

Clinical characterization of women with burning mouth syndrome in a case-control study

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ABSTRACT

Objective: Burning mouth syndrome (BMS) is a chronic orofacial pain disorder that is defined by a burning sensation in the oral mucosa. The aim of this study was to investigate the underlying factors, clinical characteristics and self-reported oral and general health factors associated with BMS.

Material and methods: Fifty-six women with BMS (mean age: 67.7) and their age-matched controls were included in the study. A general questionnaire, an OHRQL index and BMS-specific questionnaires were used. Each subject underwent an oral examination.

Results: The mean severity of the BMS symptoms (VAS, 0–100) was 66.2 (SD 19.7). Overall, 45% of the patients reported taste disturbances. More of the patients than the controls rated their general health, oral health and life situation as ‘less satisfactory’. The patients also reported more frequently on-going medications, diseases/disorders, xerostomia, allergy and skin diseases. Except for more bruxofacets among the patients, there were no significant differences regarding signs of parafunction. In a multiple logistic regression analysis, xerostomia and skin diseases showed the strongest prediction for BMS and no significant effect was found for medication, allergy or bruxofacets.

Conclusions: Skin diseases and xerostomia but not parafunction were strongly associated with BMS. Our findings provide the basis for additional studies to elucidate the causal factors of BMS.

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Introduction

Burning mouth syndrome (BMS) is a chronic pain disorder that is characterized by an unremitting oral burning or stinging sensation in the absence of any detectable changes to the oral mucosa, ruling out other obvious aetiological factors. Lack of objective diagnostic criteria of BMS may be one of the reasons why the prevalence of BMS reported in different studies varies from 0.7 to 15% [1–6]. BMS is further reported to be 2.5–7-times more common among women than men, primarily affecting perimenopausal and postmenopausal women [7,8]. The prognosis for patients with BMS is very poor [9] and these patients represent a major burden on healthcare systems.

Despite extensive research efforts, no single or direct cause of BMS has been identified to date. Associations, direct and indirect, to factors, such as xerostomia, hyposalivation, temporomandibular and tongue dysfunction/parafunction, malnutrition, anaemia, adverse drug reactions and hormonal imbalance have been reported [1,10,11]. BMS has also been associated with psychologic factors, such as stress, depression and anxiety [11–16]. The aetiology is most likely to be

multifactorial, with disease development involving interplay of hormonal, neuropathic and possibly genetic factors [17–21]. Recent developments in diagnostic method have associated BMS with either central or peripheral neuropathic pain that sometimes may overlap in the individual patients [17,18].

Large efforts have been made to treat BMS using, e.g. low-intensity laser therapy, clonazepam, paroxetine and alpha lipoic acid with promising results but there are today no treatments to cure it [22,23]. Given the lack of understanding of the disease, the development of an explanatory model for BMS is important and urgent in order to improve the diagnosis and treatment [24]. This study is part of a larger project that is investigating several potential aetiological factors for BMS, including saliva quantity and quality, taste perception, oral parafunction, behavioural and psychological factors, in larger groups of women with BMS, together with age-matched controls.

The aim of this study was to investigate the underlying factors, clinical characteristics and patients’ self-reported oral and general health factors associated with BMS and compare the characteristics of the patients to age-matched controls.

The study will form the base for further examinations on these women.

Material and method

Study sample and procedures

Case group

The patients with BMS were recruited among patients who had been diagnosed with BMS at the Clinic of Oral Medicine in Gothenburg, Sweden. A letter of invitation was sent in 2011 to 104 patients who had been diagnosed with BMS in that year or previous to that year. Of the respondents, 26 were chosen to participate in the study. Ongoing recruitment of new patients with BMS at the clinic during the study period of 2012–2014 resulted in a further 15 participants. An additional 20 women, who had learned of the study through the media or from other healthcare personnel, also joined the study. For the latter participants, a diagnosis of BMS had to be established by a specialist in oral medicine or an equivalent professional. Only three men were available in the patient register and, therefore, men were excluded in the study to avoid analytical bias. The diagnosis of BMS patients was done as per ICDH-3 beta classification system made by the International Headache Society (IHS) [25] with the exception of sensory testing. Patients diagnosed with BMS did not have asymmetric pain or other signs of neuropathies that implied other pathologies. Four patients developed diabetes long after being diagnosed with BMS.

