Original Research

STRESS: AS ETIOLOGICAL AGENT FOR ORAL LESIONS- A RESEARCH STUDY.

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Abstract: A psychosomatic disorder involves both body and mind. These diseases have physical symptoms originating from mental or emotional causes. Most common ones are stress, anxiety and depression. A wide spectrum of psychiatric disorders affects oral and para oral structures which have a definite psychosomatic cause, but unfortunately they remain unrecognized because of the common and limited nature of their presenting features. Stress is defined as a physical, mental or emotional response to events that causes bodily or mental tension. Human body is affected by various types of diseases, of these some may have an unknown or idiopathic etiology. Stress is one such etiology or predisposing factor in many diseases. This research study aims in identifying and proving the role of stress as one of the etiological factor in few oral lesions such as Oral lichen planus, Apthous ulcers, Burning mouth syndrome and Myofacial pain Dysfunction syndrome whose etiology has always remain a controversial issue.

Keywords: Oral lichen planus; Apthous ulcers; Burning mouth syndrome; Myofacial pain Dysfunction syndrome.

INTRODUCTION

Body and mind are one and hence influence each other. Diseases interact between body and mind, mind and body. The oral mucosa is highly reactive to psychological influences. In some cases oral diseases may be direct expression of emotions or conflicts, while in other instances lesions of the mouth may be indirect result of emotional problem. Mouth is directly or symbolically related to major human instincts and passions. Oral diseases with psychosomatic etiology have long been known in medicine and Mental or emotional factors may act as risk factor that could influence the initiation and progression of oromucosal diseases.

DSM-II, (1968) defines Psychosomatic Disorders as psychosomatic symptoms that are caused by emotional factors and involves a single organ system; usually under autonomic nervous innervations.⁵ Psychiatric disorders have traditionally been classified into two main groups namely organic and functional. In organic disorders, known physical etiology can be established like in dementia or delirium. In functional disorders such as schizophrenia, constitutes the large majority of

psychiatric illness in which no physical factors were present. Anxiety and depression are universally experienced neurotic symptoms, included under functional disorders.⁶

Anxiety is an emotional state, unpleasant in nature associated with uneasiness, and discomfort and concern or fear about some defined or undefined future threat.Some degree of anxiety is a part of normal life. Treatment is needed when it is disproportionate to the situation and excessive. Depression is used in everyday language to refer to a passing mood of unhappiness, sadness or the blues that all of us experience from time to time as part of the normal pattern of life. The dentist who treats patients with chronic oral diseases, must be able to recognize and obtain appropriate treatment for the depressed patient, if the dentist is to succeed in managing the patient's oral problem.8

In psychology, stress is a feeling of strain and pressure. Small amounts of stress may be desired, beneficial, and even healthy. Positive stress helps improve athletic performance. It also plays a factor in motivation, adaptation, and reaction to the environment. Excessive

amounts of stress, however, may lead to bodily harm. Stress can increase the risk of strokes, heart attacks, ulcers, and mental illnesses such as depression. Stress can be external and related to the environment, but may also be created by internal perceptions that cause an individual to experience anxiety or other negative emotions surrounding a situation, such as pressure, discomfort, etc., which they then deem stressful. 10

Humans experience stress, or perceive things as threatening, when they do not believe that their resources for coping with obstacles (stimuli, people, situations, etc.) are enough for what the circumstances demand. When we think the demands being placed on us exceed our ability to cope, we then perceive stress.

Physiological or biological stress is an organism's response to a stressor such as an environmental condition or a stimulus. Stress is a body's method of reacting to a challenge. According to the stressful event, the body's way to respond to stress is by sympathetic nervous system activation which results in the fight-or-flight response. Because the body cannot keep this state for long periods of time, the parasympathetic system returns the body's physiological conditions to normal (homeostasis). In humans, stress typically describes a negative condition or a positive condition that can have an impact on a person's mental and physical well-being.¹¹

Stress Biomarkers

Biomarkers commonly used to assess stress level are Nervous system markers, such as adrenaline, nor-adrenaline, and dopamine. Endocrine system markers, such as corticoids (Cortisol, 17-hydroxycorticosteroid and aldosterone) in the blood, urine and saliva, and ACTH in the blood. Third is the immune system markers, such as the total number of lymphocytes and its subsets T cells, B cells and natural killer cells, immunoglobulin's, and cytokines such as interleukin (IL)-1, IL-2, BL-6, interferon (IFN) and tumor necrosis factor (TNF).

