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MANAGEMENT OF SEVERE XEROSTOMIA AND ORAL CANDIDIASIS IN PATIENT WITH VALVULAR HEART DISEASE: A CASE REPORT

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ABSTRACT
Background*: Valvular heart disease is a heart valve disorder that needs complex multiple medications by administering certain drugs that cannot be replaced with other drugs because of different mechanisms of action. Beta-blockers and Angiotensin-Converting Enzyme inhibitors are drugs of choice for valvular heart disease, with diuretics and antipsychotics can cause xerostomia. Valvular heart disease patient who has a severe infection or sepsis needs long-term antibiotic treatment. Xerostomia and long-term antibiotic treatment are predisposing factors for oral candidiasis.* ***Objective****: to discuss oral candidiasis and severe xerostomia because of multiple medications in valvular heart disease patients.* ***Case****: A 58-year-old male was referred from Cardiology and Vascular Medicine Department with a chief complaint of sore tongue and pain at swallowing since 3 days ago with dry sensation of the mouth. Extraoral examination revealed dry and exfoliative lips, intraoral examination revealed fissured and lobulated tongue and white plaques could be scraped off leaving erythematous area oropharynx and tongue. The diagnoses were oropharyngeal candidiasis and severe xerostomia score of 8 according to the Chalacombe scale.* ***Case Management****: Patient was treated with nystatin, chlorine dioxide, 0.12 % chlorhexidine digluconate mouthwash, and vaseline album. Oral candidiasis was disappeared on the 22nd day of treatment.* ***Conclusion****: Xerostomia and oral candidiasis in patients with valvular heart disease require appropriate therapy, more intensive monitoring by considering the patient's general condition, and interprofessional team collaboration in the therapy of the main disease.*

Keywords: *Oral candidiasis, Valvular heart disease, Xerostomia*
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INTRODUCTION

Xerostomia is a dry sensation in the oral cavity caused by the decline in the quantity and quality of saliva thus occurring in an individual with normal or lack of salivary flow rate (hyposalivation). This condition may be prompted by aging, dehydration, autoimmune diseases such as Sjogren's syndrome, Systemic Lupus Erythematous, endocrine disorders such as diabetes, head and neck radiotherapy, salivary gland disorders, depression, stress, infections such as hepatitis C and particular drug consumption which possesses xerogenic property.

Valvular Heart Disease is a heart condition that implicates the valve and commonly requires surgery to fix. The prevalence of the disease is 0.7% among patients with heart condition aged 18-44 years old and 13.3% among patients aged older than 75 years old. Data regarding cases of valvular heart disease in England was identified in 4 million people ranging from 75-84 years old in 2018. This condition is diagnosed in 2.5% of all population in America.4,5 Patient with valvular heart disease generally prescribed with multi-medication such as antihypertensive, diuretic, antidepressant and other drugs. Severe systemic conditions may hinder the surgery. In this condition, the use of ACE inhibitors, Angiotensin Receptor Blockers and beta blockers will be the top choice that is beneficial to reduce the symptoms. Prescription of antihypertension drugs has side effects of decreasing salivary flow and increasing the risk of candidiasis. Substitutions or prescription of other drugs without any side effect of xerostomia may not be applicable as other hypertensive therapies possess different mechanism of action, therefore its use depends on the condition of the patient.2,6,7 Diuretic prescription may also induce xerostomia, but this drug is essential to limit and maintain the volume of liquid in the body so that it cannot be halted during the treatment.6,7 This condition consequently requires therapies to manage xerostomia as well as oral candidiasis for better result

without aggravating patient's condition. Heretofore, not many articles discuss about the management of xerostomia and oral candidiasis in patient with Valvular Heart Disease. This case report aims to elaborate the effectiveness of combination therapy to manage severe xerostomia and oral candidiasis in valvular heart disease with multi-medication that induces xerostomia.

