The Effect of Vitamin D Supplementation on the Improvement of Osteoarthritis activity in Taif Region.

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Abstract— Knee OA is an insidious disease related to structural changes in the joint over years. It is considered a leading cause of morbidity and reduced quality of life. Epidemiological studies have provided preliminary evidence supporting the potential use of vitamin D for the treatment of OA, Raising serum 25-OH D to sufficient levels with supplemental vitamin D may decrease the rate of bone turn-over, suppress the PTH level, increase bone mass density and even decrease fracture risk in the elderly population. Data was collected in this study through a questionnaire in which the severity of pain, joint stiffness, and physical activity of osteoarthritis were assessed using The Western Ontario and McMaster Universities Arthritis Index (WOMAC). There was an association between vitamin D supplementation and the improvement of WOMAC score in pain and stiffness parameters (OR: 0.314, 0.174, 95% CI: 0.104-0.946, 0.053-0.566, P: 0.039, 0.003 respectively), but no association between vitamin D supplementation and the improvement of WOMAC score in joint malfunction parameter (OR: 0.411, 95% CI: 0.1343 - 1.2623, P: 0.120). The results above suggest there is a statistically significant clinical benefit to vitamin D treatment in patients with OA

A long-term study to determine whether these changes are clinically important and whether they will be sustained with time.

Further studies with long-term radiologic evaluations also are recommended

Index Terms— Osteoarthritis, vitamin D supplementations, WOMAC score, non steroidal anti-inflammatory drugs

INTRODUCTION

Osteoarthritis (OA) is recognized as one of the most prevalent chronic musculoskeletal diseases worldwide. In a study on the prevalence of osteoarthritis in Saudi Arabia, Al-arfaj et al, [1] found that radiographic OA was seen in 53.3% males and in 60.9% females, and in another study done by Alballa SR et al, [2] they found that the clinical prevalence of osteoarthritis among Saudi population was 13%, and it is considered one of the most common disorders presented to the primary care physician in the over 50 years age group in the Kingdom of Saudi Arabia. [3] Ahlberg et al, [4] estimated the incidence to be 3.5% in Eastern Province.

Osteoarthritis is considered a leading cause of morbidity and reduced quality of life, while it is a disease of the joints; its effects are not just physical. In many people with osteoarthritis, their lifestyle decline which include depression, anxiety, feelings of helplessness, limitations on daily activities, job limitations, difficulty in participating in everyday personal and family joys and responsibilities. Also it has financial effects which include the cost of treatment, and wages lost because of disability. [5] The yearly global economic burden of OA measured by direct and indirect costs is in the tens of billions of dollars annually.[6]

Knee OA is an insidious disease related to structural changes in the joint over years. Progressive and irreversible articular damage results in a loss of the extracellular matrix of cartilage in addition to changes in subchondral bone. These degenerative changes result in cartilage loss, synovitis, subchondral cysts, bone marrow lesions, and osteophyte formation. It is also characterized by an attempt of the joint to regenerate tissue such as fibrocartilage. [7]

A clinical diagnosis is made on the basis of three symptoms; persistent knee pain, short-lived morning stiffness, and reduced function and identification of three signs on examination; crepitus, restricted movement, and bony enlargement without an absolute requirement for imaging. [8] Pain is recognized as one of the hallmark symptoms in knee OA and is the primary reason why patients seek medical attention. [9] It is a significant determinant of functional impairment and disability, even more so than radiographic findings. [10] The joints typically affected are located in the hands, knees, hips, and spine with varying degrees of joint deformity and swelling. [11]

Lifestyle modification such as weight loss and exercise and analgesics are the mainstay of treatment. Acetaminophen is recommended first line with NSAIDs being used as add on therapy only if pain relief is not sufficient. [12]

Epidemiological studies have provided preliminary evidence supporting the potential use of vitamin D for the treatment of OA. Raising serum 25-OHD to sufficient levels with supplemental vitamin D may decrease the rate of bone turn-over, suppress the PTH level, increase bone mass density and even decrease fracture risk in the elderly population. [13]

MAIN PROBLEM

The Effect Of Osteoarthritis disease and the role of Vitamin D supplements on its improvement.

AIMS

This study aimed to evaluate the effect of vitamin D supplements on the improvement of the activity of osteoarthritis disease by assessing the severity of pain, joint stiffness, and physical activity of patients with osteoarthritis in Taif city based on The Western Ontario and McMaster Universities Arthritis Index (WOMAC) before and after vitamin D supplementation and compared them with patients who were given analgesics only.

