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Symptom severity in burning mouth syndrome associates with psychological factors

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Abstract

Burning mouth syndrome (BMS) patients are psychologically distressed, but whether this associates with symptom severity is unclear. The aim was to investigate the association of psychological factors with pain intensity and interference in BMS. Fifty-two women (mean age 63.1, SD 10.9) with BMS participated. Pain intensity and interference data were collected using 2-week pain diaries. Psychological factors were evaluated using Depression Scale (DEPS), Pain Anxiety Symptom Scale (PASS) and Pain Vigilance and Awareness Questionnaire (PVAQ). The local ethical committee approved the study. Patients were divided into groups based on pain severity distribution tertiles: low intensity (NRS ≤ 3.7) or interference (NRS ≤ 2.9) (tertiles 1-2, n = 35) and moderate to intense intensity (NRS > 3.7) or interference (>2.9) (tertile 3, n = 17). T test, Wilcoxon's test and Pearson's correlation coefficient were used in the analyses. Patients in the highest intensity and interference tertiles reported more depression (P = .0247 and P = .0169) and pain anxiety symptoms (P = .0359 and P = .0293), and were more preoccupied with pain (P = .0004 and P = .0003) than patients in the low intensity and interference groups. The score of the pain vigilance questionnaire correlated significantly with pain intensity (r = .366, P = .009) and interference (r = .482, P = .009). Depression (r = .399, P = .003) and pain anxiety symptoms (r = .452, P = .001) correlated with pain interference. Symptom severity in BMS associates with symptoms of psychological distress emphasising the need to develop multidimensional diagnostics for the assessment of BMS pain.

KEYWORDS

biopsychosocial assessment, burning mouth syndrome, comorbid pain, pain diary, psychosocial factors, sleep disturbances

1 | INTRODUCTION

Chronic pain is generally understood in the biopsychosocial context. It is a multidimensional phenomenon, where psychological factors and other comorbidities such as sleep disturbances and other pain problems influence pain experience, complicate treatment outcome and contribute to chronicity.[1,2] During recent years, much effort has been put into developing classification systems to help to capture the multidimensional character of chronic pain with the purpose, among others, improving the prognostic judgments

and treatment decisions by clinicians treating chronic pain patients.[3-5] In the simplest form, pain intensity and interference, that is how much pain interferences with daily activities, have been used to summarise the global severity of chronic pain. In a seminal study on chronic pain patients, increasing pain intensity and interference was associated with increased psychosocial impairment and predicted the long-term pain status.[6] In oro-facial pain research, the pain severity continuum has been shown to have significant associations with, for example, psychological symptoms, other pain problems and treatment-seeking behaviour,[6-9] and to have prognostic validity.[10]

Burning mouth syndrome (BMS) is a chronic, debilitating oro-facial pain condition that is defined by a burning sensation of the oral mucosa without any identifiable oral lesions or other pathology to explain the symptoms.[11,12] The etiopathogenesis of BMS has long been considered enigmatic, but today several lines of evidence suggest a neuropathologic background for the symptoms.[13,14] Oral pain presents the cardinal symptom of BMS. It is usually described as burning in quality[15] and as mild to severe in intensity.[16] The findings from a pain diary study demonstrated, in addition to some diurnal pain variation, a considerable inter-individual variation in the intensity (NRS mean 3.1, SD 1.7, range 0.24-8. 22) and interference (mean NRS 2.5, SD 1.6, range 0.19-7.96) of BMS pain. As regards pain intensity, most patients reported mild to moderate pain, but a minority of patients, 8% to 15%, depending on the time of the day, reported severe pain (NRS = />5).[15]

Historically, much research has been devoted to the role of psychological factors in BMS. According to controlled studies, depression and anxiety are the most common and the most frequently studied psychological symptoms among BMS patients.[17] Pain-specific psychological variables such as pain anxiety or pain hypervigilance, which are suggested to be more relevant than general psychological symptoms to the understanding of chronic pain,[18] have not been studied in BMS. As regards other possible pain-related comorbidities, the occurrence of sleep disorders has received attention in BMS, and several studies have evidenced a decrease in the sleep quality in BMS patients.[19-22] However, unlike in other pain research, scarce attention has been paid to linking psychological or other pain-related symptomatology data to self-report of pain severity in BMS. Such information could possibly aid in identifying subgroups of patients with varying prognosis and treatment needs.

The aim of the present study was to investigate the association of psychological factors, sleep problems and other pain symptoms with reported pain intensity and interference in BMS. The specific aim was to study whether patients reporting most intensive and interfering pain differ from those with less severe pain symptoms.

