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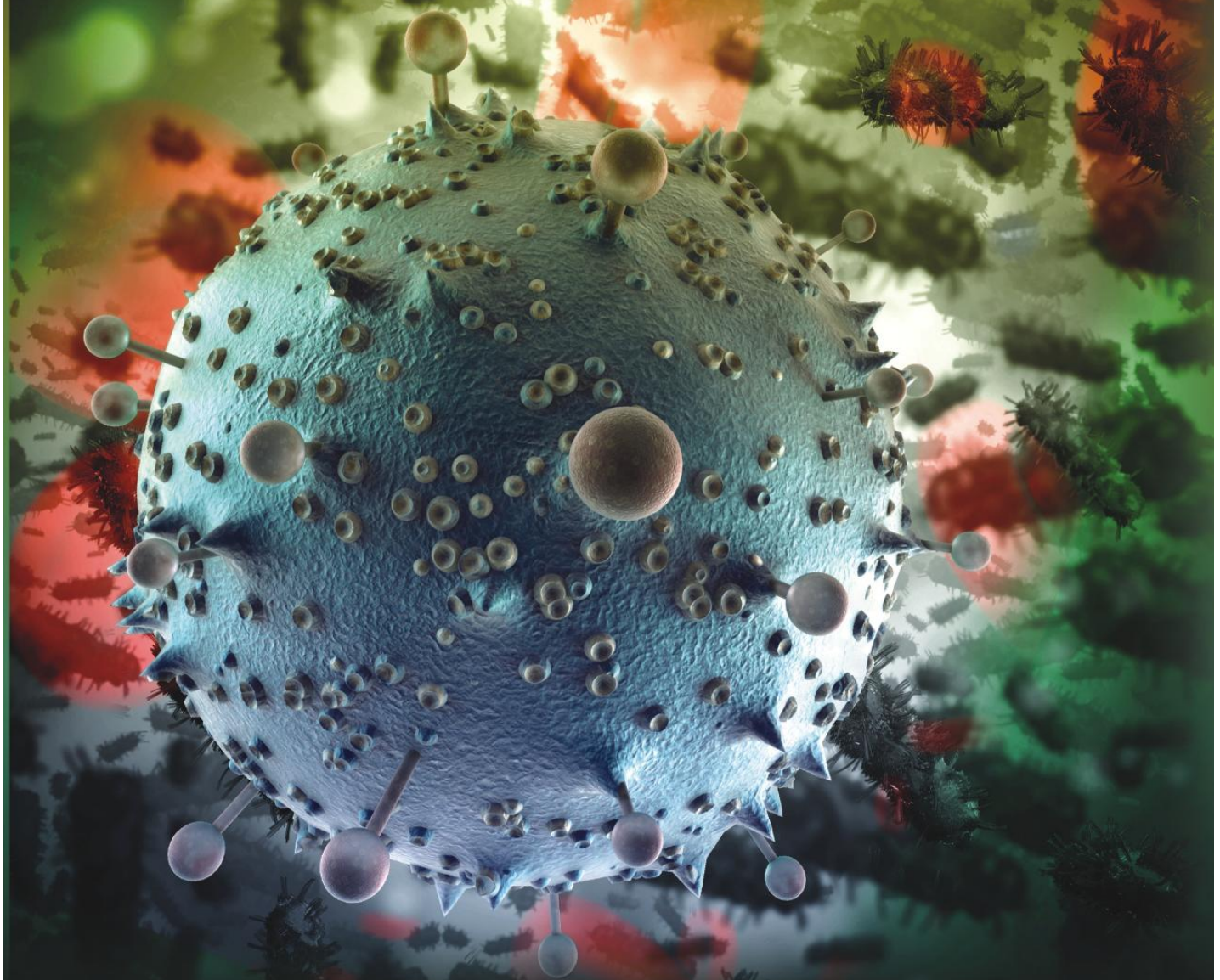

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Research Report

Medication intake and its influence on salivary profile of geriatric outpatients in Cipto Mangunkusumo Hospital

