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Correlation of ulcer size and serum cortisol in subjects with Aphthous Ulcers

Medical Science

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ABSTRACT

Background: Aphthous Ulcers are a painful oral ulcerative condition. Stress is one of the major causes for ulcer formation and cortisol level is increased in stress. This study aims at looking into the relationship between ulcer size and serum cortisol.

Methods: 40 subjects in the age group of 18-35 years with aphthous ulcers were included in the study. Ulcer size was determined and morning serum cortisol was measured in all subjects. Correlation tests were applied and significance was set at p<0.05.

Results: Ulcer size was 6.5 ±5.4 sq mm and serum cortisol was 123.3±72.6 ng/dl. There was a significant positive correlation between the serum cortisol and ulcer size when the serum cortisol was more than 100 ng/dl.

Conclusion: Serum cortisol could be a significant contributor in ulcer formation and progression. Size of the ulcer could suggest the severity of distress/Stress in the individuals.

Introduction

Aphthous Ulcers is the disorder which present as a recurrent occurrence of ulcers in the mouth of the subjects. It is also called as Recurrent Aphthous Stomatitis (RAS) or Ulcerative Stomatitis or Canker Sores. It is very common in general population (20%) and most common in university students (50-60%) [1]. Various hypotheses have been proposed for the cause of aphthous ulcers like stress, nutritional deficiencies, micro-trauma, smoking, immune dysregulation, microbial infections etc[2]. But stress in both forms, namely physical and psychological is the main contributing factor in the development of aphthous ulcers[3]. Aphthous ulcers have three forms of representation. The characteristics of these three forms i.e. minor ulcers, major ulcers and Herpetiform ulcers are described in Table 1.

Table 1: Types of Aphthous ulcers

Type of aphthous ulcers	Minor ulcerations	Major ulcerations	Herpetiform ulcerations
Size	3–10 mm	>10 mm	small, numerous, 1–3 mm
Duration (days)	10-14	> 14 (up to a month)	10-14
Duration of Pain (days)	5-7	14 - 18	5-7 (severe)
Occurrence (% of all Aphthae)	75-85	10-15	5-10

Stress is experienced by all individuals in some form. Human desires have increased beyond physical and mental limitations. A lot of effort is needed from the individuals to attain the goal. These efforts result in both eustress and distress[4]. Eustress is positive stress, constructive and recovery from this form of stress increases the person's capability to thrive in the competitive world. When stress becomes unbearable or when stress is prolonged it results in distress which has lot of adverse effects on health. One such consequence is recurrent aphthous stomatitis.

As a physiological response to stress there is an increase in serum cortisol level[5]. This increase in cortisol causes increase in the glucose level, mediates permissive action in catecholamines, causes immune modulation. As a result the person will manage and recover from stressful situations. With prolonged stress there is persistent or frequent increase in cortisol which tends to dysregulate the various homeostatic mechanisms in the body.

In this study we are trying to find the correlation between ulcer size and serum cortisol in subjects suffering from recurrent aphthous stomatitis. And hence trying to find out the extent of stress the person is suffering.

Materials and Methods:

40 subjects in the age group of 18 to 35 years suffering from aphthous ulcers were included the study between May 2011 and October 2012. All subjects were students and faculty of M S Ramaiah Medical College. Subjects with history of medications, known infections, diabetes mellitus, hypertension and Cushing's disease were excluded from the study. Ethical approval was taken according to the institutional guidelines. The study protocol was explained to the subjects and informed consent was taken. 5 ml of venous blood was taken, centrifuged, serum collected and stored at -20° C. Serum cortisol measurement was done by radioimmunoassay. (RIA kit, DRG instruments, Germany). Ulcer size was measured by using sterile threads and calipers. Length and breadth was marked with the thread with minimal contact and measurements were done with calipers. Area of the ulcer was noted in square millimeter (sq mm). Description analysis and correlation tests were applied to describe the results.

Results

Ulcer size was 6.5 ±5.4 sq mm (Mean ±SD) and serum cortisol was 123.3±72.6 ng/dl. Minimum and maximum serum cortisol measured was 24.6 ng/dl and 329.4 ng/dl respectively. Further subjects were divided into two groups with group A containing serum cortisol < 110 ng/dl and group B containing > 110 ng/dl. Mean ulcer size was 5.78 and 7.35 in group A and group B respectively (Table 2). In group A there was significant negative correlation between the ulcer size and serum cortisol in subjects (r = -0.413, p = 0.05). In group B there was positive correlation between the ulcer size and serum cortisol (r=0 .349, p=0.169).

