ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Association between preconception maternal beverage intake and in vitro fertilization outcomes

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Objective: To study whether maternal intake of beverage type affects IVF outcomes.
Design: A prospective study.
Setting: Tertiary, university-affiliated center.
Patient(s): Three hundred forty women undergoing IVF from 2014 through 2016 for infertility as well as for pregenetic diagnosis for autosomal recessive diseases were enrolled during ovarian stimulation and completed a questionnaire describing their usual beverage consumption.
Intervention(s): None.
Main Outcome Measure(s): IVF outcomes were abstracted from medical records. Total caffeine intake was estimated by summing the caffeine content for specific beverages multiplied by frequency of intake. Associations between specific types of beverages and IVF outcomes were analyzed using Poisson and logistic regression models adjusting for possible confounders.
Result(s): Higher intake of sugared soda was associated with lower total, mature, and fertilized oocytes and top-quality embryos after ovarian stimulation. Women who consumed sugared soda had, on average, 1.1 fewer oocytes retrieved, 1.2 fewer mature oocytes retrieved, 0.6 fewer fertilized oocytes, and 0.6 fewer top-quality embryos compared with women who did not consume sugared soda. Furthermore, compared with women who did not drink sugared soda, the adjusted difference in percent of cycles resulting in live birth for women consuming 0.1–1 cups/day and >1 cup/day were −12% and −16%, respectively. No associations were found between consumption of coffee, caffeine, or diet sodas and IVF outcome.
Conclusion(s): Sugared beverages, independent of their caffeine content, may be a bigger threat to reproductive success than caffeine and caffeinated beverages without added sugar. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)
Key Words: IVF, caffeinated beverages, non-caffeinated beverages, sugared soda

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Up to 10% of reproductive-age couples are infertile (1), with more than 600,000 IVF cycles performed in Europe in 2011 (2) and more than 140,000 IVF cycles performed in the United States in 2014 (www.sartcorsonline.com). Despite the relative increase in pregnancy rates with time, overall success rates of IVF remain relatively low. To date, the best characterized predictors of IVF success are unmodifiable (i.e., patient age), hence the need to investigate potentially modifiable factors, one example of which is type of beverages consumed (3–5).

Among the most popular beverages consumed by reproductive-age women are caffeinated drinks, sugared sodas, and diet sodas. Caffeine is a stimulant of the central nervous system (6). While increased caffeine consumption is associated with lower estrogen levels in the luteal phase (7–9), the effects of

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caffeinated beverages on fecundity are still inconsistent (6,10–13). Intake of sugared soda has been linked to weight gain as well as a rapid increase in circulating insulin and insulin-like growth factor-1 levels and insulin resistance due to their high glycemic content (14). Moreover, soda drinkers are potentially exposed to higher levels of endocrine disruptor chemicals such as bisphenol A, which migrate from the coating of soda cans into the liquid (15).

Most studies to date have evaluated the effects of caffeine, sugared sodas, and diet beverages either on time to conception or risk of fetal loss, and the results are still conflicting (16–20). However, the effects of these beverages on intermediate IVF cycle outcomes (i.e., number of oocytes retrieved, oocyte maturation, fertilization, and day 3 embryo quality) as well as clinical IVF outcomes (positive beta-hCG, clinical pregnancy rates, spontaneous abortions, and live births) have been less well studied (21–23).

In the most recent study on this topic, Abadia and colleagues found no association between low to moderate caffeine intake (<200 mg/day) and IVF outcomes in a prospective cohort of infertile women in the United States (24). They also found no associations with any of the specific caffeinated beverages. However, due to the low soda consumption in that cohort, the study was unable to assess whether consumption of these beverages is related with assisted reproductive technology (ART) outcomes. The aim of the current study was to evaluate the associations between preconception drinking habits of women with fresh IVF cycle outcomes in a prospective cohort of women from outside the United States consuming much higher levels of caffeine (mainly instant coffee) and sodas (both full calorie and diet).