CASE

A 58-year-old male was referred from Cardiology and Vascular Medicine Department with a chief complaint of sore tongue and pain at swallowing since 3 days ago with dry sensation of the mouth. Patient was treated in Coronary Intensive Care Unit (CICU) Hasan Sadikin Hospital Bandung and diagnosed with a suspect of endocarditis infection, valvular heart disease, acute kidney injury stage 2, inflammatory anemia, sepsis shock, suspect of embolic sepsis, reticulopathy and suspect of stroke. Current therapy includes ampicillin, sulbactam, captopril, omeprazole, vitamin B6, gabapentin, furosemide and dobutamine. Laboratory result revealed a decrease in liver and kidney function based on high SGOT, SGPT, ureum, creatinine as well as high leukocyte and WBC differential count showing the presence of infection. Laboratory screening results may be observed in Table 1.

Table 1. Laboratory Screening Results

Screening	Result	Normal Value
Haematology		
Hemoglobin	L 9.4 g/dL	14 – 17 g/dL
Hematocrit	L 28.3 %	41.5 – 50.4 %
Erythrocyte	L 3.07 million /uL	4.4 – 6.0 million /uL
Leukocyte	H 12.98 10^3/ uL	4.4 – 11.3
Trombocyte	162.000/uL	150.000 – 450.000/uL
Erythrocyte Index		
MCV	92.2 fL	80 – 96 fL
MCH	30.6 pg	27.5 – 33.2 pg
MCHC	L 33.2 %	33.4 – 35.5 %
WBC Differential Count		
Total Monocyte	H 0.65 10^3/ uL	0.12-0.62 10^3/ uL
Total Neutrophil	H 11.42 10^3/ uL	1.31-6.71 10^3/ uL
Liver Function		
SGOT (AST)	H 439 U/L	15-37 U/L
SGPT (ALT)	H 125 U/L	16-63 U/L
Kidney Function		
Ureum	H 154.0 mg/dL	15.0 – 39 mg/dL
Creatinin	H 3.56 mg/dL	0.6-1.5 mg/dL
Rheumatoid Factor@	Reactive	Non-reactive

Notes : SGOT: *Serum Glutamic Oxaloacetic*, SGPT: *Serum Glutamic Pyruvic Transaminase*, MCV : *Mean Corpuscular Volume*, MCH : *Mean Corpuscular Hemoglobin*, MCHC: *Mean Corpuscular Hemoglobin Concentration*.

Extraoral examination presented anemic conjunctives, non-icteric sclera, as well as dry and exfoliative lips (Figure 1a), submandibular and submental lymph nodes showed no abnormalities. Intraoral examination resulted in the presence of purpura and petechiae on the buccal mucosa, tongue appeared fissured and lobulated with multiple white plaque that might be scrapped off leaving erythematous area (Figure 1.d). Shallow single ulcer was discovered with irregular border surrounded by erythematous area on lingual frenum (Figure 1.b), and multiple white plaque on the oropharynx (Figure 1.c). Plaque and calculus were observed at all regions of upper and lower jaws, with profunda caries on tooth 17, 36 and impacted 48. Patient was diagnosed with oropharyngeal candidiasis, severe xerostomia scored 8 at Challacombe scale, traumatic ulcer of lingual frenum, irreversible pulpitis tooth 16 and 36, impacted tooth 48 and generalized marginal gingivitis. Patient's condition on the initial visit can be seen in Figure 1.

Figure 1. Patient's condition on the first visit: a. dry and exfoliative lips (black arrow), b. ulcer on the lingual frenum (black arrow), c. white plaque on the oropharynx (black arrow), d. white plaque that might be scrapped off leaving erythematous area (black arrow) with fissures and lobules on the dorsal surface of the tongue (black circle)

CASE MANAGEMENT

Comprehensive treatment was performed by prescribing nystatin therapy 4 x 2 ml to be gargled and swallowed to manage oropharyngeal candidiasis. Chlorine dioxide containing lemon and zinc 3 x 10 ml was prescribed to be gargled and spitted to manage xerostomia, while album vaseline was applied thinly on the lips to treat exfoliative cheilitis. Patient was also advised to consult his condition to Oral Surgery and Periodontia Department for the management of irreversible pulpitis, tooth impaction and chronic marginal gingivitis.

