

ASSESSMENT OF NEUROPATHIC PAIN IN PATIENTS WITH KNEE OSTEOARTHRITIS

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ABSTRACT

Objective: To determine the frequency of neuropathic pain in patients with knee joint osteoarthritis.

Study design: A cross sectional study.

Place and duration: Rheumatology clinic from 1st July 2021 till 31st December 2021.

Patients and methods: The study was conducted on 56 patients by using a consecutive non probability sampling technique. Fulfillment of American college of Rheumatology criteria for knee osteoarthritis was the inclusion criteria. Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to assess pain, stiffness, and physical functional ability in the knees while the Douleur Neuropathique 4 (DN4) questionnaire was used to assess neuropathic pain. Kellgren-Lawrence (KL) grading system was used for radiological classification of knee osteoarthritis.

Results: Out of the 56 patients, 44(78.6%) were female and 12 (21.4%) were male. The mean WOMAC total score in patients with neuropathy was 48.64±10.36. Neuropathic pain was found in 25(44.6%) of the study population. Their mean DN4 questionnaire neuropathy score was 4.64±0.81. *p* value of 0.02, 0.004, 0.027, 0.003 and 0.01 on the spearman rho correlation was found between the total WOMAC score, radiographic grade, neuropathic pain, WOMAC functional score and WOMAC pain score respectively, showing a significant positive correlation.

Conclusion: There was a high frequency of neuropathic pain in patients with knee osteoarthritis. The DN4 questionnaire score correlated with the WOMAC total score and the functional and pain components. It was also found that the patients with grade I, II and III osteoarthritis (KL grading system) had a significantly higher WOMAC score and DN4 questionnaire score.

Keywords:

Douleur Neuropathique four questions (DN4), Kellgren and Lawrence grading (KL grading), Osteoarthritis (OA), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

INTRODUCTION

Osteoarthritis (OA) is one of the most common diseases of the joints described to have bone remodeling i.e new bone formation, loss of cartilage and narrowing of the joint space. Roughly 25% of the world population over 18 years is some way or the other is affected by this joint

disease.¹ Decline in the functional status of the patients is a feature of this disease and thus it leads to absenteeism from work in these individuals because of pain and disability particularly the middle to older-age adults.² Symptomatic osteoarthritis most commonly presents with knee joint pain.³ In osteoarthritis, initially there is loss of articular cartilage, later there is a process of new bone formation in the form of osteophytes and furthermore there are changes in the surrounding structure of the joint like the joint capsule, muscles and their attachments and the ligaments and menisci.⁴ It is

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the involvement of all of these structures that leads to pain in patients with osteoarthritis.

Generally the pain in knee osteoarthritis is classified as nociceptive, but because of the presence of both neural and avascular tissue components in the cartilage the mechanism of pain is very complex⁵. It is thought that every component of the joint contributes differently to the degree of pain. A lot of nerve fibers are present in the subchondral tissue so damage to it can lead to damage to the nerves thus the neuropathic component of pain⁶. It has been observed that the radiographic grade of osteoarthritis and severity of pain is often mismatched and out of proportion to the degree of damage which has prompted researchers to find out about the different mechanisms of pain including neuropathy as a contributor to pain.

Neuropathic pain is considerable with prevalence of 23% or even higher⁷ in patients with knee or hip osteoarthritis as shown by a recent meta analysis. In fact a recent study done in India has shown that neuropathy in patients with knee osteoarthritis was as high as 49%⁸. Different screening tools and questionnaires have been in use for assessing neuropathic pain such as the DN4 (Douleur Neuropathique 4), pain DETECT questionnaire (PDQ) and SLANNS i.e. Self-administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire. All these questionnaires include information about the intensity of pain, character, quality, site of pain and the frequency of pain.⁹ In our study we used DN4 definition of neuropathic pain, which is a questionnaire developed by the French Neuropathic Pain Group. DN4 consists of two parts one related to history and other part is the physical examination^{10,11}. The rationale of this study was to determine the frequency of neuropathic pain in knee Osteoarthritis patients and its relation to various clinical and sociodemographic factors in the first phase of the study^{8,9}.

