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RECURRENT APHTHOUS ULCER & ORAL LICHEN PLANUS: A STUDY OF PATHO-PHYSIOLOGICAL & PSYCHOSOMATIC SIGNIFICANCE OF SALIVARY NITRIC OXIDE

Biochemistry

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ABSTRACT

Recurrent aphthous ulceration (RAU) or recurrent aphthous stomatitis (RAS) and oral lichen planus (OLP) are the most common oral mucosal disease known to human beings. The immunological imbalance & psychological stress are considered to the most prime factors for Recurrent aphthous ulcer (RAU) & Oral lichen planus (OLP).Further the oxidative stress caused by nitric oxide has a definitive role in establishing the correlation between [NO] with RAU & OLP.The present study was undertaken to study the role of nitric oxide in human saliva & its diagnostic/prognostic role in RAU & OLP.The study was carried out at Government Dental college & Hospital,Aurangabad.Twenty cases with RAU,Fifteen with OLP & Thirty healthy control individual were included in the study. The clinically diagnosed known cases of RAU & OLP were included after taking detail case history. Under all aseptic precautions, fresh saliva was collected in sterile bulp.The sample was subjected to biochemical analysis of [NO].

The RAU cases were subdivided into major & minor and OLP cases were divided into erosive or non-erosive type after clinical & histological examinations. The salivary Nitric oxide levels were found to be increased significantly in RAU & OLP group when compared with controls. Further significantly increased levels have been observed in OLP group when compared with RAU group (P<0.001).The salivary nitric oxide levels were found to be increased significantly in minor RAU than major RAU and increased in erosive type of OLP than non-erosive type of OLP. Thus this parameter can be treated as a diagnostic tool for the diffential diagnosis of RAU& OLP.

KEYWORDS

RAU (Recurrent aphthous ulcer), Oral lichen planus (OLP), Nitric oxide [NO]

INTRODUCTION

Recurrent aphthous ulceration (RAU) or recurrent aphthous stomatitis (RAS) and Oral lichen planus (OLP) are the most common oral mucosal disease known to human beings. Inspite of much clinical and research invention the causes are poorly understood, the ulcers are not preventable, and the treatment are symptomatic. Aphthous ulcers are very common with the incidence rate of 17% to 50%.The higher socioeconomic class is the maximum suffers of these conditions. These ulcers are confined to the oral mucosa and are recurrent painful, single or multiple in nature **[1].**A chronic inflammatory dematosis involving oral mucosa is oral lichen planus.It may be of erosive or non-erosive type. The immunological imbalance & psychological stress are considered to the most prime factors for the conditions like Recurrent aphthous ulcer (RAU) & Oral lichen planus (OLP).Further the oxidative stress caused by nitric oxide has a definitive role in establishing the correlation between [NO] with RAU & OLP **[2].**The etiological factors associated with recurrent Aphthous ulcers & oral lichen planus are trauma, allergy, hereditary & psychosomatic stress. Though various treatment modalities are available still the symptomatic treatment is the best option available.

Nitric oxide [NO] is pathological or pathophysiological free radicle mediator of number of diseases of CNS and PNS, cardiovascular system & kidneys. Its role in angiogenesis and tumor progression in head & neck cancer has been described by emarnula masini et al 1998 **[3].** [NO] have been reported to be present in freshly secreted human saliva & it was suggested that [NO] plays an important role in modifying physio-pathalogical processes of OMM **[4].** Therefore the present study was undertaken to estimate salivary [NO] levels in RAU &OLP with the view to ascertain its diagnostic as well as prognostic value.

MATERIAL & METHODS

The present study was carried out in the department of oral pathology & microbiology of Government Medical College & hospital, Aurangabad during the year 2015 to 2016.Total thirty five cases were studied inclusive of twenty cases of RAU & fifteen cases of OLP & thirty healthy controls were included in the study for comparion.Although case history was recorded & clinically diagnosis of RAU & OLP was confirmed. Under aseptic precautions fresh saliva was collected in sterile bulp.The sample was subjected to biochemical analysis of [NO] by diazotization reaction with adoption of the principle of Griess reagent.The RAU cases were subdivided into major RAU and OLP cases were divided into erosive type after clinical & histological examination

OBSERVATIONS:

Thirty cases in the control group comprised of equal number of males and females, however 35 cases under study group were comprised & 24 males (68.5%) and (31.5%) in (RAU and OLP) male to female ratio was 2:1:1.