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ABSTRACT

Background: *It has been well documented that several diseases or conditions and their related medications could be the risk factors for several ailments found in the oral cavity. Increased usage of medication in elderly could have impact on quality of saliva that affects oral health, eventually cause deterioration in quality of life.* ***Purpose:*** *examine the salivary pH, buffering capacity, stimulated- and unstimulated salivary flow rate profile in elderly using medications.* ***Methods:*** *Seventy-six elderly were consented and agreed to participate in this study. Interview and medical record analysis were performed to get data about their health status, chronic use of medications and complaints related to xerostomia. Collection of unstimulated and stimulated saliva samples were completed in parallel with measurement of salivary pH and buffering capacity.* ***Results:*** *The mean salivary pH was moderately acidic while having low salivary buffering capacity. The mean unstimulated salivary flow rate (USSFR) was 0.24 ± 1.8ml/min and 41of subjects (53%) were classified hyposalivation, while the stimulated salivary flow rate (SSFR) was 0.86 ± 0.49ml/min and 31 (40%) classified hyposalivation. Number of drugs-induced xerostomia intake significantly correlated with the reduction in the USSFR of subjects ($p<0.0001$), however it was not the case with salivary pH and buffering capacity ($p>0.05$). It also showed correlation with complaints related to xerostomia. The mean USSFR did not correlate with xerostomia complaints.* ***Conclusion:*** *Medications intake influenced salivary profile and had more effect in changes in xerostomia complaints and salivary quantity than to salivary pH and buffering capacity in Indonesian elderly population.*

Key words: *Medication, xerostomia, hyposalivation, elderly*

ABSTRAK

Latar belakang: *Telah lama diketahui bahwa beberapa penyakit atau kondisi sistemik dan medikasinya dapat menjadi faktor resiko terjadinya beberapa kelainan dalam rongga mulut. Meningkatnya penggunaan medikasi sistemik pada lansia dapat mempengaruhi kualitas saliva sehingga berpengaruh pada kesehatan mulut yang akhirnya menyebabkan menurunnya kualitas hidup.* ***Tujuan:*** *Mengetahui profil pH saliva, kapasitas dapar, laju aliran saliva terstimulasi (LAST) dan tanpa stimulasi (LASTS) pada lansia yang mendapatkan medikasi sistemik.* ***Metode:*** *Tujuh puluh enam lansia telah menandatangani inform consent dan setuju untuk berpartisipasi. Wawancara dan analsis rekam medis dilakukan untuk mendapatkan data tentang status kesehatan, penggunaan medikasi sistemik jangka panjang dan keluhan xerostomia. Pengumpulan saliva tanpa stimulasi dan terstimulasi dilakukan bersama-sama dengan pengukuran pH dan kapasitas dapar.* ***Hasil:*** *pH saliva subyek adalah berada dalam kelompok asam sedang dengan kapasitas dapar yang rendah. Rerata LASTS adalah 0,24 ± 1,8ml/menit dan 41 subyek (53%) mengalami hiposalivasi, sementara LAST adalah 0,86 ± 0,49ml/menit dan 31 subyek (40%) mengalami hiposalivasi. Jumlah medikasi yang dapat menginduksi xerostomia secara bermakna berhubungan dengan penurunan LASTS ($p < 0,0001$), namun tidak demikian dengan pH dan kapasitas dapar ($p>0,05$). Medikasi sistemik juga berhubungan dengan keluhan yang terkait xerostomia. Rerata LASTS tidak berhubungan dengan keluhan xerostomia.* ***Kesimpulan:*** *Medikasi sistemik pada populasi lansia Indonesia mempengaruhi profil saliva dan mempunyai pengaruh yang lebih besar pada keluhan xerostomia dan kuantitas saliva dibandingkan pH dan kapasitas dapar.*

Kata kunci: *Medikasi sistemik, xerostomia, hiposalivasi, lansia*

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INTRODUCTION

It is well documented that growing population of the elderly is very fast over other age groups of the population worldwide, especially in developing countries.[1] In less than 15 years, the number of elderly population worldwide would reach 600 million and the number would be doubled in 2050.[1] As a developing country, Indonesia is posing tremendous challenges to maintain the health status of its elderly population, since there would be shift of disease pattern. Increase number of ageing population and burden of the related chronic diseases require definite health promotion and prevention. Beside many physiological changes in the oral mucosa that increase risk of elderly to problems in the oral cavity,[2-4] degenerative diseases such as cardiovascular disease, hypertension, cancer, and diabetes mellitus, that are prevalent in old age, would also have impact to the oral health status.[1]

Saliva is one component in the oral cavity that plays an important role in maintaining oral health. Saliva functions mainly to lubricate oral mucosa, as part of its role in the stomatognatic system. It is also important for protection against pathogen microorganisms and oral mucosal repair. Reduction in the salivary bicarbonate composition would influence its buffering capacity which further interfering salivary pH and saliva remineralization function.[5] Therefore, its alteration in terms of quantity, quality and composition would interfere the oral homeostasis.[5] Several studies have included salivary flow rate, pH and buffering capacity to assess salivary function and determine the salivary profile.[6,7]

Although salivary function was thought to be physiologically decline in parallel with age, saliva composition is not significantly different among different age of healthy individuals.[8] There is growing evidence of that quality and quantity of saliva significantly influence oral health of the elderly, thus affecting quality of life.[8–10] Studies have been shown that majority of salivary dysfunction cases in elderly are related to systemic disease medication, or the presence of radiotherapy in the head and neck region.[8] Complaints of xerostomia which is usually related to subjective information, could be objectively assessed by correlating it with the salivary flow rate.