2 | METHODS

This was a multicentre study with seven participating centres in Finland (for a detailed description see Forssell et al[15]). The study protocol followed principles established in the Declaration of Helsinki[23] and was approved by the local ethical committee.

All female patients aged 18 years or more who visited the study centres during a 1-year period (2010-11) and who had had primary BMS symptoms for more than 3-month period were invited to participate in the study. The diagnosis of BMS was made by exclusion of local and systemic causes of oral burning symptoms (secondary BMS) with a thorough clinical examination of the oral mucosa and measurement of paraffin-chewing stimulated whole saliva. Smear from the oral mucosa was used to diagnose oral candidiasis. Blood tests included complete blood count, thyroid-stimulating hormone (THS), fasting blood glucose, antinuclear antibody values, as well as B12 vitamin and serum folate.

To be included in the study, the patient had to be female, 18 years old or older, the BMS pain had to be chronic (over 3 months), and the pain had to occur daily or almost daily. Exclusion criteria included pathological changes of the oral mucosa, hyposalivation, oral candidiasis, nutritional deficiencies and anaemia, abnormal TSH level, fasting blood glucose or antinuclear antibody values. All participants gave their written informed consent.

At baseline, the patients were asked to fill in a baseline self-report questionnaire including questions on demographic data, general health and use of medications. Patients were given a paper-and-pencil pain diary to fill in for fourteen consecutive days. Pain intensity and interference on normal activities were calculated as overall means from the pain diaries filled 3 times a day using 0 to 10 NRS scales (intensity: 0 = no pain and 10 = worst possible pain, interference: 0 = no pain and 10 = pain present such that I can't do anything). The pain diary results concerning pain intensity and interference have been published earlier.[15] Every morning the patients registered in the diary whether they had had problems with falling asleep because of the BMS pain (no/yes) and whether the BMS pain had disturbed their sleep during the preceding night (no/yes).

The baseline self-report questionnaire included a question: "Have you any other pain problems?" and a pain drawing where patients were asked to paint the locations of these other pains. In the analysis, the number of other pains was used. Furthermore, psychological factors were evaluated at baseline using Depression Scale (DEPS), Pain Anxiety Symptom Scale (PASS) and Pain Vigilance and Awareness Questionnaire (PVAQ). These represent current, common, easy-to-use and statistically sound self-rating scales, depicting the areas of interest in this study.

2.1 | DEPS

The self-rating Depression Scale (DEPS) was developed in Finland as a method to screen for symptoms of depression in primary care patients.[24] The psychometric properties of the DEPS have been demonstrated and found good.[25,26] The DEPS comprises 10 items depicting various aspects of depressed mood (item examples: During the last month I have "Felt low in energy or slowed down",

"Had feelings of worthlessness"). The items are rated on a Likert scale (0 not at all-3 extremely) and a sum score, ranging from 0 to 30, is calculated. The cut-off score = />9,[24] which indicates a possible depression and a need for further investigation, was used in this study.

2.2 | PASS

The Pain Anxiety Symptom Scale-20 (PASS-20) was developed by McCracken and Dhingra[27] as a self-rating scale to assess pain-related worry, fear and anxiety. It has been widely used in various pain patient groups, and its psychometric properties have been confirmed.[28] The questionnaire comprises 20 items to be rated on a six-point Likert scale (0 never-5 always). In addition to calculating a sum score (range 0-100), four subscales depicting different aspects of pain-related anxiety and including 5 items each, are formed[27,29]: Fearfulness (item example: "When I feel pain, I think I might be seriously ill"), Escape/avoidance (item example: I avoid important activities when I hurt"), Cognitive anxiety (item example: I can't think straight when I am in pain") and Physiological anxiety (item example: Pain seems to cause my heart to pound or race"). The sum score range in each of these subscales is 0-25.

2.3 | PVAQ

A Pain Vigilance and Awareness Questionnaire, PVAQ, developed by McCracken,[30] has been used in various groups of pain patients. Its psychometric properties, construct validity, criterion validity and reliability, have been found good.[31,32] The 16 items are scored on a Likert scale (0 never-5 always). In addition to a sum score (range 0-80), a two-factor solution demonstrated in previous studies (reviewed by Kuntz et al[32]) omitting two items not loading substantially on any of the factors was used in this study. The first factor or subscale, Attention to pain, comprises 8 items (item examples: "I pay close attention to my pain", "I become preoccupied with pain", sum score range 0-40). The second subscale, Attention to changes in pain, comprises 6 items (item examples "I quickly notice changes in pain,""I know immediately when pain starts or increases" sum score range 0-30).

