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A Cross-Sectional Assessment of Neuropathic Pain in Patients with Psoriasis and Psoriatic Arthritis

Psöriyazis ve Psöriyatik Artritte Ağrının Nöropatik Bileşeni: Kesitsel Bir Çalışma

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ABSTRACT Objective: Many patients with psoriasis (Ps) and psoriatic arthritis (PsA) develop a variety of sensory skin symptoms as discomfort, burning, stinging, irritation and hypersensitivity. We hypothesize that neuropathic pain (NP) is a component of these sensory skin symptoms. This study aims to assess the prevalence of NP in patients with Ps and PsA and to investigate the association between disease severity and pain scores. **Material and Methods:** We conducted a cross-sectional study on 79 Ps patients, 21 PsA patients, and 45 healthy individuals. NP was assessed by the PainDETECT Questionnaire (PDQ). Pain intensity was scored on Visual Analogue Scales (VAS). We used the Psoriasis Area Severity Index (PASI) and the Dermatology Life Quality Index (DLQI) and Nottingham Health Profile (NHP) to assess the disease severity and quality of life, respectively. **Results:** PsA patients had significantly more "likely neuropathic pain" compared with Ps patients and healthy controls (19% vs. 3.8% and 6.7%). The mean PDQ scores were higher in the Ps and PsA groups than the control group. PsA group had significantly worse scores of pain, physical activity, and fatigue compared with the Ps group. **Conclusion:** Our findings suggest that neuropathic pain may be a component of the sensory symptoms manifested in PsA patients. However, no association was found between disease severity and neuropathic pain.

Keywords: Neuropathic pain; psoriasis; psoriatic arthritis

ÖZET Amaç: Psöriyazis (Ps) ve psöriyatik artrit (PsA) olan birçok hastada, ciltte rahatsızlık, yanma, acı, tahriş ve aşırı duyarlılık gibi çeşitli duyusal cilt semptomları gelişebilir ve nöropatik ağrı bu duyusal cilt semptomlarının bir bileşeni olabilir. Bu çalışma, Ps ve PsA hastalarında nöropatik ağrı varlığını değerlendirmeyi ve hastalık şiddeti ile ağrı skorları arasındaki ilişkiyi araştırmayı amaçlamaktadır. **Gereç ve Yöntemler:** Çalışmaya 79 Ps, 21 PsA hastası ve 45 sağlıklı kontrol alındı. Nöropatik ağrı PainDETECT anketi [PainDETECT Questionnaire (PDQ)] ile, ağrı şiddeti Görsel Analog Skala [Visual Analog Scale (VAS)] ile değerlendirildi. Hastalık şiddeti ve yaşam kalitesini değerlendirmek için sırasıyla Psöriyazis Alan Ciddiyeti İndeksi (PASI) ,Dermatoloji Yaşam Kalitesi İndeksi (DLQI) ve Nottingham Sağlık Profili (Nottingham Health Profile (NHP) kullanıldı. **Bulgular:** PsA'lı hastalarda, Ps'li hastalar ve sağlıklı kontrollerle karşılaştırıldığında anlamlı olarak daha yüksek "muhtemel nöropatik ağrı" değerleri izlendi (sırasıyla; %19, %3,8 ve %6,7). Ortalama PDQ skorları Ps ve PsA gruplarında kontrol grubuna göre daha yüksek bulundu. PsA grubu, Ps grubuna göre anlamlı derecede kötü ağrı, fiziksel aktivite ve yorgunluk skorlarına sahipti. **Sonuç:** Bulgularımız nöropatik ağrının PsA hastalarında ortaya çıkan duyusal semptomların bir bileşeni olabileceğini düşündürmektedir. Bununla birlikte, psöriyazis hastalık şiddeti ve nöropatik ağrı arasında bir ilişki bulunamadı.