Stress and the Endocrine System

Several endocrine glands are involved in the body's response to stress. First, the hypothalamus, a small structure in the brain, releases a hormone that stimulates the nearby pituitary gland to secrete adrenocorticotrophic hormone (ACTH). ACTH, in-turn, stimulates the adrenal glands, which are located above the kidneys. Under the influence of ACTH, the adrenal cortex, releases a group of hormones called cortical steroids (cortisol and cortisone are examples).

Cortical steroids (also called corticosteroids) have a number of functions in the body. They boost resistance to stress, foster muscle development, and induce the liver to release sugar, which provides needed bursts of energy for responding to a threatening stressor (for example, a lurking predator or assailant) or an emergency situation. They also help the body defend against allergic reactions and inflammation.

The sympathetic branch of the autonomic nervous system, or ANS, stimulates the adrenal medulla, to release a mixture of epinephrine (adrenaline) and nor-epinephrine (nor-adrenaline). These chemicals function as hormones when released into the bloodstream. Together epinephrine and nor-epinephrine mobilize the body to deal with a threatening stressor by accelerating the heart rate and by also stimulating the liver to release stored glucose (sugar), making energy available where it can be of use in protecting ourselves in a threatening situation.

The stress hormones produced by the adrenal glands help the body prepare to cope with an impending threat or stressor. Once the stressor has passed, the body returns to a normal state. This is perfectly normal and adaptive. However, when stress is enduring or recurring, the body regularly pumps out stress hormones and mobilizes other systems, which over time can tax the body's resources and impair health. Chronic or repetitive stress can damage many bodily systems, including the cardiovascular system (heart and arteries) and the immune system. ^{12,13}Emotional stress can

produce physiologic changes that measurable in part asincrease in urinary catecholamines and 17-hydroxy steroids. There are numerous oral lesions and conditions associated with stress, these include: Oral Lichen planus [OLP], Apthous ulcers, burning mouth syndrome [BMS], Myofacial Pain Dysfunction Syndrome [MPDS], chronic periodontal disease, bruxism, dysgeusia, self mutilation, atypical facial pain xerostomia. Out of these Oral Lichen planus [OLP], Apthous ulcers, burning mouth syndrome [BMS], Myofacial Pain Dysfunction Syndrome [MPDS] are the most common oral lesions associated with stress.¹⁴

The aim of this study is to perform proper screening/diagnosis of the patients with OLP, Apthous ulcers, BMS, MPDS; evaluate the role of stress in these oral lesions and provide proper symptomatic treatment to all these patients

PROCEDURE:

This research study was conducted in a Department of Oral Medicine and Radiology, Rama Dental College, Hospital and Research Center, Kanpur over a period of two years (from March 2013- March 2015). All the patients were subjected to complete oral examination as per the proforma examination of dental patients in the Department. Patients with oral mucosal lesions like oral lichen planus, apthous ulcers, and **MPDS** affecting **BMS** the temporomandibular joint were selected and categorized into the following groups selected for the study.

Group I: 60 clinical subjects of OLP

Group II: 60 clinical subjects of Apthous ulcers.

Group III: 25 clinical subjects of BMS Group IV: 25 clinical subjects of MPDS

A proper intraoral examination was done for the patients and depending upon the clinical presentation they were categorized into the groups.

Oral lichen planus (OLP) clinical subjects presents as white striations white papules,

white plaques, erythema, erosions or blisters affecting predominantly the buccal mucosa, tongue and gingivae, although other sites are occasionally involved. Lesions are typically bilateral and often appear as a mixture of clinical subtypes. White or grey streaks (Wickham Striae) may form a linear or reticular pattern on erythematous an background. Alternatively, there may be a central area of shallow ulceration (erosion) with a yellowish surface (fibrinous exudate) surrounded by an area of erythema. Occasionally desquamation of gingiva is also seen along with radiating white striae. These lesions were treated with topical application of 1% Triamcenoloneacetonide paste in orabase 4 to 5 times daily.

Diagnosis is mostly based on the clinical appearance and the medical history. The most important diagnostic feature is a history of recurrent, self healing ulcers at fairly regular intervals. These heal within 10-14 days with size ranging from less than 1cm [Apthous minor] and larger than 1cm in [Apthous major]. Herpetiform aphthous ulcers are rare and occurs in the form of multiple small erosions that affect the coating mucosa.All clinical subjects had multiple recurrent ulcers with no history of traumatic injury and no invasive investigations were done. All the 60 clinical subjects were subjected to serum iron, Vitamin B12 and folic acid, evaluation. Few patients had deficiency of any of these nutrients. Most of the clinical subjects were students who are in the eve of examination, which also proves the significance of stress in these lesions. Topical application of antiseptic gel [Hexigel, Metrohex gel], multivitamin tablets once a day along with antiseptic /antibiotic mouth rinse, were prescribed for pain relief and asepsis.

