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Effect of pressure pain threshold in fibromyalgia syndrome and rheumatoid arthritis patients

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Abstract: *Background:* Pain is an unpleasant sensation signaling tissue damage. Objective measurement of pain helps in devising treatment strategies and relieving patients from sufferings. *Objective:* The present study was undertaken to evaluate pressure pain threshold in normal subjects, patients with fibromyalgia and rheumatoid arthritis by using algometer. Further to assess severity of pain perception by using visual analog scale. *Methods:* Measurement was done on 18 tender point sites [TePs] according to ACR criteria on 20 Fibromyalgia [FMS] patients, 20 Rheumatoid arthritis [RA] patients, and 40 healthy normal control [HNC] subjects. The pressure pain threshold [PPT] and Visual analog scale [VAS] were recorded in each TePs. *Results:* The range of PPT was 0.62 to 3.43 kg/cm^2, 0.30 to 3.90 kg/cm^2 and 1.41 to 5.35 kg/cm^2 and VAS score range was 52.90 to 67.60 mm, 30.5 to 49.00 mm and 23.65 to 41.83 mm in FMS, RA and HNC respectively. *Conclusion:* There is a significant reduction of PPT in both FMS and RA patients compared to HNC subjects. The VAS score was significantly higher in FMS suggesting altered cognitive response to pain.
Keywords: Pressure pain threshold, Algometry, Visual analog scale, Fibromyalgia, Rheumatoid arthritis.

Introduction

Pain is the most common symptom that brings a patient to medical attention [1]. Chronic pain has a major impact on physical, emotional, and cognitive function and it also affects social and family life [2]. It is very important to assess the severity of pain in chronic pain conditions like rheumatoid arthritis [RA] and fibromyalgia syndrome [FMS] for monitoring the disease progression, severity and the effects of treatment. Assessment of pain is difficult as pain is subjective and multidimensional in nature. Several assessment techniques have been developed to quantify pain. The visual analog scale [VAS] and pressure algometry are the commonly used techniques.

The VAS helps in assessing subjective pain perception. It is simple to use but influenced by patient's psychological status and ability to comprehend the instructions [3]. The PPT is the point at which a subject perceives pain on application of a pressure stimulus [4]. Our objective was to assess pain in the form of PPT and VAS as marked by the subject in chronic pain conditions like RA and FMS, and compare them with normal controls. Our secondary objective was to find out which is the better method in clinical practice to assess the prognosis of the disease.

Material and Methods

Subjects: This was a cross-sectional, comparative study comprising of 20 diagnosed FMS patients and 20 diagnosed RA patients in the 25-45 year age group, and 40 normal age and sex matched subjects. Eligible patients were recruited from the rheumatology clinic of our institute. Normal subjects were recruited from the staff and students of our institutes who consented to undergo the study. Patients with RA were diagnosed by using the criteria of the American College of Rheumatology [ACR] [5]. The FMS patients were diagnosed according to the ACR criteria for FMS, which requires tenderness at 11 or more of the 18 specific tender point sites [6]. Patients of Class 4 in RA, suspected psychiatric illness and concomitant RA with FMS, other neuromuscular disorders, and any history of fractures were excluded from the study. Informed consent was obtained from all

the study participants. The subjects were recruited in the sequence of their attending outpatient department and fulfilling eligibility criteria. The study protocol was approved by the institutional ethical committee for human research. The FMS patients were newly diagnosed cases and were on non-steroidal anti-inflammatory drugs [NSAIDs] only, while RA patients were on disease modifying anti-rheumatic drugs and a stable dose of NSAIDs, but patients were not on medication 24 hours prior to VAS and algometry recording.

Pain Assessments: Pressure Pain Threshold: The PPT was measured over specific areas by using digital algometer [manufactured by Electronics Engineering Corporation, India]. It consisted of a soft-grip handle and piston with a pressure-sensitive strain gauge at the tip [1cm^2], connected to a power supply using adapter. The instrument had 12 mm LCD digital display which showed pressure [in kg/cm^2]. The accuracy of reading was ± 3 percent. The instrument was calibrated as per manufacturer's guidelines before examining each subject. The PPT was defined as the quantity of pressure in kg/cm^2 necessary to elicit a sensation of pain distinct from that of discomfort or unpleasantness [7].

Visual Analog Scale for Pain Intensity: The subjects marked the severity of their pain when they felt it to be painful on application of pressure on the VAS. It consisted of a 100 mm horizontal line without markings, anchored by words "No pain" at the left end and "Worst possible pain" at the right end in comparison to their lifetime experience. The patient scored the pain felt on application of pressure, not the general pain they might be feeling [8].