Anahtar Kelimeler: Nöropatik ağrı; psöriyazis; psöriyatik artrit

Psoriasis (Ps) is a chronic immune-mediated inflammatory disease that affects the skin.[1] Ps affects about 1 to 3% of the worldwide population.[2] Physical skin symptoms such as discomfort, burning, stinging, irritation and hypersensitivity are not uncommon. It is reported that up to 42% of Ps patients experience pain. Studies showed that the physical symptoms of the disease including pain are attributed to poor quality of life of Ps patients.[3-5] In about 30% of Ps patients, the inflammatory process involve joints and spine leading to the development of psoriatic arthritis (PsA).[6] It is suggested that neuropathic pain (NP)

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might play a role in sensory symptoms in patients with psoriasis. NP is produced by primary neuronal lesion or dysfunction of the peripheral or the central nervous system.[7] Therefore, stimuli from psoriatic skin lesions can induce nociceptive inputs producing changes in the neural pathways and resulting in central nervous system sensitization by time. Increased excitation and reduced inhibition of neural pathways can lead to functional neuronal changes and high responsiveness to stimuli regardless of the affected body area or intensity of the stimulus.[8] In rheumatological disorders, pain occurs as a result of the prolonged stimulation of nociceptors by chronic inflammation.[9] Determining neuropathic component of pain and differentiating nociceptive pain is problematic. The PainDETECT Questionnaire (PDQ) is a tool for diagnosing NP.[10] In a study with PsA patients in 2017, consistency in pain classification with PDQ was found very strong. The authors accepted that PDQ was as an easily applied instrument that helps determination of patients' significant central pain component.[11] Few studies have investigated the presence of a neuropathic component in the pain sensation of Ps and PsA patients. Only the rates of sensory symptoms were investigated in these studies. Therefore, we conducted this study to assess NP in both Ps and PsA patients using the PDQ.

MATERIAL AND METHODS

We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement guidelines when reporting this manuscript.[12] The study was approved by the local ethics committee (Approval no. 2015/124).

STUDY DESIGN, SETTING, AND DURATION

We conducted an observational cross-sectional study in the Dermatology, Rheumatology, Physical Medicine and Rehabilitation outpatient clinics. The study was do ne within the period from May 2015 to December 2016. All included patients gave written informed consent.

STUDY GROUPS AND ELIGIBILITY CRITERIA OF THE STUDY PARTICIPANTS

Our study included three groups: Group 1 included the patients with Ps, Group 2 included the patients with PsA, and Group 3 was a control group of age- and sex-matched healthy individuals.

Patients who meet the following criteria were included in the study:

- Male and female Ps patients whose age was >18 years
- Patients who had been diagnosed with Ps or PsA according to the CASPAR criteria[13]
- Patients with a disease duration of more than one year

We excluded patients in the following conditions:

- Patients receiving treatments for any neurologic or psychiatric illness
- Patients who suffer from any accompanying rheumatologic disease
- Patients with metabolic diseases such as diabetes, chronic renal failure, thyroid dysfunction which may lead to peripheral neuropathy
- Patients with central or peripheral nervous system disorders.

SAMPLING METHOD AND SAMPLE SIZE CALCULATION

We employed a convenience sampling method. Within the study period (from May 2015 to December 2016), all Ps patients attending the study setting were eligible for inclusion in this study.

OUTCOME MEASURES

NP was evaluated by the PDQ. It is a screening tool in the form of a self-administered questionnaire that comprises seven items assessing pain qualities, course pattern of pain and pain radiation. It is scored between -1 to 38. Total score ≥19 indicates likely neuropathic pain; total score ≤12 indicates unlikely neuropathic pain and total score between 12 and 19 indicates possible NP.[14]

The Psoriasis Area and Severity Index (PASI) was used to determine the severity of Ps. It evaluates the severity of erythema, induration, desquamation according to their anatomical localization. Patients who had a PASI value ≤5 were considered to have mild Ps, a PASI value of 5-10 indicated moderate Ps and PASI ≥10 indicated severe Ps.

