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In Vitro Fertilization Outcomes and Alcohol Consumption in At-Risk Drinkers: The Effects of a Randomized Intervention

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Abstract

Background and Objectives—Women's use of alcohol in pregnancy is associated with an increase risk of fetal loss and birth defects. Also, alcohol use in women decreases the success of infertility treatment, such as in vitro fertilization (IVF). Our goal was to determine if there were differences in IVF outcomes and alcohol use parameters among at-risk drinkers randomized to a brief intervention (BI) vs. assessment only (AO).

Methods—We conducted a randomized controlled trial to determine the effect of brief intervention (BI) or assessment only (AO) among at-risk drinkers on in vitro fertilization (IVF). We studied 37 women (AO= 21; BI= 16).

Results—While the BI group had a significantly greater decrease in the number of drinks/ drinking day compared to the AO group (P=0.04), there were no differences in the likelihood of implantation failure, chemical pregnancy, spontaneous abortion, preterm birth, or live birth.

Conclusions—BI and AO contributed to a decrease in alcohol use and did not demonstrate differences in IVF outcomes. A larger study may confirm these preliminary findings.

Scientific Significance—Our results will assist care providers in treating alcohol use in pregnancy in an effective way, such that IVF cycles and the chance of pregnancy are optimized.

Alcohol use affects many aspects of reproduction in women. Moderate alcohol use (≥ 5 drinks/ week) has been associated with nearly a four-fold increase in risk of first trimester spontaneous abortion (SAB).[1] Three or more episodes of binge drinking (≥ 5 drinks/episode) has been associated with an increased risk of fetal death (≥ 22 weeks gestation) and ≥ 5 drinks/week associated 3 times greater risk of fetal death (at ≥ 28 weeks).[2, 3] Two studies report on the effects of alcohol use on in vitro fertilization (IVF). Klonoff-Cohen et al. found

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Conflicts of Interest:
Dr. Horstein received an Honorarium for UpToDate, Inc. authorship and has been on the Medical Advisory Board for WIN Fertility, both associations are not directly related to the submitted article. Other authors have no conflicts of interest to disclose. The authors alone are responsible for the content and writing of this paper.

that 1 drink/day was associated with fewer oocytes retrieved, an increased risk of not becoming pregnant if they drank during the month before the attempt, and an increased risk of miscarriage if they drank 1 week before IVF.[4] A more recent prospective cohort study demonstrated that women drinking at least 4 drinks/week had a 16% decrease in the odds of a live birth, but was not associated with increased odds of SAB.[5]

Many women stop using alcohol when they are pregnant. For those with alcohol addiction, brief interventions have proven to be successful. Pregnant women had a greater decrease in alcohol use and were more likely to be abstinent by the 3rd trimester in a brief intervention program compared to women who only had an alcohol assessment.[6, 7]

Due to the high costs of IVF (in terms of time, money, and emotional stress), it is critical that each cycle be optimized. Furthermore, alcohol cessation should be encouraged in the IVF population, in preparation for pregnancy. In this study, our objective was to determine if there were differences in IVF outcomes and alcohol use parameters among at-risk drinkers randomized to a brief intervention (BI) vs. assessment only (AO).

Methods

This study was approved by the Partners Institutional Review Board. Our analysis of IVF outcomes in infertility patients was from a randomized controlled trial of 511 women with diabetes, hypertension, infertility, or osteoporosis who were treated with BI or AO. [8] Infertile women were eligible if they practiced at-risk drinking (at least 7 drinks/week or more than 3 drinks/one day or were T-ACE positive).[9] T-ACE is a four-item screening questionnaire, validated in prenatal alcohol use studies, that asks about tolerance to alcohol, being annoyed by others' comments about drinking, attempts to decrease use, and having a drink first thing in the morning ("eye-opener").[10] Excluded were women with current treatment for alcohol or drug abuse, physical dependence on alcohol, or use of opiates, cocaine, or other illicit substances. As the number of previous IVF cycles influences her cycle success, we only included each woman's first IVF cycle with an embryo transfer.

We used a computer-generated random assignment list to randomize participants to an alcohol evaluation program that involved AO or a BI. The assessment was a diagnostic interview that measured current and lifetime alcohol and drug disorder diagnoses, daily drinking for the previous 6 months, and general health status, and then a 12 month follow-up. The BI included the assessment plus an intervention using Personal Steps to a Healthy Choice: A Woman's Guide and Helping Patients Who Drink Too Much, with 3 follow-up interviews at 3, 6, and 12 months.[9, 11] Details of the interventions have been previously described.[8] Randomization and initiation of the alcohol evaluation program occurred prior to the embryo transfer.