METHODOLOGY:

We conducted a cross sectional study in the rheumatology department of federal government polyclinic hospital, islamabad. This was a pilot study conducted on 56 patients to look for incidence of neuropathic pain in knee OA patients through non-probability consecutive sampling technique.

Inclusion criteria: all patients (age >40 years) who fulfilled the American College of Rheumatology (ACR) 1986 classification criteria for primary knee OA were included in the study¹⁰.

Exclusion criteria: patients having other causes of peripheral neuropathy like diabetes mellitus, uraemia, amyloidosis and OA secondary to other causes like rheumatoid arthritis and gout were excluded from the study.

The study was started after getting approval from hospital ethical review board. Participants gave an informed written consent. The purpose, process and benefits of research were explained to all patients included in the study. The study participants' personal information was kept confidential.

Height, weight and Body Mass Index (BMI) was measured in the rheumatology clinic of all the study participants. Clinical examination of both knees was also done for the joint line tenderness, effusion, bony hypertrophy/enlargement and crepitus.

Western Ontario and McMaster Osteoarthritis Index (WOMAC):

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scoring was done. It has three components i.e pain, stiffness and physical functional ability^{12,13}. It is scored from 0-96, a total WOMAC score, with maximum points for the physical functional ability component.

Radiological Assessment

Plain radiographs antero-posterior and lateral views of the both knees were done. The Kellgren-Lawrence (KL) grading system¹⁴ was used for radiological classification of knee osteoarthritis and help from a radiologist was taken. Relationship between radiographic grade and neuropathic pain was assessed in final data analysis.

Douleur Neuropathique 4 (DN4) Questionnaire

Neuropathic pain was defined by DN4, which is a questionnaire developed by the French Neuropathic Pain Group to differentiate somatic from neuropathic pain. DN4 has a total score of 10 and person is said to have neuropathic pain if she / he scores 4 or more. The study outcome was measured in terms of frequency of neuropathic pain in patients with knee osteoarthritis.¹⁵

Data were entered and analyzed through Statistical Package for the Social Sciences (SPSS) version 23.00. Descriptive analysis was explained using frequencies, percentages, mean and standard deviation. The association between the neuropathic pain score using the DN4 questionnaire, grade of osteoarthritis and WOMAC score was tested by using Chi square test.

RESULTS:

The study included 56 patients out of which 44(78.6%) were female. The mean age was 56.73 ± 10.04 years, mean weight was 75.10 ± 10.7 kilograms, mean height of 1.61 ± 0.07 meters, the mean BMI was 28.75 ± 4.15 kg/m². The mean duration of paracetamol use was 2.25 ± 1.58 years. The mean WOMAC overall score was 44.89 ± 11.91 while the mean WOMAC pain score was 9.80 ± 3.40 , the mean WOMAC stiffness score was 2.66 ± 1.65 and the mean WOMAC functional score was 32.41 ± 8.10 . The mean DN4 questionnaire neuropathy score was 2.64 ± 1.95 as shown in Table I.

Table I: Baseline Demographics of the study population

Baseline Demographics	Mean \pm standard deviation
Age	56.73 ± 10.04
Weight in Kg	75.10 ± 10.72
Height in m ²	1.61 ± 0.07
BMI Kg/m ²	28.75 ± 4.15
Duration of disease	2.25 ± 1.58
Baseline WOMAC score overall	44.89 ± 11.91
WOMAC Pain score	9.80 ± 3.47
WOMACS tiffness score	32.41 ± 8.10
WOMAC Functional score	2.66 ± 1.65
DN4 Questionnaire score	2.64 ± 1.95

Based on the Kellgren Lawrence grading 5 patients (8.9%) had Grade 1, 29 (51.8%) had Grade 2, 17 (30.4%) patients had grade 3 while 5 patients (8.9%) had Grade 4 osteoarthritis.

Neuropathic pain calculated by DN4 questionnaire was found in 25(44.6%) of the study population while 31 (56.4%) were found to have a score of 0-3 meaning absence of neuropathic pain.

Two sample t test was done to compare the means and also difference between the two groups i.e. with DN4 score of 0-3 and DN4 score ≥ 4 and a significant difference was found among the groups as shown in Table II.

