Peculiar alexithymic traits in burning mouth syndrome: case–control study

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Running head alexithymia in burning mouth syndrome

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ABSTRACT

Objectives. The present case-control study aims to assess the occurrence of alexithymic traits in burning mouth syndrome (BMS) subjects and to correlate alexithymic traits to anxious and depressive traits in BMS subjects.

Materials and Methods. Prospectively enrolled BMS and control subjects were administered the 20-item Toronto Alexithymia Scale (TAS-20). Anxiety and depressive traits were assessed using the Hamilton Anxiety Rating Scale and the Montgomery & Asberg Depression Rating Scale. Occurrence of alexithymic traits was compared between BMS and control subjects. Correlation tests were used to measure the importance of alexithymic traits related to demographic characteristics, pain intensity (VAS score) and to the other psychometric scores.

Results. Fifty-eight BMS subjects (46 females and 12 males) had a mean TAS-20 score significantly higher when compared to controls ($p<.001$; $r=.72$), corresponding to an occurrence rate of alexithymic traits of 79.3% versus 6.9%. Alexithymic traits in BMS subjects were just related to depressive traits ($p=.02$; $\rho=.31$).

Conclusions. The high occurrence of alexithymia in BMS is an adjunctive issue in favour of its multifactorial pathogenesis, with a not negligible role for somatization.

Clinical relevance. Clinicians should be aware of the high occurrence of alexithymic traits among BMS subjects as such traits may affect the doctor–patient relationship.

Keywords burning mouth syndrome; alexithymia; 20-item Toronto Alexithymic Scale; Somatization

INTRODUCTION

Burning mouth syndrome (BMS) is an enigmatic chronic pain condition that affects 1.5–5.5% of post-menopausal aged women[1]. The recent 3rd edition of International Classification of Headache Disorders (ICHD-III) describes it as an intraoral burning or dysaesthetic sensation, without clinically evident causative lesions[2]. The pathophysiology of BMS is uncertain and it has long generated controversies. Even if recent studies have identified dysfunctions in the peripheral and central nervous system[3, 4], controlled studies reported significant comorbidity with psychiatric or personality disorders[5-7]; in this way, interactions among systemic, local or psychogenic factors are probably involved in a large number of patients[8].

Alexithymia is a stable personality trait with characteristic ways of reacting[9]. Instead of coping with affective phenomena at a mental level, emotional arousal is frequently experienced as being somatically based[10, 11]. Alexithymic patients often complain with endless descriptions of physical symptoms with or without an identifiable cause, so that they are considered prone to somatic symptom disorders[12].

It is estimated that some psychological factors play a significant role on onset, severity, exacerbation or maintenance of pain[13] and several studies investigated the association between alexithymia and pain[14, 15]. Patients with chronic pain (back pain, headache and limb pain) in absence of organic basis, showed a higher frequency of alexithymic traits when compared to subjects suffering from medically explained chronic pain [16].

The role of alexithymia in BMS has only once been suggested in a preliminary study[17]. Recognizing subjects with alexithymic traits may be useful to correctly identify their tendency to somatization and to manage their peculiar personality traits potentially affecting the doctor–patient relationships and requiring an emphatic attitude to obtain a solid treatment alliance. Aims

of the present study were to assess the occurrence of alexithymic traits in BMS subjects compared to a matched control group assessed by the 20-item Toronto Alexithymic Scale (TAS-20) and to correlate alexithymic traits to anxious and depressive traits in BMS subjects.

MATERIALS AND METHODS

The present report fulfils the STROBE guidelines for case-control studies[18, 19]. The study was carried out according to the 'Helsinki Declaration of 1975', as revised in 2008; patient/control participation required an informed consent.

