

Vitamin D status and its associations with rheumatoid arthritis in Korean women: the Korean National Health and Nutrition Examination Survey 2008–2014

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In the present study, vitamin D status and its associations with rheumatoid arthritis in Korean women were investigated. Total 2,162 women's data from the Korea National Health and Nutrition Examination Survey during 2008–2014 were analyzed by complex sampling design logistic regression analysis and complex sampling design general linear model. Women who over 19 years old were included, and who has osteoporosis or abnormal parathyroid hormone or renal failure or liver cirrhosis or abnormal creatinine were excluded. Age and body mass index were used as covariate. In the present study, we have shown that vitamin D

status were not associated with development of rheumatoid arthritis in Korean women as well were not associated with pain and quality of life in Korean women with rheumatoid arthritis. Based on the present study and considering the effects of vitamin D on fracture and osteoporosis, it can be suggested that additional cohort study and cost-effectiveness analysis are needed.

Keywords: Arthritis, Pain, Rheumatoid arthritis, Quality of life, Vitamin D

INTRODUCTION


Rheumatoid arthritis is the most common autoimmune disease found in about 1% of adults worldwide. Rheumatoid arthritis is caused by neutrophils, macrophages, T cells, B cells and dendritic cells infiltrating the synovium of joints and causing inflammation, it causes damage to bone and disability. Finally, it induces systemic complications such as cardiovascular and cardiopulmonary dysfunction, and reduces life expectancy by about 3–10 years (Alamanos and Drosos, 2005; Picerno et al., 2015). Rheumatoid arthritis is 2 to 3 times more common in females than males (Alamanos and Drosos, 2005). Although the pathogenesis of rheumatoid arthritis has not yet been elucidated, it is known that the interaction of genetic and environmental factors influences congenital and adaptive immunity, resulting in systemic inflammation (Picerno et al., 2015).

Vitamin D not only plays a major role in the regulation of bone

mineral homeostasis but also plays a role in cell function such as cell proliferation, differentiation, apoptosis, and angiogenesis (Abourazzak et al., 2015).

Recently, appropriate level of vitamin D has been reported to reduce the risk of some chronic inflammatory or autoimmune conditions such as various cancers, infectious diseases, type 1 diabetes, multiple sclerosis, and autoimmune rheumatic disease (Agmon-Levin et al., 2013). Calcitriol or 1,25-dihydroxyvitamin D₃ (1,25(OH)₂D₃), an endogenous serum-active metabolite of vitamin D, is a kind of steroid hormone produced by cholesterol. Therefore, calcitriol has immunomodulatory properties such as glucocorticoid and gonadal hormones (Cutolo et al., 2011).

There are reports that low vitamin D intake is associated with the development of rheumatoid arthritis, or low serum vitamin D level is associated with disease activity or physical disability in rheumatoid arthritis (Haque and Bartlett 2010; Kerr et al., 2011; Merlino et al., 2004; Rossini et al., 2010). On the other hand,

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Received: November 4, 2016 / Accepted: December 13, 2016

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there are reports that vitamin D levels in patients with inflammatory joint disease are not related to arthritis activity (Braun-Moscovici et al., 2011; Craig et al., 2010).

The purpose of this study was to investigate the effect of vitamin D levels on the prevalence of rheumatoid arthritis in Korean adult women and to investigate the association of vitamin D levels with pain level and quality of life in Korean adult women with rheumatoid arthritis using the Korean National Health and Nutrition Examination Survey (KNHANES) from the Korea Centers for Disease Control and Prevention (2015).

MATERIALS AND METHODS

Subjects

This study analyzed the data of 2008–2014 from KNHANES. The subjects were women aged 19 years or older who completed a health questionnaire on rheumatoid arthritis and evaluation of vitamin D (25-hydroxyvitamin D; 25(OH)D) status.