Table II. Two sample t test shows difference in WOMAC score in both categories of DN 4 questionnaire.

	T		Sig (2 tailed)	Mean difference	Std. error difference	95% conf. interval Of the difference	
Baseline WOMAC score	-2.18	54	0.03*	-6.76	3.09	Lower	Upper
						-12.97	-0.55

$P = < 0.05$.

A p -value of 0.02, 0.004, 0.027, 0.003 and 0.01 on the spearman rho correlation was found between the baseline WOMAC overall score, radiographic grade, neuropathic pain, WOMAC functional score and WOMAC pain score respectively, showing a significant positive correlation between these entities as shown in the table III.

TABLE III. Spearman Rho Correlation analysis of the WOMAC score, Radiographic grade, Neuropathic pain

Factors		Spearman's Rho Correlation Co-efficient (r) and p-value
Baseline WOMAC score	Spearman's rho Correlation Co-efficient	0.311
	p -value	0.02
Radiographic grade	Spearman's rho Correlation Co-efficient	0.375
	p -value	0.004
Neuropathic pain	Spearman's rho correlation coefficient	0.296
	p -value	0.02
WOMAC functional score	Spearman's rho correlation coefficient	0.389
	p -value	0.003
WOMAC pain score	Spearman's rho correlation coefficient	0.341
	p -value	0.01

The comparative analysis of both the groups with the different variables studied are elaborated in table IV, showing clearly that the patients with knee osteoarthritis having neuropathy according to DN4 questionnaire had a significantly raised baseline WOMAC score (p -value 0.02). Those who had a greater radiographic damage based on the KL grading on the chi square analysis showed a significant correlation with the WOMAC pain score and the WOMAC functional score with p -value 0.008 and 0.04.

A Games-Howell post hoc analysis using the one way ANOVA between the different radiographic grades and the neuropathic pain assessed on the DN4 questionnaire showed a significant difference between the groups. The results show that the DN4 questionnaire score was significantly higher when the radiographic grade was I, II and III p -value 0.001 in comparison to grade IV. (p -value=0.79)

Our study did not show a correlation between the weight, height, BMI, age of patients and the duration of disease with the radiographic grade, however the baseline WOMAC score was worse in the female patients as compared to male (p -value=0.049) and the DN4 questionnaire score based on the independent sample t test which showed a p -value of 0.024 among both the genders.

Table IV. Comparative analysis of group 1 and 2 based on DN4 Questionnaire.

	Group 1 (without neuropathy)	Group 2 (with neuropathy)	p-value
Number	31(55.4%)	25(44.6%)	-
Age	56.9±9.45	56.52±4.28	-
Gender			-
Male	9(75%)	3(25%)	
Female	22/44(50%)	F=22/44(50%)	-
Weight	76.16±10.71	73.8±10.8	-
Height	1.61±0.07	1.60±0.06	-
BMI	28.97±4.07	28.46±4.28	-
Radiographic grade			
Grade 1	5(16.1%)	0(0%)	-
Grade2	16(51.6%)	13(52%)	-
Grade 3	6(19.4%)	11(44%)	-
Grade 4	4(12.9%)	1(4%)	-
Dn4 Neuropathy score	1.03±.706	4.64±0.81	0.045
WOMAC overall score	41.87±12.36	48.64±10.36	0.02
WOMAC pain score	9.16±3.76	10.60±2.94	0.008
WOMAC stiffness score	2.41±1.80	2.96±1.42	
WOMAC functional score	30.32±8.43	35.00±6.98	0.04

Table V. Two sample t test shows difference in WOMAC score and DN4 questionnaire in males and females.

	T	Df	Sig (2 tailed)	Mean difference	Std. error difference	95% conf. interval Of the difference	
						Lower	Upper
Baseline WOMAC score	-2.01	54	0.049*	-7.60	3.77	-15.17	-.036
DN4 Questionnaire	-2.43	20.65	0.024*	-1.34	0.55	-2.50	-0.19

P=<0.05.

The frequency of different symptoms of DN4 questionnaire in both the groups are shown below in table VI.

