Original Research Article

Pressure Pain Threshold in Musculoskeletal Disorders

Kas İskelet Hastalıklarında Basınç Ağrı Eşiği

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ABSTRACT

Aim: *Pain is the most significant symptom in musculoskeletal disorders. General hypersensitivity to pain is often associated with conditions of chronic pain. In this study we compared pain degrees of different musculoskeletal disease groups by pain pressure threshold and visual analog scale.*

Materials and Method: *Patients diagnosed with ankylosing spondylitis (n=34), fibromyalgia (n=30), myofascial pain syndrome (n=33), osteoporosis (n=34), generalized osteoarthritis (n=34) and rheumatoid arthritis (n=34) and healthy subjects (n=30) were included in the study. Beck depression inventory was used for psychological evaluation. Visual analog scale (VAS) was used to quantify clinical pain. PPT measurements made from the areas that generally not showing involvement of disease: at middle deltoid, middle ulna, hypothenar eminence, thumb, mid-tibia, and quadriceps femoris.*

Results: *VAS score for clinical pain ranged from 4.76±3.15 in ankylosing spondylitis to 7.44±2.42 in fibromyalgia. Fibromyalgia consistently had the lowest PPT across all sites of measurements indicating increased pain sensitivity. Myofascial pain syndrome and ankylosing spondylitis were the only diseases that did not show greater sensitivity to pain compared to healthy controls. Osteoporosis patients also reported an average clinical pain of 6.09±3.23 on VAS, and showed general tenderness regardless of presence of verified fractures. Overall, female gender, advanced age, depression and NSAID use correlated with lower PPT.*

Conclusions: *The level of pain sensitivity may provide a clue regarding the mechanism and treatment options of musculoskeletal disorders.*

Keywords: *pressure pain threshold; ankylosing spondylitis; myofascial pain syndrome; osteoporosis; arthritis; fibromyalgia*

ÖZET

Amaç: *Ağrı kas iskelet sistemi bozukluklarında en belirgin semptomdur. Ağrıya karşı genel aşırı duyarlılık sıklıkla kronik ağrı koşullarıyla ilişkilidir. Bu çalışmada, farklı kas-iskelet sistemi hastalık gruplarının ağrı derecelerini, ağrı basınç eşiği ve görsel analog skala ile karşılaştırdık.*

Yöntem ve Gereçler: *Çalışmaya ankilozan spondilit (n = 34), fibromiyalji (n = 30), miyofasiyal ağrı sendromu (n = 33), osteoporoz (n = 34), jeneralize osteoartrit (n = 34) ve romatoid artrit (n = 34) tanısı alan hastalar ve sağlıklı kişiler (n = 30) dahil edildi. Psikolojik değerlendirme için Beck depresyon envanteri, klinik ağrıyı ölçmek için görsel analog skala (VAS) kullanıldı. PPT ölçümleri hastalık tutulumu göstermeyen alanlardan yapıldı: orta deltoid, orta ulna, hipotenar belirginlik, başparmak, orta tibia ve kuadriseps femoris.*

Bulgular: *Klinik ağrı için VAS skoru, ankilozan spondilitte 4.76 ± 3.15, fibromiyaljide 7.44 ± 2.42 idi. Fibromiyalji, ağrı duyarlılığının arttığını gösteren tüm ölçüm yerlerinde tutarlı olarak en düşük PPT'ye sahipti. Miyofasyal ağrı sendromu ve ankilozan spondilit, ağrıya sağlıklı kontrollerle karşılaştırıldığında daha fazla duyarlılık göstermeyen tek hastalıktı. Osteoporoz hastaları ayrıca VAS'da ortalama klinik ağrı 6.09 ± 3.23 ve doğrulanmış kırıkların varlığına bakılmaksızın genel hassasiyet göstermiştir. Genel olarak, kadın cinsiyet, ileri yaş, depresyon ve NSAID kullanımı düşük PPT ile koreleydi.*

Sonuç: *Ağrı duyarlılığının düzeyi, kas-iskelet bozukluklarının mekanizması ve tedavi seçenekleri hakkında ipucu sağlayabilir.*

Anahtar Kelimeler: *basınç ağrı eşiği; ankilozan spondilit; myofasial ağrı sendromu; osteoporoz; artrit; fibromiyalji*

