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Knee osteoarthritis and menopausal hormone therapy in postmenopausal women: a nationwide cross-sectional study

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Introduction

Osteoarthritis（OA）is mainly caused by degenerative changes in the joints due to aging, but various other factors such as sex, genes, and obesity also contribute to OA development.The prevalence of OA is higher in women than in men, and the incidence of OA is particularly elevated in menopause.The incidence of OA increases after menopause, and may be related to hormonal changes in women. Estrogen has an anti-inflammatory effect at high concentrations and plays a chondroprotective role.Estrogen deficiency is known to affect the development of OA, and menopausal hormone therapy (MHT) is suggested to be related to the development of OA.

Methods

1.Theoretical basis

Estrogen promotes spontaneous repair of osteochondral defects by inhibiting osteoclasts.Estrogen can not only accelerate the speed of bone repair in the defect area, but also improve the quality of regenerated subchondral bone.

2.Study design and setting

The study was a nationwide cross-sectional observational study. Data were collected from the KNHANES, which is a nationally representative cross-sectional survey, between 2009 and 2012. The KNHANES was administered to a sample of institutionalized Korean civilians, and it was managed by the Korea Center for Disease Control and Prevention(KCDC).

3.Participants

In the 2009 to 2012 KNHANES, 5,798 postmenopausal women were over 50 years of age and had undergone knee joint radiography. After the exclusion of women who did not complete the health survey section, the final sample size for this study was 4,766 participants.

4.Main variables

a.MHT time

b.Knee joint pain

c.The radiologic criterion

5.Covariates

Age, menarche and menopause age, body mass index(BMI), hypertension(HTN), diabetes mellitus (DM), alcohol consumption, smoking status.

6.Statistical analysis

Statistical package for the social sciences (SPSS) version 23.0 (SPSS Inc., Chicago, IL) was used for all statistical analyses, and a P value <0.05 was considered significant.Chi-square tests were conducted to examine differences in the general characteristics of the postmenopausal women and knee OA prevalence between the MHT and non-MHT groups. The relationship between MHT and knee OA prevalence was calculated using odds ratios (ORs) and 95% confidence intervals (CIs)

Results

TABLE 1. *Characteristics of the study population according to menopausal hormone therapy (n = 4,766)*

	MHT (n = 441)	Non-MHT (n = 4,325)	*P*
Age (y)	61.63 ± 6.14	65.38 ± 9.21	<0.001
Menarche age (y)	15.93 ± 1.86	16.19 ± 1.99	0.018
Menopause age (y)	50.18 ± 3.90	49.55 ± 4.61	0.001
Obesity			<0.001
Underweight	5 (1.1)	112 (2.6)	
Normal	300 (68.0)	2,601 (60.1)	
Obesity	136 (30.9)	1,612 (37.3)	
HTN			0.227
Normal	131 (29.7)	1,014 (23.4)	
Prehypertension	108 (24.5)	1,008 (23.3)	
HTN	202 (45.8)	2,303 (53.3)	
DM			<0.001
Normal	285 (64.6)	2,442 (56.5)	
Impaired fasting glucose	97 (22.0)	1,104 (25.5)	
DM	59 (13.4)	779 (18.0)	
Alcohol intake			<0.001
Nondrinkers	118 (26.7)	1,585 (36.6)	
Moderate drinkers	317 (71.9)	2,697 (62.4)	
Heavy drinkers	6.0 (1.4)	43 (1.0)	
Smoking state			0.238
Never	410 (93.0)	4,003 (92.6)	
Past	18 (4.1)	161 (3.7)	
Current	13 (2.9)	161 (3.7)	
Household income			0.282
Lowest	205 (46.5)	2,845 (65.8)	
Lower middle	94 (21.3)	606 (14.0)	
Upper middle	108 (24.5)	664 (15.3)	
Highest	34 (7.7)	210 (4.9)	
Education			<0.001
Primary school or lower	104 (23.6)	1,690 (39.1)	
Middle school	116 (26,3)	1,081 (25.0)	
High school	104 (23.6)	779 (18.0)	
University or higher	117 (26.5)	775 (17.9)	
OA			<0.001
Yes	73 (16.6)	1,080 (25.0)	
No	368 (83.4)	3,245 (75.0)	

Values are presented as mean ± SD or n (%).
DM, diabetes mellitus; HTN, hypertension; MHT, menopausal hormone therapy; OA, osteoarthritis; SD, standard deviation.

In this study, four different logistic regression models were used to assess the association between MHT and knee OA.

Model I was adjusted for MHT duration;

Model II was adjusted for MHT duration, age, BMI, and menarche and menopause age;

Model III was adjusted for MHT duration, age, BMI, menarche and menopause age, HTN, DM, alcohol consumption, and smoking status;

Model IV was adjusted for MHT duration, age, BMI, menarche and menopause age, HTN, DM, alcohol consumption, smoking status, and socioeconomic status (household income and education level).

TABLE 2. *Odds ratios and 95% CIs of OA prevalence on MHT group compare to non-MHT group among postmenopausal women*

	OR	95% CI
Crude	0.59	0.45-0.78
Model I[a]	0.47	0.34-0.64
Model II[b]	0.64	0.46-0.91
Model III[c]	0.68	0.49-0.94
Model IV[d]	0.70	0.50-0.99

CI, confidence interval; DM, diabetes mellitus; HTN, hypertension; MHT, menopausal hormone therapy; OA, osteoarthritis; OR, odds ratio.
[a]Adjust for MHT duration.
[b]Adjust for MHT duration, age, obesity, and menarche, and menopause age.
[c]Adjust for MHT duration, age, obesity, menarche and menopause age, HTN, DM, alcohol intake, and smoking status.
[d]Adjust for MHT duration, age, obesity, menarche and menopause age, HTN, DM, alcohol intake, smoking status, and socioeconomic status.

DISCUSSION

MHT is effective in relieving the various symptoms of menopause, and it has been suggested as a cost-effective method of maintaining the health status of menopausal women.

Short-term MHT is effective in relieving menopausal symptoms; however, the long-term effects can only be considered when the MHT has been taken for over a year.

This study showed that MHT was associated with a lower prevalence of knee joint OA, suggesting that supplementation with exogenous female hormones after menopause may be protective against knee OA.

The main medical treatment for OA is pain control. Estrogen activates antinociception through the inhibitory pain pathway of the spinal cord.Decreased levels of estradiol in menopause increases pain severity, and estradiol supplements may alleviate pain.

CONCLUSIONS

Osteochondral defect of early osteoclast participate in regeneration of bone remodeling, middle-late if osteoclast activity still higher will lead to the subchondral bone plate crack and subchondral bone in the formation of a cystic cavity, through injection of estrogen inhibits osteoclast activity can prevent the formation of cracks and void, at the same time improve the activity of osteoblast, accelerate the speed and quality of bone repair joint action.

In this study,participants receiving MHT had a significantly lower prevalence of symptomatic knee OA compared with those who did not receive MHT. However, this cross-sectional study precludes conclusions about causal relationships, so further prospective studies and intervention trials should be undertaken to establish a causal association between knee OA and MHT.

Thank you !