RESEARCH METHODOLOGIES

STUDY DESIGN:

A cross-sectional research design using non probability convenience sampling was used in this study.

STUDY SUBJECTS:

92 patients with well diagnosed osteoarthritis (diagnosed according to ACR classification criteria) [14] recruited from King Abdul Aziz specialist Hospital, and agreed to participate in the study, were assessed with WOMAC index. 56 subjects who were scored as extreme were subdivided into two subgroups according to type of treatment given; 32 patients received treatment in the form of analgesics (non steroidal anti-inflammatory drugs or acetaminophen) and vitamin D and 24 patients received treatment in the form of analgesics only, and reassessment of the disease activity were done after treatment.

ETHICAL APPROVAL:

The study was approved by the local ethical committee at Taif University, and written informed consent was obtained from all subjects involved in the study.

DATA COLLECTION TOOL:

Data was collected in this study through a questionnaire which was developed after extensive literature search in the known database .

The questionnaire was divided into three parts; the first part included the demographic data such as age, sex, and educational level, and anthropometric measures. The Second part included disease risk factors, family and medical history, lifestyle factors, the duration of the disease, the joints involved, medication used and treatment plan. The third part included assessment of the severity of pain, joint stiffness, and physical activity of osteoarthritis using The Western Ontario and McMaster Universities Arthritis Index (WOMAC). The WOMAC measures five items for pain (score range 0–20), two for stiffness (score range 0–8), and 17 for functional limitation (score range 0–68). Physical functioning questions cover eve-

ryday activities such as stair use, standing up from a sitting or lying position, standing, bending, walking, getting in and out of a car, shopping, putting on or taking off socks, lying in bed, getting in or out of a bath, sitting, and heavy and light household duties. The Scale uses the following descriptors for all items: none, mild, moderate, severe, and extreme. These correspond to an ordinal scale of 0-4. A WOMAC test took approximately about 12 minutes.

STATISTICAL ANALYSES

Statistical analysis was performed using SPSS (Statstical package for Social Science) for Windows (version 18.0; SPSS, Chicago, IL, USA). Qualitative data were presented in the form of frequency distribution tables, number and percentage. While quantitative data were presented by mean and standard deviation. To determine the differences in terms of continuous variables among groups, unpaired student t- test was used for comparisons between two different groups, and paired student t- test was used for continuous variables to identify the differences between the condition before treatment and after treatment in the same group.To assess the relationship between categorical variables, Chi-square test was used. We divided the patients into 2 groups based on the WOMAC score into mild and moderate in one group and sever and extreme in the other and analyzed the effect of vitamin D by calculating the odds ratio (OR) together with 95% confidence intervals (CIs). Significance was set at a 2-tailed $P < 0.05$.

RESULTS

TABLE 1
THE DEMOGRAPHIC DATA OF THE STUDIED SUBJECTS:

variable		Number (92)	Percentage (%)
age	18-25	6	6.5
	26-35	10	10.9
variable		Number (92)	Percentage (%)
age	18-25	6	6.5
	26-35	10	10.9
	36-45	12	13.0
	≥45	64	69.6
Gender	male	16	17.4
	female	76	82.6
Nationality	Saudi	84	91.4
	Non Saudi	8	8.6
Education	Non educated	52	56.5
	Educated	40	43.5
Marital status	Single	15	16.3
	Married	77	83.6
	divorced	00	00
Residency	Rural	10	10.9
	urban	82	89.1
BMI	<25	18	19.6
	25-30	19	20.7
	>30	55	59.8
exercise	Yes	20	21.7
	no	72	78.3
Duration of Sun exposure	≤5 min	56	60.9
	5-30 min	32	34.8
	30-60 min	4	4.3
	≥60 min	0	0.0
smoking	yes	8	8.7
	no	84	91.3

TABLE 3
WOMAC SCORE RESULTS OF THE STUDIED SUBJECTS BEFORE TREATMENT

Variable	Severity (WOMAC score)	Number (92)	Percentage (%)
pain	Mild (0-5)	4	4.4
	Moderate (6-10)	5	5.4
	Sever (11-15)	12	13
	Extreme (16-20)	72	78.3
stiffness	Mild (0-2)	4	4.3
	Moderate (3-4)	8	8.7
	Sever (5-6)	10	10.9
	Extreme (7-8)	70	76.1
Joint malfunction	Mild (0-17)	8	8.7
	Moderate (18-34)	16	17.4
	Sever (35-51)	12	13
	Extreme (52-68)	56	60.9