The inclusion criteria for the patients with BMS were:

- Female sex.
- BMS characterized by an unremitting oral burning or stinging sensation felt superficially in the oral mucosa recurring for more than 2 h per day for more than three months, without any detectable changes in the oral mucosa.

The exclusion criteria were:

- Finding of anaemia or ongoing infections.
- Clinically visible changes in the oral mucosa/tongue.

- Increased numbers of opportunistic bacteria on the tongue.

For all women, blood tests were conducted to exclude abnormal blood values (e.g. anaemia and infections [CRP test]). Scraping samples from the tongue were also collected and analysed for the presence of opportunistic bacteria as previously described [25]. Increased opportunistic bacteria may indicate an infection that could mimic the symptoms of BMS.

Control group

The control group consisted of age-matched women (± 3 years) from public and private dental clinics and staff working at the Institute of Odontology, Gothenburg. All members of the control group were individually evaluated. The use of medication for common disorders, such as high blood pressure or high cholesterol was not a cause for exclusion.

The exclusion criteria for the controls were:

- Report of intraoral burning sensation.
- Finding of anaemia or ongoing infections.
- Increased numbers of opportunistic bacteria on the tongue.
- History of systemic disease or other more severe illnesses, e.g. rheumatoid arthritis.

All the invited subjects received a letter with an information pamphlet and questionnaires concerning their psychological profile, along with general questionnaires covering life events, medication usage and health.

Schematic of the process used to select the participants in the case-control study are shown in Figure 1.

Questionnaires

The patients with BMS and controls had to complete six questionnaires and psychometric instruments. There were two extra questionnaires for the patients with BMS: one concerning the symptoms of BMS and one psychometric index.

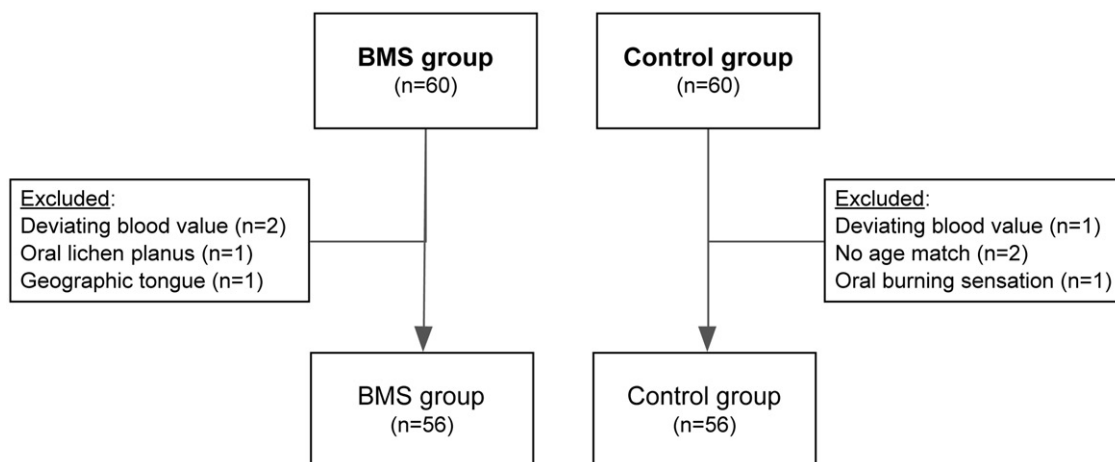


Figure 1. Schematic of the process used to select the participants in the case-control study.