We defined two types of outcomes, alcohol use outcomes and IVF cycle outcomes. Alcohol use outcomes assessed were: the change from baseline to 12 months in the number of drinks/drinking day, number of binges in past 6 months, number of weeks drinking above the safe daily limit in past 6 months, and percent of drinking days in past 6 months. For IVF outcomes, implantation failure was defined as no rise in human chorionic gonadotropin (hCG) following embryo transfer. If there was a positive hCG after transfer, but no clinical pregnancy, a chemical pregnancy was diagnosed. Spontaneous abortion was defined as a clinical pregnancy without a live birth.

Alcohol outcomes were analyzed using Wilcoxon rank sum tests. Odds ratios (OR) and 95% confidence intervals (CI) comparing IVF outcomes among the AO group to those of the BI group are from logistic regression models adjusting for age.

Results

Thirty-seven women were included (AO= 21 and BI= 16). Demographic information is presented in Table 1. At baseline, AO group had 1.8 drinks/drinking day on average, while BI subjects had 2.1 drinks/drinking day on average. In addition, there were no significant differences in the odds of implantation failure, chemical pregnancy, SAB, live birth, or preterm delivery among AO compared to BI women (Table 2).

We observed no statistically significant differences in the decrease in the percent of drinking days in the last 6 months, decrease in the number of weeks above sensible drinking limit in the last 6 months, nor decrease in the number of binges in the past 6 months between the BI and the AO groups (Table 3). However, there was a significant difference in decrease in number of drinks per drinking day (P=0.04).

Over 12 months, alcohol use fell in both the AO and BI groups, minimizing the quantifiable impact of the brief intervention. In addition, within this cohort of women with a history of at-risk drinking, rates of SAB (21%) and live birth (43%) were not unlike the general IVF population.[12]

Discussion

In this study of at-risk drinkers, women undergoing IVF may have greater decrease in some alcohol use parameters if treated with a BI compared to AO. Furthermore, similar IVF outcomes, including live birth rates, were seen between both groups.

The lack of differences seen in the IVF outcomes between groups could be related to the inclusion criteria. The mean number of drinks/drinking day was actually below the cut-off for inclusion into our study, and consequently, many participants were included based on their T-ACE positive screening. Similarly, 94% of subjects from a larger study were enrolled due positive T-ACE screen, not current alcohol use.[13] If we assume comparable enrollment, only 2 of our subjects would have been enrolled due to increased alcohol use, thus a comparison between T-ACE positive and current drinkers in the current study did not seem appropriate. Therefore, the IVF pregnancy outcomes may not be representative of women actively using alcohol and undergoing IVF. A prior study also did not find differences in IVF outcomes with alcohol use at less than 2 drinks per week.[5] However, alcohol use may be underreported due to the social perception that alcohol is not acceptable in pregnancy or those attempting to conceive. Underreporting of alcohol use may also be worsened by retrospective data collection and the type of reporting, with highest alcohol use, and presumably more accurate, with a diary, slightly lower by interview, and lowest intake with a self-administered questionnaire.[14–16] However, self-report continues to be an acceptable, major source of data collection for alcohol use studies.[17]

In addition, our study sample was small. In order to appreciate any potential impact of timing of the assessment, we felt that it was critical to have the participation in the AO or BI occur prior to the women's first embryo transfer. Therefore, many potential subjects were excluded due to these strict criteria.

Infertility and alcohol use may be related. In fact, approximately 50% of women continue to drink through their IVF cycle.[18] There is a high prevalence of anxiety and depressive disorders in the IVF population and the degree of depressive symptoms can worsen with infertility treatment duration.[19, 20] These women may be at high-risk for co-occurrence of mood disorder and coping through alcohol use.[21] If women have a history of alcohol use or mental illness, the stress associated with infertility diagnosis or treatment may exacerbate alcohol use or make it more difficult to abstain.

In conclusion, it may be beneficial for at-risk drinking women to take part in a BI or a AO, prior to starting an IVF cycle. Although the BI was associated with a significant decrease in drinks per drinking day, there were no other differences in alcohol use or IVF outcomes between BI and AO. A larger randomized controlled trial may further elucidate the optimal treatment for at-risk women drinkers and the impact this treatment may have on IVF outcomes.

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Table 1

Demographic characteristics among women with at-risk drinking.

