

Study of Reduced Salivary Secretion and Increased Caries Susceptibility in Rheumatoid Arthritis

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ABSTRACT

It is a chronic inflammatory musculoskeletal disease with extra-articular manifestations including involvement of exocrine lacrimal and salivary glands. The aim of this study was to assess the reduced salivary secretion and calculate and compare DMF index in rheumatoid arthritis patients. The salivary output was determined in unstimulated (resting) whole saliva and caries status in all individuals was determined by using the DMF index in 20 rheumatoid arthritis patients and 20 healthy control subjects. Compared with healthy control groups, rheumatoid arthritis patients had significantly decreased output of saliva and higher DMF index than in the control group. The results indicate that xerostomia in patients with rheumatoid arthritis may be indicative of increased disease activity and impacts negatively on oral health leading to increased caries susceptibility and should receive increased stomatological attention.

Keywords: Rheumatoid arthritis, Saliva, Salivary flow rate (SFR), DMF (decayed, missing, filled teeth)

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INTRODUCTION

Rheumatoid arthritis (RA) is a heterogeneous disease with a spectrum of clinical severity ranging from mild arthritis to a crippling joint disorder with internal organ involvement.

The pathogenesis of RA is characterized by prolonged, chronic inflammation of the synovial membrane accompanied by morphological alterations [1, 2]. The pathology of the disease process often leads to the destruction of articular cartilage and ankylosis of the joints [3,4].

It is a chronic inflammatory musculoskeletal disease with considerable morbidity and mortality affecting 1-2% of the population world-wide, with women affected two to three times more commonly than men [5]. The most important diagnostic criteria for RA patients are morning stiffness, arthritis and soft tissue swelling [6].

It may present with extra-articular manifestations including involvement of exocrine lacrimal and salivary glands. The

decrease of salivary function in rheumatoid arthritis is assumed to be related to the lymphocytic infiltrate present in affected glands and manifested as decrease of salivation and chemical changes [7].

The extra-articular manifestations of rheumatoid arthritis are characterized by destructive polyarthritis and extra-articular organ involvement, including the skin, oral cavity, eye, heart, lung, renal, nervous and gastrointestinal systems. Oral manifestations of RA patients include TMJ disorders, xerostomia and Sjogren's syndroms [8]. RA patients may have oral manifestations as a side effect of treatment includes: Aphthous stomatitis, Glossitis, Oral ulceration, Lichenoid eruptions, oral pigmentation, Angular Cheilitis and Candida infection [9].

Xerostomia is a condition associated with a decrease in the amount of saliva produced and an alteration in its chemical composition. It can cause a significant decline in quality of life by decreasing taste sensation and impairing chewing ability [10]. It also functions to maintain tooth integrity from dental decay by supporting ongoing remineralization of teeth by providing a reservoir of calcium and phosphate ions and forming the glycoprotein pellicle [11]. In addition, saliva functions in maintaining a neutral oral pH through bicarbonate & phosphate buffer systems [12].

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MATERIALS AND METHODS

The study was conducted in Department of Orthopedics and Rehabilitation, King George's Medical College, Lucknow. Ethical clearance for the study was obtained from the institutional ethical committee. Aim of the study was to assess the reduced salivary secretion in rheumatoid arthritis patients and calculate and compare DMF index in rheumatoid arthritis patients. 40 subjects (males and females) were enrolled in this study. Patients were divided into 2 groups:- 20 patients diagnosed clinically depending on the seven criteria of the American Rheumatism Association (ARA) [13].

20 individuals were age and sex matched healthy controls. Subjects of either sex age between 15 years to 60 years, clinically diagnosed–Rheumatoid arthritis, well – oriented to place, person and time were enrolled in the study. Subjects suffering from Diabetes mellitus, Hypertension, Cardiovascular disease and those with a history of drug intake were excluded from the study.

