http://dx.doi.org/10.5272/jimab.2013194.422

ISSN: 1312-773X (Online)

Journal of IMAB - *Annual Proceeding (Scientific Papers)* 2013, vol. 19, issue 4

FOLIC ACID AND VITAMIN B_{12} LEVELS IN BULGARIAN PATIENTS WITH BURNING MOUTH SYNDROME

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ABSTRACT

Actually the burning mouth syndrome (BMS) can be classified as idiopathic and secondary. The deficiency of vitamins (especially the group B) can be involved in BMS. In a group of 92 consecutive Bulgarian patients without oral lesions, excessive gingivitis and parodontitis or abscess, 63 patients had lower level of folic acid in serum (68%). The serum levels of vitamin B 12 were lower in 17,5% and microbes were found in 10%. The study revealed that the most frequent abnormality in Bulgarian BMS patients was the folate deficiency followed by the lower level of cobalamin and oral candidiasis. These high rates of deficiency suggest a long term folic acid supplementation.

Key words: burning mouth, folic acid, vitamin B_{12}

INTRODUCTION

The burning or tingling sensation on the lips, tongue, gums, palate, and throat or of the entire mouth is known as the Burning Mouth Syndrome (BMS) or glossodynia. Additionally, a sensation of dry mouth, increased thirst, loss or changes of taste (bitter or metallic) can appear. If pain is present, it may occur every day and can become worse as the day progresses. BMS is a chronic disorder which frequently affects women; often it is of unknown etiology and difficult for treatment and management. In some cases symptoms may suddenly go away. BMS usually doesn't cause any noticeable physical changes in the oral cavity. General symptoms can also be observed, such as sleeping disorders, anxiety, difficulty in eating. In spite of the fact that the majority of cases are not accompanied by evident organic changes and do not present health risks, BMS can significantly reduce patient's quality of life and pose challenges to both patient and dentist [9, 12]

Actually, the BMS can be classified as idiopathic (primary) or secondary. The latter can be related to dry mouth, oral candidiasis, lichen planus, allergies, dentures, excessive mouth irritation, bruxism, geographic tongue, nerve damage, diabetes, hypothyroidism, anxiety, depression, certain drugs, gastroesophageal reflux disease. The deficiency of some metals and vitamins (especially the group B) can be involved in BMS [1, 3].

AIM

The aim of our study was to evaluate the blood levels of folate and vitamin B_{12} (cobalamin) in a group of Bulgarian BMS patients without oral lesions, excessive gingivitis and parodontitis or abscess.

MATERIALS AND METHODS

92 consecutive patients (26 men and 66 women) with burning feeling in the mouth were involved in the study (average age 51,4 years, range - 16-87 years). All patients underwent face and mouth examination by a dentist to ensure that suspicious mucosal lesions, as well abscess and acute and chronic parodontitis were not present and did not develop. None of the studied subjects had a history of prior malignancy, immunodeficiency, autoimmune or mental disease.

Each patient was examined and tested as follows:

- Microbiology of the saliva and throat swabs
- Hypersensitivity to dental materials in patient's mouth
- Serum levels of B9 and B12 (40 patients)

Epicutaneous patch test was performed to assess the hypersensitivity to dental materials (IQ Chambers® - Chemotechnique Diagnostics®, Vellinge, Sweden). The serum levels of folic acid and vitamin B_{12} (cobalamin) were measured using ECLIA Roche diagnostic with normal range for B9 (10.4-42.4 nmol/l) and vitamin B_{12} (177.1-664.2 pmol/l).

RESULTS

Only 3 of all patients with mouth burning (3,2%) demonstrated allergens hypersensitivity to dental materials (Nickelsulfate in 3 patients and dental amalgam in 1 patient). In 10 patients (10,8%) different microbes were isolated, most frequently of the Candida species (table 1). 63

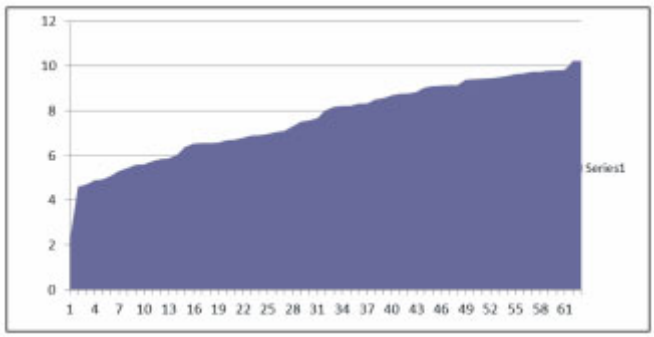

Fig. 1. Lower folic acid serum levels (nmol/l) in patients with mouth burning syndrome.

Table 1. Patients with dental materials hypersensitivity and microbes in saliva and throat swabs

Patient N	Dental materials	Microbes	Vitamin B_{12} pmol/l	Folic acid nmol/l
03	Nickelsulfate	C. non albicans spp.	210	5,6
08		St. aureus, C.albicans	157	4,9
19		C. krusei		13
20	Nickelsulfate	E. coli, C. tropicalis, C. albicans		9,8
30	Nickelsulfate and amalgame	C. glabrata, C. albicans	279	8,2
42		St. aureus	203	7,1
65		C. albicans		9,6
77		C. albicans		10,9
79		E. coli, E. faecalis		24,6
81		Kl. oxytoca		18

patients out of 92 (68,4%) had lower level of folic acid in serum. No correlation between folic acid levels and the age of patients was found. Severe deficiency – to 6 nmol/l was found in 19, 2% (average age 60,9 years); medium deficiency – 6-8 nmol/l in 24,7% (average age 49,6 years) and light deficiency – 8-10.4 nmol/l in 56,1% (average age 47,6 years) (fig.1). In patients with severe folate deficiency we observed a light negative correlation between age and serum levels (r=0,291, p=0,05).

