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Impact of etonogestrel-releasing implant and copper intrauterine device on carbohydrate metabolism: a comparative study

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Abstract

Background: We investigated the influence of an etonogestrel-releasing (ETG) implant and copper intrauterine device (IUD) on carbohydrate metabolism.
Study Design: In this nonrandomized, open-label, prospective controlled trial, 40 healthy women received an implant or IUD (20 per group). Outcome measures were fasting glucose, fasting insulin, oral glucose tolerance test (OGTT) and glycosylated hemoglobin A_1C (HbA_1C) levels at baseline and after 6 and 12 months.
Results: The groups were similar in age, body mass index and laboratory parameters at baseline. Carbohydrate metabolism was not modified by the ETG implant at baseline and at 6 and 12 months (mean±SD) (fasting glucose: 85.9±5.13, 87.05±5.36, 88.19±5.05; insulin: 7.77±2.42, 10.64±9.4, 8.82±3.73; OGTT: 94.8±25.28, 96.5±19.67, 99.47±24.6; HbA_1C: 5.27±.34, 5.55±.39, 5.7±0.37). The same was true for the IUD (fasting glucose: 88.87±7.2, 89.65±5.86, 88.75±4.79; insulin: 7.94±3.6, 8.3±4.1, 7.34±3.02; OGTT: 96.85±15.16, 97.48±13.42, 91.3±22.16; HbA_1C: 5.41±.49, 5.75±.41, 5.9±0.73).
Conclusions: The ETG-releasing implant did not affect carbohydrate metabolism in normal women after 12 months.

Keywords: Carbohydrate metabolism; Etonogestrel; Contraceptive; Copper IUD

1. Introduction

A major drawback associated with the use of hormonal contraceptives, in particular combined (estrogen+progestin) oral contraceptives, is their metabolic effects, including changes in carbohydrate metabolism [1]. Abnormalities in carbohydrate metabolism are important because even minor disturbances may increase the risk of cardiovascular disease. Of particular concern are glucose intolerance, insulin resistance and hyperinsulinemia, which are involved in the atherogenic process [2].

Progestin-only contraceptives (oral or implants) have been proposed as an alternative to avoid the side effects of combined treatments [3]. However, even though short-term use of progestin seems to induce irrelevant changes in glucose–insulin metabolism, little is known about the long-term effects of progestin use [1,2].

Implanon® is a well-known contraceptive implant containing etonogestrel (ETG), the biologically active metabolite of desogestrel, a progestin with an ethylene–vinyl–acetate copolymer as carrier material [4–11]. The use of this implant is less cumbersome than that of oral progestin-only contraceptives, which require a strict administration schedule. The ETG implant is a highly effective, long-acting, reversible contraceptive with annual pregnancy rates of 0.38% [6–8]. Nevertheless, a comprehensive review has suggested that a better evaluation is needed in order to establish the carbohydrate metabolism effects of the ETG-releasing implant [3].

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The objective of this study was to compare the impact on carbohydrate metabolism of using an ETG-releasing implant vs. copper intrauterine device (IUD) during 12 months.

2. Materials and methods

2.1. Study subjects and design

In this nonrandomized, open-label, prospective controlled trial, 46 volunteers were recruited from the Family Planning Center at Hospital de Clínicas de Porto Alegre, a teaching hospital in Brazil. Inclusion criteria were age between 18 and 35 years, regular menstrual cycles (24 to 35 days), body mass index (BMI)<30 kg/m^2, blood pressure within normal range (systolic<140 mmHg; diastolic<100 mmHg), being sexually active and absence of contraindications for the use of progestins or copper IUD. Study participants were invited to choose between the implant or the IUD. Informed consent was obtained from all subjects, and the study was approved by the local research ethics committee (protocol # 07523).

The sample size was calculated to detect a statistically significant difference of at least 1 standard deviation (SD) between the groups, considering a type I error of 0.05, type II error of 0.20 and a 10% (8 mg/dL) difference in fasting glucose. For that, at least 18 individuals were required in each group.

A bimanual pelvic examination was performed before the beginning of the study. The following parameters were measured at baseline and at 6 and 12 months after insertion of the implant or IUD: glucose, blood count, fasting insulin, oral glucose tolerance test (OGTT), and glycosylated hemoglobin A_1C (HbA_1C). On all these occasions, the participants were weighed and had their blood pressure measured. Data on adverse events (such as vaginal bleeding) were also collected at baseline and after 6 and 12 months. Women using combined contraceptives before the beginning of the study underwent a washout period (30 days) using condoms for contraception. All implants and IUDs were inserted during menses by the same experienced physician. No complications were recorded.

2.2. Laboratory measurements

Plasma glucose was estimated using an enzymatic method (Modular P, Roche Diagnostics, Mannheim, Germany) to determine plasma insulin concentrations (Modular E170, Roche Diagnostics, Mannheim, Germany) and a 75-g OGTT (GLUC-UP 75–200 mL) after an overnight fast. Hemoglobin A_1C was measured using the glycohemoglobin analyzer HCL-723GHBA1C 2.2.

2.3. Statistical analysis

Statistical analysis was performed using SPSS 18.0 for Windows. Results of group comparison were calculated using quantitative variables with mean±SD. Results of laboratory tests had normal distribution, and multiple laboratory parameters were compared using repeated-measures analysis of variance (ANOVA). Multiple measurements were compared with repeated-measures ANOVA. Student's *t* test was used to compare baseline data. Statistical significance was set at $p<.05$.

3. Results

During the study, six patients were lost to follow-up, four in the ETG group (two due to bleeding, one due to weight gain and one did not come back for at least one evaluation) and two in the copper IUD group (one case of pelvic infection and one case of IUD expulsion). No significant differences were observed between the IUD and ETG implant groups with respect to mean age, BMI and laboratory parameters (Table 1).

At the end of 12 months, no differences were observed between the groups in terms of BMI: 24±2.79 vs. 24±2.46 (mean±SD) for implant and IUD, respectively. There were no changes in carbohydrate metabolism parameters after 6 and 12 months (Table 2).

Mean fasting glucose did not differ when copper IUD and implant groups were compared after 6 and 12 months, following the same pattern of change in both groups. On the other hand, fasting insulin levels showed a slight increase after 6 months in the implant group. However, there was no statistical significance, and insulin levels remained stable after 12 months. Mean 2-h OGTT glucose levels demonstrated a mild increase in the implant group in comparison with the copper IUD group after 12 months; however, there was no statistical difference. Mean glycosylated hemoglobin remained stable after 12 months in both groups.

4. Discussion

The present study aimed to evaluate the impact of the ETG-releasing implant on carbohydrate metabolism during 12 months. Progestins have been reported to reduce insulin-dependent glucose uptake, which is compensated for by increased insulin secretion. During glucose tolerance tests,

Table 1
Characteristics of patients at baseline

Variable	ETG implant (n=20) mean (SD)	IUD (n=20) mean (SD)	p
Age (years)	26.35 (5.09)	27.85 (3.61)	.28
BMI (m^2/kg)	23.9 (2.188)	23.65 (3.1)	.77
Diastolic blood pressure (mmHg)	76 (7.36)	72.25 (6.97)	.15
Fasting glucose (mg/dL)	88.87 (7.2)	85.9 (5.13)	.14
Fasting insulin (μU/mL)	7.9 (3.6)	7.7 (2.42)	.85
2-h OGTT glucose (mg/dL)	96.85 (15.16)	94.8 (25.28)	.75
Fasting HbA_1C (%)	5.41 (0.49)	5.27 (0.34)	.28

Student's *t* test.