MATERIALS AND METHODS

Study Design

From January 2014 through August 2016, 359 women undergoing a fresh IVF cycle at a tertiary university-affiliated hospital were recruited into a study on environmental exposures and fertility. Cryopreserved cycles were excluded from our analysis. The study was approved by our local Institutional Review Board, and all patients signed informed consents. Participants were enrolled during ovarian stimulation and followed through one fresh IVF cycle. For the analysis of intermediate IVF outcomes, exclusion criteria included women with missing embryology (n = 3) or exposure (n = 2) information, women who froze their oocytes (n = 11), women using egg donors (n = 1), and women missing information on oocyte retrieval (n = 2). Thus, the final data set consisted of 340 women. For the analysis of clinical IVF outcomes, we further excluded one woman who was lost to follow-up after identification of a clinical pregnancy, bringing the final analytic sample to 339 women.

Exposure Assessment

Women reported their usual intake of caffeinated and noncaffeinated beverages on the first day of stimulation and/or on the day of oocyte retrieval. The questionnaire specifically asked women, "Do you drink any of the following 14 beverages: filtered coffee, instant coffee, boiled black coffee, mud coffee, decaffeinated coffee, cappuccino, espresso, caffeinated tea, herbal tea, chocolate drinks, caffeinated soda, caffeinated diet sodas, noncaffeinated diet sodas, and energy drinks and, if so, in what quantity (in cups)." Women were also provided with information on converting common serving sizes to cups (e.g., 1 mug = 2 cups). Total caffeine intake was estimated by summing the caffeine content for each specific beverage multiplied by their frequency of intake. We assumed the following caffeine concentrations for each caffeinated beverage: filtered coffee, 95 mg/cup; instant coffee, 63 mg/cup; boiled black and mud coffee, 115 mg/cup; decaffeinated coffee, 2 mg/cup; cappuccino, 64 mg/cup; espresso, 64 mg/shot; caffeinated tea, 26 mg/cup; chocolate drinks, 5 mg/cup; caffeinated sodas, 16 mg/cup; and energy drinks, 111 mg/cup.

Covariate Assessment

Height and weight, measured at the start of the IVF cycle by a trained nurse, were used to calculate body mass index (BMI; kg/m^2). A woman's age, smoking status, number of previous pregnancies and deliveries, duration of infertility, and IVF attempt number were abstracted from patients' medical records. On the same questionnaire as the one about the beverages, women also provided information on their country/region of birth, years of education, smoking history, and field of employment.

Outcome Assessment

Patients were treated with controlled ovarian stimulation using one of three protocols (GnRH antagonist, GnRH agonist suppressive protocol, or GnRH agonist flare-up protocol) as clinically indicated. Patients were monitored during gonadotropin stimulation for serum E_2, follicle size measurements and counts, and endometrial thickness through 2 days before oocyte retrieval. HCG was administered approximately 36 hours before the scheduled oocyte retrieval procedure to induce oocyte maturation. Women received conventional insemination or intracytoplasmic sperm injection (ICSI) as clinically indicated. Embryologists classified oocytes as germinal vesicle, metaphase I, metaphase II (MII), or degenerated. Embryologists determined fertilization 16–18 hours after insemination as the number of oocytes with two pronuclei. The resulting embryos were assessed for cell number, symmetry, and fragmentation (25). Top-quality embryos were considered to be embryos with 7–8 cells on day 3 (or in cases of day 2 transfer, 4 cells) and <10% fragmentation. Positive β-hCG (i.e., successful implantation) was defined as a serum β-hCG level >25 mIU/mL typically measured 14 days after oocyte retrieval. Embryos were scheduled for transfer on day 3 in non–preimplantation genetic diagnosis (PGD) patients. In cases for which day 3 was a holiday, transfers were performed on day 2 (n = 12 cycles). For PGD patients, embryos were biopsied on day 3 and transferred on day 4. Clinical pregnancy was defined as the presence of an intrauterine gestational sac and fetal heartbeat confirmed by ultrasound by 7 weeks of gestation, and live birth as the delivery of