General condition of the patient on D+4 showed some improvement (Figure 2a and b), therefore patient was subsequently transferred to *High Intensive Care* (HCU). Oral candidiasis had diminished and candidiasis at the dorsal of the tongue had improved. Extraction of tooth 48 and 16 as well as endoscopy was conducted on D+2 treatment in HCU. Patient was instructed not to eat a day prior to and after the treatment including the discontinuation of nystatin and chlorine dioxide application. This decision resulted in the recurrence of oral candidiasis (Figure 2.c and d). Patient was further arranged for lumbar punction that he was transferred to Geriatric Intensive Care Unit (GICU) and managed for 2 days. During the transfer, chlorine hexidine was not administered as there was no drug reconciliation. Intraoral examination revealed white plaque on the oropharynx and white plaque might be scrapped off leaving erythematous area on the dorsal of the tongue (Figure 2.e, f and g). Patient was then prescribed with additional therapy of chlorhexidine digluconate 0.12%. Patient's condition showed improvement on the following visit. Patient was transferred back to HCU and candidiasis had diminished after 26 days of treatment (Figure 2.h, i and j). Patient’s condition during the treatment may be observed in Figure 2.

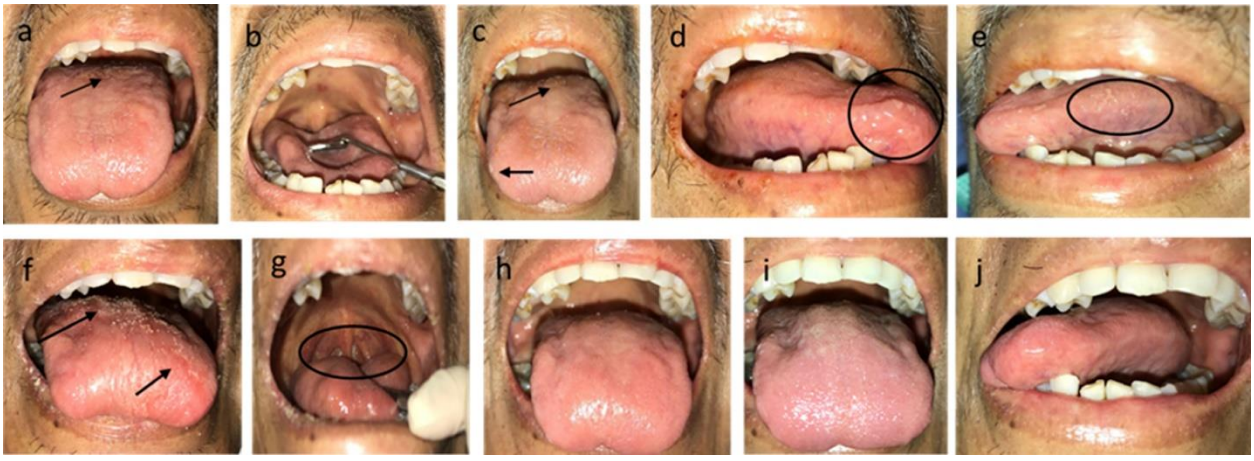

Figure 2. Patient's condition on the second day after the application of nystatin: a. white plaque on the dorsal of the tongue had diminished (black arrow), b. absence of white plaque on the oropharynx. Patient's condition after 2-day

fasting: c and d. White plaque on the dorsal of the tongue (black arrow and black circle) e. white plaque on the lateral of the tongue. Patient's condition after the discontinuation of chlorine dioxide (black circle): f. white plaque with erythematous area on the dorsal of the tongue (black arrow). g. white plaque on the oropharynx (black circle). Patient condition after additional therapy of chlorhexidine digluconate: h. absence of white plaque on the dorsal of the tongue, papilla appeared atrophic. Patient condition before the discontinuation of nystatin: i. white plaque that might be scrapped off on the dorsal of the tongue, tongue papilla had been observed on the dorsal of the tongue. j. no abnormality presented on the lateral of the tongue.