General questionnaire

All the case and control subjects filled in a general questionnaire that contained 38 questions, often with supplementary questions that began with the words: how, when, why and which. There were also questions regarding socio-demographic data (age, relationship status), general health and satisfaction with life situation. The relationship status item had six response alternatives which were dichotomized into 'living in relationship' (i.e. married, cohabiting, living together but residing apart) and 'not living in relationship' (i.e. single, divorced, widow/widower). The questions regarding general health and satisfaction with life situation were answered on a Likert scale (general health: 'very good', 'good', 'decent', 'poor', 'very poor'; and life situation: 'very satisfied', 'satisfied', 'neither/nor', 'unsatisfied', 'very unsatisfied').

The subjects also described their oral health (five-point Likert scale ranging from 'very good' to 'very poor'). Oral health-related quality of life (OHRQL) was assessed with the Oral Health Impact Profile (OHIP 14), which contains 14 items [26,27]. The responses to the OHIP 14 are scored on a Likert scale ('always', 'often', 'sometimes', 'seldom', 'never'), resulting in a score range of 14–70, with higher scores indicating poorer OHRQL.

The participants were also asked (with Yes/No response alternatives) if they: had any on-going diseases, suffered from allergy or post-menopausal symptoms, regularly took any medications, were susceptible to infections, suffered from any skin disease and experienced dry mouth [28]. An affirmative answer resulted in follow-up questions. Physical activity was assessed by a question as to how many days the subject was physically active for at least 30 min per week (defined as at least a fast-paced walk) and the answers were dichotomized into 3 d or less; and 4 d or more. The participants were also asked about past and present smoking habits. A visual analogue scale (VAS) was used to assess the severity of the xerostomia (ranging from 0 = 'not at all' to 100 = 'unbearable') and to assess sensitivity to pain by asking about perceived pain when taking a blood sample from the fingertip (ranging from 0 = 'no pain at all' to 100 = 'terrible pain').

The BMS questionnaire

A questionnaire designed specifically for the patients with BMS included 16 questions regarding the symptoms, associations connected with the debut of the symptoms and other factors related to the syndrome. This questionnaire was based primarily on the protocol of Bergdahl et al. [29]. The four alternatives regarding how the symptoms manifested themselves were: burning, scalding, numbness and prickling sensation. The severity of the BMS symptoms was assessed on a VAS that had its extremities: 'not at all' and 'unbearable'. The debut (year) of the BMS symptoms and possible association with any special event was registered. Information on how often, when during the day (or night) and for how long the symptoms appeared and lasted was registered. Furthermore, the patients were asked if any factors had triggered the symptoms (e.g. food, medicine, stress) or worsened or relieved the symptoms and if any treatment had any positive effect. In addition, the patients were asked

if they had noticed any changes in taste and if so, which taste disturbances. Finally, they were asked if they had any relative who suffered from BMS.

Clinical examinations and tests

In the clinical examination of dental status, the numbers of teeth, fillings (amalgam and composite), crowns and dentures (partial or total) were recorded. The subjects were also asked if they had any of their amalgam fillings exchanged, and if so whether there had been any noticeable change in their symptoms.

Dental wear was registered for the incisal, canine, premolar and molar regions according to the following scale: 1, no or minimal wear of the enamel; 2, wear extending into the dentin; 3, wear of one-third of the clinical crown; 4, wear extending into the secondary dentin. The scores for each region were summed and a value in the range of 0–16 was assigned to each patient. Active bruxofacets (fraying of incisal edges, shiny occlusal surfaces) were also registered in the incisal, canine, premolar and molar region, with a score of 0 or 1 for each region, yielding an overall score in the range of 0–4 for each patient. The mucosa was examined for signs of parafunction, including impressions of the tongue, bucca and lips.

The pressure pain threshold (PPT) was determined by the centre of the forehead using an electronic pressure algometer (Somedic, Sösdala, Sweden), to evaluate the general pain sensitivity of the subjects. The algometer comprises a pressure-sensitive strain gauge that is attached to a hard rubber tip. The instrument was placed perpendicular to the skin surface. Pressure was applied through the rubber tip to an area of 1 cm² at a rate of 50 kPa per second. The patients were instructed to press a signal button when the sensation of 'pressure' changed to 'pain'. The mean value of three measurements recorded at 1-min intervals was determined.