Criteria of the American Rheumatism Association^[13]

1. Morning stiffness
2. Arthritis of 3 or more joints
3. Arthritis of hand joints (1 swollen joints)
4. Symmetrical arthritis
5. Rheumatoid nodules
6. Serum rheumatoid factor
7. Radiographic changes (erosions)

Rheumatologist examined each patient and each tender and or swollen joint was calculated according to the CDAI [14]. According to this index the patients were subdivided to

1. Inactive or remission if the CDAI < 2.8
2. Mild or low disease activity if the CDAI = 2.8-10
3. Moderate disease activity if the CDAI = 10-22
4. Severe disease activity if the CDAI > 22.

$$\text{CDAI} = \text{SJC}(28) + \text{TJC}(28) + \text{PGA} + \text{EGA}$$

SJC(28): Swollen 28-Joint Count (shoulders, elbows, wrists, MCPs, PIPs including thumb IP, knees)

TJC(28): Tender 28-Joint Count (shoulders, elbows, wrists, MCPs, PIPs including thumb IP, knees)

PGA: Patient Global disease Activity (patient's self assessment of overall RA disease activity on a scale 1-10 where 10 is maximal activity)

EGA: Evaluator's Global disease Activity (evaluator's assessment of overall RA disease activity on a scale 1-10 where 10 is maximal activity)

Research Participant Preparation and Documentation

A complete check-up of the oral cavity was done in artificial light by using diagnostic dental tools (dental mirror and probe). Persons were instructed to refrain from food and beverages, except water, for two hours before saliva collection. All salivary samples were collected between 8 a.m. and 10 a.m., so that circadian influences would be minimized. Patients who were enrolled in the study were asked to rinse their mouth thoroughly with water to allow removal of debris. The first mouth –full of saliva was discarded to allow clearance of water. Unstimulated (resting) whole saliva was collected after the subjects were asked to spit all the saliva during 10 minutes into plastic graduated tubes. Salivary flow rate was immediately calculated as the volume of saliva in ml divided by the time in minutes required for collection of saliva. Saliva flow rate (ml/min) = volume/ time. Following WHO criteria, the caries status in all individuals was determined by using the DMF index. The data obtained from the procedures will be tabulated and analyzed using statistical methods.

RESULTS

Table 1 shows that both the groups were comparable in terms of age and sex.

The DMF was significantly ($p=0.02$) higher among the cases (1.55 ± 0.35) compared with controls (0.65 ± 0.16). However, saliva flow rate was significantly ($p=0.0001$) lower (0.23 ± 0.04) among cases than controls (0.37 ± 0.04) (Table 2).

Kruskall-Wallis analysis showed that there were significant ($p=0.01$) differences in DMF among all the three grades of CDAI. The multiple comparison tests showed that the DMF was significantly ($p=0.02$) lower in Grade I of CDAI as compared to Grade III (Table 3).

Table 1: Demographic features of the cases and controls

Demographic features	Cases (n=20)	Controls (n=20)	p-value
Age in years, mean ± SE (Min-Max)	25.45±1.07 (14-32)	26.75±0.94 (20-36)	0.36 ¹
Male sex, no. %	9 (45.0)	7 (35.0)	0.51 ²

¹Unpaired t-test, ²Chi-square test, SE-standard error, Min-Minimum, Max-Maximum

Table 2: Comparison of DMF and SFR (salivary flow rates) between cases and controls

	Cases(n=20)	Controls(n=20)	p-value ¹
DMF, mean ± SE (Min-Max)	1.55±0.35 (0-7)	0.65±0.16 (0-2)	0.02*
SFR, mean ± SE (Min-Max)	0.23±0.04 (0-7)	0.37±0.04 (0.1-0.8)	0.0001

¹Mann-Whitney U-test, SE-standard error, Min-Minimum, Max-Maximum, *Significant

Table 3: Comparison of DMF and SFR (salivary flow rates) according to CDAI grade

	Grade I (n=8)	Grade II (n=10)	Grade III (n=2)	p-value ¹
DMF, mean±SE	0.62±0.18 ²	2.00±0.59	3.00±1.00 ²	0.01*
SFR, mean±SE	0.26±0.07	0.21±0.05	0.17±0.05	0.17

¹Kruskal-Wallis-test, SE-standard error, ²p=0.02 (Multiple comparison test) *Significant.