3 | STATISTICAL METHODS

Descriptive statistics include means or proportions (%) with standard deviations.

Because there are no universally accepted cut-off points for pain intensity or interference,[33] patients were divided into tertiles according to pain intensity and interference. Dividing patients into tertiles according to pain intensity gave a cut-off value of 2.4 for pain intensity between the first and the second tertile and 3.7 for the second and the third tertile. The corresponding cut-off values for pain interference were 1.6 and 2.9. As preliminary statistical analyses indicated that the two lowest tertiles did not differ statistically significantly from one another on any of the other variables studied, these tertiles were combined in further statistical analyses. Thus, the patients were divided into two groups based on pain intensity distribution tertiles: tertile 1-2: mild to moderate pain intensity (NRS ≤ 3.7, n = 35) and tertile 3: moderate to intense pain intensity (NRS > 3.7, n = 17). Similarly, two groups were formed based on interference: tertile 1-2, slight to moderate interference (NRS ≤ 2.9, n = 35), and tertile 3, moderate to severe interference (>2.9) (tertile 3, n = 17). The two intensity and interference groups were compared with each other in the studied parameters using *t* test, Wilcoxon's Test and Fisher's exact test. Pearson's correlation coefficient was used to study the correlation between study parameters. Missing data were handled by listwise deletion. Statistical analyses were done using SAS version 9.4 software (SAS Institute). *P*-values < .05 were considered statistically significant.

4 | RESULTS

Fifty-two female patients (mean age 63.1, SD 10.9) with primary BMS participated in the study. The mean length of the BMS pain was 66.8 months (SD; 59.3, range 6-240 months). Twelve of the patients had no general health problems. Twenty patients reported cardiovascular diseases, eight patients had compensated hypothyroidism, one patient diabetes, one epilepsy, and five patients had asthma. Six patients had a diagnosed depression. Two patients used tranquillisers, six used antidepressants and nine patients used sleep medication. Nineteen patients reported other pain problems such as headache (six patients), joint pain (seven patients) or fibromyalgia (four patients). There were no statistically significant differences between the two intensity tertiles or between the two interference tertiles as regards the age of the patients or the numbers of patients with hypothyroidism, depression, headache, joint pain or fibromyalgia. Also, the numbers of patients using tranquillisers, antidepressants or sleep medication distributed equally among the studied tertile groups.

Completely filled diaries were received from 47 patients. In the five incomplete diaries, the maximum of incompletely filled diary days was four. Table 1 shows the amount of missing data concerning the psychological scales.

Patients reporting more intensive and interfering pain, that is those in the highest intensity and interference tertiles, reported overall significantly more depression symptoms compared to patients with less severe symptoms (Table 1). Further, more than half of the patients, viz. 9/17, in the highest intensity and interference tertiles had DEPS scores at or above the cut-off score for depressive symptoms compared with less than a third of the patients, viz. 10/35, with lower pain intensity or interference.

The patients in the highest intensity and interference tertiles also displayed significantly more pain-related anxiety symptoms than those with less severe pain symptoms. Specifically, group

TABLE 1 The values (mean, SD) of psychological, comorbid pain and sleep-related characteristics for all patients and for patients divided into groups based on pain intensity and interference tertiles

All		Pain intensity tertiles			Pain interference tertiles		
		Tertiles 1-2	Tertile 3		Tertiles 1-2	Tertile 3	
		NRS ≤ 3.7	NRS > 3.7		NRS ≤ 2.9	NRS > 2.9	
	Mean (SD)	Mean (SD)	Mean (SD)	*P*	Mean (SD)	Mean (SD)	*P*
DEPS (n = 52)	7.9 (6.7)	6.5 (5.6)	10.9 (7.9)	.025	6.4 (5.6)	11.1 (7.7)	.017
PASS (n = 52)	27.0 (19.1)	23.2 (16.5)	34.9 (18.5)	.036	23.1 (16.5)	35.2 (21.8)	.029
Fearfulness		6.2 (4.8)	8.5 (6.3)	.146	6.3 (4.7)	8.3 (6.5)	.198
Escape/avoidance		5.8 (5.0)	9.0 (5.6)	.042	5.7 (5.1)	9.2 (5.3)	.027
Cognitive anxiety		8.3 (5.2)	12.1 (6.3)	.025	8.2 (5.2)	12.3 (6.1)	.014
Physiological anxiety		2.9 (4.3)	5.3 (6.2)	.102	2.8 (4.3)	5.3 (6.1)	.090
PVAQ (n = 50)	46.5 (16.1)	41.0 (14.9)	57.2 (13.1)	.000	40.9 (14.5)	57.4 (13.6)	.000
Attention to pain		15.9 (8.7)	25.3 (8.6)	.001	15.8 (8.6)	25.5 (8.7)	.000
Attention to changes in pain		19.9 (6.0)	24.2 (4.1)	.009	19.8 (5.8)	24.4 (4.4)	.006
N of other pains (n = 48)	1.7 (1.3)	1.8 (1.3)	1.6 (1.4)	.699	1.8 (1.3)	1.7 (1.4)	.320
Difficulties in falling asleep (% of nights) (n = 52)	20.5 (27.8)	13.5 (19.5)	34.9 (36.4)	.056	11.7 (17.5)	38.6 (35.9)	.012
Disturbed sleep (% of nights) (n = 52)	5.9 (13.4)	4.3 (11.8)	9.3 (16.0)	.156	2.5 (5.8)	13.0 (12.5)	.029

