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Original article

Capsaicin-containing chili improved postprandial hyperglycemia, hyperinsulinemia, and fasting lipid disorders in women with gestational diabetes mellitus and lowered the incidence of large-for-gestational-age newborns

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SUMMARY

Background & aims: Gestational diabetes mellitus (GDM) may increase the future health risks of women and their offspring. The aim of this study was to determine the effect of capsaicin supplementation on blood glucose, lipid metabolism and pregnancy outcomes in women with GDM.
Methods: Forty-four pregnant women with GDM at 22–33 gestational weeks were randomly assigned to the capsaicin group (5 mg/d of capsaicin) or to the placebo group (0 mg/d of capsaicin) for 4 weeks in a randomized, double-blind, placebo-controlled trial. The concentrations of fasting plasma glucose and serum insulin, 2-h postprandial plasma glucose (2-h PG) and serum insulin (2-h INS), and fasting serum lipids, liver and kidney function parameters, and calcitonin gene-related peptide (CGRP) were measured at 0 and 4 weeks. The maternal and neonatal outcomes were also recorded.
Results: Forty-two women completed the trial. Compared to the placebo group, 2-h PG and 2-h INS concentrations and 2-h postprandial HOMA-IR (2-h HOMA-IR) levels, and the fasting serum total cholesterol and triglycerides concentrations significantly decreased in the capsaicin group after treatment ($P < 0.05$). Moreover, the fasting serum apolipoprotein B and CGRP concentrations significantly increased in the capsaicin group ($P < 0.05$). The changes in the 2-h PG and 2-h INS concentrations and in the 2-h HOMA-IR were negatively correlated with the change in the serum CGRP concentration ($P < 0.05$). Furthermore, the incidence of large-for-gestational-age (LGA) newborns was significantly lower in the capsaicin group than in the placebo group ($P = 0.022$).
Conclusions: Capsaicin-containing chili supplementation regularly improved postprandial hyperglycemia and hyperinsulinemia as well as fasting lipid metabolic disorders in women with GDM, and it decreased the incidence of LGA newborns.

1. Introduction

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance that begins or is first recognized in pregnancy. The expected GDM incidence has been 16%–18% of pregnancies worldwide [1]. GDM may increase future health risks for affected women and their offspring [2]. Excessive mother-to-fetus glucose transfer in pregnant women with GDM could cause adverse

Abbreviation: 2-h HOMA-IR, 2-hour postprandial HOMA-IR; 2-h INS, 2-hour postprandial serum insulin; 2-h PG, 2-hour postprandial plasma glucose; ADA, American Diabetes Association; CGRP, calcitonin gene-related peptide; GDM, gestational diabetes mellitus; HOMA-IR, homeostasis model assessment of insulin resistance; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LGA, large for gestational age; SGA, small for gestational age.

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neonatal outcomes [3,4]. For example, compared to unaffected newborns, the incidence of large-for-gestational-age (LGA) newborns was higher if their mothers had GDM. Newborns with LGA who reach adulthood may be susceptible to diabetes and other diseases. Thus, the regulation of blood glucose concentrations in women with GDM is particularly important.

Because the use of oral hypoglycemic agents may lead to several adverse effects [5–7], most women with GDM have received insulin treatment [7]. Importantly, the adjustment of suboptimal diet and lifestyle habits has been the primary therapy for GDM and an important adjunctive treatment in insulin-dependent GDM [8].

Supplementation with certain phytochemicals such as polyphenols or natural plant foods rich in these phytochemicals may be effective in improving human glucose and lipid disorders. Capsaicin, which is primarily contained in chili, exerts multiple pharmacologic and physiologic effects, such as analgesia, and anticancer, anti-inflammation, antioxidant and anti-obesity activities [9]. Moreover, capsaicin contained in chili may also reduce postprandial blood glucose and improve insulin resistance, although it did not prove to alter fasting plasma glucose in healthy humans in 1 clinical trial [10,11]. Capsaicin may exert the above effects through the release of neuropeptides, such as substance P, calcitonin gene-related peptide (CGRP), and other neurokinins from sensory nerve terminals [12].

To our knowledge, GDM mainly manifests as glucose metabolism disorders caused by insulin resistance. The hypothesis presented in this study is that an intervention of capsaicin contained in chili would improve the insulin resistance as well as glucose and lipid metabolism profiles in women with GDM, in addition to maternal and neonatal outcomes. Thus, in the current study, we conducted a randomized clinical trial of recruited women with GDM to assess the effects of regular chili consumption for four weeks on metabolic and pregnancy outcomes.

