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Is there an association between artificial sweetener consumption and in-vitro reproduction outcomes?

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KEY MESSAGE

Women consuming regular or diet soft drinks are at increased risk of oocyte dimorphisms, diminished embryo quality and a mild negative effect on blastocyst formation, implantation and pregnancy rates. Unfavourable embryo development was observed in women consuming artificially sweetened coffee.

A B S T R A C T

Previous studies have suggested an association between high intake of sweetened beverages and a number of adverse health outcomes. In this cross-sectional study, we investigated the association between daily consumption of sweetened soft drinks or coffee and the outcome of intracytoplasmic sperm injection (ICSI) treatment. Patients (n = 524) were interviewed by a nutritionist before ICSI treatment, using a food frequency questionnaire. Regression analysis showed that consumption of ≥3 servings of regular soft drinks or any amount of diet soft drinks was associated with oocyte dysmorphism, diminished embryo quality on days 2 and 3 of culture, and a mild effect on blastocyst formation, implantation and pregnancy rate. Consumption of artificially sweetened coffee was negatively associated with embryo quality on days 2 and 3. However, consumption of coffee or soft drinks was not associated with the odds of live birth. Even so, patients should be advised about the potential negative effects of sugar and artificial sweeteners before attempting infertility treatment. This study is limited by the use of a non-validated food frequency questionnaire, lack of information on quantity of sweeteners consumed, and lack of data on glucose levels in blood serum or follicular fluid. Further investigation is warranted.

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Introduction

Obesity has become a worldwide epidemic that has proven to be strongly associated with sugar intake (Sylvetsky et al., 2012). Probably due to the drastic increased prevalence of overweight and obesity, the consumption of sweeteners has sharply risen over recent decades (Ng and Popkin, 2012; Piernas et al., 2013; Spencer et al., 2016). Sweeteners, also known as low- or no-calorie sweetener, non-nutritive sweetener or artificial sweetener (Serván et al., 2014), is the term used to describe additives that provide sweetness without contributing to caloric intake (Blackburn et al., 1997; Chattopadhyay et al., 2014).

Although the potential risks of each sweetener are assessed before their approval (Olivier et al., 2015), the introduction of sweeteners onto the public market in the 1950s and 1960s has been accompanied by debates and disagreements regarding their potential nutritional and general health impacts (Rogers et al., 2016; Serván et al., 2014). Nonetheless, at present these compounds are used throughout the world in the formulation of reduced-calorie beverages and foods, and medicines (Olivier et al., 2015; Serván et al., 2014).

Soft drinks are the main sources of artificial sweeteners (Halldorsson et al., 2010; Magnuson, 2010). These beverages are often promoted as a better alternative to sugar-sweetened soft drinks, which are considered the main caloric contributor in the US diet (Block, 2004). Previous studies have suggested that both artificially sweetened soft drinks and sugar-sweetened soft drinks are positively associated with hypertension (Winkelmayer et al., 2005), metabolic syndrome (Dhingra et al., 2007; Lutsey et al., 2008) and type 2 diabetes (Schulze et al., 2004).

Considering that the human fertility rate has declined over time, it could be argued that eating habits, including the consumption of sugar and artificial sweeteners, may negatively contribute to fertility potential. The effects of nutrition on the success of intracytoplasmic sperm injection (ICSI) have previously been explored. It has been demonstrated that female obesity negatively influenced the fertilization rate and the odds of miscarriage (Ferreira et al., 2010). Moreover, a positive association between the intake of artificially sweetened soft drinks and the risk of pre-term delivery has been previously demonstrated in two epidemiological studies (Englund-Ogge et al., 2012; Halldorsson et al., 2010).

To date, the association between the consumption of sweeteners and human assisted reproduction has not been investigated. The aim of this study was to evaluate whether the oocyte quality and ICSI outcomes are influenced by the daily consumption of soft drinks or coffee, sweetened with sugar or artificial sweeteners.

Materials and methods

Study design

This retrospective cross-sectional study included 5548 oocytes retrieved from 524 patients undergoing ICSI cycles between January 2012 and December 2014.

All patients completed a questionnaire with multiple-choice questions before treatment started. Women were asked about the frequency of consumption of many food items, including regular and diet soft drinks, unsweetened coffee and coffee sweetened with sugar or any kind of artificial sweetener.

The effects of dietary habits on the oocyte quality, embryo quality on day 2 and 3, chances of blastocyst formation, pregnancy, implantation and miscarriage rates were investigated. In order to avoid any influence of seminal parameters on the results, only couples undergoing ICSI as a result of female or unexplained infertility were included in this study.

A written informed consent was obtained in which patients agreed to share the outcomes of their own cycles for research purposes, and the study was approved by the local Institutional Review Board (protocol 410/2012) on 19 December 2012.

Food consumption questionnaire

All patients were interviewed face-to-face by the same nutrition professional, with special skills in dietary assessment methods, using a non-validated food frequency questionnaire, before the beginning of the ICSI treatment. The food frequency questionnaire is a subjective measure using a predefined, interviewer-administered format, in which data are collected based on usual intake estimates over a relatively long period (e.g. 6 months or 1 year) (Shim et al., 2014).

The questionnaire contained multiple-choice questions about the average frequency of consumption of food items during the past year. The food categories investigated were (i) regular soft drinks, (ii) diet soft drinks, (iii) unsweetened coffee, (iv) coffee with sugar and (v) coffee with artificial sweetener.

In the questionnaire, participants were asked to answer 'yes' or 'no' to the following questions:

1. Do you consume coffee daily?

If you answered 'yes', please answer how do you ingest your coffee:

unsweetened;
sweetened with sugar;
sweetened with any kind of artificial sweetener.

If you answered 'yes', please answer the number of servings (a 240 mL cup = 1 serving) you ingest per day:

1 serving per day;
2 servings per day;
3 or more servings per day.

2. Do you consume soft drinks daily?

If you answered 'yes', please answer what kind of soft drink you ingest:

regular;
diet or light.

If you answered 'yes', please answer the number of servings (a 240 mL cup = 1 serving) you ingest per day:

1 serving per day;
2 servings per day;
3 or more servings per day.

Controlled ovarian stimulation

A controlled ovarian stimulation was achieved by using recombinant FSH (Gonal-F; Serono, Geneva, Switzerland) for ovarian

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