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

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ABSTRACT

Aims: 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.

Materials and methods: 60 GDM women were recruited in this study, and 30 women received a preload drink containing 20 g whey protein as group GDM-W, and the other 30 women received control flavoring drink as group GDM, and the trial lasted for 14 days. Plasma epinephrine (E), noradrenaline (NE), and cortisol were detected; we also determined levels of malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione (GSH). Homeostasis model assessment of insulin resistance (HOMA-IR) was used to assess IR.

Results: In the GDM-W group, postprandial blood glucose was decreased significantly on 3, 5, 7, and 14 days (all p < .05), plasma 2 h insulin was increased by 7.2, 8.6, and 20.5% on days 5, 7, and 14 (p < .05). HOMA-IR was decreased significantly on day 14 (p < .05). MDA was decreased by 20.7% on day 14 (p < .05) and GSH was decreased by 16.7 and 29.1% on days 7 and 14 (both p < .05). Stress hormones E and cortisol were decreased by 10.8 and 19.8%, respectively, on day 14 (p < .05). There was no significant difference in NE between the two groups within 14 days.

Conclusions: Whey protein supplementation may improve hyperglycemia by alleviating 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 can increase the risk of occurrence of type 2 diabetes mellitus (DM2) in both mothers and their off-springs, also causing adverse effects on the outcome of mothers and fetus [1-3]. 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 [4]. 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 [5,6]. We previously reported that stress adaptation disorder exists in GDM women and may be associated with the pathogenesis of GDM [7,8]. 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.
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 include maternal age, pre-gestational body mass index (BMI), and gestational weeks. Pre-BMI = pre-gestational weight (kg)/height (m²).

**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 detect cortisol levels. Results are expressed as ng/l, ng/l, and nmol/l.

Malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione (GSH) were used as markers of oxidative stress. MDA, SOD, and GSH were detected by their corresponding assay kits (Jiancheng Bioengineering Institute, Nanjing, China). Results are expressed as µmol/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 < .05 was considered statistically significant. Statistical analyses were performed with SPSS 19.0 (SPSS Inc., Chicago, IL).

**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 ($p > .05$) (Table 1).

Table 1. Maternal characteristics in GDM and GDM-W preload women ($\bar{x} \pm s$).

|                        | GDM   | GDM-W  |
|------------------------|-------|--------|
| Maternal age (years)   | 26.5 ± 2.3 | 25.9 ± 3.1 |
| Pre-gestational BMI (kg/m²) | 23.5 ± 2.7 | 24.0 ± 3.4 |
| Gestational weeks      | 26.4 ± 1.8 | 25.2 ± 2.4 |

Data are presented as mean ± SE ($n = 30$).

Figure 2. Fasting blood glucose (A), 2 h blood glucose (B), 2 h 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 3, 5, 7, and 14 days in patients with GDM. Data are presented as mean ± SE ($n = 30$).
Effects of whey preload on blood glucose-related indexes in GDM women

There was no significant difference in fasting blood glucose between two groups during the entire experimental session (p > .05) (Figure 2(A)).

In the GDM-W group, postprandial 2 h blood glucose was decreased significantly on 3, 5, 7, and 14 days compared with the GDM group (all p < .05) (Figure 2(B)).

After whey preload, plasma 2 h insulin was increased by 7.2%, 8.6%, and 20.5% on days 5, 7, and 14 in the GDM-W group (p < .05, .05, .01) (Figure 2(C)).

Whey preload decreased HOMA-IR significantly on day 14 in the experimental session (p < .05) (Figure 2(D)).

Effects of whey preload on oxidative stress injury in GDM women

The concentration of MDA in the GDM-W group was decreased by 20.7% on day 14, showing a significant difference between two groups (p < .01) (Figure 2(E)).

Anti-oxidative enzymes’ SOD in the GDM-W group was decreased by 13.4% on day 14 (p < .05) (Figure 2(F)), and the same trend was observed in the GSH, compared with GDM group, the content of GSH in the GDM-W group was decreased by 16.7% and 29.1% on days 7 and 14 (both p < .05) (Figure 2(G)).

Effects of whey preload on plasma stress hormones in GDM women

Compared with the GDM group, stress hormones E and cortisol were decreased by 10.8% and 19.8%, respectively, on day 14 (p < .05) (Figure 2(H,J)). No significant difference was observed between the two groups in NE (p > .05) (Figure 2(I)).

Discussion

Our study showed that whey protein preload can reduce hyperglycemia during 14 days supplementation in GDM women. Compared to the GDM group, there was no significant difference in fasting blood glucose between 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 [6,11–13], but the differences between the three mechanisms were 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 [14–16], and we have got a similar result, plasma 2h insulin was increased on days 5, 7, and 14 in the GDM-W group, HOMA-IR decreased significantly on day 14 in the experimental session. Some studies found that slower gastric emptying may be responsible for the reduction hyperglycemia [13,17,18].

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 hyperglycemia [19].

Pregnancy is a process of slight and chronic stress. Our previous study showed that GDM women exists stress adaptive disorder, which is related to hyperglycemia and IR [7]. This study found that stress hormones E and cortisol were decreased by 10.8% and 19.8%, respectively, on day 14 after whey protein preload. Several studies have also found that cortisol was reduced after whey protein supplementation, which is similar to our result [20,21]. 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 [22,23], while others showed that whey protein can reduce oxidative damage [24–26]. During our experiment session, oxidative stress products MDA was increased by 20.7% on day 14, anti-oxidative enzymes SOD was increased by 13.4% on day 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 patient quit because of protein flavor during the experiment. Our observations support the conclusion of whey protein preloads that could improve stress adaptation disorder, oxidative stress injury, and HOMA-IR, which should be explored with larger clinical trials in patients with GDM.

Ethics approval

Approval was obtained from Ethics committee of Yantai Yuhuangding Hospital (Approval no. 2018-104).

Disclosure statement

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

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