Recruitment

The study was carried out on patients with previously untreated BMS. They were prospectively recruited over a 24-month period at the oral medicine section of our university hospital, among subjects referring for oral burning/pain. Oral medicine practitioners, unaware of the study hypothesis, performed clinical examinations to confirm/exclude the diagnosis of BMS and to carry on the recruitment for the study purpose. It has been demonstrated that social and demographic factors such as age, gender, socioeconomic status and educational level are associated with alexithymia[10]. Therefore a control group, matched for age (five year age bands: 50-54, 55-59, 60-64, etc.), sex, educational level (length of education in years) and employment (working, retired, never working), was consecutively selected within patients attending our university hospital for conventional dental treatments (one control for each case). These subjects mainly asked for dental treatment in an university hospital for economic reasons, not for particular systemic pathologic conditions. The recruiters were not aware of the study hypothesis.

Inclusion/exclusion criteria

In accordance with previous studies[20] and with the recent ICHD-III[2], the set diagnostic criteria for BMS were the presence of an isolated complaint of chronic burning/pain in the oral mucosa revealed by a normal clinical examination, and symptoms recurring daily for more than 2 hours per day over more than 4 months with no paroxysms and not following a nerve trajectory.

To confirm the BMS diagnosis, candida infection and any other organic conditions, which could be considered as a causative factor for similar oral symptoms, were ruled out in all subjects by laboratory examinations (full blood cell count, and serum levels of iron, ferritine, folate, vitamin B12, and glucose). Subjects with diabetes that were not under effective pharmacological control were excluded. A local effect of dental materials related to contact hypersensitivity was excluded by means of patch tests in suspected cases, when symptoms were arisen after any dental rehabilitation, even in the absence of evident mucosal lesions. In case of referral of symptoms located in other sites (e.g. ENT subsites), further assessments were performed to rule out other diseases. Similarly, in presence of xerostomia (subjective dryness of the mouth), the unstimulated salivary flow rate was assessed to exclude hyposalivation. The collection of whole saliva was performed at least 1 h after eating, while subjects were at rest in a quiet room; they were asked to collect saliva in their mouth and to spit it into a wide test tube for 15 min[21].

Pain intensity

A symptom score was obtained using a visual analogue scale (VAS). The VAS consisted of a 10-cm vertical line marked from 0 (= no pain) to 10 (= most severe pain experienced)[20]. During the first clinical examination, patients were asked to indicate the mean pain intensity regarding the 2 weeks preceding the consultation.

Alexithymia assessment

The Toronto Alexithymic Scale (TAS), a self-administered psychometric questionnaire, is a validated tool to assess alexithymic traits[22, 23]. First created in 1985 (as TAS-26, with 26 items), then revised in 1992 (with a reduction to 20 items), it is currently the most commonly used and best-validated measure of alexithymia. Each answer is rated on a 5-point Likert scale corresponding to a total score ranging between 20 and 100. A different person from the recruiters

presented the questionnaire to both BMS subjects and controls; the questionnaire was self-administered. BMS subjects received the questionnaire after completion of BMS diagnosis; in this way, oral medicine practitioners who performed the clinical examination were not aware of the TAS-20 test scores. Control subjects received the questionnaire the day after the first visit. The following validated cut-off values were considered: ≤ 51 non- alexithymic, 52 to 60 borderline, ≥ 61 alexithymic[24].

Psychometric assessment

In our centre, psychiatric assessment is performed in all subjects after completion of the diagnosis of BMS; in this study, psychiatrists who did examinations were unaware of both the study hypothesis and TAS-20 test scores. The Hamilton Anxiety Rating Scale (HARS) was employed to assess anxiety symptoms using the following validated cut-off values: ≤ 17 mild anxiety, 18 to 24 mild to moderate anxiety, 25 to 30 moderate to severe anxiety. The Montgomery & Asberg Depression Rating Scale (MADRS) was employed to assess depressive symptoms using the following validated cut-off values: 0 to 6 normal/symptom absent, 7 to 19 mild depression, 20 to 34 moderate depression, >34 severe depression. Controls were only asked to fill the TAS-20 questionnaire and they did not receive a psychiatric assessment, so that psychometric assessments were just performed among the BMS group.

