glucose bewteen two groups, but postprandial blood glucose was decreased significantly during the entire experimental session. The results are consistent with previous studies that used whey protein preload[5, 10–12], but the mechanism is different. Some studies suggest that the hyperglycemia-reducing effect of whey protein preload may relate to insulin stimulation and delaying of glucose absorption in intestinal[13–15], and we have got similar result, plasma 2h insulin was increased on days 5, 7 and 14 in GDM-W group, HOMA-IR decreased significantly on days 14 in the experimental session. Some studies found that slower gastric emptying may be responsible for hyperglycemia-reducing[12, 16, 17].

E, NE and cortisol are markers of stress hormones, especially cortisol. Cortisol could increase hepatic glucose production, decrease insulin secretion and aggravate β cell function, all of which could lead to hyperglycemi[18].

Pregnancy is a process of slight and chronic stress. Our previous sutdy showed that GDM women exists stress adaptive disorder, which is related to hyperglycemia and IR[6]. This study found that stress hormones E and cortisol were decreased by 10.8% and 19.8% respectively on days 14 after whey protein perload. Several studies have also found that cortisol was reduced after whey protein supplementation, which is similar to our resul[19, 20]. It indicates that whey protein supplementation can reduce the stress adaptation disorder of GDM patients.

Previous studies on the relation of oxidative stress damage and whey protein supplementation have different conclusions. Some studies believe that supplement whey protein can increase the levels of oxidative stress products[21, 22], while others showed whey protein can reduce oxidative damage [23–25]. During our experiment session, oxidative stress products MDA was increased by 20.7% on days 14, anti-oxidative enzymes SOD was increased by 13.4% on days 14, and GSH was increased by 16.7% and 29.1% on days 7 and 14 after whey preload. So our results suggest that oxidative stress injury was decreased after supplement of whey protein.

Our study indicates that, whey protein preloading improved hyperglycemia and blood glucose related indexes, which may be related to the increase of insulin secretion, the improvement of IR, the delay of stress adaptation disorder, and the reduce of oxidative stress injury in GDM women.

Conclusion

Studies assessing effects of whey protein supplementation on diabetes are relatively few in number, and none of these studies focus on GDM. Only 60 GDM patients were included in our study, and one GDM patients quit because of protein falvour during the experiment. Our observations support the conlusion of whey protein preloads could improve stress adaptation disorder, oxidative stress injury and HOMA-IR, which should be explored with larger clinical trials in patients with GDM.

Abbreviations

GDM, Gestational diabetes mellitus;

GDM-W, Gestational diabetes mellitus preload whey protein group;

OGTT, Oral glucose tolerance test;

FPG, Fasting plasma glucose;

BMI, Body mass index;

IR, Insulin resistance;

HOMA-IR, Homeostatic model assessment of insulin resistance;

E, Epinephrine;

NE, Noradrenaline;

RIA, Radioimmunoassay;

MDA, Malondialdehyde;

SOD, Superoxide dismutase;

GSH, Glutathione.

Declarations

Conflicts of interest

None of the authors has a conflict of interest to declare.

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Authors' contributions

The authors'responsibilities were as follows：YF, QF, YP L, XNS, YHZ, JWH, YF and JWH: designed the study and wrote the manuscript; QF: performed the data analysis; XNS, YPL, YHZ, provided study oversight; all authors: approved the final manuscript. The authors report no conflicts of interest.

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Ethics approval

Approval was obtained from Ethics committee of Yantai yuhuangding Hospital [approval NO. 2018-104].