DISCUSSION

Oral cavity is covered by epithelial mucosa which functions as physical barrier to protect it from pathogens. Oral mucosa provides defenses from mechanical trauma and fungal entrance into oral mucosa by preventing the penetration of exogenous protein, inhibiting fungal proliferation and growth, as well as activating antifungal Th17 response through IL-17 expression that works synergically with antimicrobial peptides to increase the resistance and protection against infection. Oral epithelial mucosa produces antimicrobial peptides such as calprotectin, β defensin, sialo-peroxidase and cathelicidin which possess antimicrobial activity upon fungi by preventing its adhesion on the surface of epithelial cell, disrupting cell wall permeability and acting to mediates immune response through the secretion of cytokine, chemokine and arachidonic acid metabolites. Antimicrobial peptides work together with antimicrobe in saliva to foster the defense of oral cavity.[8] Saliva contains IgA, which intervene with the adherence of Candida on the oral mucosal surface, as well as antimicrobial protein and peptides such as lactoferrin, lysozyme and histatin, which are produced in salivary gland that present fungicidal and fungistatic property by inhibiting fungal adhesion and colonization on oral mucosal epithelial, inhibiting fungal growth and disrupting its cell wall.[9]

Candida is commensal microorganism in the oral cavity that may become pathogen and cause infection when there is a change in environment that promote the growth of Candida.[10] Increased incidence of Candida infection occurs as the result of several predisposing factors such as unstable and porous ill-fitting denture, xerostomia, long-term antibiotic therapy, local trauma, endocrine disorder and nutritional deficiency such as iron, folic acid, and vitamin. Oral candidiasis may induce various complaints including dysphagia, anorexia, burning sensation, dysgeusia, and weight loss thus resulting in nutritional deficiency that affects patient's quality of life.[11] Long-term use of antibiotics can lead to competitive bacterial inhibition thus providing a good environment for Candida growth.[12] Antibiotic prescription in this patient is very important because it is suspected that endocarditis infection and septic shock cannot be stopped. The patient was taking ampicillin and sulbactam since 1 month ago before being transferred to the CICU.

The patient suffered from severe xerostomia which was a predisposing factor for the occurrence of oral candidiasis. A decrease in the amount of saliva production in the oral cavity will affect the amounts of antimicrobial proteins and peptides contained in it, thereby increasing the risk of candidiasis. Drugs that may cause xerostomia include muscarinic receptor antagonists, anticonvulsants, opioids, benzodiazepines, antipsychotics, muscle relaxants, antihypertensives, and antihistamines. Antihypertensive drugs such as beta blockers, ACE inhibitors and their combination have anticholinergic properties that are competitive inhibition of acetylcholine which functions to stimulate salivary secretion produced by the parasympathetic nerves, and inhibits sympathetic nerve neurotransmission which regulates the secretion of mucin which contains antimicrobial proteins, thereby reducing the performance of salivary gland cells causing hyposalivation. Diuretic drugs such as furosemide affect the sodium-potassium-chloride cotransporter in the kidneys and other organs including the salivary glands, working by drawing fluid in and excreting it from the body. Antipsychotic drugs such as gabapentin bind to the alpha 2-delta subunit of the calcium channel gate in the dorsal horn which reduces channel opening thereby inhibiting transmission of nervous system signals.[13,14]