Statistical analysis

The sample size was calculated according to previously reported data, suggesting an overall alexithymia prevalence rate of about 10% in the general population[25] and of about 70% among BMS subjects[17]. With a power of 80% and a type I error of .05, 24 subjects (12 cases and 12 controls) had to be recruited. Data collection and management were conducted using the Microsoft Office Excel package in association with the SPSS 18.0 software package (SPSS Inc.) for

the statistical analyses. ANOVA was used to assess differences in the TAS-20 score among BMS subjects and controls. A comparative evaluation on alexithymia prevalence was also performed by comparing the percentage of positive, borderline and negative subjects among groups (Chi-square test). ANOVA and correlation tests (Pearson or Spearman two-tailed correlation analysis depending on the normal distribution of data) were used to measure the importance of alexithymic traits related to demographic characteristics, pain intensity (VAS score) and the other psychometric scores. The association was regarded as: small, if r ranged from ±.1 to ±.29; moderate, if r ranged from ±.30 to ±.49; and large, if r ranged from ±.50 to ±1.0. $P < .05$ was considered as statistically significant.

RESULTS

Despite the sample size needed, the recruitment went on until the end of the 24-month period, thus providing a sample size almost 5-fold larger than required. One hundred thirty-five patients, reporting oral symptoms suggestive of BMS, were screened for participation; among 64 BMS subjects satisfying the inclusion/exclusion criteria, 58 agreed to enter the study: 46 (79.3%) females and 12 (20.7%) males with a mean age of 65.6±10.5 years and an average educational level of 5.8 years. These demographic parameters served for the selection of a matched control group of 58 subjects. During the recruitment of the control group, before the completion of the recruitment, 12 subjects refused to enter the study. All the recruited BMS and control subjects completely filled the TAS-20 questionnaire.

The average age at BMS onset was 63.2 years (range: 30-79) with an average duration of symptoms of 2.4 years. Five subjects out of 58 were assuming psychotropic drugs at the moment of our first visit (1 subject was assuming alprazolam and bromazepam, 1 levosulpiride, 2 delorazepam and 1 amitriptyline). Nearly all BMS subjects described the perceived symptoms as burning (56/58; 96.6%), more than half (33/58; 56.9%) had xerostomia in absence of reduced unstimulated salivary flow rate and almost one quarter reported dysgeusia (14/58; 24.1%), while paresthesia and pain were less frequently recorded (8/58; 13.8% and 7/58; 12.1% respectively). The association of burning, xerostomia and dysgeusia was reported by 8/58 subjects (6.9%). The tongue, mainly the tip, was the most frequently affected oral subsite (41/58; 70.7%), followed by the gingiva (17/58; 29.3%), the palate (15/58; 25.9%) and the lips (15/58; 25.9%). Conversely, the buccal mucosa and the floor of the mouth were rarely involved (3/58; 5.2% and 2/58; 3.4% respectively). Noteworthy, few subjects (9/58; 15.5%) reported the involvement of the whole oral

cavity, while symptoms at ENT subsite were only seldom reported (4/58; 6.9%). Using a VAS-scale, BMS subjects reported an average pain intensity score of 7.6±1.7.

The VAS score resulted directly related to age (Pearson correlation test, p=.03, r=.29), conversely it was neither related to sex (ANOVA, p=.663), nor to the educational level (Spearman correlation test, p=.72).

The TAS-20 score resulted related neither to sex (ANOVA; p=.82), nor to age (Pearson correlation test, p=.08), nor to assumption of psychotropic medications (ANOVA, p=.57), but only to educational level (Spearman correlation test, p<.001, ρ=-0.35). When addressing the TAS-20 scores in BMS and controls, the BMS group revealed a significantly higher average score (ANOVA, p<.001; Pearson correlation coefficient, r=.72) and higher prevalence of alexithymic traits (chi-square test, p<.001) as shown in table 1 and figure 1.

Results of psychometric tests for depression and anxiety in BMS subjects are shown in table 2.

Table 3 shows all the comparisons among psychometric scores and pain intensities in the BMS group as assessed by Spearman correlation test. Scores for alexithymia and anxiety were not significantly related (p=.93); conversely a ρ=.31 significantly correlated scores for alexithymia and depression (p=.02). The pain intensity (VAS score) was neither significantly related to the TAS-20 score nor to any other psychometric score.

