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Problem Drinking in Women Evaluated for Infertility

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Abstract

Clinicians may wish to use the T-ACE, a screening instrument for prenatal risk drinking, for their infertile patients. Twenty-eight T-ACE negative and 23 T-ACE positive women presenting to an academic infertility clinic completed two interviews about their drinking. The 23 T-ACE positive participants were also randomized to receive a brief intervention. The T-ACE distinguished between heavier and lighter patterns of alcohol use in this sample. Moreover, it appeared that although the average quantity of alcohol consumed per drinking day was unchanged, the overall mean percentage of days drinking declined significantly from the time of enrollment to follow-up in all groups.

Defined as one year of attempted conception without success, infertility affects no fewer than six million couples in the United States.[1] Nearly half (44%) sought medical help for infertility in 1995, and it is expected that both the number of infertile women and those seeking treatment will increase in the years to come.[2] Although there are many causes of infertility, delayed childbearing and the adverse effect of increasing age on fertility have been the most frequently cited.[3]

Alcohol use is associated with altered levels of estrogen and progesterone and irregularities in the menstrual cycles and ovulation, but it is unclear how the volume of alcohol consumed will affect fertility.[4,5] However, there is increasing appreciation that such lifestyle choices can have a significant and cumulative effect on fecundability (or the ability to become pregnant in a single menstrual cycle).[6,7].

Research demonstrating the adverse impact of alcohol on fertility is accumulating. A case control study of 1050 women attending infertility clinics in the United States and Canada and 3833 control women found an increase in infertility due to ovulatory disorders (eg, anovulation and oligoovulation) or endometriosis associated with alcohol use.[8] Similarly, a study of 430 Danish couples aged twenty to thirty-five trying to conceive for the first time found that a woman's alcohol intake was associated with decreased fecundability, even among women with a weekly alcohol intake of five drinks a week or less.[9] A prospective, population-based cohort study of 7,760 Danish women identified alcohol intake to be a predictor of infertility problems in women older than thirty years and who consumed seven or more drinks a week.[10] Most recently, the long-term effects of alcohol consumption on female fertility were studied in a random sample of 7,393 Swedish women. This study found that high alcohol consumption (>140g per week, or six fluid ounces of alcohol) was associated with a significantly increased risk of infertility evaluations.[11]

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On the other hand, several other studies have not found an association between moderate alcohol consumption and reduced fecundability. A retrospective cohort study of 1,898 Canadian farm couples responding to a questionnaire about planned pregnancies in the previous thirty years did not find an association between alcohol use and infertility.[12] Moderate consumption of alcohol (defined as 2.5 to 14 drinks per week) was not associated with longer waiting times to pregnancy in a study of nearly 30,000 Danish women.[13] However, a European multi-center study on infertility and subfecundity (less than normal capacity to become pregnant in a single menstrual cycle) found an effect on time to pregnancy from a high female alcohol intake of eight or more drinks per week.[14]

While the definitive relationship between alcohol and fertility remains to be determined, it is also important to consider the prevalence of alcohol consumption by women. Among non-pregnant women of childbearing age, the use of alcohol—and, in particular, the riskier practices of frequent and binge drinking—has not changed since 1995. More than half reported at least some alcohol use, and 12.3% reported binge drinking (defined as five or more drinks per occasion) in 1999.[15] Binge drinking women reported an average of nearly 37 episodes in 2001. As binge drinking for women is more appropriately defined as four or more drinks per episode, these estimates are conservative.[16]

Thus, it seems that infertile couples seeking medical intervention might be reasonably asked to modify alcohol consumption and other lifestyle factors potentially having adverse effects on fertility.[17] Both the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists have concluded that abstinence from alcohol during pregnancy should be recommended to pre-conceptional and pregnant women.[18] As such, one strategy for physicians who invest considerable resources in the investigation and treatment of infertility is to identify women who drink alcohol and to then modify their use of alcohol through a brief intervention supporting abstinence.

The routine use of alcohol screening instruments may increase the correct identification of such women.[19] Because the goal of infertility treatment is pregnancy, the use of a screening instrument demonstrated to be effective in identifying prenatal risk drinking is practical. The T-ACE is a four-item screening questionnaire for prenatal alcohol consumption that is based on the CAGE questionnaire but substitutes a question about tolerance to alcohol for the “guilt” question, which has been demonstrated to be unreliable in women who express guilt about insignificant amounts of alcohol consumption (see Table 1).[20–22] In a study of 350 women initiating prenatal care, the T-ACE identified pregnant women with lifetime alcohol diagnoses, those who had more than two drinks per drinking day prior to pregnancy, and those who drank alcohol while pregnant. In the same study, it outperformed obstetrical staff assessment, the SMAST, and the AUDIT.[23] Hence, the T-ACE has been demonstrated to work well in groups of socially and ethnically diverse pregnant women.