Procedure: The algometer was demonstrated to the subjects. They were instructed to give verbal cue "Yes" as soon as the pressure sensation turned into a painful sensation. Four assessments were performed on sites which were not included in the study to familiarize the subjects with the algometry technique. Measurements were taken by three investigators; however, the differences in the measurements did not vary by more than five percent. Three readings were taken at each of the points and the average of these three readings was considered for analysis. Total 18 points [TePs] located bilaterally on the body were assessed in identical sequence in all subjects. These 18 TePs were proposed by the ACR for diagnosis of FMS [13]. They were located as follows: occiput [TeP 1–2], at the suboccipital muscle insertions; low cervical [TeP 3–4], at the anterior aspects of the intertransverse spaces at C5–C7; trapezius [TeP 5–6], at the midpoint of the upper border; supraspinatus [TeP 7–8], at origins, above the scapula near the medial border; second rib [TeP 9–10], at the second costochondral junctions, just lateral to the junctions on upper surfaces; lateral epicondyle [TeP 11–12], 2 cm distal to the epicondyles; gluteal [TeP 13–14], at upper outer quadrants of buttocks in anterior fold of muscle; greater trochanter [TeP 15–16], posterior to the trochanteric prominence; and knee [TeP 17–18], at the medial fat pad proximal to the joint line. Subjects were given the VAS and a pen. They were instructed to make a single vertical mark on VAS line, indicating the severity of the pain immediately after algometry. The numeric score was derived by measuring the distance in millimeters, from the left end of the VAS to the mark made by the subject. The readings at each of the TePs, as well as the marking on the VAS scale, were taken continuously.

Statistics: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented as mean ± standard deviation and results on categorical measurements are presented in number. Significance is assessed at a five percent level of significance. Analysis of variance has been used to find the significance of study parameters between three groups. Post-hoc Tukey test has been used to find the pair wise significance of parameters studied. The statistical software SPSS 15.0 was used for the analysis of the data.

Results

The mean age of FMS patients was 32 years which was 18 years younger than the RA patients. The majority of the subjects were female in all the groups [Table 1]. All the FMS patients were newly diagnosed and were not on any specific treatment of FMS, except intermittent NSAIDs, while all RA were on stable disease modifying anti-rheumatic drug therapy with regular NSAIDs.

Table-1: Baseline characteristics of the study groups				
Basic characteristics	**Normal (n=40)**	**FM (n=20)**	**RA (n=20)**	
Gender	**n (%)**	**n (%)**	**n (%)**	**Total**
Male	18(45.0)	5(25.0)	5 (25.0)	28
Female	22(55.0)	15(37.5)	15 (75.0)	52
Total	40(100.0%)	20(100.0%)	20(100.0%)	80
Age	Mean±SD	Mean±SD	Mean±SD	
Age in years (Mean ± SD)	34.30±9.01	31.55±5.45	50.35±13.66	

Table-2: Comparison of Pressure Pain Threshold between the study groups					
Parameters	**Side**	**Normal** Mean ± SD	**FM** Mean ± SD	**RA** Mean ± SD	**P value**
OCCIPUT	Right	2.35±0.93	0.73±0.71	3.11±1.53	<0.001**
	Left	2.49±1.21	0.62±0.72	3.46±1.71	<0.001**
LOW CERVICAL	Right	1.41±0.98	0.62±0.67	2.09±1.25	<0.001**
	Left	1.42±1.03	0.68±0.70	2.31±1.31	<0.001**
TRAPEZIUS	Right	3.34±1.21	1.48±0.92	0.30±0.22	<0.001**
	Left	3.36±1.24	1.36±0.84	0.37±0.32	<0.001**
SUPRASPINATUS	Right	4.00±1.35	2.03±1.20	3.03±1.59	<0.001**
	Left	3.79±1.26	1.98±1.21	2.83±1.43	<0.001**
SECOND RIB	Right	2.20±1.08	1.21±0.91	3.21±1.46	<0.001**
	Left	2.30±1.01	1.10±0.90	3.16±1.48	<0.001**
LATERAL EPICONDYLE	Right	3.05±1.22	1.41±1.08	1.66±1.18	<0.001**
	Left	3.12±1.16	1.54±1.10	1.58±1.21	<0.001**
GLUTEAL	Right	5.35±1.86	3.02±1.38	2.50±1.56	<0.001**
	Left	5.28±2.06	2.98±1.34	2.31±1.42	<0.001**
GREATER TROCHANTER	Right	5.24±1.76	3.38±1.57	3.73±2.06	<0.001**
	Left	5.19±1.62	3.43±1.42	3.90±2.22	0.001**
KNEE	Right	4.49±1.52	2.80±1.25	3.79±1.53	<0.001**
	Left	4.45±1.52	2.60±1.05	3.90±1.85	<0.001**

FM= Fibromyalgia, RA= Rheumatoid arthritis.