DISCUSSION

Age and Sex

Rheumatoid arthritis is a chronic, progressive multisystem inflammatory disorder with a prevalence of approximately 0.5-1%. It usually involves middle-aged adults with a females being affected more than males [15]. In the present study the mean age of RA patients was 25.45±1.07. 11 of RA patients were females and 9 were males.

Salivary Flow Rate (SFR)

It has been found that saliva flow rate was significantly higher in the healthy controls than in the RA patients and decreased as the grading increased. The reduction in salivary gland function as measured by saliva flow rate in the RA patients result from that the salivary glands major target organs of RA. In a similar study by Anna Zalewska *et al.* [16] on 60 RA patients and 32 controls - salivary flow rate were statistically lower in the RA patients in comparison to the Control group.

The results indicate that xerostomia in patients with RA may be a harbinger of diminished saliva production regarding quantity and quality, and may be indicative of impairment of the salivary immune system of the oral cavity in xerostomic RA patients [17]. In a similar study done by Nagler *et al.* [18] the mean salivary flow rate was lower in the RA patients than in the control group.

In RA destruction of the glandular acinar units might occur, leading to a reduction of salivary secretion. It is believed that B and T lymphocytes infiltrate the salivary glands, causing cell-mediated destruction of glandular elements; secretion of cytokines; production of autoantibodies that interfere with muscarinic receptors; and secretion of metalloproteinases that interfere with efficient glandular functions [19]. The release of acetylcholine from parasympathetic nerves initiates the stimulus-secretion coupling in the acinar cells of the salivary glands. The release of acetylcholine is brought about by an increase in the intracellular calcium level that ends in activation of the calcium-dependent K⁺ and Cl⁻ channels. Disruptions of any of these steps will bring a decrease of fluid secretion [19].

DMF (Decayed, missing, filled teeth)

We found that RA had a higher DMF index than in the control group and DMF increased as grade increased. In a similar study conducted by Anna Zalewska *et al.* [16]. DMF index was statistically higher in RA groups in comparison to the control group.

The study of Pedersen *et al.* [20] showed that patients with RA had a significantly higher DMF compared to healthy controls, Pedersen [20] claimed that RA patients harbor higher numbers of cariogenic and acidophilic microorganisms such as *Streptococcus* mutants and *Lactobacillus* species than healthy controls, and this could

be a reason for the higher DMF index. Patients with hyposalivation have more viscous and foamy saliva, losing its lubricating ability and adhering to teeth and mucous membrane. Also accumulation of plaque and an increase in the number of microorganisms in the saliva could be expected when the salivary secretion is low. This might be followed demineralization of the tooth structure leading to dental caries. The high DMF index in RA NS might reflect infraclinical involvement of the salivary glands resulting in changes in saliva biochemistry long before development of hyposalivation.

Patients with RA may require additional personal oral care instruction, dietary instruction and modifications, home/clinical fluoride therapy, home/clinical chlorhexidine therapy, treatment for their xerostomia, more frequent recall visits and radiographs and more conservative treatment plans^[21]. Thus, dental healthcare workers play an important role in recognizing signs and symptoms of RA and in advising patients to seek medical care.

CONCLUSION

The results indicate that xerostomia in patients with rheumatoid arthritis may be indicative of increased disease activity in rheumatoid arthritis patients. The demonstrated correlation between the altered salivary secretion and the severity of the disease may indicate that evaluation of the salivary status of rheumatoid arthritis patients is warranted. There were significant differences in DMF among all the three grades of CDAI. Rheumatoid arthritis disease impacts negatively on oral health and should receive increased stomatological attention^[16].

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