Table 2 –Correlation of Ulcer size and Serum cortisol

	Group A (n=23) (Mean ±SD)	Group B (n=17)
Ulcer Size (sq mm)	5.78± 3.57	7.35±7.15
Serum Cortisol (ng/dl)	73.71±22.27	190.37±62.17
Correlation	r = -0.413 , p = 0.05	r=0 .349, p=0.169

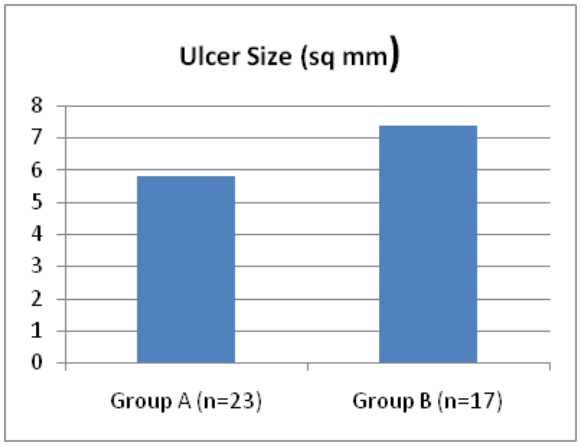

Figure 1: Mean Ulcer Size in Two groups

Discussion

It is observed that there is an increase in the serum cortisol as the size of the ulcer increases. This suggests that serum cortisol could possibly play a major role in the development of oral aphthous ulcers. Cortisol which is released in response to stress causes immune-modulation, prepares the body to fight against the stressful insult at the cellular and tissue level[6]. With prolonged stress there is persistent or frequent increase in the cortisol which tends to dysregulate the various homeostatic mechanisms in the body. Cortisol itself can alter the local immune response in the oral mucosa which can lead to formation of ulcer in the susceptible individuals[7]. These individuals might overreact to the precipitating factors like mucosal microtrauma or food allergen which could progress to ulcer development in recurrent aphthous stomatitis[8].

Is Cortisol, the molecule involved in the pathogenesis of RAS? Cortisol causes suppression of immune system, decreases lymphocyte infiltration, lymphocyte & thymocyte populations (anti-mitotic), suppresses cell-mediated hypersensitivity, and impairs phagocytes, overall decrease in inflammation. These cells mediate their actions by secreting several cytokines.

Cytokines are the major mediators in the causation of RAS. The cytokines are basically immune mediators and are classified into two 2 types 1) Type 1: Pro-inflammatory cytokines- IL-2, IL -12, interferon-α and TNF-α, induce cell mediated immunity. 2) Type-2: anti-inflammatory cytokines that promote humoral immunity and tolerance – IL-4, IL-5, IL-6, IL-10 and IL-13. This impaired cytokine ratio may mediate the ulcer formation[9]. According to Asier Eguia et al there is increase in Tumour necrosis factor-Alpha (TNF –α) in the saliva of subjects suffering from active RAS which is a proinflammatory cytokine and also increased stress[10].

Failure to suppress the inflammatory reaction initiated by trauma or other external stimuli, likely involving a functional deficiency of IL-10 in the oral mucosa, appears to be important in the pathogenesis of RAS[11]. In our study we have not noted any history pertaining to trauma in RAS groups. But it is possible that the repeated micro-trauma in the presence of the genetic predisposition can lead to triggering of the cytokine responses which leads to the autoimmune tissue destruction leading to ulcer of various sizes. Depending on the predisposing factors like stress, the ulcer may grow to larger size. As mentioned in the study by Borra et al 2004, in RAS, genetic and environmental factors may contribute to low tolerance, permitting a cytotoxic reaction against the oral epithelium[12,13]. This is evident by the fact that early intervention like relaxation techniques[14], local steroids and/or sedatives reduces the duration and severity of the ulcers.

It can be concluded that there is a definitive role of cortisol in the formation and healing of ulcer in the subjects suffering from recurrent aphthous stomatitis.

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