The assumption of psychotropic medications was observed in 5 out of 58 BMS, without significant differences when addressing genders (Fisher's exact test, p=.27) or educational levels (ANOVA, p=.97). It did not significantly affected the VAS score (ANOVA, p=.12). It implied significantly lower MADRS scores (ANOVA, p=.03), but it did not influenced the HARS scores (ANOVA, p=.58).

DISCUSSION

The clinical features of the present group of BMS subjects makes it a representative case of such condition. The group is mainly formed by postmenopausal women who complain of unremitting oral mucosal burning pain, frequently associated to dysgeusia and xerostomia. Symptoms are commonly bilateral and most often involve the tongue followed by the palate and lower lip. In contrast, the buccal mucosa and floor of the mouth are rarely affected. Also the reported pain intensity is in keeping with previous data obtained using the VAS-scale, which showed scores usually ranging from 6 to 8[20, 26-28].

The aetiology and pathogenesis of BMS are still a question of debate and have long generated controversies. Many studies explored neuropathic disorders as well as psychopathological factors, suggesting interactions among them, but a consensus has not been reached yet[29]; similarly, there is an increasing evidence on somatization among BMS subjects[13]. Such issue appears even more intriguing and potentially significant in the light of the revised classification of the somatic symptoms and related disorders in the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM–5)[30]. Currently, the distinctive characteristic of the somatic symptom disorder is not considered the somatic symptom per se, but like the way subjects present and interpret it[30]. Therefore, even in absence of any neuropathic disorders, the potential role of psychological factors, having a significant role on the way of reacting and copying with symptoms, becomes even more important.

Alexithymia is a multifaceted dimensional construct first described in the 1970s by Sifneos[31]. It represents a stable personality trait[9, 32] with a prevalence rate of about 10% among the general population[25, 33], even if an association with increasing age has been reported with a prevalence

rate as high as 20-30% among older subjects[25]. In the present study, the healthy controls (mean age 64.4±11.5 years) had a mean TAS-20 score of 48.3±7.8, which is fully comparable with that previously reported in a general population of the same age[25]. The lack of correlation between age and alexithymic traits in the present study could be reasonably due to the relatively narrow age range of BMS subjects. In 1997, Jerlang first investigated alexithymic traits in BMS; he found most of BMS subjects having alexithymic traits (14 out of 20 BMS subjects, corresponding to 70%)[17]. In the present study, the prevalence of alexithymic traits found in BMS patients is slightly higher (79.3%), but anyway comparable to previously reported data. The present study confirms a significant link between BMS and the occurrence of alexithymic traits with a noteworthy high statistical power.

Difficulty in the identification of the feelings and to distinguish them in comparison to bodily sensations of emotional arousal is one of the components of the alexithymia construct. Many factors concur to somatic symptoms presentation and some personality traits, among which alexithymia, have been regarded as risk factors for the development or persistence of medically unexplained symptoms[12, 33, 34].

Interestingly, a prospective study found that alexithymic subjects were more prone to develop somatoform disorders[35] and a recent systematic review showed that studies addressing somatoform conditions reported significantly higher degree of alexithymic traits in such subjects when compared to healthy controls, with effect sizes ranging from moderate to large (r value ranging from 0.24 to 0.67)[34]. The present results show a significant correlation between BMS and alexithymia with an even larger effect size (r=.72).

Several issues support the hypothesis of BMS as a condition associated to somatoform disorder. In a randomized controlled trial addressing the efficacy of alpha-lipoic acid in BMS, we observed that BMS had similar response to placebo when compared to atypical facial pain, which is known to have high levels of psychiatric comorbidity and psychosocial disability[20]. Cognitive behavioural therapy is known to be an efficacious treatment for the range of conditions loosely grouped under the somatoform disorders and it has been proved to be effective in the management of BMS[36]. The high occurrence of alexithymia in BMS subjects could represent an adjunctive issue in favour of a multifactorial pathogenesis of BMS with a not negligible role for somatization.

