

Menopausal hormone therapy may increase non-allergic rhinitis among postmenopausal women: Results from the Korea National Health and Nutrition Examination Survey (2010–2012)

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ABSTRACT

Objectives: To investigate the association between menopausal hormone therapy (MHT) and chronic rhinitis.

Methods: The data used in this study were derived from the Korea National Health and Nutrition Examination Survey. The analysis included 2967 postmenopausal women under 70 years of age, and with no missing data. The questionnaires about MHT, current life habits, reproductive history, and rhinitis were reviewed. The levels of total IgE and specific IgE for *Dermatophagoides farinae*, cockroaches, and dogs were measured, using approximately 10% of all samples. We compared women who were users of MHT and non-users of MHT. We also compared women with and without chronic rhinitis.

Results: Of 2967 women matching the study criteria, 567 were MHT users. The proportion of general rhinitis symptoms was greater among MHT users (24.5%) than among MHT non-users (18.9%, $p = 0.003$). The proportion of cases of rhinorrhea or posterior nasal drip was also greater among MHT users (6.3% vs. 4.3%, $p = 0.042$), while there were no differences between the two groups in the proportion of cases of nasal obstruction. There were no differences in total IgE and specific IgE levels between the two groups. MHT was used by 23.4% of women with chronic rhinitis and 18.0% of women without chronic rhinitis. Age, waist circumference, and body mass index were also increased among women without chronic rhinitis compared with those with chronic rhinitis.

Conclusions: MHT may cause non-allergic rhinitis in postmenopausal women. Age and obesity may also affect the occurrence of non-allergic rhinitis in postmenopausal women.

1. Introduction

Rhinitis is an inflammatory disease of the nasal mucosa [1]. Common symptoms are nasal obstruction, rhinorrhea, posterior nasal drip, and itching. It is an irritating disease, impeding work, study, and sleep, and causing deterioration in the quality of life [1]. Rhinitis is triggered by various causes. It has been postulated for some time that female sex hormones may cause rhinitis.

A number of studies support the association between female sex hormones and rhinitis. Philpott et al. found that estrogen β -receptors were present in the nasal epithelium and that their number correlated

with the severity of the rhinitis symptoms [2]. Hamano et al. showed that 17 β -estradiol significantly enhanced eosinophil adhesion to human mucosal microvascular endothelial cells, and its granulation [3], and that 17 β -estradiol and progesterone also increased the expression of histamine 1 receptor [4]. A further study by Topozada et al. reported that the oral contraceptive pill induced interepithelial edema, glandular hyperplasia, histiocytic proliferation, and fibrous tissue deposition in human nasal mucosa [5].

There is also indirect evidence on female sex hormones and rhinitis. The menstrual cycle affects nasal congestion [6] and 20–30% of women without rhinitis before pregnancy complain of nasal congestion after

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pregnancy [1]. Furthermore, the oral contraceptive frequently causes nasal congestion [6]. However, some studies have challenged the association between female sex hormones and rhinitis [7,8].

Menopausal hormone therapy (MHT) has long been prescribed for the treatment of postmenopausal changes, including vasomotor instability (hot flashes, sweating, and palpitations); urogenital symptoms (vaginal dryness, soreness, dyspareunia, and urinary frequency and urgency); neurogenic symptoms (mood change, insomnia, depression, and anxiety); progressive bone loss; and increased susceptibility to heart disease [9]. Different types and dosing schedules of MHT are available. We postulated that MHT could be a useful marker for evaluating the causative effect of female sex hormones on rhinitis. Firstly, we investigated the isolated effect of female sex hormones, administered as MHT, by comparison with subjects who were not receiving MHT. The effect of endogenous female sex hormones during MHT can be excluded because all participants were postmenopausal women. Conversely, the effects of uncontrollable endogenous female hormones need to be taken into account when examining rhinitis and its association with the menstrual cycle, pregnancy, or oral contraceptives. Secondly, female sex hormones are administered continuously, for a prolonged period, during MHT; therefore, we could observe the long-term effect of female sex hormones on rhinitis. The menstrual cycle involves changes occurring on a monthly-basis, unlike pregnancy with a duration of 10 months, so the effect of female sex hormones is of short duration. Furthermore, female hormonal levels fluctuate significantly during the menstrual cycle and pregnancy [10]. Despite these advantages, only one published study has examined the association between MHT and rhinitis [8]. The authors concluded that MHT does not affect the nose; however, they observed only 20 postmenopausal women and the mean period of MHT use was only 101.9 days.