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INTRODUCTION

Chronic pain is an integral part of most musculoskeletal disorders, having a negative impact on the quality of life of the patients. Although pain is regarded as the body's response to noxious stimuli, its presentation, frequency and intensity varies considerably between disease groups and individuals. Certain conditions may be associated with a general hypersensitivity to pain or tenderness, while others may be specific to the affected area. Quantitative assessment of experimentally evoked pain has been used to reveal differences between genders and age groups of healthy individuals as well as disease groups. These differences may have important implications in terms of diagnosis, disease management, prediction of treatment response and understanding the underlying pain mechanisms (1).

In this study, we compared pain pressure threshold (PPT) in areas of the body normally not affected by the disease between ankylosing spondylitis, fibromyalgia, myofascial pain, osteoporosis, generalized osteoarthritis, rheumatoid arthritis and healthy control subjects to assess the pain perception degrees, presence and extent of general hypersensitivity to mechanical stimulus.

MATERIALS and METHODS

Study design and patients

This was a prospective study comparing pain pressure threshold of different musculoskeletal disorders associated with chronic pain. Patients followed in our Physical Medicine and Rehabilitation Outpatient Clinic with a clear diagnosis of one of the following diseases were included in the study: rheumatoid arthritis (n=34), ankylosing spondylitis (n=34), fibromyalgia (n=30), myofascial pain syndrome in the trapezius muscle (n=33), osteoporosis (n=34) and generalized osteoarthritis (n=34). In addition, thirty healthy control subjects were included in the study.

Rheumatoid arthritis was diagnosed based on the 1987 American College of Rheumatology (ACR) classification criteria (2). Ankylosing spondylitis was diagnosed based on the modified New York criteria (3). Fibromyalgia was diagnosed based on the 1990 ACR criterias (4).

The presence of myofascial trigger points was determined using the diagnostic criteria described by Simons et al (5). Osteoporosis was diagnosed according to WHO definition (6). Generalized osteoarthritis was defined as bilateral involvement of fingers or involvement of the spine and both femorotibial joints (7).

Patients fulfilling diagnostic criteria for more than one of the above musculoskeletal disorders were excluded from the study. Measurement of bone mineral density (BMD) was performed by using Dual Energy X-ray Absorptiometry (DEXA). Measurements were taken in all cases and the patients who had osteoporosis and one of the any other diseases were excluded also. In addition, subjects were excluded if pregnant, younger than 18 years of age, having cognitive or mental problems, history of surgery in the upper or lower extremity or any disease that may affect upper or lower extremity performance such as polyneuropathy, vasculitis, dermatological diseases, neurovascular skin diseases, peripheral vascular disease, spinal cord injury, malignancy, burn or loss of sensation. Patients who had disease involvement in the measurement area were excluded.

The study was approved by the institutional review board. Written informed consent was obtained from all participants.

Procedures

General (clinical) pain was evaluated using the visual analog scale (VAS), where patients were asked to mark the level of pain related to their disease on a 10 cm lateral scale with one end indicating no pain and the other end indicating worst possible pain.

Pain pressure threshold was measured using a digital algometry (JTECH Medical – Algometer Commander – USA). Patients were familiarized with the algometry and a demonstration was carried out on a different part of the body unrelated to the sites of measurement (thenar area). Patients were asked to say "stop" when they feel pain first to indicate pain threshold. A 1 cm^2 probe was used and values are presented in Newton (N). Pressure was increased at a speed of 10N/s until patient reported pain and to confirm reliability three readings were taken from each site with 5 sec intervals between readings and the mean value was used in the analysis. All measurements were carried outby the same physician who was blind to the patient groups, in the same room and room temperature, using the same equipment and. Measurements were carried out bilaterally and always in the same order: middle deltoid, middle ulna, hypothenar eminence, thumb, mid tibia, and quadriceps femoris muscle.

Beck Depression Inventory (BDI) was completed by all subjects (8). BDI is a 21-item questionnaire, where a score of 21 or above represents depression.