Burning mouth syndrome is not a common symptom; hence only 25 clinical subjects were present. They were diagnosed based on their symptoms as-

1. Type 1 BMS: Patients have no symptoms upon waking but symptoms progress throughout the day reaching its peak intensity by evening. Night-time

symptoms are variable. It is linked to systemic disorders like nutritional deficiency and diabetes.

- 2. Type 2 BMS: Patients have continuous symptoms throughout the day and are symptomatic at night resulting in sleepless nights. This type is associated with chronic anxiety due to altered sleep pattern and is related to use of antidepressant drugs, which cause xerostomia.
- 3. Type 3 BMS: Patients have intermittent symptoms throughout the day with symptom-free periods. Usually seen due to anxiety or allergic reactions especially to food allergens.

Irrespective of the etiology it all the patients were symptomatically treated with topical anesthetic gel [mucopain gel-5% Xylocaine] along with topical antihistamine application [5% diphenhydramine hydrochloride].

MPDS clinical subjects were also not a common disease seen in our study, the diagnosis was based on the presence of unilateral pain in and around the ear and trigger points in the muscles of mastication insertion sites. The dental examination in all these subjects had severe attrition of the occlusal surfaces of the teeth caused due to bruxism. The most common sign and symptoms associated with MPDS includes: temporomandibular joint sounds, impaired movement of the mandible, limitation in mouth opening, preauricular pain, facial pain, headache and jaw tenderness on function. These subjects were managed with Tricyclicantidepressants [under the guidance of the concerned specialist]. Occlusal splints were fabricated for all the subjects to maintain the vertical dimension of the jaw to restore the iaw function, as attrition of all the teeth will decrease the vertical dimension.

The clinical subjects in Group I II, III, and IV were then subjected to following examination criteria.

Selection of clinical subjects under stress:

A proper medical history was taken from the patients that included past medical history just

to rule out any underlying systemic diseases e.g Diabetes mellitus, hypertension etc. The inclusion criteria for selection of the patients were based on those patients who were free from any systemic disease. These patients were subjected to anxiety and depression rating scales [HAMD AND MADRS]. If the score rate was positive for stress, then these patients were subjected to routine haemogram, serum iron, Vitamin B12, folic acid ,serum cortisole [normal 2-12.5µg/dl] and urinary cortisole levels[1.00 +/- 0.52 mg/ml]. Clinical subjects irrespective of age and sex with positive Anxiety and Depression scales, elevated serum and urinary cortisole values were alone selected for the study and others were considered as control groups. All the clinical subjects were given symptomatic treatment and were regularly followed up.

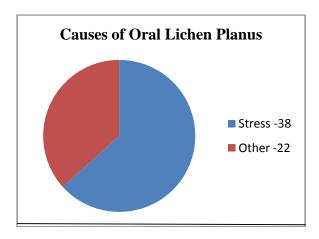
RESULTS:

This research study aims in identifying the association of stress as one of the etiological factor in few oral lesions such as (Group I)OLP, (Group II) Apthous ulcers, (Group III) BMS and(Group IV) MPDS.

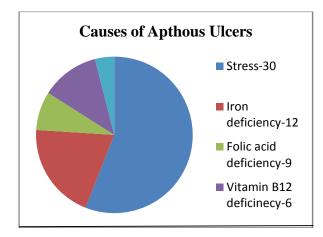
In 60 clinical subjects of OLP [Group I], 38 (63.3%)clinical subjects were diagnosed with significant stress association, based on the positive HAMD and MADRS score rates, elevated serum and urinary cortisole levels. The remaining 22(36.7%) subjects were considered as control group, as they did not have any significant association with stress (Graph 1).

In Group II, 30 clinical subjects out of 60 Apthous ulcer subjects were positive for stress as the etiological factor for these lesions. The remaining 30 subjects were considered as control group. All clinical subjects were subjected to evaluation of serum iron, Vitamin B12 and folic acid and it was found that 12 subjects had iron deficiency; vitamin B12 deficiency seen in 9 subjects, 6 of them had folic acid deficiency and in 3 clinical subjects, the cause was unknown (Graph 2).