The Korea National Health and Nutrition Examination Survey (KNHANES) is a nationwide survey of a representative population of non-institutionalized Korean residents. The survey was designed to assess national health and nutritional status and consists of a health interview, nutritional assessment, and health examination. Although KNHANES is a cross-sectional study, the population size is sufficiently large and the study quality is satisfactory, so we used the KNHANES data in this study to investigate the association between MHT and rhinitis.

2. Materials and methods

2.1. Study participants

The data used in this study were derived from the KNHANES V (2010–2012). Samples were identified using a multi-stage clustered probability design. The final sampling units for this survey were drawn from approximately 200,000 primary sampling units, geographically defined regions for the whole country. The survey used data derived from approximately 10,000 individuals each year, between 2010 and 2012. Trained interviewers conducted all the interviews using structured questionnaires to obtain information, including sociodemographic factors, health-related factors, lifestyle factors, the use of medical services, and female reproductive factors. A total of 13,918 women participated in the KNHANES V (2010–2012). The analysis in this study involved a total of 2967 postmenopausal women under 70 years of age (the youngest women's age was 38 years), and with no missing data for the question regarding MHT and outcome variables. Women who became postmenopausal due to gynecological surgery were excluded (Fig. 1). All participants agreed to provide written consent to participate in KNHANES. This study was determined exempt from ethics review by the Institutional Review Board of the Konkuk University Hospital due to the use of publicly available data.

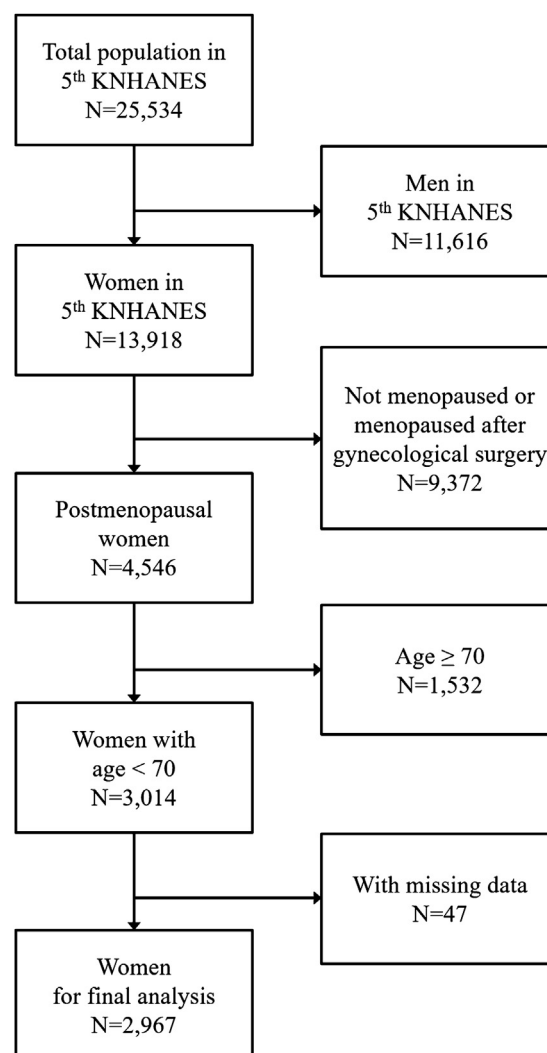


Fig. 1.

Table 1

Questionnaires about menopausal hormone therapy (MHT), current lifestyle habits, reproductive history, and rhinitis.

Questionnaires about MHT
• Have you received MHT for at least 1 month?
• When did you start MHT?
• How long have you taken MHT for?
Questionnaires about current life habits
• Do you smoke?
• Do you drink more than once a month?
• Do you exercise at a greater than moderate intensity, more than once a week?
Questionnaires about reproductive history
• How many times did you give birth?
• Did you breastfeed?
Questionnaires about rhinitis
• Have you ever experienced rhinitis symptoms, such as, sneezing, rhinorrhea, nasal obstruction, or nasal itching, which were not related to the common cold (sore throat or fever) over the past year?
• Have you experienced continuous rhinorrhea or posterior nasal drip for at least the past 3 months?
• Have you experienced continuous nasal obstruction for at least 3 months?

2.2. Measures

The questionnaires about MHT, current life habits, reproductive history, and rhinitis are summarized in Table 1. Among physical

characteristics, age, waist circumference, and body mass index (BMI) were analyzed. The body measurement was performed by a trained examiner. For IgE measurement, approximately 10% of total samples were randomly selected. The level of total IgE and specific IgE for *Dermatophagoides farinae*, cockroaches, and dogs, were measured using ImmunoCAP. Due to limited resources, the number of subjects and test items was reduced.

