Research Article

Frequency of neuropathic pain and its impact on functional status in primary knee osteoarthritis patients

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Abstract

Background: Neuropathic mechanisms are considered to play a role in development of pain in knee osteoarthritis (OA). Some OA patients developed sensitized central nociceptive circuits that enhance pain during various states of peripheral tissue insult. **Method:** 70 patients with primary knee OA were enrolled in this study. Antero-posterior knee radiographs were done using the Kellgren Lawrence scale. Pain severity was assessed by Numerical rating scale (NRS), neuropathic pain was assessed by Douleur Neuropathique en 4 (DN4) questionnaire and functional status was assessed by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale. **Results:** 52.9% of the patients had neuropathic pain according to DN4 scale. The mean pain WOMAC score and WOMAC physical function score were significantly higher in patients with neuropathic pain when compared to patients with non-neuropathic pain; 9.86 ± 2.1 versus 6.79 ± 3.59, P <0.0001 and 44.24 ± 5.43 versus 39.39 ± 10.36, P =0.015 respectively. DN4 score had a significant positive correlation with WOMAC pain (r=0.459, P<0.001), stiffness (r=0.258, P=0.031) and physical function (r=0.307, P=0.01). **Conclusion:** Chronic pain with OA has neuropathic components. Neuropathic pain is a factor that increases pain and disability and disrupts functional status in osteoarthritis patients.

Keywords: Osteoarthritis, Neuropathic pain, Douleur Neuropathique en 4 Questions

Introduction

Osteoarthritis (OA) is the most common form of joint disorder, with knee OA being a leading cause of disability among older adults globally[(1)]. It causes significant morbidity in elderly individuals, and its age of onset is gradually decreasing[(2)]. Many etiologies contribute to OA development, including age, sex, hereditary factors, and trauma[(3)].

As indicated, a common and invalidating key symptom of OA is pain[(4)]. The pain associated with OA has traditionally been attributed to peripheral pain mechanisms which involve activation of primary nociceptors in somatic tissues such as the joint and/or peri-articular structures[(5)]. Discordance between radiographic and pain severity in people with OA has led researchers to investigate the existence of other pain mechanisms to explain this discrepancy[(6)]. Recently both peripheral and central mechanisms found to contribute to OA pain[(5)].

Central sensitization in OA may present with clinical features that are characteristic of neuropathic pain (NP) conditions[(7)] Clinical features may include hyperalgesia, paraesthesia, burning pain, allodynia and numbness[(4)].

Multiple studies showed that the OA pain experience is not solely nociceptive: about 20% of hip and 20–67% of knee OA patients present neuropathic-like symptoms[(8)]. In OA, such symptoms probably arise from structural changes in joint innervation and neural changes at several levels of the nervous system[(9)].

Progressive neuropathic pain caused by OA disturbs patient's functional movement ability. This result in loss of workforce and the associated psychological effects lead to impairments in working life, entertainment, social life, and the sleep pattern of the patient, which greatly compromising quality of life[(10)].

Screening and assessment questionnaires administered to patients with neuropathic pain are valid tools that help further understanding of subjective neuropathic pain symptoms while assisting in routine monitoring and prediction of treatment response and outcomes[11].

Screening questionnaires include the Pain Detect score (PDQ), Leeds Assessment of Neuropathic Symptoms and Signs pain scale with self-report version (LANSS), Douleur Neuropathique with 4 Questions (DN4), ID pain, and the Neuropathic Pain Questionnaire (NPQ)[11].

Aim of the work

The aim of the present study was to determine the frequency of neuropathic pain in patients with primary knee osteoarthritis, and to investigate its correlation with the functional status and disease severity.

Patients and methods

Seventy patients (27 males and 43 females) who fulfilled ACR Clinical and radio-graphic diagnostic criteria for primary knee osteoarthritis[12] were consecutively included in the study.

Patients with any previous history of knee surgery, infection, rheumatoid arthritis and other pain/neurological conditions such as radiculopathies, diabetes mellitus, stroke, traumatic brain injury, and patients who were already receiving medical treatment for neuropathic pain were be excluded. Informed consent was taken from all participants in the study. The study was approved by the ethics committee of the Faculty of Medicine.