Graph 1: Showing the causes of Oral Lichen Planus



Graph 2: Showing causes of Apthous Ulcers

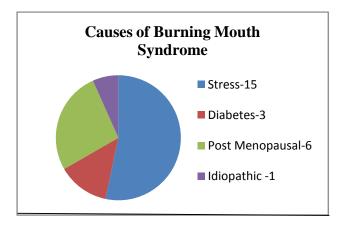


In Group II, 30 clinical subjects out of 60 Apthous ulcer subjects were positive for stress as the etiological factor for these lesions.

In Group III, 25 clinical subjects of BMS was subjected to the rating scale as well as serum and urinary cortisole levels, in which 15 subjects were positive for stress association in these lesions. The remaining 10 subjects were the control group. One more remarkable finding is that 6 out of 10 were postmenopausal woman, which proves the common manifestation of **BMS** postmenopause due to estrogen deprivation, which also plays a role in loss of epithelial integrity. Since diabetes also causes BMS in few cases, all were subjected to fasting blood sugar and 3 clinical subjects had elevated blood glucose, strongly suggesting diabetes as one of the cause for BMS. 1 subject had no

significant pathology, their blood and urine examination results were normal which also proves the idiopathic cause for BMS (Graph 3).

Graph 3: Showing causes of Burning Mouth Syndrome



In Group III, 25 clinical subjects of BMS was subjected to the rating scale as well as serum and urinary cortisole levels, in which 15 subjects were positive for stress association in these lesions.

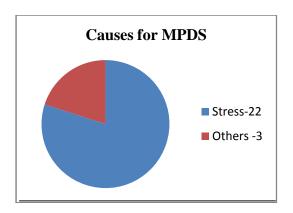
In Group IV, 22 were positive for stress and remaining 3 clinical subjects were not positive for stress. Severe attrition of all the teeth caused due to bruxism clenching and grinding of the teeth as tension relieving event] was evident in all the subjects positive for stress (Graph 4).

DISCUSSION

Human beings survive by constantly adapting to the demands of an ever-changing environment. For the purposes of this review, we define stress as a real or perceived imbalance between environmental demands required for survival and an individual's capacity to adapt to these requirements. This general model regards stress as part of a sequential process in which objective environmental circumstances (i.e., stressors) are appraised by the individual as either having no adaptive significance or as stressful

(i.e., presenting a potential threat, danger, change or challenge to one's well-being or survival). If circumstances are perceived by the individual as stressful, then this appraisal will set in motion a series of stress-response mechanisms comprised of integrated physiological, behavioral, and psychological efforts to adapt to the environmental demands. ^{15,16}

Graph 4: Showing causes of Myofacial Pain Dysfunction Syndrome



In Group IV, 22 were positive for stress and remaining 3 clinical subjects were not positive for stress.

Lichen planus is a common dermatological disorder, which may affect the skin and oral mucosa. The condition was described for the first time by Erasmus Wilson in 1869 who characterized the patients as anxious, high strung, and sensitive with a tendency to worry excessively and with periods of undue emotional stress.¹⁷

It is a chronic inflammatory disease characterized by bilateral white striations or plaques on the buccal mucosa, tongue or gingival. It is found commonly in adults (50-55 years of age) and predominantly affects women usually by a 1.4:1 ratio over men. OLP has varied clinical presentations, with the reticular, erosive, and atrophic types being the most commonly reported. In the last few years, significant advances have been made in understanding the mechanisms involved in the

pathogenesis of the disease. OLP has been reported to be associated with different medical conditions such as diabetes, hepatitis C infection, and liver disease. Although, the condition is often referred to as stress associated ulcerations of the oral mucosa and research to date hints on a psychosomatic component in the etiology and progression of OLP, very little documentation has been presented to substantiate this widely held assumption. ^{18,19}

In a study conducted by Sandhu SV et al it was reported that out of the 49 stressful life event was noted in 31 (63.2%) of the subjects at the time of OLP onset. No stressful life event was noted in 18 of the subjects at the time of OLP onset. ²⁰

In a study conducted by Maheshwari T.N and Gnanasundaram N, 29 (58%) out of 50 OLP patients were diagnosed of stress.²¹

Results of the above mentioned studies were in accordance with our study were 38 (63.3%) out of 60 OLP patients were found to be suffering from stress.

Recurrent apthous stomatitis (RAS) is the most common type of ulcerative disease of the oral mucosa, and it affects approximately 20% of the general population. The classic presentation of RAS is recurrent, self-limiting ulcers that mainly affect nonkeratinized oral mucosa. A prodromal burning sensation lasting 24 to 48 hours can often precede the onset of ulcers. Minor RAS, which makes up more than 80% of all RAS cases, is a small (up to 1 cm in diameter), shallow, painful, well-circumscribed, and round-shaped ulceration that is covered by a yellow-grayish pseudomembrane and surrounded by an erythematous halo.