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Figures

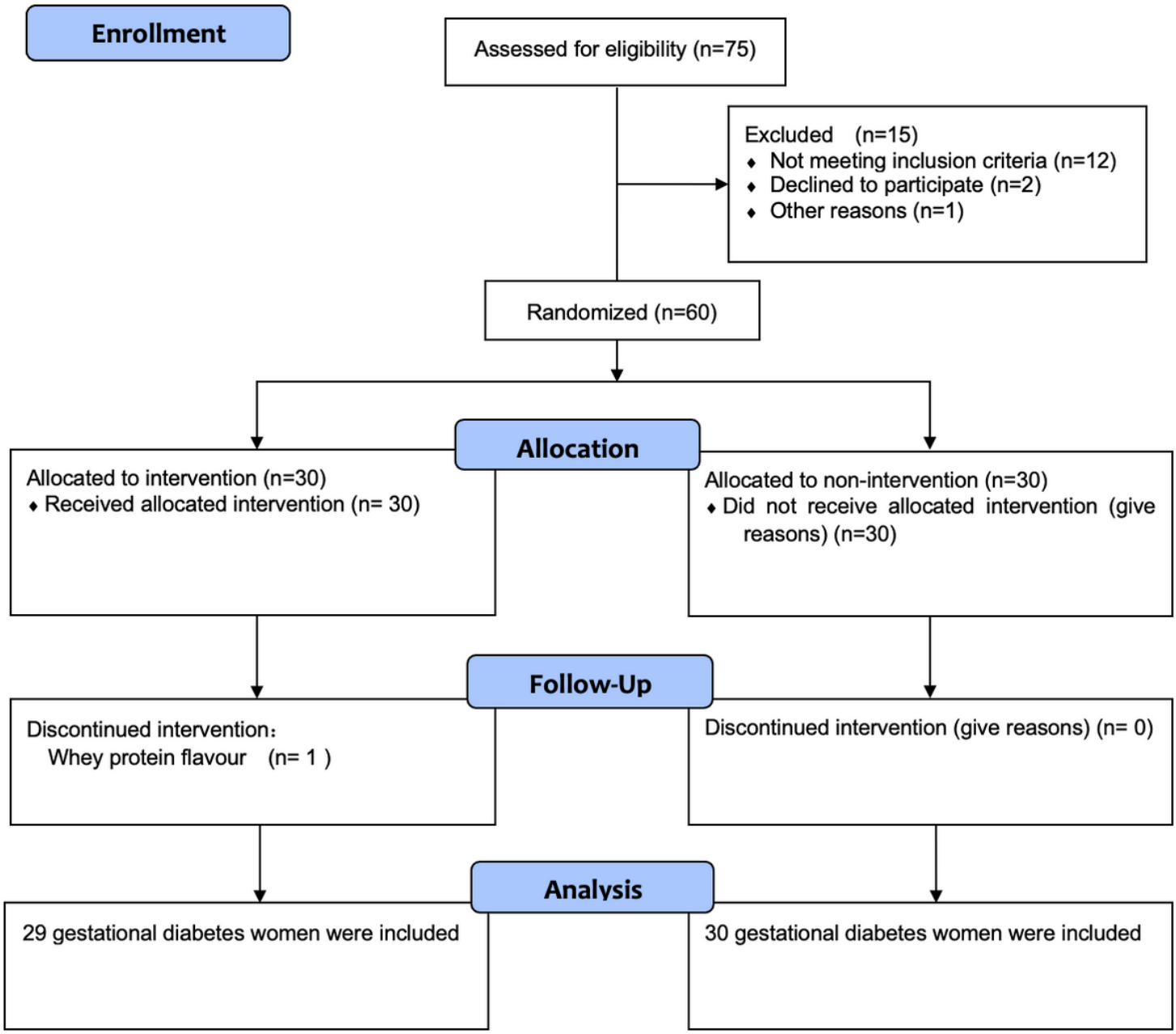

Figure 1

Flowchart of enrollment and allocation of Whey protein preloading on GDM women

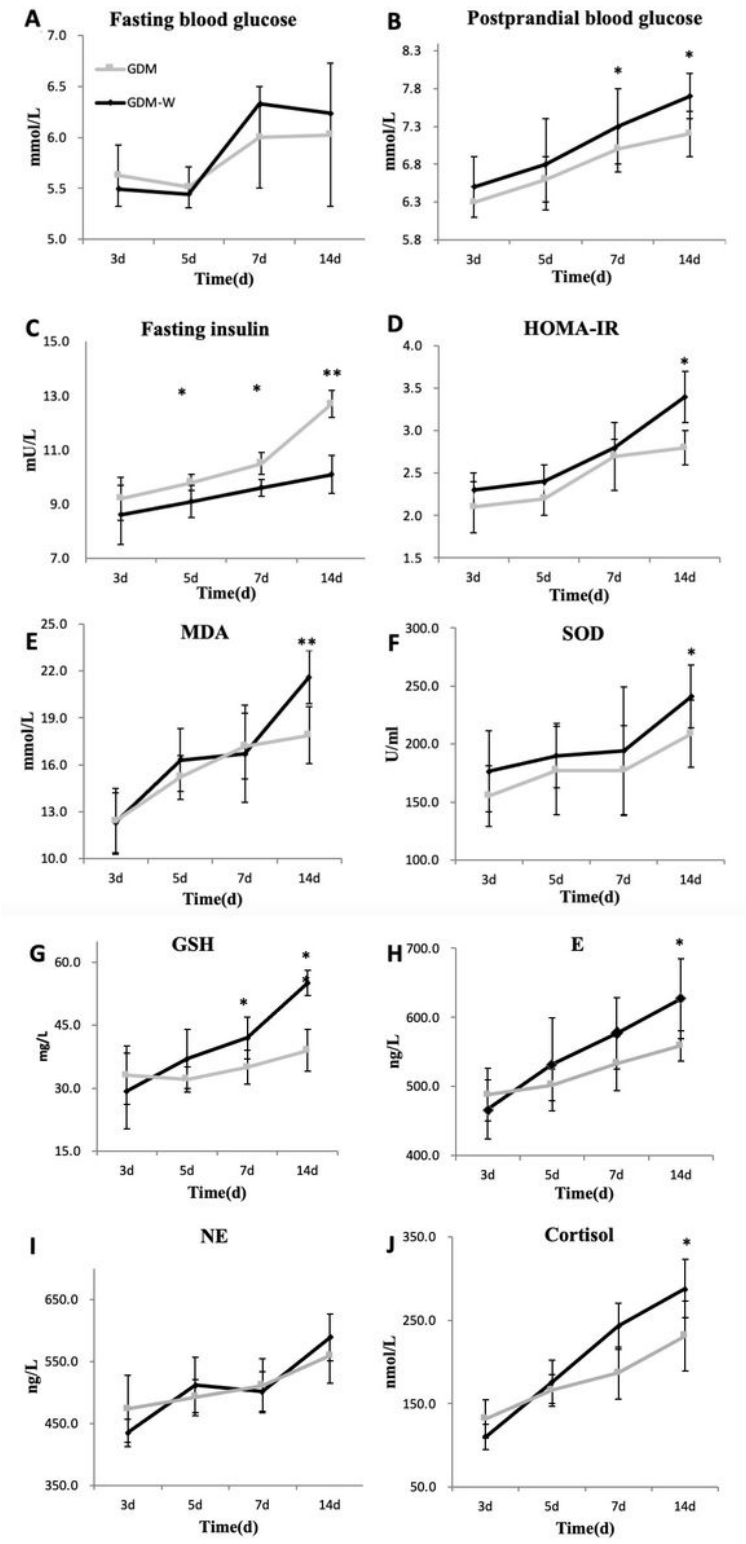

Figure 2

Fasting blood glucose (A), 2h blood glucose (B), 2h insulin (C), HOMA-IR (D), MDA (E), SOD (F), GSH (G), E (H), NE (I) and Cortisol (J) in response to whey preload 30 min before meal on 3d, 5d, 7d and 14d in patients with GDM. T-test was used to determine statistical difference. * indicate $P < 0.05$ vs. NC group and $P < 0.01$ expressed by **.