All patients were subjected to full medical history, clinical examination, pain assessment by Numerical Rating Scale (NRS) and Douleur Neuropathique 4 score (DN4), evaluation of functional status by Arabic version of The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), plain x-ray both knees antero-posterior view and radiological grading using Kellgren and Lawrence grading scale.

Statistical analysis

Analysis of data was done by personal computer using SPSS (Statistical program for social science) version 19. The data of all software patients and controls were fed into an IBM personal computer. Data were expressed as mean ± SD for parametric variables and as number and percent for non-parametric variable. Comparison between groups for parametric data was done by independent samples t-test (unpaired t-test). Chi – square (X2) test was used to compare qualitative variables. The difference was expressed as probability of value (P value). The difference was considered significant if $P < 0.05$. Pearson and Spearman correlation coefficients (r) were calculated for detection of parametric and non-parametric correlations respectively.

Results

Seventy OA patients were included in the present study, their mean age was 53.39 ± 8.004 years, and their mean disease duration was 4.69±2.91 years. The mean DN4 in the studied patients was 4.39±1.51. According to DN4 Douleur Neuropathique 4 score for neuropathic pain, 37 patients (52.9%) have neuropathic pain and 33 patients (46.9%) have non-neuropathic pain. The demographic characteristics of the studied patients are shown in Table 1

Pain, functional status and osteoarthritis severity were assessed in patients with neuropathic pain and those with non-neuropathic pain as shown in Table 2. There were a statistically significant differences between 2 groups as regarding, pain WOMAC, physical function WOMAC scores (P<0.0001, P=0.015 respectively).

The correlation of DN4 score with age, different components of WOMAC and radiological grading was done. There were significant positive correlations of DN4 with WOMAC pain score (r=0.459, P< 0.0001) (Fig.1), WOMAC stiffness (r= 0.258, P=0.031) and WOMAC physical function (r=0.307, P= 0.01) (Fig.2). Age, BMI, and other WOMAC subscale were not found to be significantly correlated with DN4 score. There was also no association of the grade of OA with neuropathic pain.

Table (1): Demographic data of the studied patients

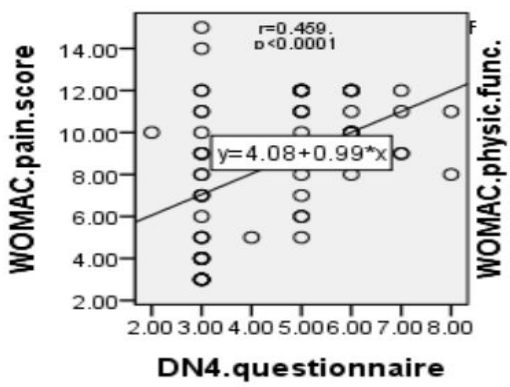
Parameter mean ± SD (range)	DN4 Score			
	Patients with neuropathic pain (n=37)	Patients with non-neuropathic pain (n=33)	t / χ^2	*P* value
Sex (Female/male)	27/10	20/13	1.209	0.271
Age (Years)	52.57± 8.5 (32-68)	543± 7.5 (40-65)	0.904	0.369
BMI (Kg/m^2)	25.6±4.14 (19.03-34.4)	25.84±4.51 (18.75-35.9)		
Normal Weight (18.5-24.9)	19 (51.4%)	13 (39.4%)	1.880	0.391
Overweight (25-29.9)	9 (24.3%)	13 (39.4%)		
Obese (>30)	9 (24.3%)	7 (21.2%)		
Disease duration(Years)	4.5±1.9 (1-11)	4.9±3.8 (1-20)	0.521	0.604

By independent sample t-test and Chi square test.