Ethical approval

This case-control study was conducted at the Institute of Odontology, The Sahlgrenska Academy at the University of Gothenburg, Göteborg, Sweden. The study was approved by the Regional Ethical Review Board in Gothenburg (Dnr. 368-10) and followed the ethical guidelines of the Helsinki Declaration. Written informed consent was obtained from all participants prior to the study.

Statistical analysis

The SPSS software package version 21.0 (SPSS, Chicago, IL) was used for all the statistical analyses. The results are shown as percentages, means and standard deviations (SD). For comparisons of two groups, an unpaired Student's *t*-test was applied for continuous variables and for ordinal scales the Mann-Whitney U-test was used. Fisher's exact test was used for comparison of proportions between the groups. Relationships were analysed using multiple logistic regression (ENTER model). The odds ratio (OR) and 95% confidence

interval (CI) were calculated. The full five-point Likert scale was used in all the analyses, even when dichotomized in the tables. The prechosen level of significance was a p value $<.05$.

Results

Responses to the general questionnaire

The 56 patients with BMS had a mean age of 67.8 years and the age-matched controls had a mean age of 67.7 ($p = .948$). The youngest participant was 43 years old and the oldest was 84 years old.

A majority of both the cases and the controls were living in a relationship (Table 1). Engagement in physical activity tended to be more common among the controls. A tendency never to have been a regular smoker was seen more frequently among the patients with BMS. None of the patients with BMS was an active smoker, as compared to four in the control group. Two of the latter were daily smokers and two smoked occasionally on a weekly basis.

Significantly fewer patients than control subjects rated their general and oral health and life situation as good or satisfactory (Table 2). Only among the patients with BMS did some experience their general health to be 'poor' or 'very poor' (25%) and were 'dissatisfied' or 'very dissatisfied' with their life situation (23%). Poor or very poor oral health was reported by 34 of the patients with BMS (61%), as compared to one control (2%). The BMS group assessed their oral health-related quality of life, as measured with OHIP 14, to be significantly poorer than that of the control group (mean OHIP 14 scores: 31.9 vs. 15.0; $p < .001$).

Table 1. Numbers of individuals in the BMS and control group who responded to questions regarding relationship status, physical activity and smoking history.

Questionnaire item	BMS		Control		p Value
	N	%	N	%	
Relationship status					
Living in relationship	41	73.2	37	66.1	.538*
Physical activity					
4 d or more/week***	25	56.1	40	70.2	.067**
Smoking habits					
Never been a regular smoker	37	66.1	29	51.8	.179*

*Fisher's exact test.

**Student's t -test.

***The continuous scale (1–7 d/week) was used in the analysis.

Table 2. Self-reported general health and oral health and life situation scores for individuals in the BMS and control groups. [AQ1]

Questionnaire item	BMS		Control		p Value*
	N	%	N	%	
Self-rating of general health					
Very good/good**	16	28.1	50	89.3	$<.001$
Self-rating of oral health					
Very good/good**	7	12.5	45	80.4	$<.001$
Life situation					
Very satisfied/satisfied**	30	53.6	55	98.2	$<.001$

*Comparison of the groups using the Mann–Whitney U-test.

**The full five-point Likert scale was used in the analysis.

A significantly higher proportion of the patients with BMS reported having one or more diseases/disorders (excluding allergy, skin disease and BMS), as compared to the controls (Table 3). The patients with BMS reported in average 1.4 (SD 1.4) diseases/disorders, as compared to 0.3 (SD = 0.7) for the controls. The most common diseases reported by these patients with BMS were osteoarthritis ($N = 8$), hypertension ($N = 9$), fibromyalgia ($N = 6$), diabetes, asthma and back pain ($N = 4$ for each). Among the controls, hypertension ($N = 5$) was the most frequently reported disease and other diseases were only reported once. Overall, 34% of the patients with BMS and 30% of the controls reported that they had had one or more serious diseases. The most common past disease was cancer, which was reported by six patients with BMS and by seven control subjects. The second most common past disease was stroke reported by three patients with BMS. Significantly, more patients with BMS reported having skin disease/problems and allergy (Table 3). The most frequently reported skin disease/problem were itching (case and control groups: $N = 4$ for each), rosacea (case group: $N = 4$), eczema (case group: $N = 4$), dry skin (case group: $N = 4$) and psoriasis (case and control groups: $N = 2$ for each). As for allergy, pollen was the most common allergen (case group: $N = 6$; control group: $N = 3$), followed by nickel (case group: $N = 4$) and penicillin (case group: $N = 4$). The patients with BMS tended to have more symptoms from the genital mucosa than the control group. Most common were dry mucosa (case group: $N = 10$; control group: $N = 5$), followed by lichen (case group: $N = 3$) and scratching (case group: $N = 2$).