Statistical analysis

Statistical analysis was performed using NCSS (Number Cruncher Statistical System) 2007 and PASS 2008 Statistical Software (Utah, USA). Data was summarized using descriptive statistics (mean, standard deviation, percentage). For variables with normal distribution one-way ANOVA was used to compare means and post-hoc Tukey HDS test was used to determine the groups differing from each other. For variables with non-normal distribution Kruskal Wallis was used to compare means and Mann Whitney U test was used to determine the groups differing from each other. In two group comparisons Student t test and Mann Whitney U test were used for normal and non-normally distributed variables, respectively. Pearson correlation analysis and Spearman's rho correlation analysis were used for normal and non-normally distributed variables, respectively. Chi-square test was used for analysis of categorical variables. Results were evaluated within 95% confidence interval and the level of significance was set at $p<0.05$.

RESULTS

Two hundred and twenty-nine subjects participated in the study. Patients were diagnosed with one of six musculoskeletal diseases including ankylosing spondylitis (n=34), fibromyalgia syndrome (n=30), myofascial pain syndrome (n=33), osteoporosis (n=34), generalized osteoarthritis (n=34), and rheumatoid arthritis (n=34). In addition, a group of healthy subjects was included as control (n=30). Due to the variety of diseases, age and gender distribution of study groups were significantly different (Table 1). Majority of the patients were women in all groups except for ankylosing spondylitis (due to the nature of disease most patients composed of males) and healthy control groups. Osteoporosis, generalized osteoarthritis and rheumatoid arthritis patients were significantly older than the rest. Median disease duration was longest for ankylosing spondylitis (9 years), followed by rheumatoid arthritis (7 years), generalized osteoarthritis (6 years), osteoporosis and fibromyalgia (3 years) and myofascial pain syndrome (2 years). Depression was more common in fibromyalgia, myofascial pain and rheumatoid arthritis patients (Table 1). On visual analog scale the level of pain experienced by the patient was lowest for ankylosing spondylitis (4.76±3.15) and rheumatoid arthritis (5.55±2.55). Non-steroidal anti-inflammatory drug (NSAID) use was highest among ankylosing spondylitis (68%) and rheumatoid arthritis (76%) patients (Table 1). Anti TNF treatment was used by 41% of the ankylosing spondylitis and 15% of the rheumatoid arthritis patients. Antidepressant use was not very common ranging between 3 and 13% in disease groups (Table 1).

For pain pressure threshold measurements, a digital algometry was used on mid deltoid, midline ulna, hypothenar eminence, thumb, mid tibia, and quadriceps femoris, always in that order bilateral. Whole body PPT was calculated as the mean value from all measurements. Fibromyalgia patients consistently had the lowest PPT across all sites of measurements. Generalized osteoarthritis patients also had low PPT compared to healthy controls across all sites.

Table 1: *Patient characteristics.*

	HC n=30	AS n=34	FS n=30	MPS n=33	OS n=34	GOA n=34	RA n=34	*p*
Age,[1] years (mean±SD)	37±12	33±8	40±10	39±11	62±9	67±9	48±12	*0.001*
Female,[2]n(%)	14 (47)	13 (38)	30 (100)	27 (82)	32 (94)	32 (94)	28 (82)	*0.001*
Disease duration,[3] years	-	9.8±6.9	3.8±3.4	3.8±5.4	3.8±4.1	10.0±9.0	9.9±9.1	*0.001*
Depression,[4]n(%)	0 (0)	10 (29)	14 (47)	15 (46)	9 (26)	8 (24)	12 (35)	*0.001*
VAS,[5]mean±SD	-	4.76±3.15	7.44±2.42	6.55±2.78	6.09±3.23	7.05±2.69	5.55±2.55	*<0.01*
NSAID use,[6]n(%)	-	23 (68)	13 (43)	6 (18)	10 (29)	15 (44)	26 (76)	*0.001*
Anti TNF use, n(%)	-	14 (41)	-	-	-	-	5 (15)	*0.015*
Antidepressant, n(%)	-	0 (0)	4 (13)	3 (9)	3 (9)	1 (3)	2 (6)	*0.303*

HC: healthy control; **AS:** ankylosing spondylitis; **FS:** fibromyalgia syndrome; **MPS:** myofascial pain syndrome; **OS:** osteoporosis; **GOA:** generalized osteoarthritis; **RA:** rheumatoid arthritis.

