Predictors of pregnancy and live birth after insemination in couples with unexplained or male-factor infertility

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Objective: To identify risk factors for pregnancy outcomes in couples treated with intracervical or intrauterine insemination, with or without superovulation for unexplained or male-factor infertility.
Design: Secondary analysis of data from a randomized superovulation and intrauterine insemination trial.
Setting: Academic medical centers.
Intervention(s): Treatment continued for four cycles unless pregnancy was achieved.
Patient(s): Out of 932 couples randomized to four treatment groups, 664 couples who had completed the lifestyle questionnaires were assessed for occurrence of pregnancy and live birth.
Main Outcome Measure(s): Pregnancy and live birth.
Result(s): The pregnancy and live birth rates were significantly higher in couples in which the female partners reported that they had consumed coffee or tea in the past or drank alcoholic beverages in the past (past users) compared with those who had never consumed coffee, tea, or alcoholic beverages. Past users also had significantly higher pregnancy and live birth rates than those currently consuming coffee or tea or alcoholic beverages. Demographic, occupational exposure, and other lifestyle factors were not significant.
Conclusion(s): Couples in which the female partners drank coffee, tea, or alcoholic beverages in the past had higher pregnancy and live birth rates compared with never or current users. When discontinuing these habits, they might have made other lifestyle changes to improve the pregnancy outcome. (Fertil Steril® 2012;97:959–67. ©2012 by American Society for Reproductive Medicine.)
Key Words: Infertility, lifestyle, pregnancy, live birth, insemination, superovulation

Infertility, defined as the inability to conceive after 12 months of unprotected intercourse, is a major public health problem affecting up to 15% of all couples (1, 2). Lifestyle factors, including smoking, caffeine use, alcoholic beverage drinking, and obesity, have been associated with subfertility and an increase in early pregnancy loss in some investigations (3–9). A variety of occupational exposures have also been linked to impaired natural fertility (10, 11). However, the effect of lifestyle factors and occupational exposures on natural fertility is not consistent from study to study (10, 12). In addition, many studies have been too small to detect an effect or have relied on retrospective information, which is subject to recall bias (13–16).

Multiple studies have investigated the impact of lifestyle factors on outcomes of in vitro fertilization (IVF). Both tobacco use and high body mass index (BMI) have been associated with a negative effect on IVF pregnancy rates (17, 18). Additionally, alcohol use has been associated with a reduction in IVF pregnancy rate (19). The relationship between caffeine use and IVF outcomes is less clear; however, a decrease in good-quality embryos has been reported in high caffeine users compared with moderate users (20).

Little is known regarding the relationship between lifestyle factors and

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pregnancy outcomes after less-aggressive infertility treatments, such as controlled ovarian stimulation (COS), intrauterine insemination (IUI), or a combination of both. Given that many couples undergo such treatment cycles to achieve a pregnancy, a better understanding of the relationship between lifestyle factors and outcomes is important to appropriately counsel patients.

To address these questions, we examined the relationship between lifestyle factors, occupational exposures and treatment outcomes in a large multicenter randomized clinical trial (21) evaluating the effectiveness of different treatments (intracervical insemination [ICI], COS with ICI, natural-cycle IUI, and COS with IUI) for unexplained infertility.

SUBJECTS AND METHODS

Study Design

From 1991 to 1997, 932 infertile couples with unexplained infertility were recruited from university-based infertility and gynecology clinics (21, 22). The couples were randomly assigned to receive ICI, IUI, COS-ICI, or COS-IUI. Treatment continued for four cycles unless pregnancy was achieved. Inclusion criteria consisted of ≥ 12 months of infertility, a detailed fertility evaluation with normal results, and the presence of motile sperm on semen analysis for male partners. Exclusion criteria included previous infertility treatment, a history of chemotherapy or radiation therapy, previous surgery (tubal surgery, myomectomy, ovarian cystectomy, or unilateral oophorectomy for women; vasovasostomy or varicocelectomy within 6 months before study, or pelvic-node dissection for men), or a medical condition related to infertility. The primary outcome studied was the establishment of pregnancy. Pregnancy was determined by an increase in the serum β-hCG concentration between luteal days 15 and 17 (21). Live birth was also recorded for the study and was defined as the delivery of a viable infant. Pregnancy loss included miscarriage, abortion, stillbirth, and nonviable infant. The Institutional Review Board at each center approved the protocol, and each of the couples gave written informed consent.

Lifestyle Factors and Occupational Exposure Assessment

Enrolled subjects completed extensive self-report questionnaires before undergoing treatment. The influence of subjects' baseline characteristics, lifestyle habits, and occupational exposures of the female partner on pregnancy outcome was evaluated. We selected the following 25 putative risk factors from a long list of variables: treatment group, age, BMI, race, education, pregnancy history, infertility length, history of smoking, coffee, tea, soda, and alcohol use, use of marijuana and cocaine, and exposure to solvents, lead, paint, pesticide, metal fumes, anesthetic gases, chemotherapeutic drugs, excess heat, vibration, and radiation during the preceding month. For smoking, "never" refers to those who had never smoked regularly or had smoked less than one cigarette per day; "current" refers to those who smoked regularly, at least one cigarette per day, within the past month; "past" refers to those who had smoked regularly, at least one cigarette per day more than 1 month before. For coffee or tea drinking, "never" refers to those who had never drunk or drank less than one 8-ounce cup of coffee or tea per week; "current" refers to those who drank at least one cup of coffee or tea per week within the past month; "past" refers to those who had drunk at least one cup of coffee or tea per week more than 1 month before. For alcoholic beverage (including beer, wine, and liquor) drinking, "never" refers to those who had never drunk or drank less than one alcoholic beverage per week; "current" refers to those who drank at least one alcoholic beverage per week within the past month; "past" refers to those who had drunk at least one alcoholic beverage per week more than 1 month before. One glass of beer equals 12 ounces; one glass of wine equals 4 ounces; one shot of liquor equals 1 ounce. The putative risk factors were selected by a combination of our knowledge and intuition. Our approach was not entirely hypothesis driven, allowing us flexibility in using the collected data; we limited the number to 25 to avoid being overly exploratory.

Data Analysis

The study sample in this analysis was used in a previous analysis looking at the efficacy of superovulation and IUI in the treatment of infertility (21). Of the 932 infertile couples recruited for that study, 268 (29%) did not complete the lifestyle or occupational exposure questionnaire. Those subjects were excluded from the present analysis, leaving 664 couples. All data management and analyses were performed using SAS (v 9.1; SAS Institute).

Baseline characteristics of the couples were compared among different treatment groups. Next, bivariate analyses were performed to determine the association between pregnancy outcome and the different factors based on a priori hypotheses. For live birth analysis, the live birth rate was the ratio of the total number of patients who delivered a live birth to the total number of patients in the groups, regardless of their pregnancy status. Pearson chi-square test was used for categoric data. Multivariable logistic regression analyses were then performed by applying the backward and stepwise procedures on the predictors introduced above (P values $<.1$ to enter and $<.05$ to stay), leading to the same final model. When the final model was obtained, the adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were computed with respect to the corresponding reference groups. We further performed an analysis on a subset of the data by including only the couples who underwent IUI (IUI and COS-IUI groups), to evaluate whether the results were changed. A two-tailed P value of $<.05$ was considered to be statistically significant. The reported P values were not adjusted for multiple comparisons.

RESULTS

Baseline Characteristics

The baseline characteristics of the 664 couples included in the following analysis are listed in Table 1. They are similar to those reported previously for the entire cohort (21).