2. Materials and methods

2.1. Subjects

Between April 1 and June 30, 2012, eighty pregnant women with GDM were screened at the Southwest Hospital of the Third Military Medical University, Chongqing, China. Ultimately, 44 eligible women with GDM were recruited into the study. According to the diagnostic criteria recommended by the American Diabetes Association (ADA) in 2011, GDM was diagnosed in pregnant women with fasting blood glucose concentrations higher than 5.1 mmol/L, or 1-h postprandial blood glucose concentrations higher than 10.0 mmol/L, or 2-h postprandial blood glucose concentrations higher than 8.5 mmol/L. Other inclusion criteria were pregnancy with a single fetus between 22 and 33 weeks of gestation; a BMI before pregnancy of between 18 and 30; and an unsuccessful prior lifestyle intervention including diet (without capsaicin) and exercise that lasted for 2 weeks. Pregnant women were excluded if they had one of the following conditions: women with a known or self-reported history of diabetes or heart, renal, or hepatic disease; a fetal anomaly; gestational hypertension; preeclampsia; fetal growth restriction; ruptured membranes, or the consumption of prescription medications for the treatment of GDM.

2.2. Study design

This study was a randomized, double-blind, placebo-controlled clinical trial. Eligible women were randomly assigned to the capsaicin ($n = 22$) or to the placebo group ($n = 22$). The randomization sequence was developed by an individual who was otherwise not involved in the trial using a computer-generated list, and was sealed until the study completion. All participants, care providers, and those who were assessing outcomes were blinded to the randomization sequence. The total duration of the trial was 4 weeks. This study was approved by the ethics committee of the Third Military Medical University, and each participant provided written informed consent. All procedures were conducted in accordance with the institutional guidelines and in compliance with the Helsinki Declaration. This trial was registered at the Chinese clinical trial registry as ChiCTR-TRC-12002193.

Before enrolling in the trial, all women accepted submission to a general physical examination and all provided health- and diet-related information. A food-frequency questionnaire including 118 food types was completed for each woman before the trial. At baseline and at the end of the trial, all of the women were asked to complete a 3-day record of their food intake, which was analyzed using the nutrition system of Chinese traditional medicine combined with Western medicine (2011) software (Dong Chen, Qingdao, China) to estimate daily energy and nutrient intake. After the 4-week intervention, all of the women attended our facility where the remaining chili powder and the related health information were collected.

2.3. Interventions

Every woman received medical nutrition therapy including an individualized recommended intake of daily energy according to the ADA and was encouraged to increase her daily physical activities. Additionally, women were instructed to consume 0.625 g of chili powder twice daily (total: 1.25 g per day) at lunch and dinner, respectively, for 4 weeks. In the capsaicin and the placebo groups, the chili powders were made from crushed *yanjiao 425* (one type of pop pepper; capsaicin content 4 mg/g) and *xingjiang sweet* (*Capsicum annuum* L, without capsaicin), respectively. The total capsaicin intake doses of women in the capsaicin and the placebo groups were 5 and 0 mg capsaicin per day, respectively. Both chili powders were packaged in unsealed aluminum foil bags. The dose of capsaicin used in the current trial was determined based on recent human and animal studies [10,13–15]. In a human study, a daily intake of 33 mg of capsaicin for 4 weeks was shown to be safe and effective in improving the attenuation of postprandial hyperinsulinemia and the inflammatory response in healthy humans [10,15]. Moreover, a single intake of 0.4 mg of capsaicin slightly increased glucose absorption and glucagon release in healthy humans [14]. In Mexico, the daily intake of capsaicin was 90–250 mg in high-capsaicin consumers who ate approximately 9–25 jalapeño peppers per day, and less than 30 mg in low consumers who ate less than 3 jalapeño peppers per day [16]. In Americans who consumed spicy foods more than 3 times every week, the mean daily intake of capsaicin was 3.6 mg [17]. Most of the Chongqing, China population consumed more than 3 dry red pod peppers (i.e., 3 g) daily. However, no clinical study has been conducted in pregnant women to our best knowledge. In an animal study, the gestating rats that consumed 7.5 mg of capsaicin per day (i.e., 30 mg/kg) for 55 days did not demonstrate a delayed thermonociceptive response of their offspring [18]. With respect to a safety factor set at 100, a dose of 18 mg capsaicin may be safe for pregnant women. However, in our previous pilot trial, 5 of 8 pregnant women were not tolerant of 2.5 g of dry red pepper powder that contained 10 mg capsaicin given daily for 2 weeks due to serious abdominal pain and diarrhea. Thus, a capsaicin dose of 5 mg was chosen for the current study.

2.4. Anthropometric measurements

Body weight was measured using electronic scales, with subjects wearing light clothing. Height was measured using a

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