2.3. Statistical analysis

We compared women who were users of MHT and non-users of MHT. We also compared women with and without chronic rhinitis. The Student *t*-test was used for all continuous variables, and the chi-square test was used for dichotomous variables. Statistical significance was set at $p < 0.05$. Age, waist circumference, BMI, and the number of childbirths, had normal distributions and are presented as mean values and standard deviations. However, IgE levels did not have normal distribution and are presented as the median value with an interquartile range. Dichotomous variables are presented as percentages.

The Statistical Package for the Social Sciences, IBM SPSS Statistics 22 (IBM, Armonk, NY, USA) was used for statistical analysis.

3. Results

Of a total of 2967 women, 567 received MHT for at least 1 month. They commenced MHT at the age of 51.3 ± 5.5 years and took it for 2.4 ± 3.2 years on average.

3.1. Comparison between women who were users of MHT and non-users of MHT

There were no differences in age between the two groups; however, waist circumference and BMI were greater among non-users of MHT than in users of MHT. There were no differences in the percentages of smoking, drinking, and regular exercise between the two groups. The number of childbirths was greater among non-users of MHT (2.6 ± 1.1) than in users of MHT (2.8 ± 1.3 , $p = 0.001$). There were no differences between the two groups in the proportion of women who were breastfeeding. Overall, 24.5% of users of MHT had general rhinitis symptoms compared to 18.9% of non-users of MHT ($p = 0.003$). The proportion of patients with rhinorrhea or posterior nasal drip was also greater among users of MHT (6.3% vs. 4.3%, $p = 0.042$). There was no significant difference between the two groups in symptoms of nasal obstruction (4.9% vs. 3.9%, $p = 0.250$). There were no differences in the levels of total IgE and specific IgE for *D. farinae*, cockroaches, and dogs, between the two groups. All comparisons between the two groups are summarized in Table 2.

3.2. Comparison between women with and without chronic rhinitis

Age, waist circumference, and BMI were greater among women without chronic rhinitis than among those with chronic rhinitis. There was no difference in the proportions of participants smoking, drinking, and taking regular exercise, between the two groups. The number of childbirths and percentage of breastfeeding were greater among women without chronic rhinitis than in those with chronic rhinitis. The percentage of MHT users was greater among women with chronic rhinitis (23.4%) than among those without chronic rhinitis (18.0%, $p = 0.003$). There were no differences in the levels of total IgE and specific IgE for cockroaches and dogs, between the two groups; however, the level of specific IgE for *D. farinae* was greater among women with chronic rhinitis than among women without chronic rhinitis. All comparisons between the two groups are summarized in Table 3.

Table 2

Comparison between women who were users and non-users of menopausal hormone therapy.

	Hormonal replacement therapy		p-Value
	Yes (n = 567)	No (n = 2400)	
Physical characteristic			
Age (year)	59.6 ± 5.8	59.3 ± 6.0	0.276
Waist circumference (cm)	80.6 ± 8.5	82.26 ± 9.1	< 0.001*
Waist circumference > 80 cm (%)	54.4%	60.5%	0.009*
Body mass index (kg/m ²)	24.0 ± 2.8	24.4 ± 3.3	0.003*
Body mass index > 25 (%)	31.9%	38.9%	0.002*
Current life habits			
Current smoking (%)	3.5	3.5	0.899
Regular drinking (%)	28.7	28.2	0.796
Regular exercise (%)	36.7	31.0	0.011
Reproductive history			
Childbirth (n)	2.6 ± 1.1	2.8 ± 1.3	0.001*
Breastfeeding (%)	88.5	88.4	0.887
Rhinitis-related symptoms			
General rhinitis symptom (%)	24.5	18.9	0.003*
Rhinorrhea or posterior nasal drip (%)	6.3	4.3	0.042*
Nasal obstruction (%)	4.9	3.9	0.250
IgE measurement			
Enrolled person (n)	63	239	
Total IgE (kU/L)	58.5 (17.6–159.0)	59.2 (26.8–136.0)	0.438
<i>Dermatophagoides farinae</i> (kU/L)	0.08 (0.01–0.47)	0.06 (0.02–0.23)	0.509
Cockroach (kU/L)	0.04 (0.02–0.08)	0.05 (0.03–0.14)	0.876
Dog (kU/L)	0.01 (0.01–0.03)	0.02 (0.01–0.03)	0.365

* p-Value < 0.05.

Table 3

Comparison between women with and without chronic rhinitis.

