Original Article

The Association between Burning Mouth Syndrome and Level of Thyroid Hormones in Hashimotos Thyroiditis in Public Hospitals in Shiraz, 2016

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KEY WORDS
Burning Mouth Syndrome;
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ABSTRACT

Statement of the Problem: Burning sensation in Hashimoto patient's oral cavity is an unknown prevalent problem.

Purpose: This study aimed to evaluate the prevalence and intensity of burning mouth syndrome (BMS) in patients suffering from Hashimoto's thyroiditis in all public hospitals in Shiraz, 2016.

Materials and Method: A total of 153 patients with Hashimoto's thyroiditis were selected based on simple random sampling. The initial level of thyroid stimulating hormone (TSH), Anti-TPO (thyroperoxidase), Anti-TG (thyroglobulin), Free T3 (triiodothyronine) and Free T4 (thyroxine) serum as the indices of Hashimoto's thyroiditis was assessed. The BMS intensity was measured according to each patient's verbal or nonverbal expression about the pain experience based on visual analog scale (VAS).

Results: Based on the clinical evaluation and interview, only 19out of 153 cases (12%) reported BMS. The mean BMS was 3 based on VAS. Statistically significant association was detected between the level of TSH (p= 0.0001), Anti-TPO (p= 0.035), Anti-TG (p= 0.0001), Free T3 (p= 0.0001), Free T4 (p= 0.0001) indices in patients with BMS. Significant association was also observed between the level of Anti-TPO (p= 0.0001), Anti-TG (p= 0.0001), Free T3 (p= 0.0001) and TSH (p= 0.0001) indices and BMS intensity. However, no significant association was found between the BMS severity and Free T4 (p= 0.056).

Conclusion: The level of TSH, Anti-TPO, and Anti-TG, Free T3, and TSH indices of Hashimoto's patients were associated with the presence and severity of BSM. However, Free T4 level was only associated with the presence of BMS and not the intensity.

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Introduction

Hashimoto's thyroiditis is a thyroid immune disease that constitutes 30% of thyroid aggressive diseases. It is more prevalent in females (about 5-10%) and patients with other kinds of auto aggressive disease. [1-3] Based on the literature, both genetics and environmental factors contribute to the etiological causes of the disease. [1]

The disease can be diagnosed by gradual thyroid enlargement and the subsequent probable hypothyroidism. At the beginning, the patient may feel fullness in the front part of the neck and a lamp-like mass when touched. The lamp-like mass may also be diagnosed by

a physician in a random clinical examination. [4] In many patients with no clinical symptoms, the thyroglobulin (TG) and thyroxidase (TPO) antibodies may be higher than normal. Hashimoto's thyroiditis can be diagnosed with the abnormal serum level of Anti-TPO. [5-6]

Thyroiditis can also occur when no signs of these antibodies are in the serum. [5] Such patients can be treated with levothyroxine medication. [7] Undoubtedly, the side effect of these hormones and medicines is a crucial concern for all healthcare professionals, including prescribers, dentists, and nurses. [8]

In terms of oral and maxillofacial pain, burning mouth syndrome (BMS) is a variant of burning sensation in the tongue or other parts of the oral mucosa, usually with no clinical reason. [9] It is classified into primary and secondary types, the former of which has no underlying factor or systemic disease, being quite idiopathic, but the latter is caused by some underlying factors.

Despite the unspecified etiology of this discomfort, experiments have confirmed the influence of underlying factors. [9] In post-menopausal women, BMS occurs commonly with no significant oral lesion, normal laboratory findings, and in association with psychological factors such as depression, which may be due to a range of factors such as hormonal factors. Besides, neuropathic changes, oral phantom pain, and inflammation of the nerves can be predisposing factors for BMS. [10]

Burning sensation usually occurs in several common areas including tongue, hard palate, and lip mucosa. The pain intensity increases during the day and reaches its maximum in the afternoon; most patients have no problem at night. [11-12] The prevalence of BMS is estimated to be 1-15% in general population. [13] However, the incidence of hypothyroidism is more frequently seen in these patients. [14]

In a research conducted in Italy (2008), 123 patients with BMS were examined, 47% of which showed symptoms of hypothyroidism in laboratory tests. The present study discusses the possible connection between hypothyroidism and BMS. [14] Moreover, since hypothyroidism is common in patients with Hashimoto's thyroiditis in different time spans and geographical zones, the present study tried to get more accurate and up-to-date results through evaluating BMS in patients with Hashimoto's thyroiditis referring to Shiraz public hospitals within the first half of 2016 over a period of 4 months.

