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The effect of premature ovarian insufficiency on nasal mucociliary clearance time

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ABSTRACT

Premature ovarian insufficiency (POI) is a global health concern for women and affects several systems, such as cardiovascular system, autoimmune disease, and psychological status. The aim of this study was to investigate the effect of POI on nasal mucociliary clearance time via saccharin test by comparing postmenopausal women and healthy controls. Thirty-five (35) patients with POI, 35 healthy postmenopausal women and 35 healthy controls were recruited in this study. All study participants underwent measurements of nasal mucociliary clearance time via saccharine test. When women with POI and postmenopausal women compared with the controls, nasal mucociliary clearance time was longer in both women with POI and postmenopausal women. When women with POI were compared with postmenopausal women, the nasal mucociliary clearance time was not difference between two groups. There was a significant prolonged nasal mucociliary clearance time in the women with POI and postmenopausal women. Lower serum estradiol levels in women with POI as well as postmenopausal women had an adverse effect of nasal mucociliary clearance time.

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Introduction

Sinus health in humans is maintained by means of the mucociliary clearance mechanism. This is the main system for the non-specific defense against constant organic and inorganic contamination transported by air. It works by trapping particles and microorganisms in the mucus and then transporting the mucous film to the pharynx, where it is eliminated via coughing or swallowing [1]. However, the ultrastructural elements of the mucosa change and delay mucociliary clearance of the nasal epithelium, causing chronic rhinosinusitis and respiratory tract diseases. The mucociliary clearance mechanism relies on the complex interaction between motile cilia, glandular secretions, and the anatomy of the sinuses and nasal environment. There is a general opinion that physiological and hormonal changes associated with various female conditions occurring during a woman's lifespan may influence rhinological functions and disease. Several changes in the nasal mucosa during the menstrual cycle, pregnancy, oral contraceptive use, and postmenopausal period were investigated in multiple studies [2–4]. Moreover, research has shown the effects of sexual hormones on otorhinolaryngology targets, both in terms of morphological and functional features [5–8].

Premature ovarian insufficiency (POI) is characterized by amenorrhea, hypo-estrogenism and elevated follicle-stimulating hormone (FSH) levels in women under the age of 40 years. This condition affects 1–2% of women younger than 40 years [9]. POI is associated with a relatively high risk of cardiovascular disease, autoimmune disorders, osteoporosis, cognitive decline, psychological distress and depression, decreased sexual and general well-being, and mortality [10]. However, there is no research on its effects on nasal functions in the literature. The aim of this

study was to investigate the effect of POI on nasal mucociliary clearance time.

Materials and methods

This prospective case-control study was carried out in the Department of Otolaryngology of Malatya State Hospital between June and December 2017. The study was approved by the local ethical review board, and all patients entered this study only after informed consent was obtained. The same otorhinolaryngology specialist (I.K.) who was blind to the patient's hormonal status performed ear and nasal examination of all study participants and saccharine test.

One-hundred and five (105) patients were enrolled in the study, and they were divided into three groups, as follows: women with POI ($n = 35$); women in the postmenopausal period ($n = 35$); and a control group ($n = 35$). POI was diagnosed by amenorrhea for at least 6 months and serum follicle stimulating hormone (FSH) levels found to be greater than 40 mIU/mL on two occasions, at least 1 month apart, and age under 40 years [10]. Postmenopausal period was defined as amenorrhea for at least 1 year, with FSH levels up to 40 mIU/mL, estradiol (E_2) levels lower than 30 pg/mL, and age over 50 years [10]. The control group consisted of healthy women who still menstruated regularly. The body mass index (BMI) (kg/m^2), FSH, E_2 , luteinizing hormone (LH), thyroid-stimulating hormone (TSH), prolactin (PRL), blood glucose level and hemoglobin values of all patients were investigated.