**Analysis of variance (ANOVA) with Post-hoc Tukey test applied to test for significance between three groups.

Table-3: Comparison of Pressure Pain Threshold by VAS					
Parameters	**Side**	**Normal Mean**	**FM**	**RA**	**P value**
OCCIPUT	Right	39.80±18.01	67.60±9.51	41.50±22.31	<0.001**
	Left	41.83±19.33	67.35±7.50	43.00±25.15	<0.001**
LOW CERVICAL	Right	40.33±16.80	66.70±8.33	42.00±25.67	<0.001**
	Left	39.68±17.01	67.25±6.91	43.50±25.81	<0.001**
TRAPEZIUS	Right	33.23±16.90	64.20±8.73	40.00±24.49	<0.001**
	Left	34.58±18.44	65.10±8.74	39.50±23.28	<0.001**
SUPRASPINATUS	Right	33.50±17.53	63.05±11.66	45.50±29.11	<0.001**
	Left	32.25±14.31	63.10±11.30	39.00±23.37	<0.001**
SECOND RIB	Right	37.30±18.07	63.20±11.35	46.50±26.21	<0.001**
	Left	37.68±16.66	64.50±11.98	49.00±27.13	<0.001**
LATERAL EPICONDYLE	Right	38.13±17.62	62.10±8.66	45.50±31.03	<0.001**
	Left	36.85±17.39	63.55±9.38	44.00±20.88	<0.001**
GLUTEAL	Right	25.63±14.43	56.20±10.21	30.50±22.82	<0.001**
	Left	24.80±13.50	57.05±10.55	35.00±25.44	<0.001**
GREATER TROCHANTER	Right	24.08±14.92	52.95±11.81	35.00±26.46	<0.001**
	Left	23.65±13.54	52.90±12.16	39.50±29.64	<0.001**
KNEE	Right	28.68±16.06	53.75±9.21	38.00±23.53	<0.001**
	Left	29.45±16.09	55.80±10.96	38.50±25.40	<0.001**

FM= Fibromyalgia, RA= Rheumatoid arthritis.

**Analysis of variance (ANOVA) with Post-hoc Tukey test applied to test for significance between three groups.

Pressure Pain Threshold: Table 2 shows that maximum PPT of 3.02±1.38 has been recorded in the gluteal area, and a minimum PPT of 0.62±0.67 was recorded in low cervical area in FMS patients. Maximum PPT of 3.90±1.85 has been recorded in the knee area and a minimum PPT of 0.30±0.22 was recorded in low cervical area in RA patients. The maximum PPT in HNCs has been recorded in gluteal area as 5.35±1.86, and a minimum PPT of 1.41±0.98 was recorded in low cervical area. The above findings show that in RA patients, PPT was lower in most of the areas with the exception of areas like the occiput, the cervical area, and over ribs, where PPT was higher than the HNCs. The PPT was significantly lower in the FMS group as compared to HNCs. The PPT was more in FMS patients as compared to RA patients in the trapezius and gluteal areas.

Visual Analog Scale: Table 3 presents VAS in three study groups. The scores were comparable in RA and HNCs except in the supraspinatus [right], second rib [left], gluteal [left], greater trochanter, and knee [right], while in FMS patients it was significantly higher compared to the other two groups at all the sites. It was observed that there were significant differences in mean scores of PPT between the three groups, RA, FMS, and

HNC, and these differences were observed to be statistically significant at all the study points. There was a significant higher VAS scoring in FMS patients as compared to the HNCs and RA patients. There were no significant differences between the RA and the HNC groups. The PPT varied between different points within the group [Figure 1] whereas the difference between VAS scores were not significantly different at different points within the group [Figure 2].