It was reported that osteoporosis or increased parathyroid hormone affects vitamin D level (Aloia et al., 2006), and parathyroid hormone has inverse correlation with the conversion of vitamin D (25(OH)D) to active form of vitamin D, calcitriol (1,25(OH)₂D₃) (Pagan and Pagana, 2010). Thus, in the present study, patients with osteoporosis were excluded from the study until the year 2012 when health questionnaires and examinations for related items were discontinued. Parathyroid hormone abnormalities were also excluded in cases of over 65 pg/mL, according to the previous study (Aloia et al., 2006). Vitamin D is metabolized to the active form of calcitriol (1,25 (OH)₂D₃) in the liver and kidneys (Christakos et al., 2012), thus, patients with renal insufficiency or liver cirrhosis (Abourazzak et al., 2015) or those with thyroid disease or those with creatinine levels above 2.0 mg/dL were also excluded (Hansen et al., 2014).

Study design

The subjects were divided into whole female or fertile period and postmenopausal period. In each group, subjects were divided into five groups using the 5th quintile according to the serum level of vitamin D. The odds ratios of the five groups of rheumatoid arthritis according to the level of vitamin D in the serum were checked and the degree of pain and quality of life of the rheumatoid arthritis patients were analyzed. Pain intensity was assessed by visual analogue scale (VAS) ranging from 0 to 100, and quality of life was assessed using the EQ-5D questionnaire.

Statistics

KNHANES was recommended to be analyzed by complex sampling design (Korea Centers for Disease Control and Prevention, 2015). Thus, in this study, weights of each year were multiplied by the ratio of the surveyed population by year to generate integrated weights.

Demographic information used frequency and descriptive statistics of complex sampling design. The odds ratio of rheumatoid arthritis according to the level of vitamin D was determined by complex sampling design logistic regression. The degree of pain and quality of life of patients with rheumatoid arthritis according to their vitamin D levels were determined by the complex sampling design general linear model.

In the analysis of odds ratio, pain level and quality of life, we compared the value of the 5th group with the highest vitamin D level, and the values of the remaining four groups and found that there was a statistically significant difference. When there is a statistically significant difference, the *P* for trend of the complex sampling design general linear model is conducted to confirm the linear trend.

Age and body mass index are major risk factors for rheumatoid arthritis (Qin et al., 2015) and also affect vitamin D level (Derdemezis et al., 2011; Holick et al., 2007). Thus, age and body mass index were used as covariates to control the effect of age and obesity on the association of rheumatoid arthritis and vitamin D level. In model 1, only age was used as covariate, and in model 2, both age and body mass index were used as covariates.

The values of the continuous variables were expressed as mean (standard error; SE), and the results of complex sampling design logistic regression analysis showed odds ratio and 95% confidence intervals (CIs).

Statistical analysis was performed using IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA). All statistical significances were *P* < 0.05.

RESULTS

Demographic information

A total of 2,162 unweighted subjects were included in the study and their mean vitamin D was 15.80 ng/mL and the prevalence of rheumatoid arthritis was 12.0%. The numbers of unweighted subjects in fertile period female was 1,179, the mean vitamin D was 14.54 ng/mL, and the prevalence of rheumatoid arthritis was 5.7%. The numbers of unweighted subjects in postmenopausal period female was 983, and their mean vitamin D