The purpose of this pilot study is to test the utility of the T-ACE in a sample of women presenting for evaluation of infertility at the Center for Reproductive Medicine at the Brigham and Women’s Hospital in Boston, Mass., and to evaluate a brief intervention offered to a random subset of women meeting criteria for risk drinking.

METHODS

New patients waiting for evaluation appointments at the Center for Reproductive Medicine were asked to complete a Health and Habits Survey that included questions about cigarette use, diet, exercise, sleep, alcohol consumption, the T-ACE, stress, and willingness to participate in the study. The T-ACE was considered positive with a score of 2 or more. The tolerance question was scored 2 points if the respondent said more than two drinks to feel the

effects of alcohol. The other questions were scored one point for each positive answer. The T-ACE questions are listed in Table 1. Individuals who agreed to be contacted by phone were checked for study inclusion criteria. They were informed that data obtained as a result of the study would not become part of their medical record and their answers would not be disclosed to their physicians at the Center for Reproductive Medicine.

A consecutive sample of alcohol screen negative and alcohol screen positive subjects totaling about fifty participants was planned. This number was based on estimates of a 1:1 ratio of alcohol screen positive to negative subjects, 95% confidence, 80% power, and 10% risk drinking in the alcohol screen negative group, based on previous studies.[23,24] Inclusion criteria for the alcohol screen negative subjects were a T-ACE score less than 2 and agreement to complete diagnostic and follow-up interviews. Inclusion criteria for the alcohol screen positive subjects were a T-ACE score of 2 or more, usual alcohol consumption in excess of seven standard drinks per week or more than two drinks per episode (the National Institute on Alcohol Abuse and Alcoholism sensible drinking limits for adult women), and agreement to study terms, which included a diagnostic interview, randomization to a brief intervention session, and a follow-up interview.[25]

The diagnostic interview was administered by a research assistant and consisted of:

1. alcohol and drug abuse modules from the Structured Clinical Interview for DSM-IV to generate current and lifetime alcohol and drug diagnoses according to criteria from the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed.[26]
2. an alcohol timeline followback interview to obtain estimates of daily drinking for the three months prior to study enrollment.[27]
3. a readiness-to-change questionnaire, a twelve-item, self-administered questionnaire to measure an individual's readiness to change drinking behaviors.[28]
4. questions about whether the participant recalled her CRM physician discussing alcohol, caffeine, or cigarette use in any visit.

The alcohol screen positive participants were randomized by computer-generated assignment to receive a brief intervention with the first author that was completed after the diagnostic assessment. The brief intervention included a review of the subject's current health status, feedback on her current drinking habits and sensible drinking limits for women, establishment of the subject's drinking goal, and identification of her personal risk situations for drinking and strategies to manage the risk situations. *Personal Steps to a Healthy Choice: A Women's Guide*, was reviewed, annotated, and given to the subject for review.[29]

Sixty days after the initial assessment, all alcohol screen positive and alcohol screen negative participants completed a follow-up interview. It consisted of two measures: 1) the Timeline followback interview to obtain drinking history for the past sixty days, or the interval since the diagnostic interview: and 2) questions regarding their recollections of a CRM physician discussion about alcohol, caffeine, and tobacco smoking. The CRM physicians did not change their usual practice in this area because of the study. The Human Subjects Committee of the Brigham and Women's Hospital approved this study.

DATA ANALYSIS

Data were analyzed with *SAS 6.11* (SAS Institute, Cary, NC, 1995). Results are reported as percentages, means with standard deviations, and medians. Due to the small sample size, measures of association are not included for all measures. Nonparametric measures of association however, are presented for alcohol use variables. For comparisons of mean levels of alcohol consumption between the alcohol screen positive (brief intervention and control

subjects) and alcohol screen negative groups, the Kruskal-Wallis test was used. The Wilcoxon signed-rank test was used to evaluate change in alcohol use over time for each of the three groups. The chi-square test was used for categorical comparisons. Statistical significance was assumed for $p \leq .05$.

RESULTS

Sixty-one of approximately 75 women who returned the screening survey (81%) indicated initial interest in participating. However, three (5%) were found to be ineligible, and an additional seven (11.5%) subsequently declined to participate further. Fifty-one women (84%), of whom 23 were alcohol screen positive and 28 were alcohol screen negative, completed the initial diagnostic and sixty-day follow-up interviews. All ten screen positive participants randomized to the treatment condition completed the brief intervention after the diagnostic assessment. The overall mean age of participants was 35 years: most were married or in a committed relationship (84%). Most of the participants were European-American (71%); 11% did not disclose their ethnic/racial background and 8% were African-American. There were no significant demographic differences between the alcohol screen positive and negative subjects. Overall, three-quarters reported regular exercise and sleep habits, with an average of seven hours a night. Although not statistically significant, alcohol screen positive women were more likely to be current cigarette smokers (13% versus 7.1 %) and satisfy DSM-IV diagnostic criteria for lifetime (but not current) alcohol abuse or dependence than the alcohol screen negative group (13% versus 7.1 %). Table 2 summarizes subjects' characteristics.

