THE PREVALENCE OF RECURRENT APHTHOUS STOMATITIS IN PATIENTS WITH HEMATINIC DEFICIENCY

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ABSTRACT

BACKGROUND
Recurrent Aphthous Stomatitis (RAS) is one of the most common oral mucosal diseases, characterised by recurrent painful mucosal ulcers. The aim of this study was to evaluate the prevalence of RAS in patients with hematinic deficiencies (HD).

MATERIALS AND METHODS
This cross-sectional study consisted of 201 patients with at least one HD parameter including iron, ferritin, folic acid, vitamin B12 and/or related complete blood count changes. The control group consisted of 200 healthy subjects, visited our clinic for dental check-ups.

RESULTS
There was no statistically significant difference between study and control groups in terms of RAS presence (16.4%, 13.5%; $p > 0.05$). However, RAS history was present in 11 (27.5%) of 40 patients with vitamin B12 deficiency ($p = 0.03$), which was statistically significant.

CONCLUSION
Previous studies indicate HD may cause RAS and all these studies investigated the HD presence in patients with RAS. In order to assess whether HD is a cause of RAS or not, the presence of RAS in patients with HD should be taken into account. This study is the first study designed to assess the relationship between the two clinical conditions in this manner. There was no statistically significant relationship between RAS and serum iron, folic acid deficiency and anaemia, but only with B12 deficiency.

KEYWORDS
Hematinic Deficiency, Recurrent Aphthous Stomatitis.

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BACKGROUND

Recurrent Aphthous Stomatitis (RAS) is one of the most common oral mucosal diseases, characterised by recurrent painful mucosal ulcers which cause increased salivation and pain during eating, drinking and speaking. RAS affects approximately 20% of the general population, but the incidence ranges from 5% to 60% in different ethnical or socioeconomic groups.[1]

RAS is generally a topic of general medical practice, dental practice, internal medicine and dermatology. In spite of many investigations and studies, the aetiology of the RAS still remains unclear. Predisposing factors such as Hematinic Deficiencies (HD), heredity, immune dysregulation, certain foods, drugs, stress, local trauma, hormonal disturbances, infections, smoking habits and poor oral hygiene may play a role in onset of RAS as well as preventing the disease.[2-7]

The role and prevalence of HD such as iron, folic acid and vitamin B12 deficiencies in the aetiopathogenesis of RAS are not well known and many conflicting results have been reported in the literature.[4,5,7-10] Wray et al[8,11] reported increased incidence of HD in RAS patients and suggested haematological screening in such patients. While many researchers supported this relationship,[5,9-13] conflicting studies exist as well.[4,14,15] Olson et al[14] pointed out that serum deficiencies do not play a significant role in the aetiology of RAS. Koybasi et al[4] reported a significant correlation between RAS and vitamin B12 deficiency, while there is no direct association between serum iron, ferritin and haemoglobin levels and RAS.

In the majority of the studies investigating the relationship between RAS and HD, patients with RAS diagnosis were analysed for HD and the results were compared with healthy subjects who had no RAS history. However, if HD is considered a cause of RAS, then the analysis should be made by investigating the RAS prevalence in patients with HD, not investigating the HD prevalence in patients with RAS. Based on the reported high prevalence of

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HD in RAS patients, we expected to find a high RAS incidence in patients with HD when compared with the normal population in terms of HD. We evaluated the RAS incidence in patients with HD and compared it with healthy control subjects.

METHODS

The study was designed as a cross-sectional study. The study group consisted of 201 patients only experiencing HD (188 Females, 13 Males, mean age 41.59±14.83, range: 15-84). Patients were randomly selected from a group of patients who were referred to the outpatient clinic between August 2012 and January 2013.

Patients with a deficiency in at least one of the following hematinic parameters, serum iron, ferritin, folic acid, vitamin B12 and haemoglobin (Hb) were included in the study. Blood samples were obtained between 09:00 am - 10:00 am. The control group consisted of 200 age-sex matched healthy control subjects (187 females, 13 males; mean age: 41.92±15.18, range: 15-84) without HD and systemic disorders who were referred to our clinic for dental check-ups. Patients and subjects with any systemic disorder using any pharmacological therapies and/or drugs containing iron or vitamins, patients with Behcet's disease, coeliac disease and other gastrointestinal or dermatological diseases in which RAS is part of their clinical manifestation were excluded from the study.

A detailed medical history was recorded and intraoral clinical examination was performed on all patients and healthy subjects within the same day by two experienced surgeons. The RAS diagnosis was made based on medical history and clinical examination. Patients having at least one aphthous ulcer, defined as round or oval ulcers with a gray-white pseudomembrane and an erythematous halo less than 5 mm in diameter were considered as RAS positive.[6]

Biochemical analyses were carried out with a Roche Hitachi E170 modular system, vitamin B12 was measured with Architect i2000 and i4000, and total blood count was analysed with the Cell Dyn-3700 from Abbott. The reference values for the parameters are as follows: 60-175 µ/dL for iron, 30-400 ng/mlt (Male) and 13-150 ng/mlt (Female) for ferritin, 3.1-17.5 ng/mlt for folic acid, 200-663 pg/mL for vitamin B12 and 13-15.5 g/dL (Male) and 12-15.5 g/dL (Female) for Hb. All haematological analyses were evaluated by two haematologists.

All patients signed informed consent form and the procedures performed in this study involving human participants were in accordance with the ethical standards of the Declaration of Helsinki and approved by Istanbul University, Istanbul Medical Faculty Ethics Committee (Project No: 2013/1734). Data were analysed by using SPSS 20.0 statistic program (SPSS Inc., Chicago, IL, USA). Chi-square tests were used to evaluate the relationships between HD and RAS. Independent t-test was used to determine the means of samples. P value ≤ 0.05 was considered statistically significant.

