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Randomized control trials

Diabetes mellitus and abnormal glucose tolerance development after gestational diabetes: A three-year, prospective, randomized, clinical-based, Mediterranean lifestyle interventional study with parallel groups

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SUMMARY

Background & aims: Women with prior gestational diabetes mellitus (GDM) have a high risk of developing type 2 diabetes mellitus (DM2) in later life. The study aim was to evaluate the efficacy of a lifestyle intervention for the prevention of glucose disorders (impaired fasting glucose, impaired glucose tolerance or DM2) in women with prior GDM.

Methods: A total of 260 women with prior GDM who presented with normal fasting plasma glucose at six to twelve weeks postpartum were randomized into two groups: a Mediterranean lifestyle intervention group ($n = 130$) who underwent an educational program on nutrition and a monitored physical activity program and a control group ($n = 130$) with a conventional follow-up. A total of 237 women completed the three-year follow-up (126 in the intervention group and 111 in the control group). Their glucose disorders rates, clinical and metabolic changes and rates of adherence to the Mediterranean lifestyle were analyzed.

Results: Less women in the intervention group (42.8%) developed glucose disorders at the end of the three-year follow-up period compared with the control group (56.75%), $p < 0.05$. The multivariate analysis indicated a reduction in the rate of glucose disorders with a BMI of less than 27 kg/m^2 (OR 0.28; 0.12–0.65; $p < 0.003$), low fat intake pattern (OR 0.30; 0.13–0.70; $p < 0.005$), low saturated fat pattern (OR 0.30; 0.13–0.69; $p < 0.005$) and healthy fat pattern (OR 0.34; 0.12–0.94; $p < 0.04$).

Conclusions: Lifestyle intervention was effective for the prevention of glucose disorders in women with prior GDM. Body weight gain and an unhealthy fat intake pattern were found to be the most predictive factors for the development of glucose disorders.

Current Controlled trials: ISRCTN24165302. http://www.controlled-trials.com/isrctn/pf/24165302.

1. Introduction

Lifestyle changes that impact modifiable risk factors have been unequivocally demonstrated to be highly efficient for the prevention of type 2 diabetes mellitus (DM2) in people at risk, achieving reductions of up to 58% in the conversion rate to DM2 over a period of three years [1–3]. Long-term reductions of approximately 43% in 10 years have been successfully maintained [4–6]. In addition, lifestyle interventions have been demonstrated to be at least as efficient as pharmacological interventions with an outstanding reduction in adverse effects, and are also cost-effective [4,7]. The translation of these preventive programs into clinical practice using the available resources is currently the most important question.

Women who have previously presented gestational diabetes mellitus (GDM) have a well-known increased risk of developing glucose disorders in later life with conversion rates to DM2 from 20 to 50% by 10 years postpartum [8]. Moreover, these women exhibit an increased long-term cardiovascular risk [9]. Obesity, weight gain

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during pregnancy and shortly after in the postgestational period and a sedentary lifestyle are the main modifiable risk factors for the development of postgestational diabetes [10].

GDM represents a growing health problem with increasing prevalence in our population; however, the optimal lifestyle intervention that achieves an effective reduction in the risk of DM2 in the postgestational period under the real conditions of clinical practice has not yet been defined [11–13].

One of the most interesting aspects examined over the last few years is the potential modification of nutritional patterns as the key to preventing postgestational diabetes [14].

The Mediterranean diet is broadly recognized as a healthy nutritional pattern and has recently demonstrated a relevant reduction in the incidence of DM2 and a reduction in cardiovascular risk compared with other nutritional patterns [15,16].

The hypothesis of the present study is that a Mediterranean-pattern lifestyle intervention and a monitored program of physical activity are able to reduce the development of glucose disorders three years postpartum in women who have previously presented with GDM under the real conditions of clinical practice.

2. Materials and methods

2.1. Study design

The present study was an interventional, randomized, controlled trial with two parallel groups. The primary outcome was a comparison of the effects of a standard follow-up with a nutritional intervention and a monitored physical activity program on the prevention of glucose disorders three years after gestational diabetes development. The term glucose disorder includes prediabetes (impaired fasting glucose and/or impaired glucose tolerance) and DM2.