Two patients with BMS and one control subject still had menstrual periods. Postmenopausal symptoms were or had been common in both groups (Table 3). In the BMS group, 21 (38%) had postmenopausal symptoms and 20 (36%) still had these symptoms, as compared to 28 (50%) and 17 (30%), respectively, in the control group. In the BMS group, 30 (54%) never had used oestrogen drugs vs. 39 (70%) of the controls. Nine of the patients with BMS (16%) and three of the controls (5%) answered in the affirmative to the question

Table 3. Numbers of individuals in the BMS and control groups reporting intake of drugs, skin disease, symptoms of the genital mucosa, susceptibility to infection, allergy, post-menopausal symptoms and xerostomia.

Questionnaire item	BMS		Control		p Value*
	N	%	N	%	
On-going diseases/disorders					
Yes	40	71.4	15	26.8	$<.001$
Medication					
Yes	48	85.7	30	53.6	$<.001$
Skin disease					
Yes	22	39.3	8	14.3	.005
Symptoms genital mucosa					
Yes	15	26.8	6	10.7	.051
Susceptibility to infection					
Yes	7	12.7	4	7.1	.360
Allergy					
Yes	24	42.9	13	23.2	.044
Postmenopausal symptoms					
Yes (have/have had)	41	73.2	45	80.4	.502
Xerostomia					
Yes	42	75.0	11	19.6	$<.001$

*Comparison of the groups using Fisher's exact test.

asking if they presently used oestrogen on the recommendation of their physician. However, scrutiny of the medicine lists revealed that 16 of the patients with BMS (29%) and 7 (13%) of the controls used oestrogen in some form. More patients with BMS than control subjects experienced dryness of the mouth (Table 3). Among those reporting xerostomia, the intensity of the problem scored on a VAS was on average 50.4 (SD 28.3) for the BMS group and 25.3 (SD 26.1) for the control group ($p = .011$).

General sensitivity to pain was assessed on a VAS (perceived pain when taking blood sample from the fingertip) and by determining the PPT (forehead). No significant differences were found between the patients with BMS and the control subjects for either the VAS [BMS group: mean =12.7, SD 16.5; control group: mean =13.3, SD 15.4 ($p = .832$)] or for PPT [BMS group: mean =262, SD 139; control group: mean =286, SD 126) ($p = .345$).

Clinical examination

The average number of teeth was high in both groups (Table 4). Two patients had a full denture in one jaw and one of them also had a partial denture in the other jaw. The control group had significantly more amalgam restorations (Table 4). Ten patients in the BMS group had their amalgam fillings exchanged, compared with none in the control group. None of the patients reported any subjective perceivable change of symptoms after the restorations were exchanged. The dental wear patterns were similar in both groups, although a higher number of active bruxofacets was seen in the BMS group.

Regarding oral signs of parafunction in the tongue, cheeks and lips, tongue impressions were more common in the BMS group and cheek strips and lip impressions were more common in the control group, but none of these differences were statistically significant (Fisher's exact test): tongue impressions, $p = .195$; cheek strips, $p = .072$; and lip impressions, $p = 1.0$ (Figure 2).

A logistic regression analysis was performed to assess the impacts of the seven significant variables from Tables 3 and 4. Four of the independent variables made significant contributions to the model (Table 5). Xerostomia had the strongest impact on BMS, recording an OR of 11.7, followed by skin diseases with an OR of 7.4. The model as a whole explained between 46.8% (Cox and Snell R^2) and 62.3% (Nagelkerke R^2) of the variance and correctly classified 81.3% of the cases.