RESULTS

There was no statistically significant difference between study and control groups in terms of RAS ($p > 0.05$) (16.4% and 13.5%, respectively). Mean age was 41.93±15.71 and 39.25±13.51 in patients with and without RAS in the study group, respectively. In the control group, mean age was 40.58±14.29 and 41.03±16.08 in patients with and without RAS, respectively. There was no statistically significant difference between groups in terms of age ($p > 0.05$).

A great majority of the patients (n=172, 85.5%) in the study group had deficiencies in at least two hematinic parameters. Twenty-three of 146 patients with iron deficiency had an RAS history; however, there was no statistically significant relationship between iron levels and RAS ($x^2=0.17$; $p=0.17$). Out of 40 patients (27.5%) with B12 deficiency, RAS was observed in 11 patients and the relationship between B12 deficiency and RAS was statistically significant ($x^2=4.46$; $p=0.03$). RAS was observed in 22 patients out of 157 patients with anaemia and the relationship was not statistically significant ($x^2=3.02$; $p=0.08$) (Table 1-2).

Biochemical Analysis	Deficiency was Seen (n, %)
Iron Deficiency	146 (72.6%)
Ferritin Deficiency	125 (62.2%)
Vitamin B12 Deficiency	40 (19.9%)
Hb Deficiency	157 (78.1%)

Table 1. Hematinic Deficiencies of the Study Group (n=201, Multiple HD was Included)

Deficiencies	Patients with RAS (n, %)	P-value
Iron Deficiency (n=146)	23 (15.8%)	p=0.17
Ferritin Deficiency (n=125)	19 (15.2%)	p=0.55
Vitamin B12 Deficiency (n=40)	11 (27.5%)	p=0.03*
Hb Deficiency (n=157)	22(14%)	p=0.08

Table 2. RAS Prevalence in HD Patients (n=201, Multiple HD was Included)

Chi-square test was used * $p < 0.05$.

DISCUSSION

RAS is a common inflammatory ulcerative condition affecting the oral mucosa. It is an important condition that can be distressing and causes suffering and pain.[16] Numerous studies have reported a high incidence (4-56, 2%) of HD in patients with RAS.[5,8,11,15-18] Iron, vitamin B12 and folic acid deficiencies were reported as predisposing factors in RAS in several studies.[4,5,8,10,11,16,18]

Porter et al[18] have determined the frequency of anaemia and/or HD in RAS. They indicated that 11.6% of RAS patients had low iron storage when compared with 4.9% of control subjects and also indicated that neither patients nor control subjects had anaemia. Wray et al[8] investigated 130 RAS patients for vitamin B12, folic acid and iron deficiencies and found that 23 patients (17.7%) had HD. When compared to the control group, iron and folic acid deficiencies were found twice as frequently in RAS patients and vitamin B12 deficiency was five times more common in RAS patients. On the other hand, Rogers and Hutton[19] studied 102 patients with RAS and found only 5.9% of patients to be anaemic.

Sun et al[13] reported a significant relationship between RAS and Hb, iron, vitamin B12 and folic acid deficiencies. They suggested that these deficiencies may result in atrophy of the oral epithelium, which may contribute to or facilitate RAS development by breakdown of the oral epithelium.

Lopez-Jornet et al[15] found a higher overall frequency (14.14%) of HD in the RAS group versus the control group (6.39%), but the difference was not statistically significant. Koybasi et al[4] only found an association between vitamin B12 levels and RAS history. In clinical practice, vitamin B12 deficiency has multiple symptoms and signs in the oral mucosa. The most well-known finding is glossitis, which presents as a burning feeling in the mouth.[20] Several studies have reported the role of vitamin B12 deficiency in RAS aetiology.[4,5,8,13] It is also a well-known fact that vitamin B12 deficiency should be evaluated with folic acid level, which can be seen simultaneously.[20,21] In the present study, a statistically significant difference was found between RAS and vitamin B12 deficiency, but no relationship was found between RAS and folic acid level.

Although, HD is proposed as a predisposing factor in the aetiology of RAS, all of the studies investigating the relationship between these two conditions are designed to determine whether or not HD is present in patients with RAS. However, studies also need to investigate the RAS prevalence in patients with HD in order to see if HD is a predisposing factor or not. Since there are conflicting results in the literature about the role of HD in RAS aetiology, we aimed to assess the relationship between these two conditions from another point of view. Therefore, we decided to investigate RAS prevalence in patients with HD. Based on existing literature on the relationship between these two conditions, we expected RAS incidence to be increased in patients with HD. But contrary to our expectations, RAS ratio was 16.4% in HD patients and 13.5% in control group subjects and this difference was not statistically significant ($p > 0.05$).

CONCLUSION

Without several studies investigating the relationship between HD and RAS, these results are still not confirmatory; there is no accepted consensus regarding HD screening protocol of RAS patients in the literature. This study aimed to investigate the relationship between RAS and HD from this point of view. Although, we did not find a statistically significant relationship between RAS and serum iron, ferritin, folic acid deficiencies and anaemia, we found a relationship between vitamin B12 deficiency and RAS history. The major limitation of this study was the non-uniform distribution of the patient population in terms of gender, which is composed of a high number of female patients. However, this limitation was an expected one, since HD is a more common condition in female patients. In conclusion, a definite statement with regard to the relation of RAS and HD could not yet be made yet, leaving the aetiology elusive. Taking account of many study results including this study it seems that HD screening, especially for vitamin B12 might be helpful in the management of RAS.

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