The alcohol screen positive women reported significantly more alcohol consumption in the ninety days prior to enrollment than did the alcohol screen negative group. The alcohol screen positive women had more drinks per episode (mean 2.1, SD = 1.6 drinks/drinking day versus 1.3, SD = .7 drinks/drinking day, respectively, $p < .05$) and had more drinking days overall (mean 59.2% drinking days versus 30.3%, respectively, $p < .05$).

As measured by the readiness to change questionnaire, three stages of behavior change with regard to alcohol consumption were identified. The *precontemplation stage* describes those who have no intention to change their behaviors.[30] The majority (64.3%) of the alcohol screen negative subjects and nearly 40% of the alcohol screen positive subjects were at this stage (chi square = 3.21, df = 2, $p = .07$). The *contemplation stage* describes those who intend to change in the future, and only four of the 23 alcohol screen positive subjects were at this stage. The *action stage* describes those who are already making changes. Fewer than half of the alcohol screen positive (43.5%) and alcohol screen negative (35.7%) subjects were at this stage (p = NS).

All 51 participants completed the sixty-day post-assessment, follow-up interview. While the average drinks per drinking day did not change in the alcohol screen positive brief intervention group, the mean percentage of drinking days declined from 53.2% to 13.4% after the brief intervention ($p < .01$). A similar pattern was observed in the alcohol screen positive control group, which completed only the diagnostic assessment. They had no significant change in drinks per drinking day (2.2) but a reduction in the mean percentage of drinking days from 63.8% to 19.1% ($p < .001$). The alcohol screen negative group did not only change its mean drinks per drinking day (1.3) over time, but also reduced its mean percentage of drinking days from 30.3% at enrollment to 7% at follow-up ($p < .001$). Overall, the alcohol screen positive groups had more percent drinking days than the alcohol screen negative subjects at follow-up ($p < .01$).

Of note, different patterns of recollection about CRM physician discussion regarding the use of alcohol, caffeine, and tobacco use were observed when subjects were queried at the time of

assessment and then later at follow-up. At follow-up, more alcohol screen positive brief intervention subjects recalled physician discussion of alcohol use than when asked at assessment (40% versus 30%, p = NS). In contrast, fewer patients from the alcohol screen positive control group recalled physician discussion about alcohol use at follow-up than at assessment (23.1% versus 53.9%, p = NS). About one-third of the alcohol screen negative subject reported physician discussion about alcohol use at both assessment and follow-up. All three groups were fairly consistent in recalling physician discussion about caffeine use, about a third overall at both time points. All three groups demonstrated declines in recall about physician counseling regarding smoking at follow-up, with the alcohol screen positive control group having the greatest reduction. Table 3 compares the alcohol screen positive and negative groups in terms of their enrollment and follow-up health habits.

DISCUSSION

Alcohol has been identified as having a potentially adverse effect on reproductive health in women. Since alcohol consumption is widespread and increasing among women of child-bearing age, even a minor effect on fertility is of public interest.[11] The main findings of this pilot study are that the T-ACE screening instrument for pregnancy risk drinking distinguishes between heavier and lighter patterns of alcohol use in a group seeking treatment for infertility. Moreover, although it appears that the average quantity consumed per drinking day did not change in any of the groups, the overall mean percentage of days drinking declined significantly from the time of diagnostic assessment to follow-up in all groups. As in other treatment studies, the subjects seemed to respond therapeutically to assessment batteries, which in other circumstances might be considered to be the first step in treatment.[31,32]

An interesting observation is that more than half of the T-ACE-positive women who exceeded NIAAA sensible drinking limits for non-pregnant adult women and were seeking infertility treatment were not actively modifying their drinking behavior. This may signal a teaching opportunity for physicians to instruct their patients who may be otherwise unaware of the potential adverse impact of alcohol on fertility.

The effect of the brief intervention on drinking behavior is less clear-cut, but it may have reinforced awareness of the risk of drinking on pregnancy. In this study, the percentage of the alcohol screen positive control group that recalled discussing alcohol with their physician declined markedly from enrollment to follow-up, suggesting that the previous conversations were largely forgotten. In contrast, the percentage of women in the alcohol screen positive brief intervention group who recalled their physicians talking to them about alcohol increased from 30% at assessment to 40% at follow-up. Although these changes were not statistically significant, there may be some clinical importance in that the brief intervention may have reinforced the information that was already provided. It is also possible that treatment group participants conflated the brief intervention session with their usual care.