Patients with any of the following condition were excluded: with a diagnosis of any nasal pathology, chronic sinusitis, allergy or asthma, coexisting systemic diseases, prior nasal surgery history, and with upper respiratory tract infection during the previous

2 months. In addition to women with smoke cigarette and used any medication were excluded from this study.

The saccharin test is an easy, low-cost and painless clinical test for defining nasal mucociliary clearance time [11]. The patients did not to eat or drink anything for 1 h before the test. Then, 1/4 of a saccharin tablet is placed on the surface of the inferior nasal concha. The patients must breathe normally without sneezing or blowing their noses during the test. The saccharine particle is carried by means of ciliary transport along the entire nostril until it reaches the oropharynx, consequently a characteristic sweet taste can be perceived. The time was recorded to the minute (min) and the test was considered complete [12].

Statistical analysis

All analyses were conducted using SPSS 15.0 (SPSS® for Windows 15.0, Chicago, USA). The normality of the distribution was assessed using the Kolmogorov–Smirnov test. Variables with a normal distribution were presented as the mean ± standard deviation, and variables with a skewed distribution were presented as the median and interquartile range (IQR). The groups were compared with the Student *t*-test for parametric data and Mann–Whitney U-test for nonparametric data. A *p* values less than .05 was considered statistically significant.

Result

The baseline characteristics and hormone levels of study participants are shown in Table 1. Among women in the POI group, the mean age was 31.7 ± 5.6 years, while postmenopausal women group, it was 54.8 ± 5.8 years. The mean age of controls was 29.6 ± 5.6 years. There was no statistically significant difference regarding the age of the women with POI and controls (*p* = .08). However, the mean age of postmenopausal women was statistically significantly higher than both the mean ages of women with POI and controls (*both values p* < .001). The mean BMI was 28.8 ± 2.6 kg/m² in women with POI, 29.1 ± 3.4 kg/m² in postmenopausal women, and 27.9 ± 3.0 kg/m² in the controls. There was no statistical significance between the three groups. The median FSH level was 68.6 (43.2–95.9) mIU/mL in women with POI, 52.2 (41.1–73.7) mIU/mL postmenopausal women, and 6.2 (4.1–8.2) mIU/mL in the controls. The median E₂ in women

with POI was 21.8 (11.5–34) pg/mL, while it was 16 (12–31) pg/mL in postmenopausal women and 76 (53–111) pg/mL in the controls.

When women with POI and postmenopausal women were compared with the controls, serum FSH levels were higher in both study groups than controls (*both p* values < .001). When the median FSH level of women with POI was compared with that of postmenopausal women, there was no statistically significant difference between the two groups (*p* = .96). The median LH level was 48.8 (36.3–61.3) mIU/mL in women with POI, 47.3 (30–61.4) mIU/mL in postmenopausal women, and 6.1 (4.1–8.3) mIU/mL in the controls. When women with POI and postmenopausal women were compared with controls, serum LH levels were higher in both study groups than controls (*both p* values < .001). When median LH level of women with POI was compared with that of postmenopausal women, there was no statistically significant difference between the two groups (*p* = 0.81). When the median E₂ levels of women with POI and postmenopausal women were compared with those of the controls, the median E₂ serum level was lower in both study groups (*both p* values < .001). When women with POI were compared with postmenopausal women, the serum E₂ levels were not statistically significantly different between the two groups (*p* = .43). The median PRL values were 9.7 (6.9–17.4) µg/L in women with POI, 15.7 (7.5–23.1) µg/L in postmenopausal women, and 11.8 (7–16.5) µg/L in controls. The median TSH level was 1.7 (1.1–2.3) mIU/L in women with POI, 1.7 (1.2–2.5) mIU/L in postmenopausal women, and 1.4 (1.1–1.9) mIU/L in controls. The median hemoglobin values were 13.8 (12–14.8) g/dL in women with POI, 12.8 (11.9–14.5) g/dL in postmenopausal women, and 12.5 (11.9–14.7) g/dL in controls. The median glucose level was 99 (89–110) mg/dL in women with POI, 95 (89–101) mg/dL in postmenopausal women, and 93 (87.5–95.7) mg/dL in controls. There was no statistically significant differences in PRL, TSH, glucose and hemoglobin levels between the three groups (Table 1).