To date, data on the condition of salivary profile and its relation to medication intake in elderly population in Indonesia is still not well documented. Therefore, this study aimed to examine the salivary pH, buffer capacity, unstimulated and stimulated salivary flow rate profile in elderly using medications in elderly attending the outpatient geriatric clinic in Cipto Mangunkusumo General Hospital, Jakarta Indonesia. This study would provide additional information regarding elderly in Indonesia.

MATERIALS AND METHODS

Seventy-six elderly, who were attending the geriatric outpatient clinic in Cipto Mangunkusumo Hospital, Jakarta, were consented and agreed to participate in this study. Interview about their health status, chronic use of medications and complaints related to xerostomia using modified xerostomia questionnaire was performed.[11] This study collected the xerostomia complaints using three questions modified from Xerostomia Inventory,[11] which were "Do your mouth feel dry?", "Do you get up at night to drink?" and "Do you need to sip liquid to aid in swallowing food?".

After that, the unstimulated salivary flow rate (USSFR) was collected in the morning of the next visit to the clinic approximately at 10 am. The subjects were ask to avoid eating or drinking about 1 hour prior saliva collection. The USSFR was collected in 5 minutes time, where patient was asked to expectorate the saliva every 60 seconds. The analysis of salivary pH and buffer capacity was performed using the USSFR sample. Collection of the stimulated salivary flow rate (SSFR) sample was performed by asking the patient to chew paraffin wax for 5 minutes, then expectorating the saliva every 60 seconds. All the procedure was carried out using Saliva-Check BUFFER Kit from GC (900200 GC America, Inc.).

One-way ANOVA test was used to compare mean values of all measurement. Correlation of salivary profile with xerostomia complaints was analyzed using Pearson correlation test. Spearman correlation was used to analyze any correlation between medication intake and xerostomia complaints.

RESULTS

The study showed that the mean of USSFR and SSFR for the sample group were 0.24 ± 1.8 ml/min and 0.86 ± 0.49 ml/min respectively. Although the mean value of the USSFR and SSFR were not categorized as hyposalivation, this study showed 41 subjects (53%) were classified having hyposalivation based on USSFR measurement, while according to SSFR measurement, 31 subjects (40%) were classified having hyposalivation, and the difference was not significant ($p > 0.05$). Analysis of salivary pH showed that the majority of this elderly population having moderately acidic pH, whilst having low buffering capacity according the GC Saliva-Check BUFFER Kit (Table 1). Although, we found that 9 of subjects (11%) had highly acidic saliva with very low buffering capacity, quite high number of subjects still had normal salivary pH 27 (36%) and normal buffering capacity 25 (33%) (Figure 1).

Table 1. Salivary profile of the subjects

Saliva	Salivary Flow Rate (ml/min) Mean ± SD	Number of Subjects with Hyposalivation n (%)	pH Mean ± SD	Buffering Capacity Mean ± SD
USSFR	0.24 ± 1.8	41(53)	6.6 ± 0.5	7.6 ± 2.8
SSFR	0.86 ± 049	31(40)	-	-

Hyposalivation USSFR < 0.2 ml/min, SSFR < 0.7ml/min; pH score: highly acidic = 5.0–5.8, moderate acidic = 6.0–6.6, normal = 6.8–7.8; buffer capacity score: very low = 0–5, low = 6–9, normal = 10–12.