Table 1. Characteristics of participants

Period	Percentile	No. of unweighted participants	Age (yr)	Body mass index (kg/m ²)	Vitamin D (ng/mL)	Rheumatoid arthritis patients (%) ^a	Present smoking (%) ^a
Female	1st	396	39.02 ± 0.82	22.92 ± 0.22	8.52 ± 0.08	10.3	8.8
	2nd	426	40.42 ± 0.82	22.78 ± 0.24	11.94 ± 0.04	9.0	8.7
	3rd	433	41.14 ± 0.75	23.13 ± 0.22	14.66 ± 0.04	10.9	6.3
	4th	419	43.45 ± 0.84	23.19 ± 0.22	17.91 ± 0.07	14.3	6.9
	5th	488	49.56 ± 0.77	23.23 ± 0.18	25.97 ± 0.30	15.2	6.0
	Total	2,162	42.72 ± 0.32	23.05 ± 0.10	15.80 ± 0.19	12.0	7.3
Fertile period	1st	220	33.24 ± 0.77	22.50 ± 0.30	8.15 ± 0.09	6.1	10.0
	2nd	235	32.41 ± 0.73	22.54 ± 0.43	11.29 ± 0.05	5.0	8.8
	3rd	241	33.24 ± 0.63	22.47 ± 0.24	13.83 ± 0.05	6.3	7.5
	4th	233	34.02 ± 0.66	22.44 ± 0.32	16.59 ± 0.07	7.0	6.9
	5th	250	35.35 ± 0.72	22.70 ± 0.25	22.85 ± 0.34	4.2	9.1
	Total	1,179	33.66 ± 0.27	22.53 ± 0.14	14.54 ± 0.21	5.7	8.5
Postmenopausal period	1st	199	57.24 ± 0.98	23.99 ± 0.30	9.44 ± 0.13	20.4	5.9
	2nd	192	56.98 ± 0.95	23.82 ± 0.28	13.25 ± 0.07	18.5	9.1
	3rd	185	57.74 ± 0.95	24.01 ± 0.28	16.53 ± 0.09	28.8	5.2
	4th	198	58.46 ± 0.78	24.39 ± 0.29	20.55 ± 0.13	20.0	3.3
	5th	209	59.41 ± 0.87	23.39 ± 0.24	29.75 ± 0.44	24.5	3.8
	Total	983	57.97 ± 0.31	23.92 ± 0.123	17.92 ± 0.2.94	22.4	5.5

Values are presented as mean ± standard error.

^aPercentages were calculated by weighted number.

was 17.92 Ng/mL, and prevalence of rheumatoid arthritis was 22.4%, both of which were higher than those of fertile period female (Table 1).

Association between rheumatoid arthritis and vitamin D status

The odds ratios of rheumatoid arthritis according to the level of total vitamin D in the whole female was statistically significantly lower in the lowest vitamin D group and the second lowest vitamin D group than in the group with the highest vitamin D before using covariance. However, after using the covariates, all of these statistical differences disappeared.

The results of the subdivided into fertile period female and postmenopausal period female showed that the odds ratio of rheumatoid arthritis according to the level of serum vitamin D was not statistically significant (Table 2).

Association between rheumatoid arthritis'VAS and vitamin D status

In whole rheumatoid arthritis female group, the difference in pain level was not statistically significant depending on the level of vitamin D, and also was not statistically significant in fertile period rheumatoid arthritis female group.

In postmenopausal period rheumatoid arthritis female group, the third highest vitamin D group had significantly higher pain intensity before using the covariate than the group with the highest vitamin D.

There was statistically significant difference between the group with the most severe pain and the group with the mildest pain in the models 1 and 2. However, there was no statistically significant difference in the degree of pain compared to the group with the highest vitamin D.

In the *P* for trend, *P* = 0.879 before using covariance, *P* = 0.702 in model 1 and *P* = 0.606 in model 2 were not statistically significant. Thus, the difference in pain level according to the level of vitamin D was not linear (Table 3).

Association between rheumatoid arthritis'EQ-5D index and vitamin D status

There was no statistically significant difference in the quality of life among the whole rheumatoid arthritis female according to their levels of vitamin D.

In fertile period rheumatoid arthritis female, the group with the lowest vitamin D had significantly lower quality of life before using covariance and model 1 than the group with the highest vitamin D. However, there was no statistically significant difference