The median nasal mucociliary clearance time was 9.3 (7.05–12.07) min. in women with POI, 9 (7.4–11.6) min. in postmenopausal women, and 6.2 (4.–8.1) min. in controls. The mean nasal mucociliary clearance times were statistically longer in both the study groups than controls (*both p* values < .001). However, the median nasal mucociliary clearance time was not statistically significantly different between women with POI and postmenopausal women (*p* = .75) (Figure 1).

Table 1. Clinical characteristics and hormonal profile of study participants

	POI <i>n</i> = 35	Menopause <i>n</i> = 35	Control <i>n</i> = 35	<i>p</i> ₁	<i>p</i> ₂	<i>p</i> ₃
Age (y)	31.7 ± 5.6	54.8 ± 5.8	29.6 ± 5.6	.08	<.001*	<.001*
BMI (kg/m ²)	28.8 ± 2.6	29.1 ± 3.4	27.9 ± 3.0	.54	.27	.49
FSH (mIU/mL)	68.6 (43.2–95.9)	52.2 (41.1–73.7)	6.2 (4.1–8.2)	<.001*	<.001*	.96
Estradiol (pg/mL)	21.8 (11.5–34)	16 (12–31)	76 (53–111)	<.001*	<.001*	.43
LH (mIU/mL)	48.8 (36.3–61.3)	47.3 (30–61.4)	6.1 (4.1–8.3)	<.001*	<.001*	.81
PRL (µg/L)	9.7 (6.9–17.4)	15.7 (7.5–23.1)	11.8 (7–16.5)	.81	.27	.30
TSH (mIU/L)	1.7 (1.1–2.3)	1.7 (1.2–2.5)	1.4 (1.1–1.9)	.30	.13	.43
Glucose (mg/dL)	99 (89–110)	95 (89–101)	93 (87.5–95.7)	.08	.33	.3
Hemoglobin (g/dL)	13.8 (12–14.8)	12.8 (11.9–14.5)	12.5 (11.9–14.7)	.3	.78	0.52
NCT (min)	9.44 ± 2.7	9.3 ± 2.6	6.04 ± 1.9	< 0.001*	<.001*	.75
Cigarette Smoking	-	-	-			
Alcohol Consumption	-	-	-			

NCT: Nasal mucociliary clearance time.

Variables with a normal distribution were presented as mean ± standard deviation, and variables with a skewed distribution were presented as median and interquartile range (IQR).

*p*₁ = group POI vs control;

*p*₂ = group menopause vs controls;

*p*₃ = group POI vs group menopause. **p* < .005.