1, OS and GOA mean age significantly higher than the rest ($p<0.001$); RA mean age significantly higher than HC, AS, FS, MPS ($p<0.05$)

2, Significantly more women in FS, MPS, OS, GOA and RA ($p<0.001$)

3, AS, GOA, RA disease duration significantly longer compared to FS, MPS, OS ($p<0.001$)

4, FS, MPS and RA patients had significantly more depression compared to the rest ($p<0.01$)

5, VAS score of AS significantly lower than FS ($p=0.001$), MPS ($p=0.025$), GOA ($p=0.003$); VAS score of RA significantly lower than FS ($p=0.002$) and GOA ($p=0.003$)

6, NSAID use in AS and RA significantly higher than the rest ($p<0.01$); NSAID use in MPS significantly lower than the rest except for OS ($p<0.01$).

Table 2: *Pressure pain threshold (PPT) values (mean±SD) at different body sites.*

	HC	AS	FS	MPS	OS	GOA	RA	*p*
Mid deltoid [1]	4.47±1.54	4.57±1.60	3.15±0.82	5.02±1.59	3.94±0.89	4.02±1.24	4.42±1.40	*0.001*
Midline ulna [2]	5.32±1.40	4.59±1.74	3.44±0.82	5.15±1.60	4.03±1.03	3.96±1.24	4.22±1.39	*0.001*
Hypothenar eminence [3]	5.50±1.71	4.64±1.78	3.71±1.00	4.97±1.86	4.44±1.02	3.89±1.45	4.04±1.61	*0.001*
Thumb [4]	4.43±1.17	3.55±1.23	2.57±0.58	3.72±1.35	3.25±0.70	2.97±1.18	2.87±1.16	*0.001*
Mid tibia [5]	4.80±1.60	3.76±1.11	2.91±0.77	4.34±1.55	3.56±0.91	3.18±1.07	3.53±1.33	*0.001*
Quadriceps femoris [6]	6.36±2.29	5.89±1.96	3.59±0.83	5.76±1.83	4.49±1.28	3.98±1.38	4.65±1.76	*0.001*
Whole body PPT [7]	5.15±1.50	4.50±1.40	3.23±0.64	4.83±1.43	3.95±0.80	3.67±1.08	3.96±1.25	*0.001*

HC: healthy control; **AS:** ankylosing spondylitis; **FS:** fibromyalgia syndrome; **MPS:** myofascial pain syndrome; **OS:** osteoporosis; **GOA:** generalized osteoarthritis; **RA:** rheumatoid arthritis.
1, FS significantly lower than HC, AS, MPS and RA (p<0.01). OS and GOA significantly lower than MPS (p<0.05)
2, FS significantly lower than HC (p<0.01), AS(p<0.05) and MPS (p<0.01). OS and GOA significantly lower than HC and MPS (p<0.05). RA significantly lower than HC (p<0.05)
3, FS significantly lower than HC (p<0.01) and MPS (p<0.05). GOA and RA significantly lower than HC (p<0.01)
4, FS significantly lower than HC, MPS and AS (p<0.01). GOA and RA significantly lower than HC (p<0.01) and MPS (p<0.05). AS and OS significantly lower than HC (p<0.05).
5, FS and GOA significantly lower than HC and MPS (p<0.01). AS, OS, RA significantly lower than HC (p<0.05).
6, FS, GOA and OS significantly lower than HC (p<0.01), MPS (p<0.05) and AS (p<0.05). RA significantly lower than HC (p<0.01) and AS (p<0.05).
7, FS significantly lower than HC, MPS and AS (p<0.01). OS, GOA and RA significantly lower than HC (p<0.01) and MPS (p<0.05).

Table 3: *PPT score correlation with age, disease duration and VAS.*

	Age		Disease duration		VAS	
	r	*p*	r	*p*	r	*p*
HC	-0.079	*0.680*	-	-	-	-
AS	0.148	*0.402*	0.204	*0.247*	0.238	*0.176*
FS	-0.075	*0.694*	-0.280	*0.134*	0.223	*0.237*
MPS	-0.017	*0.923*	-0.026	*0.885*	0.053	*0.770*
OS	0.111	*0.531*	0.061	*0.732*	0.073	*0.680*
GOA	-0.028	*0.876*	0.157	*0.377*	0.255	*0.145*
RA	0.416	*0.014**	-0.097	*0.586*	-0.182	*0.303*
All subjects†	-0.136	*0.039**			-0.133	*0.045**

HC: healthy control; **AS:** ankylosing spondylitis; **FS:** fibromyalgia syndrome; **MPS:** myofascial pain syndrome; **OS:** osteoporosis; **GOA:** generalized osteoarthritis; **RA:** rheumatoid arthritis.
***** p<0.05
† All subjects did not include healthy controls for disease duration and VAS.