Both somatization and alexithymia are associated with common psychopathologies such as depression and anxiety. In the present study, both depression and anxiety were assessed by clinician-administered tests. Depression was assessed by MADRS, which has a reliability comparable to that of the Hamilton Rating Scale for Depression, by far the most used in research, with the advantage of a smaller number of items; conversely, anxiety was assessed by HRSA, a 14-item interview addressing both psychic and somatic symptoms of anxiety. Recently, it was found that alexithymia was strongly associated with depressive and anxiety disorders[37, 38]. Nevertheless, alexithymia does not seem to be affected by depressive episodes[39], thus confirming that it is a stable trait rather than a state-dependent feature. Therefore, alexithymic traits imply an increased risk of developing depressive or anxiety disorders and cannot be interpreted as a consequence of psychopathologies[9, 40]. The preliminary study by Jerlang showed that alexithymic traits in BMS subjects were only weakly correlated to depressive symptoms, but were not correlated to pain intensity, depression or anxiety[17]. Even if already reported by Jerlang, the lack of correlation between pain intensity and TAS-20 score could be unexpected, as a linear relation between TAS-20 and VAS values has seldom been reported in

studies addressing other kind of pain[41, 42]. In the present study, the lack of correlation could be due to the quite narrow range of the VAS score (7.6±1.7). Nevertheless, other studies failed to find a correlation between alexithymia and pain intensity[43]. Even with limitations due to the lack of a complete psychometric assessment of control subjects, the present study is absolutely in keeping with such results, showing very similar interactions among alexithymia, anxiety, depression and pain when just considering BMS subjects. Even if we observed quite high scores for anxiety and depression in BMS subjects, the lack of a complete psychometric assessment of control subjects prevented us from confirming the already known significant comorbidity of BMS with anxiety and depression. About 9% of BMS subjects were already assuming psychotropic medications as prescribed by their general medical practitioner. This resulted in significantly lower scores at the MADRS test, even if not related to the TAS-20 score.

Chronic orofacial pain patients generally desire to be understood and to feel cared for, with acknowledgement of their pain as real; they need a multidisciplinary approach with peculiar attention to the patient-doctor interaction. Particularly, in alexithymic subjects, an emphatic attitude may represent the basis for a solid treatment alliance[44]. Therefore, clinicians should be aware of a high occurrence of alexithymic traits among BMS subjects as such kind of traits may have important implications for medical treatment[45] and may affect the patient-doctor relationships.

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TABLES

Table 1. Alexithymia prevalence and TAS-20 score in BMS and control subjects

	No alexithymia	Borderline alexithymia	Alexithymia	TAS-20 score mean±SD	Total
BMS	5 (8.6%)	7 (12.1%)	46 (79.3%)	70.6±13.2	58
Control	39 (67.2%)	15 (25.9%)	4 (6.9%)	48.3±7.8	58

Table 2. Prevalence of anxiety and depression as assessed by the psychometric tests in BMS subjects

Anxiety (HARS)*	Mild	Mild to moderate	Moderate to severe	Score mean±SD	
	11 (19.3%)	18 (31.6%)	28 (49.1%)	23.5±8.2	
Depression (MADRS)*	Normal	Mild	Moderate	Severe	Score mean±SD
	29 (50.9%)	27 (47.3%)	1 (1.8%)	0 (0.0%)	7.8±5.1

*= data available for 57 subjects

Table 3. Correlations among psychometric scores and pain intensity in BMS subjects

		TAS -20	MADRS*	HARS*	VAS
TAS-20	Spearman's rho	1	.31	.01	.23
	p value (2-tails)		.02	.93	.09
MADRS*	Spearman's rho	.31	1	.14	.01
	p value (2-tails)	.02		.29	.95
HARS*	Spearman's rho	.01	.14	1	.05
	p value (2-tails)	.93	.29		.69
VAS	Spearman's rho	.23	.01	.05	1
	p value (2-tails)	.09	.95	.69	

*= data available for 57 subjects

FIGURE

Figure 1. TAS-20 score distribution among BMS subjects and controls