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Should fertile women quit drinking alcohol to produce better quality oocytes?

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Research Article

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Summary

Alcohol consumption has long been shown to affect both fetal health and pregnancy. In this study, antral follicle count, maturation level of oocytes including morphological assessment and number of metaphase I (MI), metaphase II (MII) and germinal vesicle (GV) stage oocytes obtained from young women (age < 30 years old) with or without alcohol consumption were investigated. In total, 20 healthy women who were social drinkers and 36 healthy women who do not consume alcohol were involved in this study. Women in both study and control groups were undergoing controlled ovarian stimulation. The antral follicle count and the number and quality of the oocytes retrieved were evaluated and recorded. In total, 635 antral follicles, 1098 follicles and 1014 oocytes with 820 MII, 72 MI and 78 GV stage oocytes were collected from the social drinkers. In the control group, 628 antral follicles, 1136 follicles and 1085 oocytes with 838 MII, 93 MI and 102 GV stage oocytes were evaluated. The results of this study showed that the antral follicle count was very similar in both groups. The number of oocytes and MII stage oocytes was slightly higher in the control group, although it was not a significant difference. This study showed that although the consumption of alcohol may have adverse effects post-implantation, it may not have a solid effect during oogenesis in young women. The results of this study are especially important in clinical settings as some women who are social drinkers undergo *in vitro* fertilization treatments.

Introduction

Infertility, defined as the inability of a natural conception following 1 year of unprotected sexual intercourse, has been shown to be affected by many factors. Both genetic and epigenetic factors may influence the reproductive lifespan. Additionally, lifestyle options, such as the use of alcohol, caffeine intake and smoking, have been shown to effect the fertility status. The effects of alcohol consumption for fetal health and pregnancy on obstetrics has long been acknowledged (Larkby and Day, 1997). Alcohol use has been associated with longer duration of pregnancy (Mutsaerts *et al*., 2012), lower rates of implantation (Rasch, 2003) and conception (Hakim *et al*., 1998), and higher risks of miscarriage (Rasch, 2003) and fetal death (Gill, 2000; Bailey and Sokol, 2011; Greenwood *et al*., 2014). Although previous studies have reported that alcohol use may affect parity (Greenlee *et al*., 2003), more recent studies have failed to show this outcome (Mikkelsen *et al*., 2016). Problems both in females [including anovulation, luteal phase dysfunction and abnormal blastocyst development (Gill, 2000)] and males [including sperm motility (Gaur *et al*., 2010), morphology, teratozoospermia and oligozoospermia (Li *et al*., 2011)] have been associated with alcohol use. Therefore, alcohol consumption has been suggested to lead to infertility (Greenwood *et al*., 2014). Studies specifically focusing on the effect of alcohol use on infertility treatment showed a negative association with the number of oocytes retrieved (Klonoff-Cohen *et al*., 2003), low fertilization rates (Rossi *et al*., 2011) and embryo qualities (Wdowiak *et al*., 2014). Furthermore, with increasing levels of maternal alcohol consumption, the number of oocytes retrieved was shown to be lowered by 13% (Klonoff-Cohen *et al*., 2003) with lower quality embryos (Wdowiak *et al*., 2014) and live birth rates were decreased by 16% (Klonoff-Cohen *et al*., 2003). When both partners were reported to have more than four drinks per week, live birth rates were lowered by 21% (Klonoff-Cohen *et al*., 2003). However, a recent cohort study reported that there was no association between alcohol intake and IVF outcomes (Firns *et al*., 2015). Therefore, to date, although some studies investigated the effect of alcohol use in *in vitro* fertilization (IVF) cycles, there was not a comprehensive conclusion. Furthermore, to our knowledge there have been no studies investigating the effect of alcohol use on IVF treatment in young fertile oocyte donors. Investigating the effects of alcohol intake on follicle growth and oocyte maturation in young fertile females may provide more valuable information rather than the analysis of infertile females. It is also important to determine all the factors that may lower live birth rates due to the invasiveness and high cost of IVF treatment. Therefore, in this study, we aimed to investigate the association on pre-conception alcohol use

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with the antral follicle count (AFC) and number, as well as quality, of oocytes retrieved in young fertile oocyte donors.

Materials and methods

Study population

The study group included fertile women who were eligible to be oocyte donors in the IVF Clinic at the Near East University Hospital between May 2015 and June 2019. Ethical approval was granted by the institutional review board (YDU/2019/71-839). The donors were between 18–30 years old. They were interviewed to obtain detailed medical history and underwent gynaecological check-up. Only the applicants with no known chronic disease and with AFC suitable with age were accepted as donors. The other criteria of being an oocyte donor included negative screening for standard infectious diseases, including HIV, hepatitis B and C and syphilis, negative screening for haemoglobinopathies and normal karyotyping analysis.

Controlled ovarian stimulation

Transvaginal ultrasound was performed for each donor between days 1 to 3 of the menstrual cycle just before ovarian stimulation to determine the AFC. Antral follicles were accepted to be follicles between 2–9 mm. The donors with follicle sizes of 10 mm or more were excluded from the stimulation protocol. Controlled ovarian stimulation cycles were started between days 1–5 of the menstrual cycle using the short antagonist protocol. Different doses of recombinant follicle-stimulating hormone were administered to each donor daily depending on AFC, body mass index (BMI) and age. An ultrasound check was performed on days 4–6 of stimulation and followed up every other day. Gonadotropin releasing hormone (GnRH) antagonist was also started to be administered daily when at least three follicles reached 14 mm in diameter. Ovulation was triggered with recombinant hCG when at least three follicles reached 17 mm in diameter. Oocytes were retrieved after 35.5 h of ovulation trigger.