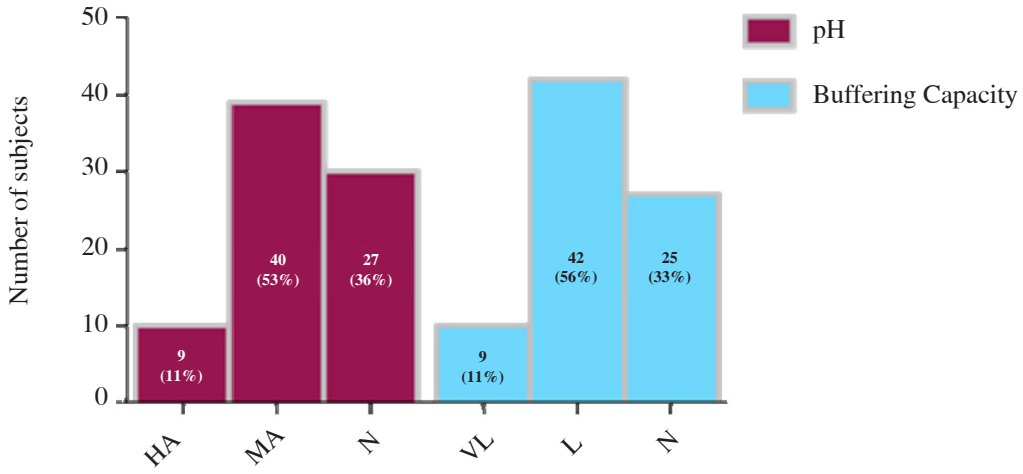

Figure 1. Salivary pH and buffering capacity of the USSFR sample of the subjects showed that mostly were having moderate acidic pH dan low buffer capacity. HA = highly acidic, MA = moderate acidic, VL = very low, L = low, N = normal.

The majority of subjects were on medications to treat the related systemic diseases. This study noted 14 different types of systemic disease/conditions that required medications. Data on patients medication was then classified into five types of drug-induced xerostomia according to previously published review (Table 2).[12] This study found that many subjects had taken more than one type of medications to treat multiple systemic diseases. We therefore analyzed the difference between salivary pH, buffering capacity and USSFR with the number of drugs-induced xerostomia intake in the subjects (Table 3). There was no difference in salivary pH and buffering capacity between the three groups of patients ($p > 0.05$). However, number of drugs-induced xerostomia intake strongly influenced the USSFR of the subjects in this study ($p < 0.0001$).

According to the modified xerostomia questionnaire that was used in this study, the number of subjects having complaints of xerostomia were 58 (76%), however 27 subjects (37%) with xerostomia complaints were found to have normal salivary flow rate (Table 4). Therefore there was no correlation

Table 2. Intake of drugs-induced xerostomia

Type of drugs	Number of subjects n (%)
Antihypertensive	58 (76)
Bronchodilator	14 (18)
Diuretics	3 (3)
Antidepressants	2 (2)
Cytokines	2 (2)

Table 3. Salivary pH and buffering capacity of subjects with different number of drug-induced xerostomia intake

Number of drug-induced xerostomia intake	n	Salivary pH Mean ± SD	Buffering Capacity Mean ± SD	Mean ± SD USSFR
0	18	6.8 ± 0.58	7.80 ± 2.74	0.39 ± 0.17
1	29	6.75 ± 0.51	7.86 ± 2.2	0.22 ± 0.18
> 2	29	6.57 ± 0.62	8.06 ± 2.5	0.16 ± 0.09
p value*		0.32	0.93	< 0.0001

* One-Way ANOVA

Table 4. Salivary flow rate of patients with xerostomia complaints

Number of xerostomia complaints	n	Mean ± SD USSFR	Number of subjects with hyposalivation
0	18	0.24 ± 0.15	1
1	29	0.20 ± 0.16	18
2	23	0.20 ± 0.09	13
3	6	0.35 ± 0.3	6
		p value = 0.17*	r = 0.17** 95% CI = –0.94 to 0.97 p value = 0.8 R square = 0.02

* : One-way ANOVA, ** : Pearson correlation

Table 5. Number of drugs-induced xerostomia in subjects having xerostomia complaints

Number of drug-induced xerostomia intake	Number of xerostomia complaints				Correlation analysis*
	0	1	2	3	
0	8	7	2	1	r = 0.86 p value = 0.86
1	8	7	9	5	
>2	12	4	9	4	
n	28	18	20	10	

* Spearman correlation

between xerostomia and condition of hyposalivation in this study (R square = 0.02, p value = 0.8, Pearson correlation). It was also confirmed that there was no significant difference between mean value of USSFR and xerostomia complaints (p > 0.05, one-way ANOVA) (Table 4) and there was also no correlation between number of drugs-induced xerostomia intake and xerostomia complaints (r = 0.86, p value > 0.05) (Table 5).

DISCUSSION

Saliva plays a very important role in maintaining an individual's oral mucosa health. Aging was considered to be the cause of reduction of salivary function, although it is now accepted that the production of saliva and its composition are actually not influenced by age in healthy people.[8,12] Reduction in salivary function in the elderly is usually correlated with the effects of systemic diseases and the related medications. It is very common to find complaints of dry mouth or so called xerostomia, a consequence of reduction of salivary flow rate or hyposalivation, in the older people. Many studies and reviews have shown information about the correlation between quantity and quality of saliva in the elderly in relation to the systemic diseases and medication intake.[13-15] Similar reports or reviews in relation to Indonesia are not well documented, therefore this study provided additional information regarding elderly in Indonesia.[16]

This study focused on the elderly population attending Geriatric Outpatient Clinic in the Cipto Mangunkusumo Hospital in Jakarta, Indonesia. This was a small survey study only sampled elderly population who came to Cipto Mangunkusumo Hospital, since basic information about salivary profile in the elderly in terms of salivary pH, buffering capacity and flow rate in relation to systemic diseases and medication intake has not been available. Since Cipto Mangunkusumo Hospital is a type A general hospital with many patients referred from different part of Indonesia, data generated from this study might be useful as baseline. Further multicenter study using bigger sample size should be done to generalize the condition of Indonesian elderly.