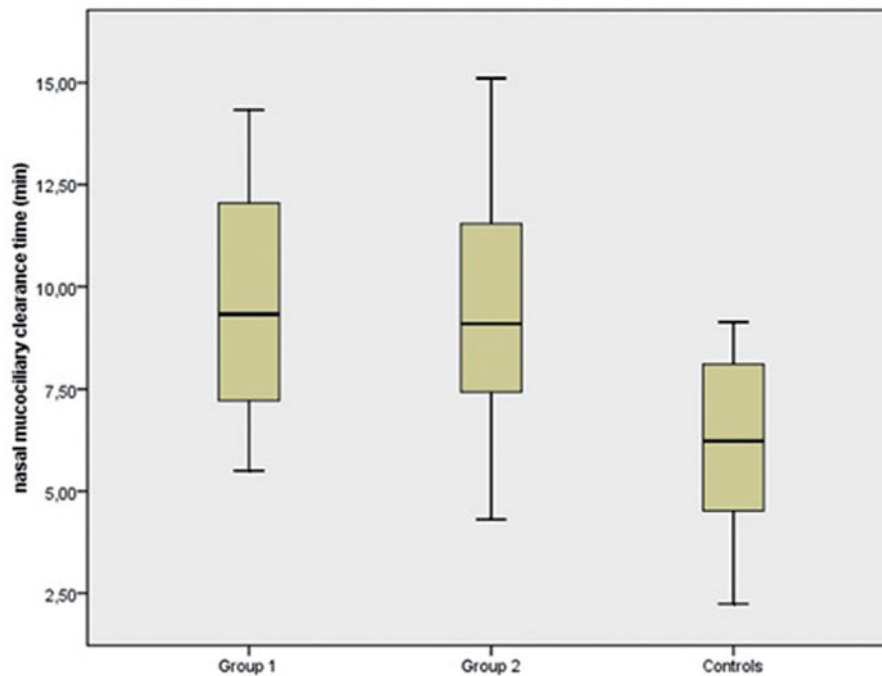


Figure 1. Mean nasal mucociliary clearance time of the study groups. Group 1 = women with POI, Group 2 = women with menopause

Discussion

In this study, we found that women with POI had prolonged nasal mucociliary clearance time. To the best of our knowledge, this is the first study showing the adverse effects of POI on nasal mucociliary clearance functions.

All measurements were performed by the same otolaryngologist, who was blind to the hormonal and medication status of the subjects. In addition, women with POI and controls were cross-matched for age and BMI. These represent the strengths of this study. However, the limitations of the study are the small sample size and nasal mucociliary clearance time was only analyzed via the saccharin test.

In this study, the nasal mucociliary clearance times of both study groups were prolonged compared with those of the controls. In the present study, women with POI had elevated FSH and decreased E_2 levels. In an animal study, Brittebo et al. showed that estrogen receptors are also present in the nasal mucosa [13]. Moreover, Philpott et al. found that estrogen receptors are present in the human nasal mucosa. In addition, they showed that there is a significant positive relationship between the mean number of positive estrogen receptors cells and nasal symptoms [14]. Caruso et al. investigated the cytological characteristics of the nasal respiratory epithelium, and they found that the nasal respiratory epithelium is an estrogen target, with similar morphological features to the vaginal mucosa [15]. The cytological features of epithelial smears from both organs showed similar trophic characteristics in postmenopausal women. The significance of these receptors is unclear, as the mechanism of interaction has yet to be understood [16]. Finally, Topozada et al. [4] demonstrated that the menopausal period causes several transformations in the nasal structures, and these changes are due to low blood estrogen level.

In this study, we found that postmenopausal women had prolonged mucociliary clearance times. In a clinical study, the researcher demonstrated that a statistically significantly high proportion of postmenopausal patients reported at least one symptom of rhinitis within a 1-year period [17]. Likewise,

questionnaire-based survey of 3724 women found a statistically significantly higher reporting of rhinitis symptoms in the postmenopausal subgroup [18]. In contrast, Yildirim et al. found that the results of acoustic rhinometry, rhinomanometry, and peak inspiratory nasal flow were not affected in postmenopausal period [19]. Ozler et al. investigated the effects of menopause on the nasal mucociliary clearance time by comparing the results of premenopausal and postmenopausal women. They found that the nasal mucociliary clearance time in postmenopausal women was significantly longer than in premenopausal women; however, the participants in this study belonged to similar age group and the groups probably had similar FSH and E_2 levels, although the study did not clarify this [20].

Conclusions

This study showed that both women with POI and postmenopausal women had prolonged nasal mucociliary clearance times. The result of this study showing lengthened nasociliary mucosal clearance time may increase the tendency toward upper respiratory tract infections due to disrupted nasal physiology. To confirm the possible clinical outcomes of this study, there is a need for epidemiological studies revealing the incidence of sinus and nasal clinical problems in POI and postmenopausal period.

Disclosure statement

The authors report no conflict of interest.

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