Sex Distribution

Group	No. of cases	Age range in yrs	Mean age in yrs	Male	Female
Control	**30**	**15-55**	**28.1**	**15**	**15**
Recurrent apthous ulcer (RAU)	**20**	**15-66**	**30.8**	**15**	**05**
Oral Lichen planus (OLP)	**15**	**24-55**	**37.2**	**09**	**06**
Total	**65**			**39**	**26**

Age Distribution

Group	No. of cases	Age in Yrs			
		11-20	21-30	31-40	>40
Control	30	04	19	03	04
RAU	20	04	08	04	04
OLP	15	-	03	06	06
Total	65	08	30	13	26

The patients in the age range of 11-20 years were 4 each in control and RAU gr.19,08 &03 in the age range of 21-30 yrs,3,4 & 6 in the age range of 31-40 yrs & 4,4 and 6 cases in the age range above 40 yrs in control RAU and OLP groups.

Salivary nitric oxide levels in various age ranges in all the groups & their comparison with the control grp is as under.

Nitric oxide Levels observed in Control group in various Age Range

Number of cases	Age Range in Yrs	Nitric oxide levels (µgm%)
04	11-20	216.8 ± 32
19	21-30	201.6 ± 0.1
03	31-40	213.3 ± 2.3
04	>40	115.7 ± 0.1

Nitric oxide Levels observed in OLP group in various Age Range

Number of cases	Age Range in Yrs	Nitric oxide levels (µgm%)
-	11-20	-
04	21-30	389.75 ± 3.75
06	31-40	340.33 ± 1.33
05	>40	312.4 ± 5.5

Mean Salivary Nitric oxide levels Observed in Various groups

Group	Number of cases	Nitric oxide levels (µgm%)
Control	30	214.35 ± 42
RAU	20	339.7 ± 6.72
OLP	15	352.3 ± 12.0

Comparison of Salivary Nitric oxide levels in Control grp with RAU & OLP grp

Group	Number of cases	Nitric oxide levels (µgm%)	SD	't'	P value
Control	30	214.35 ± 42	-		-
RAU	20	339.7 ± 6.72	19.09	22.72	<0.001
OLP	15	352.3 ± 12.0	5.26	62.91	<0.001

P<0.001(Highly significant)

Comparison of Salivary Nitric oxide levels Observed in RAU & OLP grp

Group	Number of cases	Nitric oxide levels (µgm%)	SD	't'	P value
RAU	20	339.7 ± 6.72			
OLP	15	352.3 ± 12.0	3.95	9.33	<0.001

P<0.001(Highly significant)

Salivary [NO] levels were found to be increased significantly in RAU & OLP grp when compared with control (p<0.001) which is statistically highly significant in all age ranges studied.

Comparison of Salivary Nitric oxide levels Observed in:

Age Range 11 to 20 years in all Groups

Group	Number of cases	Nitric oxide levels (µgm%)	SD	't'	P value
Control	04	213.6 ± 3.2	-		-
RAU	04	346.0 ± 6.72	19.09	22.72	<0.001
OLP	-	-	-	-	-

Age Range 21 to 30 years in all Groups

Group	Number of cases	Nitric oxide levels (µgm%)	SD	't'	P value
Control	19	201.6 ± 0.1	-		-
RAU	08	328.3 ± 15.0	63.00	4.76	<0.001
OLP	03	393.0 ± 1.0	02.52	57.2	<0.001

Age Range 31 to 40 years in all Groups

Group	Number of cases	Nitric oxide levels (µgm%)	SD	't'	P value
Control	03	201.6 ± 0.1	-		-
RAU	04	313.2 ± 15.0	3.00	43.59	<0.001
OLP	06	351.1 ± 31.8	26.9	07.24	<0.001

Age Range Above 40 years in all Groups

Group	Number of cases	Nitric oxide levels (µgm%)	SD	't'	P value
Control	04	215.7 ± 0.1	-		-
RAU	04	371.5 ± 5.5	3.88	75.14	<0.001
OLP	06	312.8 ± 3.2	2.53	82.60	<0.001

P<0.001(Highly significant)

In the age range of 21-30 yrs salivary [NO] levels were increased significantly (p<0.001) in OLP grp when compared with RAU.

In age range 31-40 yrs salivary [NO] levels were increased significantly p<0.001 in OLP grp when compared with RAU.

In age range above 40 yrs the contrast results were observed i.e. salivary [NO] levels were significantly increased in RAU when compared with OLP grp.