	Chronic rhinitis		p-Value
	Yes (n = 593)	No (n = 2374)	
Physical characteristic			
Age (year)	58.8 ± 5.9	59.5 ± 5.9	0.011 [*]
Waist circumference (cm)	80.8 ± 8.8	82.2 ± 9.1	< 0.001 [*]
Waist circumference > 80 cm (%)	53.6%	60.8%	0.002 [*]
Body mass index (kg/m ²)	23.9 ± 3.0	24.4 ± 3.2	< 0.001
Body mass index > 25 (%)	33.9%	38.5%	0.041 [*]
Current life habits			
Current smoking (%)	4.2	3.3	0.261
Regular drinking (%)	27.5	28.5	0.647
Regular exercise (%)	33.1	31.8	0.589
Reproductive history			
Childbirth (n)	2.6 ± 1.2	2.7 ± 1.3	0.049 [*]
Breastfeeding (%)	84.7	89.4	0.001 [*]
Menopausal hormonal therapy (%)	23.4	18.0	0.003 [*]
IgE measurement			
Enrolled person (n)	58	244	
Total IgE (kU/L)	67.7 (19.2–176.0)	58.0 (26.0–119.0)	0.743
<i>Dermatophagoides farinae</i> (kU/L)	0.08 (0.02–0.55)	0.06 (0.02–0.23)	< 0.001 [*]
Cockroach (kU/L)	0.06 (0.03–0.12)	0.04 (0.02–0.12)	0.380
Dog (kU/L)	0.02 (0.01–0.04)	0.01 (0.01–0.03)	0.324

* p-Value < 0.05.

4. Discussion

Our main finding was that the prevalence of chronic rhinitis among women who underwent MHT was 24.5% and 18.9% among women who did not take MHT. Therefore, the absolute risk of MHT-induced rhinitis is presumed to be 5.6%. Although this study was cross-sectional, a causal association is relatively clear, because rhinitis was defined only when symptoms were present during the 12 months preceding the surveys and the women had been taking MHT for an average of 8.3 years up to the surveys. Therefore, it follows that MHT use has an impact on the subsequent development of rhinitis.

Rhinitis is classified into allergic and non-allergic rhinitis [1]. Allergic rhinitis is an IgE-mediated inflammation, triggered by airborne allergens, including house dust mite, pollens, animal dander, fungus, and cockroach [1]. Non-allergic rhinitis is a heterogeneous disease caused by a range of factors, including viruses, air pollutants, food, cold temperature, exercise, and autonomic dysregulation [1]. Differentiation between allergic and non-allergic rhinitis is important because prognosis and treatment are different [1]. Differential diagnosis relies on allergic testing, including the skin prick test or specific IgE measurements of allergens, rather than on clinical symptoms or findings on physical examination of the patient [1]. In this study, general rhinitis symptoms were more common among users of MHT. However, no differences in total IgE and specific IgE levels between users and non-users of MHT were detected; therefore, MHT is believed to induce non-allergic rhinitis, rather than allergic rhinitis. Further evidence supporting this argument is the finding that rhinorrhea or posterior nasal drips were more common among users of MHT than among non-users of MHT, while the incidence of nasal obstruction was comparable between the two groups. Non-allergic rhinitis, rhinorrhea, and posterior nasal drip are common symptoms, while nasal obstruction is a common symptom for allergic rhinitis [11].

Our results indicate that women with chronic rhinitis received MHT more frequently than those without chronic rhinitis (23.4% vs. 18.0%, $p = 0.003$). Further differences between the two groups were age, BMI, and waist circumference. Women with chronic rhinitis were slightly younger and more slender than those without chronic rhinitis, challenging previous reports that rhinitis increased with age and BMI. The elderly complain of rhinorrhea, nasal obstruction, and even olfactory problems, more frequently than younger persons [12]. Recently, research has focused on obesity as a cause of rhinitis [13]. We could not identify any plausible explanation for our conflicting results. The level of specific IgE for *D. farinae* was greater among women with chronic rhinitis than among those without chronic rhinitis; however, there were no differences in the levels of total IgE and specific IgE for cockroaches and dogs. This finding implies chronic rhinitis among postmenopausal women is, in part, triggered by *D. farinae*, the most common cause of allergic rhinitis among Koreans. However, as mentioned above, chronic rhinitis caused by MHT is non-allergic rhinitis.

Although KNHANES involved a large study population and the quality was satisfactory, this study has several limitations. First, every cross-sectional study cannot be free from the causality problem [10]. We could not exclude women who had experienced rhinitis before the use of MHT. Second, the definition of rhinitis was made on the basis of a single simple question. However, many surveys have used a similar question to define rhinitis and its validity has been accepted [14,15].

Third, different types and schedules of MHT are available [9]. Moreover, the duration of MHT also varied significantly among studies. We simplified the issue and defined user of MHT if they underwent any type of MHT for at least 1 month.

5. Conclusion

MHT may increase non-allergic rhinitis among postmenopausal women. Aging and obesity may negatively influence the occurrence of non-allergic rhinitis among postmenopausal women.

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Conflict of interests

None declared.

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