Table (2): Pain, functional status and osteoarthritis severity in OA patients:

Parameter mean ± SD (range)		DN4 Score: Patients with neuropathic (n=37)	DN4 Score: Patients with non-neuropathic (n=33)	t (x^2)	*P* value
NR Score		6.57±1.59 (3-9)	6±1.46 (3-8)	1.550	0.126
WOMAC	pain score (0 to 20)	9.86± 2.1 (5-12)	6.79±3.59 (3-15)	4.439	**<0.0001***
	stiffness score (0 to 8)	3.57±1.2 (1-6)	4± 1.2 (2-6)	1.527	0.131
	physical functional score (0 to 68)	44.24± 5.43 (35-56)	39.39± 10.36 (21-60)	2.491	**0.015***
	overall score (0 to 96)	56.81 ± 6.62 (42-70)	52.52±11.36 (31-75)	1.959	0.054
KL scale	Grade II	17(45.9%)	19(57.6%)	1.124	0.570
	Grade III	16(43.2%)	12(36.4%)		
	Grade IV	4 (10.8%)	2(6.1%)		

By independent sample t-test



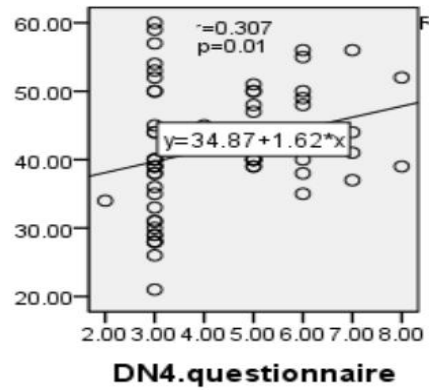


Fig.1:Correlation between DN4 score & WOMAC pain
Fig. 2:Correlation between DN4 score & WOMAC physical function

Discussion

Osteoarthritis (OA) is a common arthritic disorder, often associated with pain and local tenderness or pressure hyperalgesia around the affected joint(s) [13].

Although knee OA has been considered the archetypal model of inflammatory or nocicep-tive pain [9], it is increasingly apparent that people with knee OA may present with different pain phenotypes. It is now recognized that some individuals with knee OA exhibit features of neuropathic pain [9].

In our study, neuropathic pain was detected in 52.9 % of patients based on the DN4 scale in consistent with our study neuropathic pain in OA patients was detected in 28% in a study by Turovskaya and Alekseeva 2013 [14], 51.9% in a study by Oteo-A´lvaro et al., 2015[15], whereas 24% in a study by Go¨lge et al., 2015 [16] using the same questionnaire, another study by Radwan and Borai 2018[17] neuropathic pain detected in 17.6% of patients, 46.7% in a study by Askin et al., 2017[18], 49% in a study by Narayan et al., 2017[19], 40% in a study by YILDIRIM et al., 2019[20].

In our study, there was no statistically signifi-cant difference between neuropathic and non-neuropathic groups based on DN4 score as regarding disease duration, in agreement with our study Aşkın et al., 2017[18] found also no statistically significant difference between two groups as regarding disease duration.

In our study, we found that WOMAC subscales pain, and physical function were significantly higher in neuropathic than non-neuropathic groups with ($p < 0.0001$, $p = 0.015$ respectively), this was consistent with a study by Narayan et al., 2017[19].

There was a significant positive correlation between total DN4 score and WOMAC pain score ($r = 0.474$, $p < 0.0001$), WOMAC physical function score ($r = 0.289$, $p = 0.015$) this was in agreement with a study by Go¨lge et al., (2015)[16], Askin et al., (2017)[18],

Narayan et al., (2017)[19] and Radwan & Borai 2018[17]. In the present study, by using DN4 we found no statistically significant difference between the studied OA groups (neuropathic and non-neuropathic) as regarding different Kellegren Lawrence scale grades. This was consistent with a study by Murphy et al., 2011[21] and Finan et al., 2013[6].

The association between radiographic severity in OA and pain remains indeterminate. There are many patients who have radiographic evidence of OA in the absence of pain and those who have little radiographic evidence of OA with moderate to severe pain[22].

Finan et al., 2013[6] suggested that central sensitization in knee OA is apparent among patients with high levels of pain in the absence of moderate-to-severe radiographic evidence of knee OA.

In conclusion, Chronic pain with OA has neuropathic components. Neuropathic pain is a factor that increases pain and disability and

disrupts functional status in osteoarthritis patients.

We recommend that, neuropathic pain should be assessed and questioned in OA patients.
using further assessment tools for neuropathic pain associated with Knee OA pain and neuropathic pain treatment should be taken as part of the treatment of OA.

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