TABLE 2
THE CLINICAL DATA OF THE STUDIED SUBJECTS

		Number (%)	Percentage (%)
Diabetes mellitus	yes	36	39.1
	spine	8	8.7
	hands	7	7.6
	all	24	26.1
Duration of the disease	<1 year	22	23.9
	1-5 years	48	52.2
	>5years	22	23.9

TABLE 4
THE SIGNIFICANCE DIFFERENCE OF WOMAC SCORE RESULTS BEFORE AND AFTER TREATMENT IN EACH GROUP

	Group1 (n=32) ($\overline{X}$±SD)	t	P value	Group2 (n=24) (($\overline{X}$±SD)	t	P value
Pain before treatment	20±0.0	3.24	.023*	19.4±1.3	2.51	.040*
Pain after treatment	9.3±8.04			17±3.3		
Stiffness before treatment	7.8±0.4	3.14	.026*	7±2.6	0.46	.654
Stiffness after treatment	3.7±3.2			6.6±1.6		
Joint malfunctions before treatment	64±8.0	3.22	.023*	65.9±5.2	1.92	.095
Joint malfunctions after treatment	32.2±27.9			58.9±9.6		
WOMAC before treatment	91.8±7.9	3.25	.023*	92.2±6.0	2.4	.047*
WOMAC after treatment	45.2±39.1			82.5±13.4		

Group 1: Patients treated with analgesics and vitamin D supplement.

Group 2: Patients treated with analgesics only.

$\overline{X}$: Statistical mean SD: Standard deviation

P ≤ 0.05 is significant *: Statistically significant

TABLE 5
THE SIGNIFICANCE DIFFERENCE OF WOMAC RESULTS AFTER TREATMENT BETWEEN THE 2 STUDIED GROUPS

	Group 1 (n= 32) ($\overline{X}$±SD)	Group2 (n= 24) ($\overline{X}$±SD)	t	P value
Pain	9.3±8.04	17±3.3	.770	0.607
Stiffness	3.7±3.2	6.6±1.6	.759	0.611
Joint malfunctions	32.2±27.9	58.9±9.6	.839	0.584
WOMAC	45.2±39.1	82.5±13.4	.80	0.59

Group 1: Patients treated with analgesics and vitamin D supplement.

Group 2: Patients treated with analgesics only.

$\overline{X}$: Statistical mean SD: Standard deviation

P ≤ 0.05 is significant

TABLE 6
THE ASSOCIATION BETWEEN VITAMIN D SUPPLEMENTATION AND THE DEGREE OF WOMAC SCORE

	WOMAC score	Group 1 n=32 (%)	Group 2 n=24 (%)	OR	95% CI	P value
Pain	0-10	21 (34.4)	9 (12.5)	0.314	0.104-0.946	0.039*
	11-20	11 (15.6)	15 (25.0)			
stiffness	0-4	21 (34.4)	6 (00.0)	0.174	0.053 -0.566	0.003*
	5-8	11 (15.6)	18(25.0)			
Joint malfunction	0-34	16 (34.4)	7 (16.7)	0.411	0.1343 - 1.2623	0.120
	35-68	16 (31.2)	17 (37.5)			

Group 1: Patients treated with analgesics and vitamin D supplement.

Group 2: Patients treated with analgesics only.

OR: Odds ratio CI: Confidence interval

*: Statistically significant P ≤ 0.05 is significant

DISCUSSION

Osteoarthritis is an age-related disease of the articular cartilage lining of a joint; it produces a multi-dimensional clinical syndrome, which often includes symptoms of pain. Associated pathological changes such as joint effusion, stiffness, decreased range of joint motion, joint instability and malalignment are common, and can progressively impair the efficiency of musculoskeletal functioning in this population. [15]

In the present study, 92 patients with well diagnosed osteoarthritis were involved in the study, It was noticed that most of the subjects have age ≥45 (n= 64, 69.6%), and the majority of them were females (n= 76, 82.6%), this results are in accordance with previous studies that concluded that the incidence of hand, hip, and knee OA increased with age, and women had higher rates than men, especially after age 50.[16-18]

In the present study 59.8% (n= 55) of the studied subjects were obese (BMI >30), this results are in accordance with many epidemiological studies [19-21] which showed an increased prevalence of osteoarthritis of the knee and hand with increased BMI. The connection between obesity and osteoarthritis can be explained by genetic factors and by the accumulation of tear and wear. Overweight occurs prior to knee joint degeneration, not as a result of diminished activity due to joint degeneration, and weight control seems to be an influential tool in the prophylaxis of overweight-specific joint degeneration.