Table 2. Association between rheumatoid arthritis and vitamin D status

Period	Percentile	Crude			Model 1			Model 2		
		% ^{b)}	OR (95% CI) ^{a)}	P-value	% ^{b)}	OR (95% CI) ^{a)}	P-value	% ^{b)}	OR (95% CI) ^{a)}	P-value
Female	1st	20.0	0.629 (0.40–0.99)	0.043	20.0	1.194 (0.74–1.93)	0.469	20.0	1.167 (0.72–1.89)	0.530
	2nd	19.9	0.551 (0.36–0.85)	0.007	19.9	0.914 (0.58–1.44)	0.699	19.9	0.913 (0.58–1.44)	0.696
	3rd	20.0	0.686 (0.44–1.07)	0.097	20.0	1.154 (0.72–1.86)	0.555	20.0	1.153 (0.72–1.85)	0.556
	4th	20.1	0.913 (0.57–1.47)	0.710	20.1	1.330 (0.80–2.21)	0.269	20.1	1.329 (0.80–2.20)	0.268
	5th	20.0	Reference		20.0	Reference		20.0	Reference	
	Total ^{c)}	2,162			2,162			2,160		
Fertile period	1st	19.9	1.470 (0.65–3.34)	0.357	19.9	1.647 (0.70–3.86)	0.249	19.9	1.651 (0.70–3.88)	0.249
	2nd	20.1	1.202 (0.52–2.78)	0.667	20.1	1.405 (0.59–3.35)	0.442	20.1	1.408 (0.59–3.37)	0.441
	3rd	20.0	1.526 (0.65–3.58)	0.331	20.0	1.750 (0.73–4.21)	0.211	20.0	1.764 (0.73–4.27)	0.207
	4th	20.0	1.696 (0.73–3.94)	0.219	20.0	1.870 (0.78–4.48)	0.160	20.0	1.887 (0.78–4.54)	0.156
	5th	20.0	Reference		20.0	Reference		20.0	Reference	
	Total ^{c)}	1,179			1,179			1,179		
Postmenopausal period	1st	20.0	0.790 (0.45–1.40)	0.416	20.0	0.864 (0.49–1.53)	0.615	19.9	0.841 (0.47–1.49)	0.554
	2nd	20.0	0.698 (0.41–1.19)	0.183	20.0	0.773 (0.46–1.32)	0.342	20.0	0.775 (0.46–1.30)	0.335
	3rd	20.0	1.247 (0.67–2.33)	0.488	20.0	1.400 (0.73–2.68)	0.310	20.0	1.404 (0.74–2.68)	0.302
	4th	19.9	0.768 (0.44–1.35)	0.358	19.9	0.792 (0.45–1.38)	0.411	20.0	0.796 (0.46–1.37)	0.412
	5th	20.1	Reference		20.1	Reference		20.1	Reference	
	Total ^{c)}	983			983			981		

Model 1 was adjusted for age. Model 2 was adjusted for age and body mass index.

^{a)}Crude and each model's odds ratios (ORs) and 95% confidence intervals (95% CIs) calculated by Complex samples logistic regression analysis. ^{b)}Percentage of participants in each percentiles were calculated by weighted number. ^{c)}Unweighted number.

Table 3. Association between rheumatoid arthritis' visual analogue scale and vitamin D status