Table 4: *Mean PPT scores by gender, presence of depression and NSAID use.*

	Gender (male/female)			Depression (yes/no)			NSAID use (yes/no)		
	n	Mean ± SD	*p*	n	Mean ± SD	*p*	n	Mean ± SD	*p*
HC	16	5.74±1.65	*0.020**						
	14	4.47±0.98							
AS	21	4.74±1.26	*0.184*	10	4.21±1.75	*0.496*	23	4.55±1.25	*0.897*
	13	4.11±1.57		24	4.62±1.25		11	4.41±1.74	
FS	0	-	-	14	3.21±0.69	*0.884*	13	3.36±0.59	*0.615*
	30	3.23±0.64		16	3.25±0.62		17	3.13±0.68	
MPS	6	4.97±1.81	*0.455*	15	4.98±1.43	*0.600*	6	4.04±1.02	*0.112*
	27	4.80±1.37		18	4.70±1.45		27	5.00±1.46	
OS	2	4.56±0.05	-	9	4.14±0.91	*0.740*	10	3.62±0.88	*0.199*
	32	3.92±0.82		25	3.89±0.77		24	4.10±0.75	
GOA	2	4.84±0.35	-	8	3.25±1.23	*0.180*	15	3.85±1.07	*0.340*
	32	3.60±1.07		26	3.80±1.02		19	3.53±1.10	
RA	6	4.79±1.59	*0.086*	12	3.35±1.01	*0.040**	26	3.89±1.27	*0.685*
	28	3.78±1.13		22	4.29±1.27		8	4.17±1.27	
All subjects	53	5.07±1.47	*0.001**	68	3.90±1.36	*0.039**	93	3.95±1.15	*0.030**
	176	3.91±1.16		161	4.30±1.30		136	4.34±1.43	

HC: healthy control; **AS:** ankylosing spondylitis; **FS:** fibromyalgia syndrome; **MPS:** myofascial pain syndrome; **OS:** osteoporosis; **GOA:** generalized osteoarthritis; **RA:** rheumatoid arthritis.
***** p<0.05

Osteoporosis patients had low PPT in the arm and moderately low PPT in the leg, while rheumatoid arthritis patients had low PPT in the hand and moderately low PPT in the leg. PPT of ankylosing spondylitis patients were mostly close to the PPT values of healthy subjects with a significant difference detected only on the mid tibia readings. Myofascial pain syndrome patients had the highest PPT among different patient groups with no significant difference from healthy subjects at any sites of measurement (Table 2).

The effect of age, disease duration and actual clinical pain (VAS score) on PPT was assessed using correlation analysis. There was a moderate positive correlation between age and PPT in rheumatoid arthritis patients (r: 0.416, p=0.014), but a weak negative correlation was observed for all subjects (r: -0.136, p=0.039) (Table 3). PPT was not correlated with disease duration, while it showed a weak negative correlation with VAS when all patients were considered (r: -0.133, p=0.045) (Table 3).

PPT was significantly higher in men compared to women (5.07±1.47 vs. 3.91±1.16, p=0.001). A similar difference was seen in the healthy control group, but not in ankylosing spondylitis, myofascial pain or rheumatoid arthritis groups. The effect of gender on PPT could not be measured on the other disease groups as the number of men was insufficient for statistical analysis. Patients with depression had significantly lower PPT scores in the rheumatoid arthritis group (3.35±1.01 vs. 4.29±1.27, p=0.040) and in the overall analysis of all subjects (3.90±1.36 vs. 4.30±1.30, p=0.039). NSAID users had lower PPT in the overall analysis of all subjects (3.95±1.15 vs. 4.34±1.43, p=0.030) but no significant difference was detected in the analysis of individual disease groups.