The secondary objectives were to evaluate the clinical changes and biochemical parameters in the intervention and control groups, the adherence to lifestyle changes and predictive factors of conversion to glucose disorders in the postpartum period.

2.2. Subjects

The inclusion criteria were as follows: women diagnosed with GDM between 24 and 28 weeks of gestation with the Carpenter-Coustan criteria who were assisted and followed during pregnancy in the Gestational Diabetes Unit of Hospital Clinico San Carlos (HCSC) between January 2007 and December 2008. The exclusion criteria were the presence of impaired fasting plasma glucose ($\geq$100 mg/dL) in the first postpartum evaluation and plan for new pregnancy during the three years of follow-up. All patients signed informed consent forms, and the protocol was approved by the Ethical Committee of HCSC and followed the Declaration of Helsinki.

A total of 300 consecutive women diagnosed with GDM and assisted in our unit between January 2007 and December 2008 were invited to join the study. Fig. 1 shows the participant flow chart.

Of the total population selected, seven refused to participate, and 33 were excluded because of impaired fasting glucose at their first postpartum visit. Finally, a total of 260 women provided informed consent and were randomized 1:1 according to age, ethnicity, BMI and use of insulin during pregnancy to either the intervention group ($n = 130$) or the control group ($n = 130$). During the follow-up, 23 women, four in the intervention group and 19 in the control group, did not complete the first annual evaluation and were excluded because of a new pregnancy ($n = 10$) or a change of address ($n = 9$). The final sample that was analyzed for intention to treat included 237 patients (126 in the intervention group and 111 in the control group). Both groups displayed similar characteristics at entry without any significant differences in the demographic data (Table 1).

2.3. Intervention

During pregnancy, all of the participants received the same recommendations about a healthy diet based on the Mediterranean pattern and recommendations about physical activity according to the diabetologic education program in the GDM Unit of HCSC [17].

In the last visit before delivery, which occurred between 37 and 39 weeks of gestation, the women were provided an appointment to be evaluated at 7–12 weeks postpartum in our unit, and blood analyses were performed 6 weeks postpartum.

The patients participated in a 2-h group session at the first visit (7–12 weeks postpartum), that included the additional participation of a nurse, a registered dietitian and one endocrinologist. The women received information regarding the risk of DM2 after presenting GDM and how it can be prevented and were educated regarding healthy nutritional habits, the practice of physical activity and the importance of smoking cessation.

The nutritional recommendations for both groups consisted of as much adherence as possible to the Mediterranean diet pattern: high consumption of fruits and vegetables (five or more serving a day), high consumption of legumes (more than two serving per week), high consumption of nuts (more than three serving a week), daily use of virgin olive oil (more than 40 cc per day), at least three serving per week of oily fish, low consumption of red and processed meats (less than two serving per week) and low consumption of non-skimmed dairy products (less than two serving per week). To guide these recommendations, a semiquantitative questionnaire, which will be described later in the text, was utilized.

The objective of the intervention was to achieve a nutrition score greater than 5 based on the previously reported Diabetes Nutrition and Complications Trial (DNCT) [18].

The physical activity program was monitored by a physiotherapist with a monthly evaluation by the doctor of the Rehabilitation Unit of HCSC and was only implemented in the intervention group. The control group received recommendations to practice aerobic exercise (brisk walking, bicycle, paddle, tennis, etc.) for at least 150 min per week.

Group and individual sessions were programmed during a period of 10 weeks between 3 and 6 months post delivery in the intervention group. After this program, 1-h reinforcement sessions were added at the end of and three and six months after the monitored physical activity period.

The exercises consisted of aerobic activities and muscular conditioning, and these were progressive and practiced on a regular basis with moderate intensity. The exercises were performed during sessions of 50–60 min four days per week (two days at the hospital and two days at home).

The exercise sequence was as follows: warm-up exercises (10 min), aerobic activity; cycle ergometer and treadmill (15 min); muscular strengthening exercises, biceps, triceps, abdominals, quadriceps, with two to three sets of eight to ten repetitions for each muscular group (15 min); resting periods between the sets (10 min); and relaxation exercises (5 min).

At the same time, there was a non-monitored physical activity program in which the patients practiced the exercises at home, with the objective of introducing the habit into the patient's daily life. The patients registered their daily physical activity, duration, type and heart rate at the beginning and the end of the exercise in a log book.