Patient	Percentile	Crude			Model 1			Model 2		
		% ^{b)}	Mean ± SE ^{a)}	P-value ^{a)}	% ^{b)}	Mean ± SE ^{a)}	P-value ^{a)}	% ^{b)}	Mean ± SE ^{a)}	P-value ^{a)}
Female rheumatoid arthritis patients	1st	18.6	62.19 ± 3.47	0.519	18.6	60.23 ± 3.55	0.400	18.3	59.47 ± 3.59	0.315
	2nd	20.3	70.81 ± 3.42		20.3	69.87 ± 3.36		20.4	69.85 ± 3.32	
	3rd	19.1	67.07 ± 5.93		19.1	67.19 ± 5.82		19.2	67.16 ± 5.81	
	4th	20.3	65.11 ± 3.98		20.3	65.46 ± 3.81		20.3	65.44 ± 3.80	
	5th	21.7	65.11 ± 3.94		21.7	67.25 ± 3.88		21.8	67.43 ± 3.92	
	Total ^{c)}	283			283			281		
Fertile rheumatoid arthritis patients	1st	20.1	67.84 ± 3.66	0.454	20.1	68.29 ± 2.73	0.504	20.1	68.54 ± 3.65	0.710
	2nd	22.4	69.80 ± 4.09		22.4	69.99 ± 4.15		22.4	70.00 ± 4.12	
	3rd	20.7	77.07 ± 4.69		20.7	76.40 ± 4.33		20.7	76.25 ± 4.66	
	4th	18.5	54.98 ± 13.36		18.5	55.33 ± 13.63		18.5	55.37 ± 13.79	
	5th	18.3	73.19 ± 3.49		18.3	72.88 ± 3.32		18.3	72.71 ± 3.52	
	Total ^{c)}	71			71			71		
Postmenopausal rheumatoid arthritis patients	1st	17.3	59.55 ± 4.17	0.031	17.3	58.63 ± 4.02	0.022	16.8	57.65 ± 4.07	0.015
	2nd	19.6	64.75 ± 4.44		19.6	66.40 ± 4.22		19.7	66.33 ± 4.12	
	3rd	21.5	75.85 ± 3.65 ^{d)}		21.5	72.71 ± 2.46		21.7	72.79 ± 2.49	
	4th	20.5	60.45 ± 5.09		20.5	62.42 ± 5.56		20.6	62.34 ± 5.49	
	5th	21.1	62.84 ± 5.32		21.1	63.37 ± 4.88		21.2	63.38 ± 4.85	
	Total ^{c)}	212			212			210		

Model 1 was adjusted for age. Model 2 was adjusted for age and body mass index.

^{a)}Crude and each model's means, standard errors, and P-value were calculated by complex samples general linear analysis. ^{b)}The percentage of participants in each percentiles were calculated by weighted number. ^{c)}Unweighted number. ^{d)}Compared to 5th percentile group.

Table 4. Association between rheumatoid arthritis' EQ-5D index and vitamin D status

Patient	Percentile	Crude			Model 1			Model 2		
		% ^{b)}	Mean ± SE ^{a)}	P-value ^{a)}	% ^{b)}	Mean ± SE ^{a)}	P-value ^{a)}	% ^{b)}	Mean ± SE ^{a)}	P-value ^{a)}
Female rheumatoid arthritis patients	1st	19.6	0.85 ± 0.03	0.822	19.6	0.84 ± 0.03	0.675	19.3	0.84 ± 0.04	0.755
	2nd	19.6	0.88 ± 0.02		19.6	0.88 ± 0.02		20.0	0.88 ± 0.02	
	3rd	20.1	0.83 ± 0.05		20.1	0.83 ± 0.05		20.1	0.83 ± 0.05	
	4th	20.1	0.88 ± 0.03		20.1	0.88 ± 0.03		20.2	0.88 ± 0.02	
	5th	20.4	0.86 ± 0.03		20.4	0.88 ± 0.03		20.4	0.87 ± 0.03	
	Total ^{c)}	319			319			317		
Fertile rheumatoid arthritis patients	1st	19.7	0.92 ± 0.01 ^{d)}	0.025	19.7	0.92 ± 0.01 ^{d)}	0.048	19.7	0.94 ± 0.02	0.165
	2nd	19.9	0.94 ± 0.01		19.9	0.94 ± 0.01		19.9	0.95 ± 0.02	
	3rd	20.4	0.93 ± 0.02		20.4	0.93 ± 0.02		20.4	0.91 ± 0.03	
	4th	20.2	0.73 ± 0.12		20.2	0.73 ± 0.12		20.2	0.74 ± 0.11	
	5th	19.8	0.96 ± 0.01		19.8	0.96 ± 0.01		19.8	0.94 ± 0.02	
	Total ^{c)}	80			80			80		
Postmenopausal rheumatoid arthritis patients	1st	19.7	0.81 ± 0.04	0.244	19.7	0.80 ± 0.04	0.570	19.3	0.80 ± 0.04	0.673
	2nd	20.2	0.83 ± 0.02		20.2	0.84 ± 0.02		20.3	0.85 ± 0.02	
	3rd	20.2	0.90 ± 0.03		20.2	0.88 ± 0.03		20.3	0.87 ± 0.03	
	4th	20.0	0.82 ± 0.03		20.0	0.84 ± 0.04		20.1	0.85 ± 0.03	
	5th	19.9	0.86 ± 0.04		19.9	0.87 ± 0.03		20.0	0.86 ± 0.03	
	Total ^{c)}	239			239			237		