Figure-1

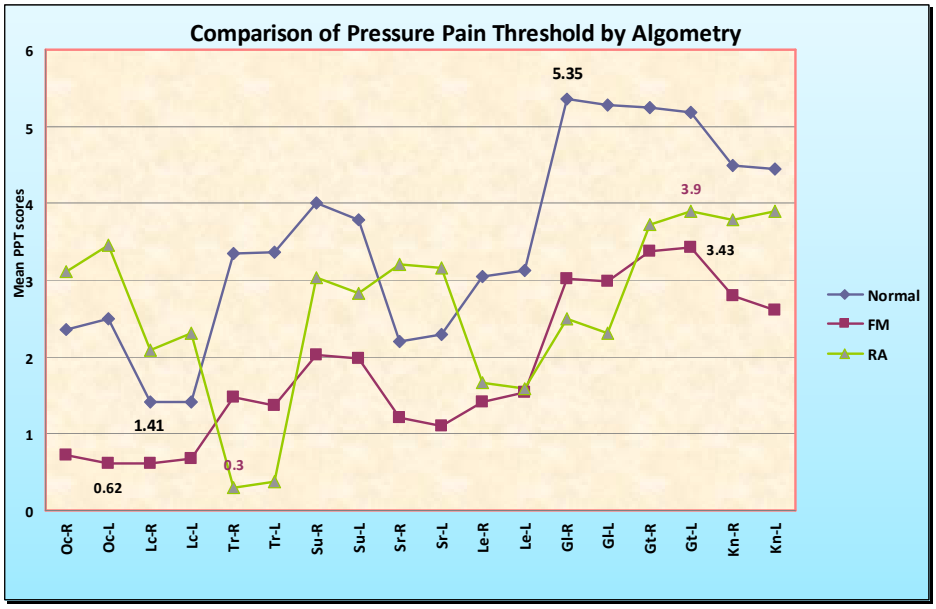
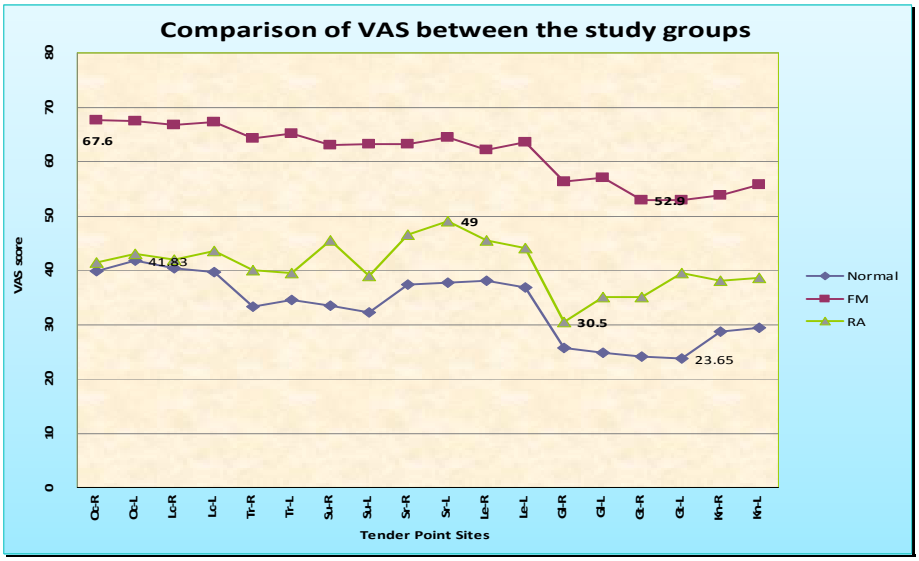


Figure-2



Key to abbreviation of graphs:

Oc-R = OCCIPUT RIGHT
Oc-L = OCCIPUT LEFT
Lc-R = LOW CERVICAL RIGHT
Lc-L = LOW CERVICAL LEFT
Tr-R= TRAPEZIUS RIGHT
Tr-L=TRAPEZIUS LEFT
Su-R = SUPRASPINATUS RIGHT
Su-L = SUPRASPINATUS LEFT
Sr-R = SECOND RIB RIGHT
Sr-L= SECOND RIB LEFT
Le-R = LATERAL EPICONDYLE RIGHT
Le-L = LATERAL EPICONDYLE LEFT
Gl-R =GLUEAL RIGHT
Gl-L = GLUEAL LEFT
Gt-R = GREATER TROCHANTER RIGHT
Gt-L = GREATER TROCHANTER LEFT
Kn-R= KNEE RIGHT
Kn-L= KNEE LEFT

Discussion

We found that PPT has been decreased in both RA and FMS groups, as compared to the HNC group. The reduction in PPT was seen in all the designated TePs in FMS, while PPT was reduced in the majority of TePs in the RA group. In RA, the VAS values at TePs were not significantly different from healthy individuals, whereas in FMS, the VAS was significantly higher in almost all the TePs [Figure 2]. We can infer that though the pain threshold has come down in both RA and FMS patients, the proportion of pressure at which an RA patient discriminates pressure as pain [to be ascertained by them to be tender] remains the same with reference to HNCs. However, in patients of FMS, the point at which they experience the pain was perceived as more painful [as represented in VAS value], and was proportionately higher compared to HNCs.