Alcohol consumption

Information on alcohol consumption was collected for each donor. Donors were categorized according to their alcohol consumption; group one involved the control group with donors who did not consume any alcohol, whereas group two involved donors who were considered as social drinkers with one or two drinks per week. Social drinking falls into the category of moderate drinking, which is defined as 85–168 g of alcohol per week (Li *et al.*, 2020). Heavy drinkers were not accepted as oocyte donors. Effects of alcohol consumption on the AFC and number of oocytes retrieved with the quality of oocytes in young and fertile donors were evaluated using Student's *t*-test and GraphPad prism software. These parameters were also associated with BMI. Body weight (kg) was divided by the square of height (m^2) to calculate BMI.

Results

In this study, 56 fertile donors were analyzed. Of these donors, 20 were social drinkers, whereas 36 did not consume any alcohol. The mean age of the women who were both social drinkers and non-drinkers was 25 ± 5. The average BMI for social drinkers was 21.4, whereas for non-drinkers it was 23.4. The mean AFC for social drinkers was 19 (635 in total), the mean number of follicles collected was 32 (1098 in total) and the mean number of oocytes collected was 30 (1014 in total; Table 1). Of the 30 oocytes collected, the mean metaphase II (MII) was 24 (820), two (72) were metaphase I (MI), three (72) were germinal vesicle (GV) and two had anomalies. The women who did not consume any alcohol had a mean AFC of 20 (628 in total), 34 follicles (1136) collected with 32 (1085) oocytes. Of these oocytes, a mean of 25 (838) were MII, three (93) were MI, three (102) were GV and one had cytoplasmic anomaly with vacuoles and fragments (Table 1). Although the AFC, number of follicles and oocytes were higher in women who do not consume any alcohol compared with women who were social drinkers, there was no statistical difference in these parameters ($P > 0.05$). Furthermore, the numbers of GV, MI and MII oocytes were similar in each group. Cytoplasmic anomalies of the oocytes were same per number of follicles at the time of oocyte retrieval. Ratios of MII oocytes per antral follicle count and number of follicles at the time of oocyte retrieval were also similar in both groups (MII/AFC = 1.29 and MII/follicles = 0.75 in social drinkers; MII/AFC = 1.33 and MII/follicles = 0.75 in non-drinkers).

Table 1. Summary of oocyte details

	Social drinkers	Non-drinkers
Mean AFC (total number)	19 (645)	20 (628)
Mean number of follicles at ovum pick-up (total number)	32 (1098)	34 (1136)
Mean number of oocytes (total number)	30 (1014)	32 (1085)
Mean number of MII (total number)	24 (820)	25 (838)
Mean number of MI (total number)	2 (72)	3 (93)
Mean number of GV (total number)	3 (72)	3 (102)
Number of oocytes with cytoplasmic anomalies	2	1

Discussion

Fertility of both females and males are affected by many factors, including lifestyle choices. Alcohol consumption is one of the aspects that has an influence in female reproduction as well as fertility. Infertile patients are more willing to change their lifestyle when they are trying to conceive, especially during IVF treatments. Although couples tend to reduce their alcohol consumption during IVF treatments, there is no clear-cut recommendation for these couples. Therefore, it is crucial to investigate the possible adverse effects of alcohol use in gametogenesis, embryogenesis and during fetal development to provide these couples the essential counselling. Therefore, this study investigated the effects of alcohol consumption on the AFC and total number and quality of the oocytes retrieved.

The results of this study showed that, although the numbers of oocytes collected as well as the number of MII stage oocytes were slightly higher in the women who do not consume any alcohol, there was no significant difference. Furthermore, ratios of MII oocytes per AFC and numbers of follicles at the time of oocyte retrieval were also similar in both groups. Correspondingly both the numbers of oocytes retrieved, as well as the pregnancy outcome, have been shown to be affected by the alcohol intake, although these were not statistically different in drinkers and non-drinkers (Klonoff-Cohen *et al.*, 2003). Similar results were

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also reported by previously published studies (Jong *et al*., 2014; Firns *et al*., 2015). To our knowledge, no previous study has investigated cytoplasmic anomalies in oocytes in women who consume alcohol. The results of this study showed that one or two alcoholic drinks per week did not have an effect on cytoplasmic anomalies of the oocyte. Studies investigating the IVF outcome reported an unfavourable association with alcohol consumption (Klonoff-Cohen *et al*., 2003; Rossi *et al*., 2011). It is possible that the amount of alcohol consumption is the key factor, as with increased number of drinks, such as more than four alcoholic drinks per week, the live birth rates were decreased by approximately 20% (Klonoff-Cohen *et al*., 2003). Therefore, the amount of alcohol intake influences live birth rates (Rossi *et al*., 2011). Furthermore, although alcohol consumption was reported not to affect the first cycle of IVF, everyday alcohol use showed a two-fold higher miscarriage rate in the first IVF cycle (Dogde *et al*., 2017). However, more recent data have shown that social drinking does not influence the number of embryos and pregnancy rates, although in the first cycle, a two-fold increased miscarriage risk was observed in daily drinkers compared with non-drinkers (Dogde *et al*., 2017).

In conclusion, it is crucial to determine the role of alcohol intake in reproduction. As IVF is an invasive, tedious and expensive procedure in which the patients are not only affected economically, but also psychologically, it is important to guide and counsel patients properly to achieve the best outcome. The results of this study suggested that pre-pregnancy social alcohol consumption did not affect oogenesis in young fertile women. However, more detailed studies, including the exact amount as well as the type of alcohol, will be performed. Future studies will focus on the pre-implantation embryo development of women, as well as men, who are social drinkers.

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Conflicts of interest. None.

Ethical standards. Ethical approval was granted by the institutional review board (YDU/2019/71–839).

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