In this case, there was a decrease in the amount of saliva production induced by the ACE inhibitor captopril, the antipsychotic gabapentin and the diuretic furosemide, thus increasing the risk of xerostomia. Xerostomia can induce dental caries, increase the risk of candidiasis, bad breath, burning sensation in the mouth, taste disturbances, and difficulty in chewing, speaking and swallowing.[2] Candidiasis in this case was a pseudomembranous candidiasis found on the dorsum of the tongue and oropharynx. Pseudomembranous candidiasis gives clinical manifestations in the form of yellowish white plaques consisting of candida, desquamated epithelial cells, fibrin, inflammatory cells and debris on the mucosa which can be cleaned by means of a scraping, leaving the mucosal surface reddish or bleeding underneath, may be accompanied by pain or burning, most commonly often found on the tongue, palate and buccal mucosa. The diagnosis of pseudomembranous candidiasis is generally based on clinical criteria, confirmed by microscopic examination using KOH

or culture. Candidate identification can be done by cytological examination with periodic acid Schiff and/or Papanicolaou staining.[11]

Fluconazole, which belongs to the triazole group, is an option for the treatment of oropharyngeal candidiasis especially the pseudomembranous type, but presents with hepatotoxic side effects. Hepatotoxicity of this drug category causes liver damage which is characterized by an increase in the level of SGOT and SGPT, namely serum alanine transaminase (ALT) or serum aspartate transaminase (AST) more than three times higher of the normal value, alkaline phosphatase (ALP) more than twice higher of the normal value, or the total bilirubin level more than twice higher of the normal value.17 The patient in this case had liver problems which was characterized by an increase in the SGOT level of 11 times above the normal value, while the SGPT value was 1.98 times above the normal values, so the chosen antifungal drug is nystatin. Nystatin is the first-line antifungal drug to treat oral candidiasis, because it is less or not absorbed by the intestinal tract and most of the antifungals are excreted unchanged, so they do not demonstrate hepatotoxicity side effect.

The use of nystatin is highly dependent on adherence to medication by the patient because it has an unpleasant taste, in addition, the lubrication and maintenance of saliva causes the nystatin suspension to be swallowed quickly resulting in better efficiency.[15,16] The administration of nystatin gives good results, but after 6 days of use, the patient requires endoscopy and root extraction, so fasting and nystatin is stopped for 2 days, this results in worsening of oral candidiasis. Continuing the management of giving nystatin back was an option due to liver problems in this patient. Discontinuation of chlorine dioxide for 2 days caused xerostomia to recur and oropharyngeal candidiasis remission, so chlorhexidine digluconate gargle was added, which provided good results.

Chlorhexidine is a cationic antiseptic, which binds to the oral mucosa, has bacteriostatic and fungistatic activity. Chlorhexidine contains dicationic chlorophenyl biguanide which binds non-specifically to proteins and phospholipids of the cell wall structure of bacteria and fungi, thereby changing surface tension and disrupting metabolism and causing cell death. The cationic nature of chlorhexidine allows it to bond with the surface of the teeth and oral mucosa that may inhibit the attachment and interfere with the growth of bacteria and fungi. A total of 30% from the total dose of chlorhexidine is retained in the oral cavity for 24 hours after gargling for 1 minute, but most is lost within the first hour due to dilution and self-cleaning by saliva.[17-21] The use of chlorhexidine should not be more than 2 weeks because it can cause an imbalance of the biofilm layer in the oral cavity. In addition, the biofilm which contains saliva and bacterial glycoproteins has a function to maintain moisture by retaining water content so that long-term use of mouthwash is one of the risk factors for the occurrence of xerostomia.[1,21] In this case, the patient was given 0.12% chlorhexidine digluconate and nystatin in alternating times to amplify the antifungal effect. Research by Scheibler et al. in 2018 and Baldino et al. in 2020 showed that antagonistic interactions between nystatin and chlorhexidine caused a decrease in pharmacological effects when used together in less than 30 minutes. A sufficient time interval is needed to maintain the effectiveness of the drug combination.[22,23] The effectiveness of the combined administration of chlorhexidine and nystatin for oral candidiasis therapy in immunocompromised patients was reported by Amalia et al in 2019.[24]
Eliminating predisposing factors is part of therapy. Although discontinuation or replacement of ACE inhibitors, anticonvulsants and diuretics as well as discontinuation of long-term antibiotics in this case was unattainable, other predisposing factors such as xerostomia can be removed. Management of xerostomia aims to reduce complaints and increase salivary flow, among others, by increasing hydration, avoiding foods or products that irritate the oral mucosa that cause pain. Giving mouthwash containing chlorine dioxide containing xylitol and zinc acetate is one option in overcoming xerostomia. Chlorine dioxide maintains a normal pH in the oral cavity is an oxidizing agent that is bactericidal, viricidal and fungicidal, inhibiting microbial growth by interfering with nutrient transport through cell membranes. Zinc acetate keeps the oral cavity moist, while xylitol is antimicrobial which reduces the risk of infection in the oral cavity due to xerostomia. Aloe vera reduces inflammation, irritation and pain. The lemon contained in it stimulates saliva production and gargling activity can stimulate a temporary increase in salivary flow, thereby reducing the risk of infections such as oral candidiasis.[21,25–27]

