Effect of Hookah (water pipe) smoking on Anti-Mullerian Hormone levels

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Abstract

Purpose: Hookah (water pipe) smoking, an ancient method of tobacco smoking, is regaining widespread popularity all over the world. Although research in this field is still lacking, its harmful effect on human health through the increased risk of cardiovascular disease, infection, and cancer has been proven. Cigarette smoking has been found to have a detrimental effect on reproductive function. However, no data about the effect of hookah smoking on human fertility or reproductive outcomes are available. In this study, we aimed to determine if smoking hookah has a harmful effect on human ovarian reserve, anti-Mullerian hormone levels, and cycle regularity. **Methods:** A total of 100 healthy women within the 25-35 years age range undergoing laboratory investigations were randomly chosen to participate. After obtaining consent, they filled a questionnaire about smoking habits and menstrual data. Blood samples were withdrawn for anti-Mullerian hormone testing. The anti-Mullerian hormone levels of 50 women smoking hookah but not cigarettes were compared to 50 non-smoking women. Collected data were analyzed by analysis of variance and independent samples T-test. **Results:** There were no significant differences in mean anti-Mullerian hormone levels and cycle regularity between hookah smokers and non-smokers. **Conclusion:** Hookah smoking has no significant effect on anti-Mullerian hormone levels.

Introduction

Hookah (shisha or water pipe) is a method of smoking tobacco invented in the 16th century as an attempt to purify the smoke by passing through water, which is an unproven concept (Kadhum et al., 2015). Due to this misconception, its consumption has risen worldwide, especially among teenagers and college students (Bou Fakhreddine et al., 2014). Contrarily to the widespread misconception, water pipe smoking is associated with different short- and long-term adverse health effects (El-Zaatri et al., 2015). For example, it has been reported that hookah smoking may increase the risk of coronary heart disease and arrhythmias (Kadhum et al., 2015). Moreover, it has been found that hookah smokers have higher levels of low-density lipoprotein (Al Numair et al., 2007).

A systematic review and meta-analysis included 50 studies and found that hookah smoking was significantly associated with chronic obstructive pulmonary disease, oral cancer, lung cancer, low birth weight, metabolic syndrome and cardiovascular diseases (Waziry et al., 2016).

Anti-Mullerian hormone (AMH) concentration is proportional to the number of the developing antral follicles since it is mainly derived from its granulosa cells. As the number of the antral follicles is comparable to the primordial follicle pool, AMH can indirectly represent the ovarian reserve. Accordingly, it is considered as a marker of ovarian aging (Dewailly et al., 2014).

The AMH level is relatively stable through the menstrual cycle, as indicated by multiple studies. This is explained by the fact that the dominant follicle and corpus luteum do not secrete AMH; moreover, AMH serum levels are not affected by the growth of the dominant follicle (Dewailly et al., 2014; Broer et al., 2014). Apoptosis is the mechanism for follicular depletion during the reproductive life (May-Panloup et al.,

2016). In fact, more than 99.9% of oocytes present at birth undergo atresia at some point of their maturation stages (Sükür et al., 2014; Li et al., 2012; Alviggi et al., 2009). To maintain a regular menstrual cycle, a threshold number of follicles is essential (Alviggi et al., 2009). Therefore, irregular menstrual cycles is a characteristic of the peri-menopausal period (Alviggi et al., 2009). For that reason, in normally ovulating women, menses are usually predictable and regular (Practice Committee of the American Society for Reproductive Medicine, 2018). Consequently, cycle regularity is considered as a clinical indicator of regular ovulation (Fritz and Speroff, 2011).

It has been found that blood nicotine concentration in daily hookah smokers is similar to that found in half-pack daily cigarette smokers (Neergaard et al., 2007). Furthermore, hookah smokers are exposed to high concentration of toxicants (Barnett et al., 2017). A typical hookah session, which may last at least 45 minutes, exposes users to high amounts of carbon monoxide, 30 times more carcinogenic polycyclic aromatic hydrocarbons, and 40 times more tar compared to smoking a single cigarette (Barnett et al., 2017). Some studies have shown that chemicals in cigarette smoke appear to expedite follicular depletion and the loss of reproductive function, expressed by a lower antral follicle count and serum AMH levels (Practice Committee of the American Society for Reproductive Medicine, 2018; Firms et al., 2015). Furthermore, it has been demonstrated by longitudinal studies that AMH levels decline more quickly in smoking women within reproductive age (Practice Committee of the American Society for Reproductive Medicine, 2018).

Little is known about the effects of hookah smoking, especially after long-term exposure, on female reproductive health. Hannoun et al. (2010) found no significant difference in the clinical pregnancy rate between hookah (43.6%) and non-hookah smokers (51.0%); however, a lower rate was found in cigarette smokers (23.8%).

AMH is primarily expressed by the granulosa cells of growing secondary, pre-antral, and early antral follicles. It is strongly related to ovarian follicle status and it is a marker of assisted reproductive technology outcomes (Freour et al., 2008). Several studies showed a detrimental effect of cigarette smoking on AMH levels but no studies analyzed the effect of hookah smoking on female fertility or AMH levels (Szkoup et al., 2018; Fuentes et al., 2013; Waylen et al., 2010). To the best of our knowledge, this is the first study to explore the effect of Hookah smoking on ovarian reserve and AMH levels.