Potential limitations to this study include the small sample size, administration of the brief intervention by a physician not directly related to the Center for Reproductive Medicine, and reliance on self-report of alcohol consumption and physician counseling. While it is possible that a brief intervention given by the CRM staff may have been perceived to be more “valid” by participants, it is also possible that subjects may have been less forthcoming about the extent of their alcohol use, due to wishes to “look good” for fertility treatment. Similarly, the desire to “look good” may have resulted in the underreporting of alcohol consumption particularly at follow-up, although our previous work with pregnant women supports the idea that women are forthcoming about their alcohol consumption in a no-contingency setting and, in fact, self-report more prenatal drinking than their collateral reporters.[33,34] Other researchers have also found that study volunteers do not minimize their drinking, so that biochemical tests and

collateral informant reports are not necessary.[35] Fortunately, the tolerance question of the T-ACE is less likely to trigger denial, as the "socially correct" answer is not known and patients feel less stigmatized to answer honestly.[36] Finally, patient recall of physician health counseling was not compared to either the medical record or the gold standard of audiotape or videotape analysis. Other researchers have found that when queried, patients overestimate health promotion activity in their physician encounters and medical records underestimate them.[37]

The identification of alcohol use by women of child-bearing age is enhanced by the use of appropriate screening instruments, and it appears that the T-ACE, when self-administered to women seeking evaluation and treatment for infertility, is successful in distinguishing those with heavier from lighter patterns of regular alcohol use.[38–41] While the T-ACE positive and negative groups did not change their average consumption per drinking day, all groups reduced the number of drinking days after completing the diagnostic interview. Future work should include larger scale studies of the impact of systematic identification of and intervention for risk-drinking women with infertility on their subsequent alcohol consumption and outcome of fertility treatment.

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TABLE 1

The T-ACE[21]

T	**Tolerance:** how many drinks does it take to make you feel high?
A	Have people **annoyed** you by criticizing your drinking?
C	Have you ever felt you ought to **cut down** on your drinking?
E	**Eye-opener:** have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover?

Scores are calculated as follows: a reply of more than two drinks to the **T** question is considered a positive response and scores 2 points. An affirmative answer to the **A**, **C**, or **E** questions scores 1 point each. A total score of 2 or more points on the T-ACE is positive.

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TABLE 2

Characteristics of study subjects'

	Alcohol screen positive (*n* = 23)	Alcohol screen negative (*n* = 28)
Mean age (SD)	35 (5.3)	35 (5.4)
Marital status		
Married	83%	86%
Single	17%	14%
Ethnic background		
European American	90%	90%
African American	4%	4%
Hispanic/Latina	2%	2%
Other, including unknown	4%	4%
Health habits		
Current cigarette smoking	13%	7.1%
Regular exercise	70%	75%
Usual hours of sleep	6.9 (1 .6)	7.1 (.6)
Stress level (0 [none] to 3 [great])	2 (moderate)	2 (moderate)

Differences between the two groups were not statistically significant.

TABLE 3

Comparison of the alcohol screen positive and negative groups

At enrollment	Alcohol screen positive brief intervention (*n* = 10)	Control (*n* = 13)	Alcohol screen negative (*n* = 28)
DSM-IV lifetime alcohol Dx, %	10.0	15.4	7.1
Stage of change			
Action, %	40.0	46.2	35.7
Contemplation, %	20.0	15.4	0.0
Pre-contemplation, %	40.0	38.5	64.3
Alcohol consumption, mean drinks/drinking day*			
Enrollment	2.1 (.7)	2.3 (2.0)	1.3 (.7)‡
Follow-up	2.0(1.5)	2.2 (.8)	1.3 (.7)‡
Change	0.1 (1.0)	0.1 (1.6)	0(.6)
Mean percentage drinking days			
Enrollment	53.2 (29.7)	63.8 (59.4)	30.3 (37.2)†
Follow-up	13.4(9.6)	19.1 (20.3)	7.0 (11.5)§
Change	39.8 (24.3)¶	44.7 (44.5)¶	23.3 (30.2)¶
Recollection of physician discussion, %‡			
Alcohol, enrollment	30.0	53.9	32.0
Follow-up	40.0	23.1	32.1
Caffeine, enrollment	20.0	38.5	32.0
Follow-up	20.0	38.5	35.7
Cigarettes, enrollment	40.0	33.3	28.0
Follow-up	30.0	15.4	25.0

*Drinks per drinking day at enrollment is based on a sample of 47, and drinks per drinking day at follow-up is based on a sample of 44.

†Sample sizes for recollection data are 48.

‡$p < .05$, intergroup comparison. The Kruskal-Wallis test was used for enrollment and follow-up data.

§$p < .01$, intergroup comparison. The Kruskal-Wallis test was used for enrollment and follow-up data.

¶$p < .001$, intragroup comparison. The Wilcoxon signed rank test was used to evaluate change.