Table 4. Dental status of the patients with ($N = 56$) BMS and the control group ($N = 56$).

Clinical findings I	BMS		Control		p Value*
	mean	SD	mean	SD	
Teeth	25.4	4.3	26.3	3.1	.245
Amalgam fillings	3.9	3.6	6.2	4.3	.003
Composite fillings	6.5	4.4	6.1	4.1	.594
Porcelain/metallic crowns	5.2	5.5	5.6	5.8	.700
Active bruxofacets	1.6	1.1	1.0	0.8	.005
Dental wear	3.1	2.3	2.8	1.2	.280

*Comparison of the groups using the student's t-test.

Responses to the BMS questionnaire

On average, the patients had suffered from BMS for 7.6 years (SD 6.5; range: 0.5–33 years). For 30 of the patients (55%), the onset of BMS was >5 years ago, for 29% it was >10 years ago and for three patients it was >20 years ago.

The patients with BMS described their BMS symptoms using the four alternatives of burning, scalding, numbness and a pricking sensation (Figure 3). The majority had more than one of these symptoms. Burning and scalding were the two most common symptoms, being always reported either alone or together with any of the other symptoms. The severity of the BMS symptoms on a VAS scored on average 66.5 (SD 19.6). None of the patients scored <20, 53% scored 50–79 and 36% scored ≥ 80 on the VAS.

The BMS symptoms were reported to be present: 'always' by 80% of the patients; 'now and then, but often' by 16%; and 'now and then, but seldom' by 4% of the patients. The patients experienced the symptoms: during both the night-time and daytime (66%), during the daytime only (25%), in the morning (5%) and in the evening (4%). None of the patients reported symptoms during the night-time only.

Overall, 16 of the patients (29%) reported factors that could trigger the BMS symptoms and 31 (55%) reported factors that aggravated the symptoms. The most common factors reported as initiating the symptoms of BMS were salt, sweets and strong spices. These factors together with sour taste, wine, antibiotics and stress were also reported to aggravate the symptoms.

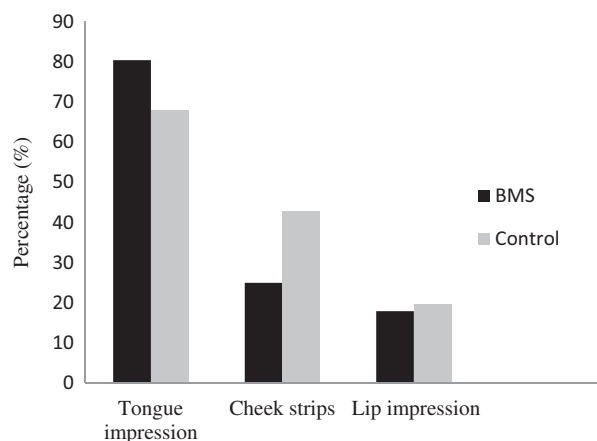


Figure 2. Percentages of individuals in the BMS and control groups with signs of parafunction in the tongue, cheeks and lips.

Table 5. A multiple logistic regression (ENTER model) of the clinicopathologic data with the patients with BMS and the controls as the dependent variable and the significant variables from Tables 3 and 4 included as the independent variables.

Independent variable	OR	95% CI	p Value
Diseases/disorders	2.2	1.1–4.3	.022
Allergy ^a	1.0	0.3–3.0	.941
Xerostomia ^a	11.7	3.6–37.5	<.001
Amalgam	0.85	0.74–0.99	.033
Bruxofacets	1.8	0.997–3.4	.051
Medications	1.1	0.8–1.5	.628
Skin diseases ^a	7.4	1.8–30.4	.006

^aYes (having disease, allergy, xerostomia and skin disease).