Materials and Method

This cross-sectional study evaluated the presence and intensity of BMS and also primary thyroid stimulating hormone (TSH), Anti-TPO, Anti-TG, Free T3 (triiodothyronine) and Free T4 (thyroxine) serum levels as the indicators of Hashimoto's thyroiditis all at the same time regardless of their delays and priorities.

The study was conducted in the first half of 2016 over a 4-month period (one third) on patients referring to all Shiraz public hospitals that had training ward under the supervision of Shiraz University of Medical Sciences. Each patient who met the inclusion criteria was given a code. Then, numbers were randomly selected out of the sample codes by using random numbers table. They were referred to the related hospital for finding the corresponding patients. The patients were contacted through telephone and they were met during the routine examinations. If no preset time was considered, an appointment was set. Our sample size was selected based on statistician's opinion.

The objectives of the study were thoroughly described for the patients. If willing to participate, they completed the written voluntary consent forms for accessing their files and evaluating the BMS. Participation in this study was voluntary and did not affect the patient's examinations and normal therapies.

This study included adults above 18 years old with confirmed Hashimoto's thyroiditis that had not previously received and were willing to take part in the study.

The exclusion criteria were reluctance to participate in the study, wearing dentures, age below 18, geographic tongue, oropharyngeal candidiasis, menopause, diabetes, xerostomia, consumption of diuretics and drugs, atrophy of lingual papillae, and psychological disorder. Those who had already started pharmacotherapy or whose initial experiment result was not available were also excluded. [15]

The research method and the study were patiently explained according to the patient's literacy [10] so that they would be encouraged to cooperate with the examiner. First, the test results were recorded to assess the

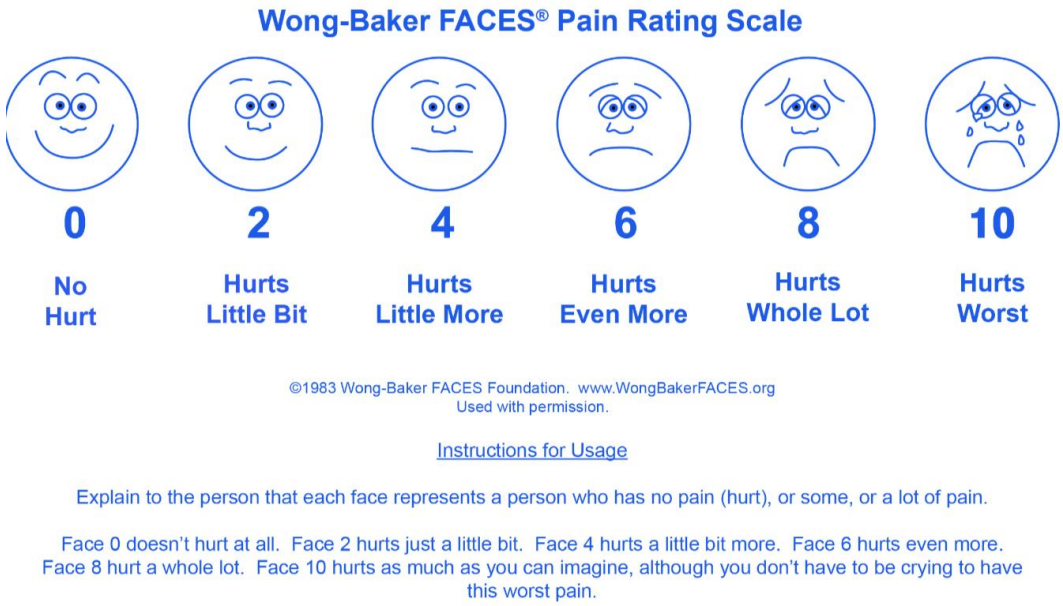

Figure 1: Wong-Baker FACES used as a pain rating scale for patients who did not understand the numerical rating

initial TSH, Anti-TPO, Anti-TG, Free T3, and Free T4level as the indices of Hashimoto's thyroiditis.