The combination of multiple medications in valvular heart disease patients with long-term use of antibiotics has a high potential for xerostomia in the oral cavity, which can pathogenic transformation of Candida because of its opportunistic nature. Eliminating predisposing factors is one part of therapy, but discontinuation of a causative drug is not always possible. Oral candidiasis and severe xerostomia in patients with valvular heart disease require appropriate therapy, more intensive monitoring, taking into account the general condition of the patient and interprofessional teamwork in treating the main disease. Good coordination and cooperation between related disciplines is very important for the care of patients with a diagnosis of valvular heart disease.

REFERENCES

1. Chevalier M, Sakarovitch C, Precheur I, Lamure J, Pouyssegur-Rougier V. Antiseptic mouthwashes could worsen xerostomia in patients taing polypharmacy. Acta Odontol Scand. 2015 May;73(4):267-73.
2. Barbe AG. Medication-Induced Xerostomia and Hyposalivation in the Elderly: Culprits, Complications, and Management. Drugs Aging. 2018 Oct;35(10):877-885.
3. Nadig SD, Ashwathappa DT, Manjunath M, Krishna S, Annaji AG, Shivaprakash PK. A relationship between salivary flow rates and Candida counts in patients with xerostomia. J Oral Maxillofac Pathol. 2017 May-Aug;21(2):316.
5. Iung B, Vahanian A. Epidemiology of valvular heart disease in the adult. Nat Rev Cardiol [Internet]. 2011;8(3):162–72.
6. Eacts CS, Germany CH, Rosenhek R, France EL, Rodriguez D, Tornos P, et al. 2017 ESC / EACTS Guidelines for the management of valvular heart disease The Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European. 2017. 2739–2791 p.
7. Balakumar P, Kavitha M, Nanditha S. Cardiovascular drugs-induced oral toxicities: A murky area to be revisited and illuminated. Pharmacol Res. 2015 Dec;102:81-9.
8. Feller L, Khammissa RA, Chandran R, Altini M, Lemmer J. Oral candidosis in relation to oral immunity. J Oral Pathol Med. 2014 Sep;43(8):563-9.
9. Bergmeier LA. Oral Mucosa in Health and Disease. Vol. 2, Medical Journal of Australia. Springer International Publishing; 2018: 881–881 p.
10. Williams D, Lewis M. Pathogenesis and treatment of oral candidosis. J Oral Microbiol. 2011;3:10.3402/jom.v3i0.5771.
11. Kohli S, Shinde CV. Candidiasis and Oral Cavity : A Review. Int J Res Rev. 2019;6(5):336–7.
12. Mason KL, Downward JRE, Mason KD, Falkowski NR, Eaton KA, Kao JY, et al. Candida albicans and bacterial microbiota interactions in the cecum during recolonization following broad-spectrum antibiotic therapy. Infect Immun. 2012;80(10):3371–80.
13. Einhorn OM, Georgiou K, Tompa A. Salivary dysfunction caused by medication usage. Physiol Int. 2020;107:195–208.