The ulceration generally heals without scarring after 10 to 14 days. *Major* RAS is characterized by ulcers that are typically larger and deeper than *minor* RAS. Furthermore, they heal more slowly and often cause scarring. Herpetiform ulcers manifest as

multiple recurrent clusters of small ulcers (less than 4 mm in diameter) that are scattered throughout the oral mucosa. These ulcers may further coalesce into larger ulcerations. ^{22,23}

The etiology of RAS still remains unclear, and the currently available therapy remains inadequate. Many factors have been implicated in the promotion and/or exacerbation of RAS; these include positive family history, local trauma, nutritional deficiency, food hypersensitivity, immune disturbance, smoking cessation, and psychological stress, among others.²⁴

Previous studies have suggested that psychological disturbances such as stress and anxiety could play a role in the onset and recurrence of RAS lesions. However, the obtained results were rather varied. 25, 26

In the study conducted by Gallo CB el al. 50 patients were enrolled in the trial. 25 RAS patients constituted the study group and another 25 non-RAS patients who were similarly matched for sex, age socioeconomic status constituted the control group. Each patient was evaluated in terms of the four domains of stress (emotional, physical, social and cognitive) using an internationally validated questionnaire, which was comprised of 59 items and measured the frequency and intensity of stress symptoms. The RAS group was interviewed during an active RAS episode. Completed questionnaires were submitted to proper analytical software and interpreted by an expert psychologist.

The results of this trial showed that RAS patients exhibited higher stress levels than the control group during their active episodes. 12/25 (48%) RAS patients exhibited stress levels of 4–5 while only 4/25 (16%) of the control patients exhibited the same stress levels. Additionally, most patients in the RAS group indicated a positive relationship between stress and ulcerative episodes.²⁷

In another study conducted by Maheshwari T.N and Gnanasundaram N, 26(52%) out of

50 recurrent apthous stomatitis patients were diagnosed of stress.²¹ These results are in accordance with the results seen in our study where 30(50%) out of 60 patients with apthous ulcers were found to be having stress in their life.

Burning mouth syndrome is associated with burning sensation of tongue, lips and other mucosal surfaces. Post – menopausal symptoms was rated significantly high by burning mouth patients. Sleep disturbances were common among the burning mouth syndrome patients. Treatment needs to be customized to the etiological factors identified in an individual patient with attention also given to symptomatic relief and management of any associated behavioral or psychiatric disorders.²⁸

In the research study conducted by Maheshwari T.N and Gnanasundaram N, 12(48%) out of 25 BMS patients were diagnosed of stress.²¹ The results of the research study we conducted were slightly more as compared to above mentioned study; in our study where 15(60%) out of 25 patients with MPDS were found to be having stress in their life.

One of the most common forms of temporomandibular joint (TMJ) disorders is myofacial pain dysfunction syndrome. Pathology in masticatory apparatus can lead to pain and poor function of TMJ. It is not uncommon that patient suffering from myofacial pain dysfunction syndrome (MPDS) consult dentist for tooth ache. MPDS is usually associated with joint pain, pain in muscles of mastication, limited mouth opening and deviation of headaches, ear ache and fracture of teeth. Occlusal disharmony and psychosocial variable also have been shown to play an aggravating role in MPDS. Current management of MPDS now also takes into account the psychological aspects of this disorder. There is however still an ongoing debate regarding the primary cause of the problem 29

In the research study conducted by Maheshwari T.N and Gnanasundaram N, 21(84%) out of 25 MPDS patients were diagnosed of stress.²¹ These results are in accordance with the results seen in our study where 22(88%) out of 25 patients with MPDS were found to be having stress in their life.

CONCLUSION: Stress also induces oral lesions, but stress may not be the cause in many of the lesions in some subjects. Proper history and essential investigations will ensure correct diagnosis of the etiological factor and thus results in successful treatment plan. Oral lesions not related to stress, if subjected to antipsychotic measures, it might lead to further complications. Dentists, in their daily practice frequently come across patients with psychosomatic disorders, patients who are emotionally disturbed frequently presents with oral symptoms, and recognition of such emotional disturbance benefits both the patient and clinician. This Research study thus emphasizes the need to consider the role of stress in these oral lesions namely OLP, Apthous ulcers, BMS and MPDS.A positive finding of stress requires immediate psychological counseling and anti-anxiety management. This is not it, the dentist show do periodic follow up which not only helps in gaining faith but also sympathetic as well as symptomatic treatment of these patients.

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