The serum levels of vitamin B 12 were lower in 7 (17,5 %) out of 40 examined patients with mouth burning syndrome and combined cobalamin and folate deficiency was observed in 6 patients – 15% (average age - 48,8 years). No correlation between vitamin B_{12} levels and the patient's age was found. There was no correlation between cobalamin and folate serum B9 levels.

DISCUSSION

The association between BMS and nutritional deficiencies was examined [6]. Occasionally, BMS patients exhibited low levels of blood serum vitamins B_1, B_2, and B_6, but a decrease in serum vitamin B_{12} was the most common finding in this subgroup of patients [2, 8, 14]. Vitamin B complex replacement therapy, however, often proves ineffective for pain relief. Other minor findings of nutritional deficiency in BMS subjects may include low levels of blood serum folic acid and iron, suggesting a possible role of some type of anemia in the pathogenesis of this syndrome [6, 8].

Based on the above reported circumstances, we aimed to evaluate a possible connection between mouth burning and deficiencies of folic acid and cobalamin in Bulgarian patients.

Vitamin B_{12} has a number of functions. It works with folic acid in DNA, RNA, protein synthesis and the production of red blood cells. Vitamin B_{12} deficiency can be caused by: lack of a gastric protein called intrinsic factor (pernicious anemia), atrophic gastritis (up to 30% of people aged 50 and older), gastric resection, small intestine diseases (Crohn's disease, celiac disease, bacterial growth, or a parasite), excessive alcohol consumption, long-term use of acid-reducing drugs, hyperthyroidism, pregnancy. Vitamin B_{12} deficiency can also occur in strict vegetarians.

A deficiency of vitamin B_{12} and/or folic can lead to macrocytic anemia with pale skin and sore tongue and all the anemic syndrome signs. If the deficiency is not corrected it can damage the nerve cells, the consequences being tingling or numbness in fingers and toes, difficulty in walking, depression, memory loss. Older adults with vitamin B_{12} levels between 200 and 500 pg/mL may also have symptoms.

Folate deficiency may lead to glossitis, diarrhea, depression, confusion, megaloblastic anemia, and fetal neu-

ral tube defects and brain defects (during pregnancy). The most common folic acid deficiency cause is a low daily intake from foods (lack of fresh green vegetables, legumes), and prolonged storage and cooking can cause a 50% to 95% loss of folate. Other factors that may cause folic acid deficiency are alcoholism, malabsorption, certain drugs, pregnancy, lactation and elderly age. Folic acid deficiency in the early stages may not be obvious. It may take up to four months before any signs or symptoms are manifested.

V. Vucicevic-Boras et coworkers found no differences in serum levels of iron, folic acid, calcium and magnesium between patients with burning mouth syndrome and the controls. The authors proved lowered vitamin B12 levels in burning mouth (14).

Values of less than 200 pg/mL are a sign of a vitamin B12 deficiency. People with this deficiency are likely to have or develop symptoms of burning in the mouth [7].

In our patients with feeling of mouth burning only 17% had vitamin B_{12} deficit (below 177pmol/l), but 2/3 had folic acid deficit and 15% demonstrated simultaneous folate and cobalamin deficit.

The daily folate requirement for unstressed adults is estimated to be approximately 50 mcg/day. Folate deficiency is treated with supplemental oral folate of 400 to 1000 mcg/day. This treatment is very successful in replenishing tissues [12]. The vitamin B_{12} supplementation with 500-100 mcg injections usually corrects the deficiency and the symptoms.

Delayed-type hypersensitivity reaction or type IV allergic reaction can cause different oral manifestations including BMS. The results of patch testing showed that the most common proven allergens are gold sodiumthiosulphate (14%), nickel sulfate (13%), mercury (10%), palladium chloride (7%), cobalt chloride (5%), and 2-hydroxyethyl methacrylate (6%). There is no specific association between a specific oral presentation and a particular allergen [1, 5].

Some studies suggest that BMS can be caused by hypersensitivity to dental materials, although others have not found any aetiologic [4, 11]. In our BMS group we found hypersensivity to nickelsulfate in only 3%.

In 124 patients R. Marino did not find any significant association between the patients and positive patch test reactions – 13% positive patch test [10]. Using a panel of 25 potential denture allergens J.Helton and F.Storrs_ cannot indict contact dermatitis, contact urticaria or pressure urticaria as a cause for the BMS in denture-wearing patient of normal-appearance mucosa [4]. Contact allergy in BMS seems not to play a primary role; nevertheless, it is advisable to perform patch tests in selected patients to identify a possible aetiological agent [1, 13].

There are a number of possible causes for the burning mouth syndrome, including oral candidiasis. Candidiasis in conjunction with hyposalivation may induce glossodynia without manifestation of objective abnormalities [11]. In 10 % of our BMS patients we found microbes in the oral cavity. In 8 % different candida species were isolated. In this subgroup of 10 patients with oral candidiasis and/or presence of other microbes the frequency of lower folate levels is like in the rest of the studied patients. The three patients with hypersensivity to nickelsulfate demonstrated simultaneously oral candidiasis and low folic acid serum levels.

CONCLUSION.

The most frequent abnormality in Bulgarian BMS patients without oral lesions, excessive gingivitis and parodontitis or abscess was the folate deficiency followed by the lower level of cobalamin and oral candidiasis. These high rates of deficiency and the presence of severe folate deficiency suggest a high dose long term folic acid supplementation.

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