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Dietary patterns and the phenotype of polycystic ovary syndrome: the chance of ongoing pregnancy

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KEY MESSAGE
Adherence to a healthy dietary pattern is inversely associated with the hyperandrogenic polycystic ovary syndrome phenotype and to an increased chance of ongoing pregnancy.

A B S T R A C T

Polycystic ovary syndrome (PCOS) is generally considered a complex disorder caused by interactions between genetic and environmental factors. In a sub-cohort of women with PCOS visiting the preconception outpatient clinic of a tertiary hospital with follow-up in a periconception cohort, we identified specific dietary patterns and adherence in patients with PCOS with and without hyperandrogenism and the chance of ongoing pregnancy. Food frequency questionnaires were available from 55 patients diagnosed with PCOS during follow-up in routine clinical practice, including 25 with hyperandrogenism and 30 without hyperandrogenism. Strong adherence to the healthy dietary pattern was inversely associated with the hyperandrogenic PCOS phenotype (Adjusted OR 0.27; 95% CI 0.07 to 0.99). In women with PCOS overall, a strong adherence to the healthy dietary pattern showed a

three-fold higher chance of ongoing pregnancy (adjusted OR 3.38; 95% CI 1.01 to 11.36) and an association with anti-Müllerian hormone concentration (β –0.569 µg/L; 95% CI –0.97 to –0.17). The effect of this dietary pattern on the chance of ongoing pregnancy and AMH suggests causality, which needs further investigation in prospective studies in the general population.

Introduction

Polycystic ovary syndrome (PCOS) is an endocrine disorder with a prevalence of 5–10% and characterized by oligoovulation or anovulation, hyperandrogenism, polycystic ovaries, or all these symptoms (Azziz et al., 2004; Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004; Ezeh et al., 2013). Nowadays, PCOS is generally considered a complex genetic disorder with interactions between environmental factors, such as diet, obesity, and genetic susceptibility caused by single nucleotide polymorphisms (Barber and Franks, 2013; Franks et al., 1998). These gene-nutrient interactions, in particular, influence gene expression, resulting in a variety of diseases even with transgenerational effects (Waterland and Jirtle, 2004). The one carbon (1-C) pathway plays an essential role in epigenetics, in which methyl groups derived from nutrients such as B vitamins are used for DNA synthesis and phospholipid and protein biosynthesis (Steegers-Theunissen et al., 2013). Previous studies have shown that dietary patterns rich in these B vitamins are associated with increased chances of pregnancy and decreased chances of adverse pregnancy outcome, confirming the involvement of the 1-C pathway (Obermann-Borst et al., 2011; Timmermans et al., 2012; Twigt et al., 2012; Vujkovic et al., 2007, 2009, 2010).

Dietary intervention studies of specific nutrients have shown various improvements in the features of PCOS, substantiating the hypothesis that nutrition affects biological processes involved in the clinical spectrum of PCOS phenotypes (Douglas et al., 2006a; Gower et al., 2013; Graff et al., 2013; Mehrabani et al., 2012; Sorensen et al., 2012; Stamets et al., 2004; Toscani et al., 2011; Vargas et al., 2011). Moreover, we recently showed that the use of a self-initiated diet and diet inadequacy are associated with PCOS and with the severity of the PCOS phenotype, which is further substantiated by a positive association between diet inadequacy and anti-Müllerian (AMH) concentration (Huijgen et al., 2015).

In this continuous search for the best treatment for PCOS, to the best of our knowledge no observational studies have assessed dietary patterns in relation to the heterogeneity of the PCOS phenotype. Therefore, we explored which dietary patterns are distinctive for women with PCOS and whether these dietary patterns are associated with the more severe hyperandrogenic PCOS phenotype or the mild non-hyperandrogenic PCOS phenotype (Daan et al., 2014). Additionally, we investigated whether the established dietary patterns are associated with the chance of ongoing pregnancy.

Materials and methods

Design

Couples referred to our hospital because of subfertility visited the preconception tailored nutrition and lifestyle counselling clinic during their first visit at the Department of Obstetrics and Gynaecology at the Erasmus MC, University Medical Centre Rotterdam, a tertiary hospital in the Netherlands, between October 2010 and October 2012. They were additionally invited to participate in the ongoing Rotterdam Periconceptional Cohort, the Predict study (Hammiche et al., 2011; Steegers-Theunissen et al., 2016). Women with oligoovulation or anovulation were screened for ovulatory dysfunction. Trained professionals diagnosed PCOS according to a standardized protocol, based on the Rotterdam criteria (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004), including the presence of oligoovulation or anovulation, hyperandrogenism (Ferriman-Gallweyscore ≥9, a Free Androgen Index >4.5, or both), polycystic ovaries, or both. Two subtypes of PCOS were distinguished according to the severity of the phenotype: hyperandrogenic PCOS and non-hyperandrogenic PCOS (Daan et al., 2014; Huijgen et al., 2015). The AMH was also used as marker of PCOS severity, as elevated levels are the result of an arrest of the selection of the dominant follicle with a concomitant increase in the number of small (pre)-antral follicles in the polycystic ovary. During the visit at the outpatient clinic, standardized anthropometric measurements, i.e. height, weight and circumferences, and non-fasting blood samples, were obtained. Participants completed a general questionnaire and a food frequency questionnaire (FFQ) at baseline, which were used for counselling during the visit. Couples were counselled twice with a fixed time interval of 3 months (Hammiche et al., 2011). From the general questionnaire, data were obtained on age, ethnicity, educational level, the use of a diet, the use of folic acid or vitamin supplements, medication, alcohol or tobacco and physical exercise. The validated semi-quantitative FFQ consisting of 196 food items was developed by the division of Human Nutrition, Wageningen University, The Netherlands, and was used to estimate habitual food intake over the previous 4 weeks before the preconception visit (Huijgen et al., 2013; Siebelink et al., 2011; Verkleij-Hagoort et al., 2007). To calculate the individual micro- and macro-nutrient intakes, the nutrient densities as reported in the Dutch Food Composition Database of 2011 were multiplied by the consumed amounts of foods with consideration of preparation methods and portion sizes (RIVM, 2011). Twenty-three food groups were classified, to reduce the 196 food items by the summation of food items with a similar nutrient content (Supplementary Table S1) (Slimani et al., 2002; Vujkovic et al., 2010). Dietary patterns were extracted from the women with PCOS only, because of the heterogeneity of the subfertile control group comprising women with ovulatory disorders (such as imminent ovarian failure, WHO 1), tubal infertility or unexplained subfertility. Clinical and fertility outcome parameters, such as type of fertility treatment, ongoing pregnancy (intrauterine pregnancy with positive heart action confirmed by ultrasound at 12 weeks gestation; yes/no), and time to pregnancy were extracted from medical records and follow-up stopped in January 2015.

Biomarkers

Venous blood samples were collected and the biomarkers of 1-C metabolism were determined; serum and red blood cell (RBC) folate,