TABLE VI. Frequency of the components of DN4 Questionnaire in both the groups

	Group 1 (without neuropathy)	Group 2 with neuroopathy	p-value
Number	31(55.4%)	25(44.6%)	-
Interview of patient			
Burning	8/31(25.8%)	10/25(40%)	0.25
Painful cold	5/31(16.1%)	12/25(48%)	0.01*
Electric shock	8/31(25.8%)	21/25(84%)	0.000*
Tingling	2/31(6.4%)	10/25(40%)	0.002*
Pins and needles	2/31(6.4%)	16/25(64%)	0.000*
Numbness	4/31(12.9%)	17/25((68%)	0.000*
Itching	1/31(3.2%)	10/25(40%)	0.001*
Examination of patient			
Hypoesthesia to touch	0/31(0%)	9/25(36%)	0.000*
Hypoesthesia to pinprick	0/31(0%)	1/25(4%)	0.26
Brushing	2/31(6.4%)	11/25(44%)	0.001*

DISCUSSION:

Osteoarthritis is the commonest cause of functional

decline and disability, particularly in the middle age to old age people leading to a poor quality of life. Osteoarthritis leads to limitation in the mobility of around 80% of the patients and out of them 25% cannot do their daily activities.¹⁶ Good physical therapy and patient education has been the main stay of treatment in OA knee patients alongside paracetamol, topical and systemic NSAIDs and on need basis intra-articular steroid injections. Other entities like hyaluronic acid, chondroitin sulfate, kinesiotaping, radiofrequency ablation etc. have conditional recommendations in particular situations.¹⁷

Pain in knee osteoarthritis is proposed to have two components; nociceptive and neuropathic. These can be mediated by peripheral pathway i.e. mechanical or the central pathway leading to hyperalgesia.¹⁸ We focused on the neuropathic component of pain in this study and would emphasize to treat neuropathic pain in patients with osteoarthritis.

Previously done studies show a wide range of prevalence of neuropathic pain in knee i.e. from 5.4– 52%.^{19,20} In our study, we found that 44.6% patients had neuropathic component of pain which is comparable to the figures of a study performed in India where 49% patients had neuropathy⁸. A Spanish community based study showed a figure of 52%. However after removing confounders like other neuropathy causing conditions, the prevalence reduced to 33%.²¹ In both these studies DN4 questionnaire was used as a tool to assess neuropathy.

Other scales for measuring the neuropathy, like the Pain DETECT questionnaires and the Self-administered Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire (S-LANSS) have also been used in different studies to assess the neuropathic pain in knee OA. The results from these tools also show almost similar prevalence of neuropathic pain. Examples include a study done in the United Kingdom showing that 27% of 179 respondents had neuropathic pain²² and an Indonesian study in which 45.9% of patients were found to have neuropathic pain.²³

As regards WOMAC scoring system, in our study it was seen that the total WOMAC score of the participants, the functional component and pain component of WOMAC score were analogous to the study done by Polat et al in Turkey in which WOMAC score in the neuropathy group was 58.5 vs 42.5.²⁰

The relationship between radiographic grade, WOMAC score and neuropathic pain was not linear as found in our results and supported by study done by Finan et al that also showed an indeterminate relationship between radiographic damage and the degree of neuropathic pain.²⁴

Our study also did not show any correlation between the weight, height, BMI, age of patients and the duration of disease with the DN4 questionnaire and the WOMAC score. This is also supported by previously done studies for example a study by Yildirim MA et al in Turkey did not show significant difference in the anthropometric measures of both the groups.²⁵ However, the literature review does show the results of some studies where patients with neuropathic pain component had slightly shorter height as compared to those without neuropathy.^{19,26}

SHORT COMINGS:

There were several limitations in our study. First of all sample size was small. Secondly neuropathic pain was defined by using the DN4 questionnaire but not confirmed by the nerve conduction studies. Lastly, depression is an important component for somatization of pain and this component was not addressed in our study.

CONCLUSION

There was a high frequency of neuropathic pain in patients with knee osteoarthritis. The DN4 questionnaire score correlated with the WOMAC total score and the functional and pain components. It was also found that the patients with grade I, II and III osteoarthritis (KL

grading system) had a significantly higher WOMAC score and DN4 questionnaire score.

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