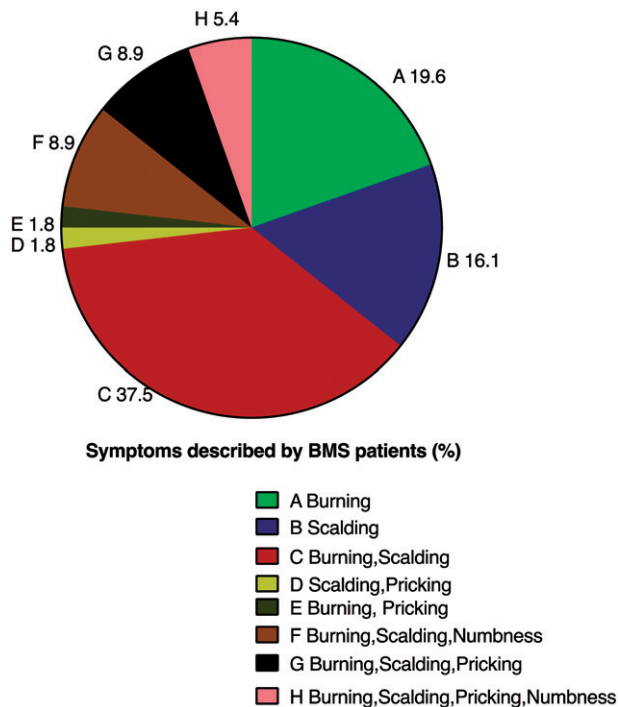


Figure 3. Distributions of symptoms described by the patients with BMS (%).

Factors that could ease the BMS symptoms were reported by 35 patients (63%). The most commonly reported relieving factor was to chew chewing gum, as reported by 16 patients. Other relieving factors included mineral/tap water ($N=4$) and saliva substitute gel ($N=3$). To the specific question 'Have you received any treatment for your problems resulting in a positive effect?' 10 patients responded in the affirmative. These treatments were: medication ($N=6$), dental splint ($N=4$) and acupuncture ($N=2$).

Twenty-five patients (45%) reported taste disturbances. The most common taste disturbances involved sensation of a metallic ($N=7$), sour ($N=5$), salty ($N=5$), bitter ($N=4$) or sweet ($N=2$) taste. Fifteen patients (27%) reported one taste disturbance, while two tastes were changed in six patients and three in one patient. Three of the patients with BMS reported that they had relatives (mother, grandmother and sister) who suffered from BMS.

Discussion

In this study, we evaluated and compared the characteristics of the patients with BMS and the age-matched controls. Skin diseases were found to have a strong association with BMS, along with self-reported symptom of xerostomia.

The controls for the patients with BMS were age-matched. Although a difference of three years was accepted in a few cases, the average age was basically the same in both groups, indicating that the matching worked well. The mean age of the BMS group in this study is somewhat higher than those described in previous studies [30]. More than half of the patients with BMS in this study had their first diagnosis more than five years previously, and some patients were diagnosed more than 20 years ago, which may explain the higher mean age.

The patients with BMS and controls did not differ with respect to the background factors, such as living in a relationship, level of physical activity and smoking habits. In this study, slightly more of the controls than the patients with BMS stated that they had been or still were smokers although the difference between the groups was not statistically significant. There have been contradictory findings regarding association between BMS and smoking where some studies associated BMS to smoking while others did not [10,30].

In accordance with other studies [16,31,32], the BMS group reported significantly poorer general health, oral health, oral health-related quality of life and life situation, as compared with the control group. Although the majority of the patients with BMS experienced poor oral health, it was surprising to discover that 10% reported 'good' oral health. Quite a few of the patients with BMS (but none of the controls) were 'dissatisfied' or 'very dissatisfied' with their life situation and reported 'poor' or 'very poor' general health. To be included in the control group, the participants had to state that they did not suffer from any serious chronic disease or burning mouth sensations, which may explain why the controls were more satisfied with their life situation and general health. Very few of the controls (but quite a few of the patients with BMS) reported suffering from chronic pain, as in arthritis, fibromyalgia and back pain, in addition to their BMS symptoms, which is in accordance with the results of earlier studies [33,34]. However, in patients with BMS, other co-occurring pain symptoms are rare according to a recent review [35]. The poor general health and dissatisfaction with the life situation reported by the patients with BMS are important. Psychological and/or psychiatric factors have previously been reported accompanying BMS, especially anxiety and depression [36]. However, as with any chronic condition, it is difficult to link cause and effect, as any long-term illness can produce psychological disturbance. Within the present project, the BMS-patients and their controls have responded to several well-established psychometric instruments and single questions regarding, e.g. personality traits, psychiatric health and presence of stressful life/life events. The psychopathology of the BMS patients and their controls will be addressed in a future study.