	Assessment Only (n=21)	Brief Intervention (n=16)
Age (Mean (SD) in years)	36.4 (3.4)	34.9 (4.5)
Range	30.0–44.8	27.2–42.1
Body mass index (kg/m^2)		
Missing	15 (71.4%)	10 (62.5%)
18.5–24.9	3 (14.3%)	5 (31.3%)
25–29.9	3 (14.3%)	0 (0.0%)
30–34.9	0 (0.0%)	1 (6.3%)
Race		
Missing	11 (52.4%)	13 (81.3%)
White	8 (38.1%)	3 (18.8%)
Black	1 (4.8%)	0 (0.0%)
Asian	1 (4.8%)	0 (0.0%)
Infertility Diagnosis		
Missing	4 (19.0%)	4 (25.0%)
Unexplained	6 (28.6%)	2 (12.5%)
Ovulatory	5 (23.8%)	2 (12.5%)
Endometriosis	1 (4.8%)	2 (12.5%)
Tubal	1 (4.8%)	0 (0.0%)
Male Factor	4 (19.0%)	6 (37.5%)
Prior Delivery		
Missing	16 (76.2%)	9 (56.3%)
No	1 (4.8%)	6 (37.5%)
Yes	4 (19.0%)	1 (6.3%)
Lifetime alcohol use/dependence		
No	16 (76.2%)	9 (56.3%)
Yes	5 (23.8%)	7 (43.8%)
Current alcohol use/dependence		
No	21 (100.0%)	14 (87.5%)
Yes	0 (0.0%)	2 (12.5%)

AO= Assessment only group, BI = Brief intervention group. Data reported at IVF cycle start.

“Missing” indicates that the information was not recorded in the medical record. Statistics are displayed are n, mean (SD), min-max for continuous variables, and n (%) for categorical variables.

Table 2

Odds ratios and 95% confidence intervals Brief Intervention and In Vitro Fertilization outcomes.

	Assessment Only (n=21)	Brief Intervention (n=16)	Overall (n=37)
Implantation Failure			
n (%)	6 (28.6%)	6 (37.5%)	12 (32.4%)
Crude OR (95% CI)	1.00 (Referent)	1.50 (0.38 – 6.00)	
Age-adjusted OR (95% CI)	1.00 (Referent)	1.82 (0.43 – 7.73)	
Chemical Pregnancy Only			
n (%)	3 (14.3%)	0 (0.0%)	3 (8.3%)
Crude OR (95% CI)	--	--	
Age-adjusted OR (95% CI)	--	--	
Spontaneous abortion[1]			
n (%)	2 (20.0%)	2 (22.2%)	4 (21.1%)
Crude OR (95% CI)	1.00 (Referent)	1.14 (0.13 – 10.39)	
Age-adjusted OR (95% CI)	1.00 (Referent)	1.51 (0.15 – 15.35)	
Live birth[1]			
n (%)	8 (42.1%)	7 (43.8%)	15 (42.9%)
Crude OR (95% CI)	1.00 (Referent)	1.07 (0.28 – 4.10)	
Age-adjusted OR (95% CI)	1.00 (Referent)	0.92 (0.23 – 3.72)	
Preterm delivery[1]			
n (%)	2 (25.0%)	2 (28.6%)	4 (26.7%)
Crude OR (95% CI)	1.00 (Referent)	1.20 (0.12 – 11.87)	
Age-adjusted OR (95% CI)	1.00 (Referent)	1.32 (0.13 – 13.61)	

Multivariate models adjusting for continuous age and continuous BMI did not converge.

[1]At the time of the analysis, 2 subjects were pregnant, and thus were excluded from the spontaneous abortion, live birth and preterm analysis.

Table 3

Simple Rank Tests for Brief Intervention and alcohol outcomes.

	Assessment Only (n=21)	Brief Intervention (n=16)
Decrease in number of drinks on a drinking day		
n	21	16
Median (Q1–Q3)	0.2 (0.0–0.5)	0.7 (0.2–1.8)
Mean (SD)	0.4 (1.0)	1.0 (1.0)
P-value		0.040
Decrease in % of drinking days in past 6 months		
n	21	16
Median (Q1–Q3)	0.1 (0.0–0.2)	0.1 (0.0–0.3)
Mean (SD)	0.1 (0.2)	0.2 (0.3)
P-value		0.177
Decrease in number of weeks drinking above SDL in past 6 months		
n	21	16
Median (Q1–Q3)	0.0 (0.0–2.0)	0.5 (0.0–7.0)
Mean (SD)	1.7 (3.5)	5.6 (9.0)
P-value		0.127
Decrease in # of binges in past 6 months		
n	21	16
Median (Q1–Q3)	0.0 (0.0–2.0)	0.5 (0.0–4.0)
Mean (SD)	1.2 (4.5)	14.5 (44.4)
P-value		0.198

One-sided P-values are from Wilcoxon exact tests.