differences were noted in two of the subscales, escape-avoidance and cognitive anxiety (Table 1).

Patients in the highest intensity and interference tertiles were more preoccupied with the pain compared with patients with less severe pain. Between-group differences were noted for both of the factors of PVAQ, that is attention to pain and attention to changes in pain (Table 1).

The correlations between DEPS, PASS and PVAQ sum scores were high, varying between $r = .46$-$.59$ ($P < .001$).

The sum score of the PVAQ was found to correlate significantly with pain intensity ($r = .366$, $P = .009$) and interference ($r = .482$, $P = .009$). Depression ($r = .399$, $P = .003$) and pain anxiety symptoms ($r = .452$, $P = .001$) correlated with pain interference, but correlations with pain intensity did not reach statistical significance ($r = .243$, $P = .082$ and $r = .269$, $P = .053$ for depression and anxiety, respectively).

There was no association between the number of other pains and BMS pain intensity or interference (Table 1). Patients reporting high pain interference had difficulties in falling asleep because of the pain more often, and they also experienced more often pain-related sleep disturbances (Table 1).

5 | DISCUSSION

5.1 | Main findings

In accordance with the biopsychosocial model of chronic pain that emotional and cognitive factors play a role in pain experience, the results of the study demonstrated that BMS patients reporting more intensive and interfering pain reported more depressive and pain-related anxiety symptoms and more pain hypervigilance compared with patients with less severe pain intensity and interference. Patients reporting higher pain interference also reported more pain-related sleep problems. Depression and pain anxiety were found to correlate especially with pain interference, whereas pain hypervigilance correlated also with pain intensity.

Depressive symptoms were prevalent among BMS patients, and more than a third of the patients (19/52) had DEPS scores above the cut-off score for possible depression. The results are in line with previous research indicating that depression is highly prevalent in BMS patients.[17]

As regards pain anxiety and pain hypervigilance, the results are novel, as these pain-specific psychological factors have not earlier been assessed in BMS patients. They are part of the fear-avoidance model of chronic pain according to which pain initiates a set of emotional, cognitive and behavioural processes, which may exacerbate pain and disability.[34,35] Symptoms of pain anxiety correlate with pain intensity and disability in chronic pain patients[36] and do so more consistently in comparison with the general anxiety symptoms.[18] In line, in our study, BMS patients reporting most intensive and interfering pain displayed significantly more pain anxiety symptoms than those with less severe pain. The pain and interference groups differed specifically in respect to escape-avoidance (stopping or avoiding activities) and cognitive anxiety (difficulties to concentrate on other things) aspects of pain-related anxiety; the more pain and interference, the more these types of symptoms. Knowledge of the specific type of pain anxiety symptoms may facilitate development of individualised treatment interventions.

Excessive attention to pain or pain hypervigilance has been reported to associate with higher pain intensity, disability and emotional distress in different pain patient populations[30,31] and has been suggested to influence disability more than other psychological factors.[37] The findings of the present study showing a significant association between pain intensity and interference with pain hypervigilance may indicate that pronounced attention to pain may be an important factor also in BMS pain. Both subscales, "attention to pain" and "attention to changes in pain", differed significantly, indicating that the suggestion by Roelofs et al[31] to use a total PVAQ sum score is justified.

A recent study on pain-related cognitive factors in BMS patients focused on pain catastrophising, that is a tendency to magnify the threat value of pain stimulus and to feel helpless in the context of pain.[22] In this study, catastrophising was found to be associated with pain experience emphasising the role of maladaptive cognitive responses in BMS pain.