^{a)}Crude and each model's means, standard errors, and P-value were calculated by complex samples general linear analysis. ^{b)}The percentage of participants in each percentiles were calculated by weighted number. ^{c)}Unweighted number. ^{d)}Compared to 5th percentile group. Model 1 was adjusted for age. Model 2 was adjusted for age and body mass index.

in model 2. And, in postmenopausal period rheumatoid arthritis female group, the difference in quality of life according to the level of serum vitamin D was not statistically significant (Table 4).

DISCUSSION

Vitamin D levels in the body are most important to be produced by exposure to sunlight, which affects sun exposure, including skin pigmentation, clothing style, use of sunscreen, physical activity, and age. However, in case of inadequate exposure to sunlight increases the importance of food intake. And vitamin D levels are also affected by obesity, calcium, and parathyroid hormone (Lips et al., 2014). Obesity has been reported to reduce vitamin D (Derdemezis et al., 2011), and increasing age also reduces vitamin D, leading to a reduction in vitamin D to about 1/4 of that of younger adults (Holick et al., 2007).

However, in this study, postmenopausal period female with higher body mass index and higher age showed higher levels of vitamin D than fertile period female. Meta-analysis of vitamin D levels showed that there were differences according to age and region. Children and adolescent vitamin D levels were lower in the Asia/Pacific region than adults and elderly, however, children and

adolescent vitamin D levels were higher in the Middle East/Africa region than adults and elderly (Hilger et al., 2014). Moreover, in Korea's previous study, serum vitamin D levels were the lowest in the 20s and gradually increased with age up to 60s in both sexes (Nah et al., 2015). In industrialized countries, relatively younger women tend to use clothing or sunscreen agents, to reduce exposure to sunlight. In addition, the higher proportion of indoor occupation than undeveloped country may have reduced vitamin D in young cases (Nah et al., 2015). The elderly can maintain a sufficient level of vitamin D when exposed to the appropriate amount of ultraviolet light. Therefore, postmenopausal period female with higher occupation rate of occupations with a lot of outdoor activities such as agriculture and a higher rate of participation in outdoor activities such as sports may have a relatively long exposure time to sunlight (Lips et al., 2014).

The immune function of vitamin D is mediated by the vitamin D receptor. Vitamin D inhibits proliferation of activated B lymphocytes expressing vitamin D receptors and inhibits proliferation and differentiation of T cells. Vitamin D also has been shown to inhibit the production of interleukin (IL)-2, interferon gamma of T helper (Th) 1 cells and to inhibit the production of IL-17 of Th17 cells. Therefore, vitamin D has been reported to inhibit the

proinflammatory response (Abourazzak et al., 2015). However, in this study, there was no significant difference in the odds ratio of rheumatoid arthritis according to the level of vitamin D. There have been some preclinical studies that suggest that vitamin D may be helpful in the treatment of Th17 mediated inflammatory diseases such as rheumatoid arthritis (Abourazzak et al., 2015).

However, in clinical studies and research results, many cases were not. In cross-sectional studies, there was no difference in the activity of arthritis, C-reactive protein, and erythrocyte sedimentation rate according to serum vitamin D levels in patients with inflammatory arthritis such as rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis (Braun-Moscovici et al., 2011). Preclinical rheumatoid arthritis may be caused by a subclinical inflammatory process as well as a decrease in vitamin D levels due to reduced sun exposure due to decreased physical activity and changes in dietary intake. However, it is unclear whether low levels of vitamin D increase the risk of rheumatoid arthritis or whether inflammatory conditions due to preclinical rheumatoid arthritis lower vitamin D levels (Hiraki et al., 2014).