The observations indicate a significant gap in the perception of pain between RA and FMS, which was not seen between RA and HNCs. We hypothesized that the subject's experience with pain should be proportionate to when a person considers the pressure sensation as uncomfortable; this should not differ significantly, despite the variation in pain threshold. We observed that a VAS value of 20 to 45 by both HNC and RA patients were considered uncomfortable. Otherwise 20 to 49 percent of their worst pain experiences were considered perceivably tolerable. That is the range of VAS score that was observed in HNC and RA together. While applying pressure and eliciting pain by PPT method or eliciting tenderness, the instruction to the patient is to indicate when he feels the application of pressure uncomfortable. We did observe that the range of VAS score represented across all points in a subject [patient and normal] was not significantly different between the points in all three groups. Even the differences between VAS points were much narrower in the HNCs than the other patients. The VAS score was higher and the range was more in the FMS group. In FMS group, the VAS was more than 50 and increased in all the 18 TePs, and had no relationship to the PPT. This difference indicates that there is a perceived difference in pain in patients suffering from FMS, compared to RA patients. This altered perception of pain has been observed in several other studies using different methods [neuron, pain, etc.]. This has been attributed to the behavior of catastrophizing [9], "heightened awareness" [10], etc.

The marking of pain on VAS pain scale was influenced by defective perception of pain by patients. In contrast there was no influence of variation or reduced PPT on marking of VAS pain scale by the patients. This fact is substantiated by the observation that in conditions like RA where a pathological disturbance [e.g., inflammation in RA] has altered PPT, the interpretation on to the VAS was not influenced by altered pain and was close to normal. Hence, the proportion of pain, as per the individual experience of pain, becomes uncomfortable and is not altered. In the hypothesis we speculated that the VAS is the perceived level of discomfort, whereas the PPT measures the quantity of pressure applied to elicit the discomfort. Thus VAS represents the perceptional component of pain, while PPT measures the objective change in the pain threshold. In RA and FMS patients, the change in pain threshold is not limited only to TePs, it is more diffuse even in other areas [11-12]. Our study substantiates the same view. Studies have demonstrated that the change in PPT was proportionate to inflammatory load and was inversely related to C-reactive protein [13] and cytokines like tumor necrosis factor-alpha and interleukin-1 [14]. Pain pressure threshold changes over a period of time in a single person [15]. However, several studies have evaluated PPT as a measure for monitoring pain and have found it to be consistent and a useful tool, especially when used by single observer [16-17]. When used by experienced persons PPT could be a useful tool to measure pain even in normal healthy individuals [18].

Factors like anatomical locations [11], gender [19], inflammatory status [13-14], hormones cycles [20], stress, and anxiety [21] influence the PPT. Similarly, VAS is also influenced by psychological status and ability to comprehend the instructions. Marking on the VAS may also be influenced by the patients expectations and understanding the importance of his/her act. The PPT has a distinct advantage being not altered by use of analgesics [22], while both the VAS and

number of TePs alter with use of NSAIDs [23]. The primary pathological problem in RA is deregulated increased inflammatory process. Measures used in assessing disease activity in RA should be the measure reflecting the process of inflammation. The VAS pain scale, number of tender joints and other measures which are influenced by patients' perception as well as by factors other than inflammation may not quantify the disease process more accurately. The patient's anxiety, as well as other regional problems not attributable to synovitis, influences the process of elicitation of tenderness. Non-steroidal anti-inflammatory drugs can influence the number of tender joints as well as the marking on VAS. To minimize these factors utilization of altered pain threshold as a measure in RA would be more accurate as it is greatly influenced by both inflammatory cytokines and CRP, and least influenced by cognitive function. Our study throws light on the fact that in FMS the patient has a distorted impression of pain, which is responsible for exaggerated markings on a VAS scale, which is significantly higher than both HNC and RA groups. This suggests the fact that in FMS, the cognitive distortion of pain perception contributes to the disease. The gap between the VAS scoring and altered PPT as measured at the point as observed in our study should help to differentiate the cognitive impact on perception of pain in addition to altered sensitivity. These two different aspects of pain, the perception and absolute change if proved with further studies, should help in management and following up with these patients. Further studies are needed for standardizing PPT as a measure and VAS score in both RA and other chronic pain syndromes.

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