In addition to pain-related psychological factors, also patients' self-reported pain-related sleep problems were associated with pain experience in the present study. Patients reporting high pain interference reported difficulties in falling asleep more often and experienced sleep disturbances more often. Two studies assessing sleep disturbances with validated sleep scales in BMS patients reported a corresponding association.[20,22]

Much attention has been paid to the frequent co-occurrence and overlap of pain syndromes in chronic pain, with consequent pain amplification and perpetuation of the pain condition.[38] Comorbid pain conditions have been reported to be common among patients with different oro-facial pain conditions and to correlate with increasing pain severity.[9,38,39] To the contrary, a recent systematic review found no evidence of an association between BMS and other pain symptoms.[40] Herein, no association was found between the number of other pains and BMS pain severity. The finding may support the notion that BMS is a distinct intra-oral disease entity depending on specific mechanism at the trigeminal level.[40]

In the correlation analysis, the studied psychological parameters associated more with pain interference, a positive correlation with pain intensity was found only for pain hypervigilance. Likewise, no correlation was found between psychological symptoms and pain intensity in a previous study on the correlation of psychological symptoms with pain intensity in BMS patients.[41] The findings in BMS patients are in keeping with earlier findings of a more strong association of cognitive and affective measures to pain interference than to pain intensity in different chronic pain patient populations.[42,43] The statistically significant correlations between the psychological parameters (DEPS, PASS and PVAQ) suggest that they may be regarded as indicators of a more general psychological distress continuum.

5.2 | Methodological considerations

Pain intensity and interference figures were based on prospective pain diary data.[15] Prospective responses are considered more accurate compared to retrospective responses, which tend to show more inflation.[44] The amount of missing data was low; at the most, some data were missing from 4 patients (Table 1), supporting the use of listwise deletion in the statistical analysis.

The depression questionnaire, DEPS, used in this study was developed and validated as a screening instrument for patients in primary care,[24] while the internationally recommended Depression Scales have been developed for psychiatric patients. The validity of the commonly used Depression Scales in patients with somatic symptoms such as pain has been questioned. For example, sleep disturbance, loss or change of appetite, and fatigability have been regarded as "somatic" symptoms which, in the case of somatic illness, do not necessarily indicate depression.[45-48] DEPS, except for the item of sleep problems, does not include any of the"somatic" symptoms found problematic in earlier studies on pain patients and is therefore probably better suited to depict depression in this patient group. Further research is however needed to explore the validity and reliability of DEPS in the field of chronic pain. Regardless of the assessment method, diagnosing depression in chronic pain remains a challenge and requires careful interpretation of symptoms.

In this study, the focus was on symptoms of depression, pain-related anxiety and attention to pain, all of which present aspects of psychological vulnerability to chronic pain. Paying attention in future studies also to resilience aspects of pain, such as pain acceptance and positive psychological resources, would broaden the picture of the role of psychological factors in BMS pain experience.

The cross-sectional nature of the study limits causal interpretation of the relationships between pain intensity and interference and psychosocial factors. The most obvious limitation of the present study is the modest sample size, which prevented us from using more complicated statistical models to study the relative contribution of different comorbid factors on BMS pain experience.

5.3 | Clinical implications

According to the results of the present study, patients suffering from BMS symptoms are not a homogenous group. Patients experiencing different levels of symptom severity differed also in terms of comorbid symptoms so that patients with high pain intensity and interference were more psychosocially distressed compared to patients with less severe pain. The study thus identified subgroups of BMS patients likely having differing prognosis and treatment needs. As psychological factors are considered to be highly relevant in terms of treatment outcome and prognosis in pain, the prevailing view is that they should be addressed as part of the assessment in any pain condition.[2,49]

The findings of the present study are in line with findings from other oro-facial pain research,[6-9] where pain severity continuum assessments have generally also been used as tools to tailor treatments to patients' symptoms.[49,50] Treatment tailoring has so far not been applied to the treatment of BMS, which may in part explain the modest treatment outcomes achieved by different

treatment methods.[11] The present results underline the need to develop the diagnostics and treatment of BMS in a multidimensional direction.

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CONFLICT OF INTEREST

The authors report no conflicts of interest that may have affected the work.

AUTHOR CONTRIBUTIONS

Heli Forssell and Ann-Mari Estlander initiated the study project. Tuija Teerijoki-Oksa participated in the gathering of the study subjects. Pauli Puukka planned and performed the statistical analyses. Heli Forssell wrote the manuscript. All authors reviewed and revised the manuscript, and approved the final version of the manuscript.

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