Pain severity was assessed by the Visual Analogue Scale (VAS).[15]

Quality of life was assessed by the Nottingham Health Profile (NHP)and the Dermatology Life Quality Index (DLQI). NHP evaluates emotional, social and physical health problems perceived by the individual. It consists of 38 questions and evaluates 6 subsections regarding energy level, pain, physical activity, sleep, emotional reactions, social isolation. Questions are answered as "Yes" or "No". Each section is scored between 0-100. While 0 indicates the best health status, 100 indicates the worst health status. The DLQI includes ten items on patients perception of symptoms, feelings, daily activities, leisure work, school, personal relationships and treatment.[16,17]

Statistical Analysis

Categorical data were described as frequency and percentages while continuous data were described as mean and standard deviation. Data normality was tested using the Kolmogorov Smirnov test. The association between categorical variables (gender, groups for disease severity) was tested by the Chi-square test. For comparing continuous variables (age, disease duration, NP score, VAS pain, NHP, PASI, DQOI) we used the student t-test and the Mann Whitney U test for normally (DQOI) and non-normally (other continuous variables) distributed data, respectively. Continuous variables were compared with one way analysis of variance (ANOVA) (age) or Kruskal-Wallis analysis (other continuous variables) in PsA, Ps and control groups. An alpha level below 0.05 was considered for statistical significance. All analyses were performed using SPSS version 17.0 software.

RESULTS

DEMOGRAPHICS AND CHARACTERISTICS

Our study included 145 individuals divided into three groups: the Ps group included 79 patients (47 females, 32 males; mean age 41.9±13.7 years), the PsA group included 21 patients (15 females, 6 males; mean age 41.7±13.7),and a third group (control group) consisting of 45 healthy individuals (26 females, 19 males; mean age 36.7±9 years). The baseline characteristics of the study population in the groups are shown in Table 1.

PAIN SCORES OF THE PAIN DETECT QUESTIONNAIRE

The percentage of patients with "likely neuropathic pain" was higher in the PsA group than the Ps group and the control group (19% vs. 3.8% and 6.7%, respectively). The percentage of patients with "possible neuropathic pain" was 14.3%, 7.6%, 4.4%, respectively. No neuropathic pain was observed in 66% of patients with PsA, 88.6% in patients with Ps and 88.9% in the control group. Moreover, higher PDQ scores were found in the Ps and PsA groups compared with the control group. The mean (SD) of PDQ scores in the three groups were as follows: (Ps: 11.1±6.2, PsA: 6.6±5.7, and control: 5.6±5.9). The mean difference between PsA group and the control group was statistically significant (p=0.002).

VAS PAIN SCORE AND NOTTINGHAM PAIN SCORE

The VAS scale showed that PsA group had significantly higher pain score than the Ps group (4.5 vs. 1.6, respectively, p=0.001). The Nottingham Pain Subscale showed higher pain scores in the PsA group than the Ps group (34.6 vs. 18.2, p= 0.008, Table 2).

TABLE 1: Characteristics of patients and controls.

	Ps group n=79	PsA group n=21	Control n=45	p value
Age (years)	41.9±13.7	41.7±13.7	36.7±9.1	0.07
Gender (female) n, %	47 (59.5%)	15 (71.4%)	26 (57.8%)	0.54
Disease duration (years)	11.4±10.8	11.4±9.6	NA	0.66
PainDETECT Score	6.6±5.7	11.1±6.2	5.6±5.9	0.002*
Likely NP (%)	3.8%	19%	6.7%	0.04*

* Statistically significant. Continuous variables are expressed as mean (SD), while categorical variables are presented as number and percentages.
Ps: Psoriasis; PsA: Psoriatic arthritis; NP: Neuropathic pain.

TABLE 2: The disease severity, pain scores, and quality of life of patients in the Ps and PsA groups.

	Ps Group n=79	PsA Group n=21	p value
VAS	1.6±2.7	4.5±3.3	0.001*
PASI	4.9±3.3	4±2.3	0.55
DLQI	16.5±9.2	16.6±9.6	0.96
Nottingham Health Profile scores			
NHP-Pain	18.2±28.3	34.6±34	0.008*
NHP-Physical Activity	14.8±20.2	26.7±23.4	0.01*
NHP-Fatigue	44.9±43.5	66.6±42.8	0.04*
NHP-Social Isolation	31.8 ±40.6	30.1±44.2	0.66
NHP-Sleep	36.4±31.2	37.1±31.1	0.88
NHP-Emotion	42.5±40.2	36.9±39.2	0.49
Disease Severity			
Severe Ps %	11.4%	0%	
Moderate Ps %	27.8%	19%	
Mild Ps %	60.8%	81%	

* Statistically significant. Continuous variables are expressed as mean (SD), while categorical variables are presented as percentages.
VAS: Visual Analog Scale; PASI: Psoriasis Area Severity Index; DLQI: Dermatology Life Quality Index; NHP: Nottingham Health Profile; Ps: Psoriasis; PsA: Psoriatic Arthritis.