In this study, 89.1% (n= 82) were living in urban areas. In addition greater part of the subjects were non educated (n= 52, 56.5%), this findings were in agreement with Seavey et al, [22] who didn't find any association between education, income and osteoarthritis

We found most of the subjects were non smokers (n= 84, 91.3%), and this results are in accordance with previous studies [23,24] who found varying between having no effect on future knee problems and a protective effect.

The clinical data of the studied subjects showed that 30.4% (n= 28) only of the subjects were hypertensive, and only 39.1% (n=36) were diabetic. After making literature review, there was mixed evidence of the association of hypertension with onset of knee OA with two cohort studies investigating it showing a significant positive association [22,25] and one case–control study revealing no significant effect of hypertension.[26] As regarding diabetes mellitus previous study show that long-standing type 2 diabetes is independently associated with advanced OA of knee and hip joints [27], and this is not in agreement with our results which may be explained by the small sample size, and this results need more further investigations.

In this study, we found 17.4% (n= 16) only had history of trauma to the joints, Of studies investigating previous joint injury, [21,28,29] two only concluded that it was an important risk factor, and this is in agreement with our results.

56 (60.9%) subjects are exposed to sun less than 5 minutes daily, and only 4 (4.3%) are exposed to sun from 30 to 60 minutes daily. In a previous study investigating vitamin D levels and OA performed by Lane et al, [30] It showed a 3-fold increased risk of incident joint space narrowing at the hips of women with lower serum 25-hydroxy vitamin D levels at baseline, and in a recent study of Berking et al, [31] suggests vitamin D status influences the incidence and progression of knee radiographic OA.

In the present study, all the subjects involved in the study were assessed with WOMAC index to detect the degree of disease activity before they took any treatment, then they were stratified into mild, moderate, sever, and extreme as regarding pain, joint stiffness, and joint malfunction. 78.3 % (n=72) of them had extreme pain and extreme joint stiffness, and only 60.9% (n= 56) had joint malfunction.

The group of extreme score was divided into two groups according to the treatment modality given, a group who was treated with analgesics and vitamin D supplement (group 1), and a group who was treated with analgesics only (group 2).

When we compare the WOMAC score of all parameters (pain, stiffness, and joint malfunction) in all patients before and after treatment, we found that there is significant difference in pain, stiffness, and joint malfunction before treatment and after treatment in patients treated with analgesics and vitamin D supplement (group1) (p= 0.023, 0.026, 0.023 respectively), and there is significant difference in pain only before treatment and after treatment in patients treated with analgesics only (group 2) (p= 0.040). (Table 4)

When we compare the mean score of all WOMAC parameters (pain, stiffness, and joint malfunction) after treatment in both groups, it shows that there is no significant difference between the mean score of any of WOMAC parameters (pain, stiffness, and joint malfunction) after treatment in both groups (p= 0.607, 0.611, 0.584 respectively) (Table 5).

But after stratification of the score of WOMAC parameters into two subgroups in each; for pain, the number of patients that has score from 0-10, and the number of patients has score from 11-20. For stiffness, the number of patients has score from 0-4, and the number of patients has score from 5-8, and for joint stiffness, the number of patients has score from 0-34, and the number of patients has score from 35-68, and then we compared between them by Chi square test, and calculated the Odds ratio, we found that there is an association between vitamin D supplementation and the improvement of WOMAC score in pain and stiffness parameters (OR: 0.314, 0.174, 95% CI: 0.104-0.946, 0.053-0.566, P: 0.039, 0.003 respectively), but no association between vitamin D supplementation and the improvement of WOMAC score in joint malfunction (OR: 0.411, 95% CI: 0.1343 - 1.2623, P: 0.120).

These results are in agreement with epidemiological studies and experimentally induced animal models which suggest that the status of vitamin D is associated with the severity of inflammatory diseases such as rheumatoid arthritis [32] and osteoarthritis [33], and they found that vitamin D deficiency has been positively associated with knee and hip OA progression, cartilage loss, and low bone mineral density. However, it has also been shown that vitamin D deficiency is associated with only certain age groups, and with certain factors, such as pain, rather than with radiographic changes, while other studies have found no association between vitamin D and OA, even in patients diagnosed with OA who were using vitamin D supplements. [34]

CONCLUSION

The results above suggest there is statistically significant clinical benefit to vitamin D treatment in patients with OA, although we recommend a long-term study to determine whether these changes are clinically important and whether they will be sustained with time. Further studies with long-term radiologic evaluations also are needed.

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