14. Turner MD. Hyposalivation and Xerostomia: Etiology, Complications, and Medical Management. Dent Clin North Am. 2016 Apr;60(2):435-43.
15. Garcia-Cuesta C, Sarrion-Pérez MG, Bagán JV. Current treatment of oral candidiasis: A literature review. J Clin Exp Dent. 2014 Dec 1;6(5):e576-82.
16. Epstein JB, Beier Jensen S. Management of Hyposalivation and Xerostomia: Criteria for Treatment Strategies. Compend Contin Educ Dent. 2015 Sep;36(8):600-3.
17. Pakfetrat M, Nikoo MH, Malekmakan L, Tabande M, Roozbeh J, Reisjalali G, *et al*. Risk Factors for contrast-related acute kidney njury according to risk, injury, failure, loss, and end-stage criteria in patients with coronary interventions. Iran J Kidney Dis. 2010 Apr;4(2):116-22.
18. Rao PK, Chatra L, Shai P, M VK. Oral Candidiasis – A Review. J Indian Dent Assoc. 2013;(5):8–13.
19. Ellepola ANB, Joseph BK, Khan ZU. Cell surface hydrophobicity of oral Candida dubliniensis isolates following limited exposure to sub-therapeutic concentrations of chlorhexidine gluconate. Mycoses. 2013;56(1):82–8.
20. Fathilah AR, Himratul-Aznita WH, Fatheen AR, Suriani KR. The antifungal properties of chlorhexidine digluconate and cetylpyrinidinium chloride on oral Candida. J Dent. 2012 Jul;40(7):609-15. d
21. Yadav SR, Kini VV, Padhye A. Inhibition of Tongue Coat and Dental Plaque Formation by Stabilized Chlorine Dioxide Vs Chlorhexidine Mouthrinse : A Randomized , Triple Blinded Study. J Clin Diagnostic Res. 2015;69–74.
22. Baldino MEL, Medina-Silva R, Sumienski J, et al. Nystatin effect on chlorhexidine efficacy against Streptococcus mutans as planktonic cells and mixed biofilm with Candida albicans. Clinical Oral Investigations. 2021 Jun. DOI: 10.1007/s00784-021-04041-0.
23. Scheibler E, da Silva RM, Leite CE, Campos MM, Figueiredo MA, Salum FG, Cherubini K. Stability and efficacy of combined nystatin and chlorhexidine against suspensions and biofilms of Candida albicans. Arch Oral Biol. 2018 May;89:70-76.
24. Amalia T, Setiadhi R. Terapi Kandidiasis pada Anak dengan Lupus Eritematosus Sistemik disertai Ko-infeksi Tuberkulosis. J Kedokt Gigi Univ Padjadjaran. 2019;31(3):201–6.
25. Sung E, Hernawan I. Tatalaksana serostomia akibat penggunaan metformin: laporan kasus (Management of metformin-

induced xerostomia: case report). MDJ (Makassar Dent Journal). 2018;7(1):14–20.
26. Nugraha AP, Ernawati DS, Harijanti K, Parmadiati AE. Psychological Induced Xerostomia and Hyposalivation: The Case Study in Indonesian Female Patient. J Int Dent Med Res 2019; 12(1): 216-219
27. Asmi Usman N, Hernawan I. Tata Laksana Xerostomia Oleh Karena Efek Penggunaan Amlodipine: Laporan Kasus. Insisiva Dent J Maj Kedokt Gigi Insisiva. 2017;6(2). https://doi.org/10.18196/di.6284