Comparison of Salivary Nitric oxide levels Observed in:

Age Range 21 to 30 years in RAU & OLP Groups

Group	Number of cases	Nitric oxide levels (µgm.%)	SD	't'	P value
RAU	08	328.3 ± 15.0	-	-	-
OLP	03	393.0 ± 1.0	-	-	<0.001

Comparison of Salivary Nitric oxide levels Observed in Age Range 31 to 40 years in RAU & OLP Groups

Group	Number of cases	Nitric oxide levels (µgm.%)	SD	't'	P value
RAU	04	313.2 ± 3.4			
OLP	06	351.1 ± 31.8	25.2	3.6	<0.001

Comparison of Salivary Nitric oxide levels Observed in: Age Range Above 40 years in all Groups

Group	Number of cases	Nitric oxide levels (µgm.%)	SD	't'	P value
RAU	04	371.5 ± 5.5	-	-	-
OLP	06	312.8 ± 3.2	17.7	7.92	<0.001

The patients in the OLP grp were advised oral steroids along with the tropical application for fifteen days. Only four cases followed regular medical schedule and came after fifteen days as advised. Salivary [NO] levels were found to be 181.0 ± 13.5ugm%.Three cases in OLP grp turned up after one month who have applied topical medications without oral steroids. The salivary [NO] levels observed were 300.0 ± 4.0 µgm%.

Comparison of pre and Post treatment levels of Salivary Nitric oxide in OLP Group

Group	Number of cases	Pre t/t levels (µgm.%)	Post t/t levels (µgm.%)	SD	't'	P value
OLP	10	359.71± 57.1	240.8 ± 74.4	68.84	8.6	<0.001

Mean salivary post treatment levels of [NO] in OLP grp were found to be decreased significantly P<0.001 when compared with mean pretreatment levels of salivary [NO]. Statistical analysis was carried out by applying paired 't' test

DISCUSSION:

Recurrent Aphthous ulcers are characterized by painful recurring ulceration of oral mucosa and oral Lichen planus is clinically recognizes as persistent while striations and patches associated with mucosal atrophy and erosion **[5, 6].** Common histological features of these diseases are characterized by basal cell destruction and presence of lymphocytic infiltrate. Numerous studies have reported hereditary, dietary, endocrine, infections, allergic, immunologic and psychological stress disturbances in their etiology **[7].**The common etiologic factors especially on the psychological background and microscopic features were specifically selected for the study to evaluate salivary nitric oxide levels. It is believed that there is a specific correlation exists between the psychological stress & salivary nitric oxide levels in RAU & OLP.RAU occurs at any stage with the highest frequency in young adult usually non-keratinized mucosa of the oral cavity is involved **[8`, 9].**The histologic feature is non-pathogenic with central zone of destruction, increased vascularity in the connective tissue with mixed cellular infiltrate i.e. Lymphocytes, histocytes, PML and plasma cells**. [10].**

The RAU grp revealed salivary nitric oxide levels of 346.0 ± 1.5, 332.7 ± 11.7, 313.2 ±1.7 and 356.8 ±4.3 µgm% in the age grp 11-20, 21-30, 31-40 and above 40 yrs respectively. Maximum levels were observed in age grp above 40 yrs, followed by 11-20 yrs.pre pubertal age or premenstrual age range and post-menopausal age range were more prone to the emotional stress and hormonal imbalance which results into the elevation of salivary [NO] levels. This may be probable due to the process of ageing. Reactive oxygen species (ROS) generates in

bulk quantities which results into the elevated [NO] levels in RAU **[8].**

Salivary (NO) levels observed in various age range in OLP gr.were 289.7 ±375,340.3±1.3 and 312.4±5.5 µgm in the age range 21-30,31-40 and above 40 yrs. respectively. This may be due to psychological stress or physiological stress which may causing excess (NO) release in the hypothalamic pituitary adrenal axis (HPA).Also the hormonal imbalance leads to the highest salivary (NO) concentrations **[4, 11].**

The reactive oxygen species (ROS) such as superoxides, hydrogen peroxide, hydroxyl radical, nitric oxide.etc.usually termed as free radical or oxidants. The involvement of ROS in gastric ulceration was first evident from the gastric mucosal injury**.[12,13]** It has been reported that submandibular or parotid salivary glands did not show any gross difference in the concentration of (NO).Therefore the whole saliva was used for the quantitation of salivary (NO). It is believed that [NO] is synthesized by variety of cells and tissues including brain. [NO] acts as crucial mediator of various metabolic functions and serves as retrograde messenger **[14].**

CONCLUSION:

Thus in the present study the diagnostic value of salivary [NO] in RAU & OLP was evaluated and prognostic value in OLP was assessed. This parameter can also be used for the differential diagnosis of RAU & OLP. Still further studies are required to establish concrete relation between salivary [NO] and RAU & OLP.

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