DISEASE SEVERITY AND PS AREA SEVERITY INDEX (PASI)

Disease duration was approximately similar in both groups (11.5 vs. 11 years). The PASI score in the Ps group showed that 11.4% of the patients had severe disease, 27.8 %had moderate disease, and 60.8% had mild disease. While in the PsA group, none of the patients had severe disease, 19% had moderate disease, and 81% had mild Ps. There was no association between the sensory pain scores and the severity of the disease.

DERMATOLOGY LIFE QUALITY INDEX AND NOTTINGHAM HEALTH PROFILE

The Dermatology Quality of Life Index did not differ significantly between the two study groups (Ps: 19.4±10.2 vs. PsA: 16.5±9.17, p=0.96). There was no significant difference between the two groups in terms of the Nottingham social isolation, sleep, and emotions score. However, higher scores of pain and fatigue were reported in the PsA group compared with the Ps group (Table 2).

DISCUSSION

SUMMARY OF MAIN FINDINGS

Our study showed that patients with Ps and PsA had significantly higher pain scores assessed by PDQ, VAS and NHP than the control group. Moreover, PsA patients were more likely to suffer from NP and to experience more physical activity limitations and fatigue.

AGREEMENTS AND DISAGREEMENTS WITH PREVIOUS STUDIES

These findings are consistent with the literature suggesting that many patients with Ps are experiencing different types of sensory skin symptoms including pain.[18] Several studies were carried out to assess the sensory skin symptoms in Ps patients, which include hypersensitivity, burning, stinging, cramping, tingling, aching, irritation and itching. Many of these sensory symptoms include a neuropathic component. However, some studies failed to confirm this.[3]

Ahmed et al. used the PDQ to evaluate NP in patients with rheumatoid arthritis (RA), they found that 28% of patients with RA had possible NP and 5% had likely NP.[19] In our study, we found that 14.3 of patients with PsA had possible NP and 19% had likely NP. In the study of Ahmed et al., a positive correlation was found between VAS and the PDQ suggesting that there might be a non-inflammatory neuropathic component that is mediating pain perception in RA. These results were supported by Christensen et al. who found that among RA patients with high PDQ scores,

there is a non-inflammatory pain component affecting the disease activity score (DAS28) and patient-reported outcomes in general.[20]

Rifbjerg-Madsen et al. also used the PDQ in patients with RA, they found relatively higher neuropathic pain scores in RA patients, and they suggested that a total PDQ score ≥19 at baseline can predict a poor clinical response on initiating anti-inflammatory therapy.[21]

Another study by Koop et al. showed that about 17% of RA patients had likely NP although 75% of them were in DAS28 remission. Despite the low disease severity, nearly half of the patients reported significant pain; this led them to conclude that inflammation is not the only contributing factor to pain, but other factors such as NP might play a role.[22] Similar to this study 19% of PsA patients had likely NP in our studyNP was not related to disease severity in our study, which is on the contrary to the other studies that suggest an association between PASI and sensory skin symptoms.[6] Sampogna et al. did not find any correlation between symptoms and PASI. This was justified that the PASI might be an inadequate assessment to evaluate Ps patients since the PASI only assesses skin lesions but does not evaluate sensory symptoms.[23]

STRENGTH AND LIMITATIONS

To the best of our knowledge, this is the first study to assess NP in both Ps and PsA patients using the PDQ. Some limitations of our study are worth noting. The relatively small sample size may have affected our results, and while the majority of our patients had mild to moderate Ps (65%, 23% respectively), patients with severe Ps (12%) may be the reason behind finding no association between disease severity and both NP and dermatologic quality of life. Further studies with larger sample size are needed to confirm whether there is an association between NP and disease severity.

Authors' Conclusion

Our findings suggest that Neuropathic pain may be a component of the sensory symptoms manifested in PsA patients. However, no association was found between disease severity and pain.

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