The occurrence of BMS in perimenopausal and postmenopausal women suggests that hormonal status plays some role in the pathogenesis. However, in this study, postmenopausal symptoms were somewhat more commonly reported among the controls. Studies on hormone replacement therapy in BMS show contradictory results [37–39]. In this study, about half of the patients with BMS and a third of the controls used or had used oestrogen medication. An interesting observation is that there was a discrepancy between the number of persons who said that they used oestrogen and the number who acknowledged such use in their medical list, both of which were self-reported. More oestrogen drugs were reported in the medical list, which may be related to the use of oestrogen-containing drugs not prescribed by a physician.

Another interesting finding is the higher proportion of skin diseases/symptoms among the patients with BMS,

as compared with the controls. To the best of our knowledge, this is a new observation.

It has been speculated that BMS has an immunologic aetiology [40,41]. This notion is supported in our study in that the BMS group reported significantly more allergies than the control group. Also, xerostomia was noted more frequently in the BMS group, with these patients reporting experiencing dry mouth with twice the intensity, as compared to the controls. In addition, the frequencies of diseases/disorders and medication differed significantly at group level.

The multiple logistic regression analysis reflected in large part the results of the analyses performed at group level. However, the significant factors medication and allergy were shown to have much less influence on BMS when adjusting for other factors. For obvious reasons, age and gender were not included in the regression analysis.

In a simple group comparison, the presence of bruxofacets was more common in patients with BMS. In the regression analysis, bruxofacets were, however, not contributing to the model. Previous studies have reported contradictory results regarding the frequencies of teeth grinding/clenching and/or tongue thrusting [10,42,43]. However, most of these earlier studies have based their conclusions on subjective reports of parafunction, in contrast to this study in which the focus is on clinically visible active bruxofacets, which we believe allows a more accurate assessment of current parafunction. Other signs of parafunction did not differ significantly between the groups. The registration of signs of parafunction in the teeth, lips, tongue and bucca may have been affected by the fact that the examiners were not blinded. In a separate study (unpublished data), intra-oral photographs from the patients with BMS and controls (eight photos/person) were examined in a blinded fashion. In that blinded study, more tongue impressions ($p = .035$) and cheek strips ($p = .006$) were found among the controls. These findings, together with the findings of this study and previous reports [44] confirm that parafunction may not be a common characteristic of BMS.

While it has previously been debated as to whether or not the mercury in dental amalgams could cause BMS, the replacement of fillings did not result in relief of the BMS symptoms [12]. In this study, the patients with BMS had fewer amalgam fillings than the controls. This was mainly due to the replacement of amalgam with other materials, which does not seem to have affected the BMS symptoms. However, no information is available on whether the replacement of fillings was linked to the BMS.

In agreement with previous studies [45,46], the patients with BMS were not more sensitive to pain than the controls.

The mean severity of BMS pain among the patients assessed on a 0–100 mm VAS was within the range of 50–80 mm, which is similar to what has been reported in previous studies [47]. Most patients experienced the symptoms both during night-time and daytime, which is in accordance with previously reported results [48]. None of the patients reported symptoms during the night-time only.

Studies have reported that as many as 70% of patients with BMS experience changed taste perception, most commonly a metallic after-taste [49,50]. This was also frequently

reported in this study, in which close to half of the patients reported taste disturbances.

In this study skin diseases and xerostomia but not parafunction were found to be strongly associated with BMS. The characterization of the BMS patients and controls reported in this study are important for the evaluation of the planned additional studies with the aim of gaining new insights into possible causal factors of BMS.

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Disclosure statement

The authors declare no conflicts of interest.

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