The BMS symptoms were confirmed through clinical examinations and the patient's declaration. Then, it was evaluated according to the patient's verbal or non-verbal expression of the pain experience. Besides, the visual analogue scale (VAS) was used as the graded method of measurement of pain severity. VAS is a 10-cm line graded from zero (analgesia) to 10 (worst possible pain). The patient determined the pain intensity on a spot at the line and the resulting number was measured from zero.

Numerical [1-10] and descriptive scales (analgesia, little, moderate and severe pain) were used to evaluate the pain intensity. If the patient could not understand the numerical rating, Wong-Baker FACES figures were employed (pain intensity drawn in faces), and then matched with the numbers in VAS (Figure 1). Finally, statistical methods were used to assess the BMS prevalence and average intensity in patients with Hashimoto's thyroiditis, as well as its association with the level of TSH, Anti-TPO, Anti-TG, Free T3, and Free T4serum.
Frequencies and percentages were determined for qualitative data mean, and standard deviation (SD) was determined for quantitative data. Chi square and Fisher's exact test were used to compare the qualitative data. Mann-Whitney test was used to compare the two qualitative groups. Spearman's correlation coefficient and Pearson's correlation coefficient were used to determine the association between pain intensity (VAS) and quantitative variables.

Table 1: The patients' demographic data (n=153)

	N	Minimum	Maximum	Mean
Age	153	20.0	60.0	38.00
Height	153	141.0	190.0	159.000
Weight	153	49.0	119.0	71.000
BMI	153	19.0	39.0	27.000
Waist	153	70.0	114.0	92.00
Hip	153	82.0	128.0	105.00

Results

Out of 153 patients with Hashimoto's thyroiditis who were randomly selected and examined in this study, 32were males (20%) and 121were females (80%). (Table 1) Based on the clinical evaluation and interview, burning mouth sensation was reported in only 19 cases (12%). The average BMS was measured to be 3based on VAS scale (0-10) with maximum of 6 and minimum of 1.

TSH

The mean value of TSH hormone was 6.02in patients with Hashimoto's thyroiditis (maximum = 108.27, minimum = 0.3, and median value =3.09). Hypothyroidism was observed in 62 out of 153 patients (40%). The frequency of hypothyroidism patients with BMS was more than without BMS (Table 2). Chi square test revealed that presence of BMS was significantly related with the TSH level in patients with Hashimoto's thyroiditis and hypothyroidism (p= 0.0001).

Table 2: The patients with or without BMS according to their TSH level (Total number=153)

Burning		N	Percent
Without BMS	Normal	81	60.0%
	Hypothyroidism	53	39.0%
With BMS	Normal	10	52.0%
	Hypothyroidism	9	47.0%
Total		153	

Mann-Whitney test showed that the mean TSH hormone in patients with BMS (mean= 87.00) was more than that in patients without BMS (mean=75.00). Furthermore, significant association was detected between the TSH level and presence of BMS (p= 0.0001). Likewise, Spearman's correlation coefficient confirmed significant association between the TSH level and BMS intensity (p=0.0001).

Anti-TPO

The mean value of Anti-TPO was 655in Hashimoto's patients with the maximum of 2349.10, minimum of 6.50, and a median value of 386.Mann-Whitneytests showed that the mean Anti-TPO in patients with BMS (mean=968) was more than that in patients without BMS (mean=586). In addition, significant association was detected between the Anti-TPO level and presence of BMS (p= 0.035).Spearman's correlation coefficient revealed a significant association between the Anti-TPO level and the BMS intensity (p= 0.0001).

Anti-TG evaluation

The mean value of Anti-TG was 353 in patients with Hashimoto's thyroiditis, with the maximum of 3016.70, minimum of 0.80, and a median value of 115.Mann-Whitney test showed that the mean TSH hormone in patients with BMS (69.00) was more than that in patients without BMS (64.00). There was also significant association between the Anti-TG level and presence of BMS (p=0.0001). Spearman's correlation coefficient confirmed significant association between the Anti-TG level in patients with BMS and the intensity of burning sensation (p=0.0001).