Medication intake was analyzed based on the type of medication and the number of medications used. Several reviews have listed names of drugs that induced xerostomia.[12] The salivary profile was also analyzed to see the possible correlation with xerostomia complaints. It showed that the types of medication having influences to xerostomia were antihypertensive, bronchodilators, diuretics, antidepressants and cytokines, as previously published.[12,17] Many subjects in this study took more than one type of drugs that could induce xerostomia, which is in line with other study and the subjects were divided into three groups (Table 3). Mechanism behind this phenomenon might be resulted from synergistic effect of different drugs consumed by the patients. Differences at the number and type of drugs consumed by the subjects of the study showing

importance of thorough assessment of patients' medical history. This information could be useful for the dentist to find out the results of presence oral complaints.

The mean salivary pH for the whole subjects in this study was moderately acidic while having low salivary buffering capacity. However, there was no difference in salivary pH and buffering capacity between the three groups of subjects in this study ($p>0.05$). Although the difference was not statistically significant, changes in pH and buffering capacity would have role in the presence of diseases or conditions found in the oral cavity of this group of population. Possible explanation might be based on the fact that remineralization of teeth structure in the oral cavity is sustained by the presence of calcium and phosphate ions in the saliva that would happen in neutral salivary pH.[8] Several oral conditions have been found in the subjects of this study as previously published.[2] Further analyzes of salivary profile might be needed to elucidate other possible factors influencing those oral findings.[2] The status of important enzymes, immunoglobulin A, lactoferrin, histatins and defensins that would provide antimicrobial activity of the saliva that protects oral mucosa and the teeth from dangerous agents as well as providing lubrication to helps chewing, swallowing, speech and preventing trauma to the oral tissue.[8]

Xerostomia complaints found in this study were not correlated with the mean USSFR. It is a common oral discomfort symptom related to elderly population and could potentially be problematic.[16,18] Although it is a clinical complaint, many cases found to have been correlated with dysfunction of salivary gland. This study has found that 76% of subjects having xerostomia complaints, although only 37% of those were having hyposalivation. Subjects who were not found to have hyposalivation should be encouraged to do several preventive measures of hyposalivation. Recently, the use of 1% malic acid was proven to increase salivary flow rate in patients consuming antihypertensive drugs.[19] The ones who have true hyposalivation should be considered to be treated aiming to reduce the symptoms, increase salivary flow rate or to use saliva substitute.[10,20]

Drug-induced xerostomia would have impact on to the cholinergic and/or sympathetic systems of the autonomic nervous system.[12,21] Muscarinic receptors located on the cell surface are the major responsible aid for fluid secretion, while the protein secretion is controlled by adrenergic and other receptors. The stimulation of these receptors results in a complex cascade that is mediated by intracellular calcium, eventually causing saliva secretion.[21] Significant difference between number of medication intake and reduced salivary flow rate was found ($p < 0.001$) in this study. This finding is in agreement with several studies showing that medication is responsible for reduction of USSFR.[14,22] The results of this study also showed possible synergistic effect of multiple drug intake to USSFR. Possible mechanism of hyposalivation caused by medications in this study population may include dysfunction in neurotransmitter receptors, destruction or disorder of the parenchymal salivary gland, dysregulation of immune system, DNA damage and alterations in fluid and electrolytes or combination of them.[10]

It is important to consider applying modification when choosing type of drugs in the elderly, since the systemic treatment is usually for a long term one. This might have influenced the findings of oral health problems related to xerostomia and/or hyposalivation in the elderly. Management of patients having complaints of xerostomia and/or hyposalivation should be designed based on the underlying causes, which might not be applicable for every problem. However, it is important consider the quality of life of the elderly who is already a frail individual and is having many systemic diseases and medication usage.

In conclusion, medications intake influenced salivary profile and had more effect in changes in salivary flow rate than to salivary pH and buffering capacity in this elderly population. The types of medication having influences to xerostomia were antihypertensive, bronchodilators, diuretics, antidepressants and cytokines.

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