Moreover, in Nurses' Health Study (NHS) and Nurses' Health Study II (NHS II) cohort studies confirmed the relationship between the incidence of rheumatoid arthritis and vitamin D intake. There was no significant association between the incidence of rheumatoid arthritis and in NHS II, even with an intake of 400 IU/day or more of vitamin D, resulted in an increase in rheumatoid arthritis (Costenbader et al., 2008). A randomized double-blind placebo-controlled study of vitamin D in patients with rheumatoid arthritis for 12 months showed that vitamin D treatment was not effective in improving parathyroid hormone, bone mineral density, disease activity and cytokines in patients with rheumatoid arthritis (Hansen et al., 2014).

Although there was no statistically significant difference between the two groups, fertile period female group had higher odds ratios of rheumatoid arthritis at lower vitamin D levels, whereas postmenopausal period female group showed lower odds ratios of rheumatoid arthritis at lower levels of vitamin D, in this study. The incidence of rheumatoid arthritis is high in case of nulliparity or when there was no experience of oral contraceptive use (Doran et al., 2004), or when breastfeeding is not performed after first birth (Brennan and Silman, 1994) Thus, female hormone changes have been reported to affect the risk of rheumatoid arthritis. Interactions between the endocrine system and the immune system are the basis for causing differences in the development of autoimmune diseases in women of childbearing and postmenopausal age. Diseases, induced by B cells, peak at reproductive years in women

due to the effects of serum estrogens and their metabolites synthesized by the endocrine system. After that, the role of endocrine system decreases with age. When women become older and the majority of estrogen is made at a peripheral aromatase, the immune and inflammatory responses of men and women become similar (Cutolo et al., 2014). Calcitriol (1,25(OH)₂D₃) inhibits the expression of aromatase, an enzyme that catalyzes the production of estrogen at the periphery, using androgen under normal conditions (Cutolo et al., 2014). The high prevalence of autoimmune rheumatoid disease in women is due to a decrease in the down regulation of aromatase due to the deficiency of calcitriol (1,25(OH)₂D₃), leading to an increase in estrogen production in the periphery, which increases the risk and severity of rheumatoid arthritis (Krishnan et al., 2010).

The present study showed that the relationship between vitamin D levels and pain was statistically significant in postmenopausal period rheumatoid arthritis female group. However, there was no significant difference in linear trend between pain and vitamin D level. Severe deficiency of vitamin D (< 10 ng/mL) is associated with symptoms such as musculoskeletal pain and symptomatic improvement in vitamin D supplementation has been reported (Haque and Bartlett, 2010). However, a randomized, double-blind, placebo-controlled study reported no significant trends in patients' self-reported health status and visual pain rating (VAS), which were reported to be significantly worse in the vitamin-supplemented group (Hansen et al., 2014).

In the present study, there was no difference in quality of life according to the level of vitamin D. In some studies, univariate analysis showed an inverse correlation with increased functional impairment at low vitamin D levels. However, there was no significant difference in multivariate analysis (Abourazzak et al., 2015). The limitations of this study are that despite the data for many years, the actual number of patients with rheumatoid arthritis is not large enough, and seasonal effects, sun exposure time, use of drugs, such as disease modifying antirheumatic drugs or glucocorticoids, were not controlled.

The current recommendation for vitamin D supplements focuses on bone mineral density and fracture, and the Korean Society of Bone Metabolism (2015) recommends a daily intake of 800 IU of vitamin D. Although vitamin D has not been statistically associated with the development of rheumatoid arthritis, it has been reported that vitamin D may be an appropriate adjuvant therapy for patients with rheumatoid arthritis due to its low cost and harmless (Dehghan et al., 2014).

The results of this study showed that there was no difference in

the incidence of rheumatoid arthritis according to the level of vitamin D in Korean adult women and that there was no difference in pain and quality of life when rheumatoid arthritis occurred. However, it is necessary to clarify the relationship through a large-scale cohort study that reflects the results of recently reported genome studies. Considering the effect of vitamin D supply on bone density and fracture, and the low price, vitamin D administration with effectiveness analysis is also needed.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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