Free T3 evaluation

The mean value of Free T3 was 3, with maximum of 15.90, minimum of 1.90 and a median value of 3. According to Mann-Whitney test, the mean value of Free T3in patients with BMS (57.00) was more than that in patients without BMS (66.00). Moreover, the Free T3level was significantly related with the BMS presence (p=0.0001). Pearson's correlation coefficient proved a significant association between the Free T3level and BMS intensity (p= 0.0001).

Free T4 evaluation

The mean Free T4 was 15, with a maximum of 70.50, minimum of 3.10, and a median value of 15.Mann-Whitney test showed that the mean value of Free T4in patients with BMS (mean=51.00) was more than that in patients without BMS (mean= 67.00). There was also significant association between the Free T4level and presence of BMS (p= 0.0001).Spearman's correlation coefficient showed no significant association between the Free T4level and BMS intensity (p= 0.065).

Discussion

According to the statistical tests, the presence of BMS in patients with Hashimoto's thyroiditis without preceding pharmacotherapy was significantly associated with the level of TSH in patients with hypothyroidism, Anti-TPO, Anti-TG, Free T3, Free T4, and TSH indices. Significant association was also detected between the level of Anti-TPO, Anti-TG, Free T3 and TSH indices and the BMS intensity.

Some studies have evaluated the correlation between BMS and mental disorder and functional neurons. They have mostly tried to prove a psychological background and neuron disorder for BMS. [16-17] Hence, management of basilar disorder is recommended prior to pharmacotherapy. Likewise, cognitive-behavioral therapy has also been reported to help in controlling BMS. [18]

Investigations on patients with BMS also showed that thyroid disorders negatively affected the taste and increased the sensitivity of trigeminal nerves. [19] However, no abnormality was reported in morphological examinations of the tongue mucosal tissue. [20] Anti-xerostomia drugs could not treat BMS. [21] Only one single study mentioned the microvascular dilation in the burning area. [22]

BMS has been reported to be an autoimmune disease. [23] According to other research, the decreased level of some hematological parameters (such as hemoglobin, iron, and vitamin B12) and the high level of homocysteine and gastric parietal cell antibody could be the determining factors in BMS. [24] It is also reported that in patients with type 1 diabetes, environmental neuron disorders could be considered as an etiologic factor

for BMS. [25]

In a study conducted in Nepal on 123 patients with BMS, it was found that individuals with the parenchymal or thyroid gland changes could develop BMS; meanwhile, hypothyroidism might be also responsible for irritation or disruption of taste in such cases. [14] The presence of Hashimoto's thyroiditis can be considered as one of the BMS causal factors, the early treatment of which can help preventing the symptoms in potential patients. Only a few studies have been performed on oral irritation in patients with Hashimoto's thyroiditis; thus, further investigations are highly needed on factors contributing to oral irritation in patients with Hashimoto's thyroiditis.

The current study evaluated indices such as TSH, Anti-TPO, Anti-TG, Free T3, and Free T4 serum level as the potential factors causing oral irritation in patients with Hashimoto's thyroiditis. Yet, evaluations are needed to assess other factors accountable in Hashimoto disorder.

The retrospective nature of this study is likely to include a few unwanted limitations concerning the patients' side; however, the data were collected with the utmost precision. Moreover, inclusion of only adults in the study helped eliminating the effect of irregular hormonal changes in early menstruation. Further case-control studies are suggested to assess the possible causes of BMS.

Conclusion

In patients with Hashimoto's thyroiditis, who had not previously received pharmacotherapy, the level of TSH in patients with hypothyroidism, Anti-TPO, Anti-TG, Free T3, Free T4 and TSH indices was associated with BMS and was effective in presence of BMS. Therefore, it seems the level of different hormones, especially in hypothyroidism, is one of the factors affecting BMS. Besides, the level of Anti-TPO, Anti-TG, Free T3, and TSH indices was related to the BMS intensity.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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