Material And Methods

One hundred healthy non-cigarette smoking women between 20–35 years old were divided into two groups according to hookah smoking status (50 hookah smokers and 50 non-smokers). As fertility and ovarian reserve decline after the age of 35, women over this age were not included. Exclusion criteria also included having either a chronic medical illness, e.g., diabetes, hypertension, thyroid disease, autoimmune disease or connective tissue disease; and using hormonal contraception.

After obtaining Ethical Committee Board approval, participants were chosen randomly from women who met the inclusion criteria attending Josante Healthcare laboratory for general investigations such as

annual complete blood count and vitamin D level. Fifty current hookah smokers and 50 non-hookah smokers were selected. After proper counseling and signing the consent form mentioning that participating in the study will include answering a questionnaire, in addition to providing a blood sample for AMH testing with the confirmation that all information will be confidential, a validated questionnaire was filled by each participant and a blood sample was withdrawn. Before starting the study, the questionnaire was presented to 3 gynecology consultants and 3 patients meeting the inclusion criteria and were asked to answer the questionnaire to make sure it was clearly understood. The questionnaire consisted 3 sections: demographic information; hookah smoking status; and menstrual cycle regularity, frequency, and dysmenorrhea. Participants were asked two questions to assess cycle regularity. The first was a yes/no question asking whether the cycle was regular or not. Participants were then asked to record menstruation frequency; those who answered yes to the first question and had a variation in frequency of not more than 3 days were considered as having cycle regularity. Five cc of blood were collected and allowed to clot for 30 minutes. After that, centrifugation for 10 minutes at 4500 cycles per minute was performed before analysis using Cobas 6000 (F. Hoffmann-La Roche Ltd, Basel, Switzerland). A total of 2–3 cc of serum was used for the analysis. Calibration and measurement of AMH levels was done using an Elecsys AMH kit (F. Hoffmann-La Roche Ltd, Basel, Switzerland) was used. Mean AMH levels were compared between Hookah smokers and non-smokers using a one-tailed independent samples t-test. Frequencies of different clinical parameters were compared with smoking Hookah. Correlation between different parameters and smoking Hookah was determined using Pearson's Chi-Square test.SPSS for Windows 17.0 (IBM, Armonk, NY) was used for all analyses. P values < 0.05 were considered significant.

Results

The average age of participants was 25 ± 0.9 years. The AMH levels of hookah smokers and non-smokers are expressed as means $\pm$ standard error. The mean AMH level was 2.654 ± 0.270 ng/ml in hookah smokers and 2.449 ± 0.259 ng/ml in non-hookah smokers. This difference was not significant, P value 0.55. (Table 1)

Table 1
Mean AMH levels in hookah smokers versus non-smokers

Smoking status	Mean AMH value (ng/ml) $\pm$ SE
Hookah smokers	2.654 ± 0.270
Hookah smokers	2.449 ± 0.259

SE: standard error

The pattern of menstrual cycle regularity was similar between hookah smokers 44(88%) and non-smokers 44(88%). There was no difference in the percentage of patients with irregular menstrual cycle in

the hookah smoking 6(12%) and non-smoking groups 6 (12%), P value 0.088.

The sub-analysis of mean AMH levels between Hookah smokers and non-smokers with regular and irregular cycles found no significant difference in mean AMH levels between participants with regular cycles, as shown in Table 2, P value 0.074.

Table 2
AMH values in relation to cycle regularity.

Smoking status	Cycle regularity	Mean AMH values (ng/ml) ± SE
Hookah smokers	Regular	2.77759 ± 0.289
	Irregular	2.44050 ± 0.895
Non-smokers	Regular	2.4158 ± 0.272
	Irregular	2.2822 ± 0.861

SE: standard error

Discussion

No significant differences were found in AMH serum levels or cycle regularity between hookah smokers and non-smokers. A further sub-analysis of AMH levels among patients with irregular cycles also showed no differences.

Nevertheless, considering the quantity of toxicants presents in hookah, it would be expected to find a harmful effect of hookah smoking. Plante et al. (2010) found that active cigarette smoking is associated with lower AMH levels in the late reproductive age, between 38–50 years old. Furthermore, it is known that active cigarette smoking is associated with an earlier age of menopause (Oboni et al., 2016). This could be explained by the smoking effect on ovarian reserve. However, no studies addressed the mechanism of these changes or investigated the effect of hookah smoking on ovarian reserve, AMH levels, or menstrual cycle characteristics.

Our findings could be explained by the low number of patients, which may not reflect the real effect of hookah smoking. Our preliminary data support the development of further studies among heavy hookah smokers to identify any changes in AMH levels and at which level of smoking they start to appear. In addition, measuring the antral follicle count would reinforce the results.

Conclusion

Our findings indicate that Hookah smoking has no effect on ovarian reserve. Hookah smoking is a globally emerging habit and it is crucial to conduct high-quality studies with a larger number of

participants to explore its effect in female reproductive function.

Declarations

Ethical Approval:

Ethical approval was obtained from Institutional Review Board of Jordan University of Science & Technology- King Abdullah University Hospital- Jordan

Availability of Data

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author Contributions:

Soha Albeitawi: Conceptualization, methodology, project administration, resources, supervision, visualization, writing original draft, writing review and editing

Lama Al-mehaisen: Methodology, validation, review and editing

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