DISCUSSION

In this study, we compared general pain sensitivity of patients with a variety of musculoskeletal disorders based on measurements at unaffected body sites. This is the first study which compares PPT in six different frequent diseases and healthy individuals.

The VAS is a well known subjective pain scale with simple application. VAS improved long time ago, has been found to be valid and reliable tool for assessing pain relief and pain intensity (9). International Association for the Study of Pain (1986) outlined the pain threshold as "the minimum intensity of a stimulus that is perceived as painful" (10). PPT is a reliable test for hyperalgesia in superficial body structures (11, 12).

Our results showed a clear difference in pain sensitivity between inflammatory joint disorders. AS patients had no evidence of tenderness in unaffected body sites, while RA and GOA patients had overall tenderness. Previous studies comparing pressure pain threshold in AS and RA patients also concluded that in contrast to RA, there is no generalized tenderness in AS patients (13-15).

Differences in the presentation of these arthritic diseases may account for the differences in pain perception. AS is manifested as enthesitis and is characterized by spinal involvement. On the other hand, RA begins at the synovium and involves the extremities. Also, genetics may play a role through increased susceptibility to pain in RA compared to AS.

In the Gerecz-Simon et al., study hip or knee OA patients were compared with AS, RA and healthy controls. In their study PPT of OA patients were higher than healthy controls and RA, similar to AS patients. However, subsequent studies conducted on knee OA patients determined decreased PPT near the affected knee as well as at distant body sites suggesting central sensitization (16-19). Similarly, our patients with generalized OA also showed tenderness across all the tested body sites.

Fibromyalgia is a chronic muscle pain disease characterized by widespread allodynia and/or hyperalgesia (20). A diagnostic criterion for fibromyalgia involves pain sensitivity to a pressure of 4 kg at eleven out of eighteen tender points.

However, it is established that tender points are not the source of pain, rather they are anatomically more sensitive spots to be used in diagnosis (21). We found the lowest PPT scores in fibromyalgia patients for all body sites, indicating general tenderness in accordance with previous studies (22, 23). The underlying mechanism for tenderness in fibromyalgia is thought to involve central sensitization and impaired pain modulation in addition to peripheral sensitization (20).

As expected PPT was higher in MPS compared to FS, even though the clinical pain scored by VAS were not significantly different between these groups. Although both syndromes involve muscle tissue and can be found concomitantly in some patients, MPS is a regional

pain syndrome characterized by trigger point in a taut band, in contrast to the diffuse pain experienced in FS (24).

As far as we know this is the first study investigating pressure pain threshold in osteoporosis patients. Although osteoporosis is often described as a silent disease, osteoporotic pain has a serious impact on the patient's quality of life (25). Chronic back pain in osteoporosis patients is usually related to vertebral compression fractures resulting in deformities in the spine. In this study, clinical pain of osteoporosis patients were comparable to the other chronic pain conditions studied and generalized sensitivity to pain was observed compared to healthy control subjects.

One limitation of this study is that disease groups and healthy control subjects were not age and gender matched due to the differences in demographics of the diseases. Comparison of pain perception between younger and older age groups show varying results based on the methodology used to inflict experimental pain.

Most studies conducted on healthy individuals support an increase in pain threshold with advanced age (26-28). In contrast, a weak negative correlation suggesting lower PPT with advanced age was determined when all subjects were considered in our study. Moreover, OS and GOA, two groups composed of patients with advanced age had significantly lower PPT compared to the younger groups.

Similarly, studies show that there is a gender bias in pain perception such that women have a lower threshold to experimental pain stimuli (29, 30). While it could be argued that a more balanced representation of men in healthy control and AS groups may account for the higher PPT values, equally high PPT values of MPS group composed predominantly of women patients contradicts this line of reasoning.

In conclusion, perception of pain in general is not affected in AS and MPS, while hypersensitivity is seen in RA, GOA, OS, and FS. Overall, female gender, advanced age, depression and NSAID use correlated with lower PPT. A weak negative correlation was detected between VAS and PPT when all patients were considered, but no significant correlation was present within the disease groups. Long-term chronic pain may lead to overall tenderness via central and peripheral sensitization and impaired pain modulation. Intrinsic hypersensitivity to pain may also play a role in chronic pain disorders.

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