"Case Report"

Management of Xerostomia and Hyposalivation in Hypertensive Patient's Using Candesartan Cilexetil

Shely Wandhila1, Dwi Suhartiningtyas2
1School of Dentistry, University of Muhammadiyah Yogyakarta, Special Region of Yogyakarta, Indonesia
2Department of Oral Medicine, Faculty of Dentistry, University of Muhammadiyah Yogyakarta, Special Region of Yogyakarta, Indonesia
Corresponding author: shely.w.fkik21@mail.umy.ac.id

Abstract

Saliva’s disorder and dry mouth (xerostomia) are related to routine medication as antihypertensives. Candesartan cilexetil is an angiotensin receptor blocker (ARB) hypertension drug that indirectly affects saliva by changing fluid and electrolyte balance. To examine the management of xerostomia and hyposalivation in hypertensive patients due to use of candesartan cilexetil. A 70 year old female patient complained her mouth felt dry since 1 year ago when she was diagnosed with hypertension. The patient consumes candesartan cilexetil once daily, 8 mg. Intra oral showed were edentulous areas on the entire upper and lower jaw with the patient's oral mucosa being dry, saliva thick, sticky and frothy. In this case, saliva’s rate measurement showed a result of 0.16 mL/minute. After intervention using dry mouth gel for two weeks, a saliva rate of 0.38 mL/minute. During the control, patient didn’t complaining dry mouth. This is accordance with the literature, dry mouth gel can improve signs and symptoms of dry mouth a and increase the patient's ability to swallow. Patient’s take antihypertensive drugs have manifestations in form of xerostomia. The treatment carried out to improve the condition of patient's oral cavity is providing education on maintaining healthy teeth as well as using dry mouth gel applied to the entire oral mucosa. In this case, an increase salivary rate from 0.16 mL/minute to 0.38 mL/minute. The concluded, use of dry mouth gel is effective in treating xerostomia and can increase the rate of saliva in the oral cavity.

Keywords: candesartan cilexetil, hypertension, dry mouth gel, salivary flow rate

INTRODUCTION

Saliva is a fluid in the oral cavity that can reflect a person's body condition and has an important role in oral health. Saliva is clear and contains water with a pH of 6-7 which is secreted by the parotid, submandibular, sublingual glands and several small glands in the oral cavity. The rate of saliva secretion is regulated by the autonomic nervous system through specific receptors found in the salivary glands. This secretion can be stimulated by neurotransmitters found in the sympathetic and parasympathetic nerves. Stimulation of the sympathetic nerves can influence the composition and protein content in saliva, while stimulation of the parasympathetic nerves affects the performance of saliva secretion. In elderly patients, saliva has an important role related to the health of their oral cavity. Elderly patients begin to experience changes in the composition and production of saliva so that it cannot function properly. This complaint, which is usually complained of by elderly patients, is also called dry mouth (xerostomia). Xerostomia is a symptom that is defined as a person's perception of a dry mouth and may or may not be related to a decrease in the rate of saliva flow (hyposalivation). Examination of the oral cavity is very important in identifying clinical signs that are pathognomonic for hyposalivation. Several signs have been proposed by Osailan at al., (2011), there are several signs including: (1) sticking of the mouth mirror to the intraoral mucosa of the buccal side and tongue, (2) no saliva pooling on the floor of the mouth, (3) loss of the dorsum of the tongue, (4) foamy saliva, (5) the tongue is lobed or cracked, (6) the oral mucosa,
especially the palate, looks shiny, (7) the gingival architecture is changed/smooth, (8) there is caries on the cervix of more than two teeth, (9) mucosal flakes on the roof of the mouth (except the area covered by the denture plate)\(^5\).

The normal stimulated saliva flow rate is 1.5-2.0 mL/minute while the unstimulated saliva flow rate is approximately 0.3-0.4 mL/minute. The most common causes experienced by patients are related to hyposalivation due to the consumption of certain routine medications such as anticoagulants, antidepressants, antihypertensives, anti-inflammatory drugs, hypoglycemics, levothyroxine, supplements and vitamins and steroid inhalers\(^6\).

Antihypertensive drugs are drugs that are often used in patients with hypertension to reduce the frequency of strokes, coronary heart events and kidney failure. Based on the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNC), hypertension is a condition where blood pressure is ≥ 140 mmHg. Antihypertensive drugs have an elimination pathway that leads to the kidneys, so they can affect the accumulation of chemicals that can worsen the prognosis in the kidneys. Considering this prognosis requires attention in selecting antihypertensive drugs that are good for the kidneys. Based on recommendations by the Eighth Joint National Committee and the Guidelines of Clinical Care Ambulatory, the initial option for using antihypertensive drugs is an Angiotensin Converting Enzyme Inhibitor (ACEI) or Angiotensin Receptor Blocker (ARB) \(^7\). \textit{Candesartan cilexetil is an antihypertensive drug from the type I angiotensin II receptor antagonist (ARB) class. ARB has a mechanism of action by interacting with amino acids in the transmembrane domain which can prevent angiotensin II from binding to its receptor. Antagonism of angiotensin II will directly cause vasodilation of blood vessels, decreased blood pressure, water, glucose and blood salt. This class of drugs will indirectly affect saliva by changing fluid and electrolyte balance}\(^8\).

**CASE REPORT**

A 70-year-old female patient came complaining that her mouth felt dry. This complaint began one year ago when the patient started taking routine antihypertensive medication. The dry mouth that patients complain about is felt every day. The patient feels a little saliva in his mouth. The patient does not complain of a burning sensation in the oral cavity, does not feel hot in the oral cavity and sometimes only feels his lips are dry.

Based on the oral health history, the patient no longer has any teeth and has been routinely cleaning his gums and complete dentures 3 times a day, in the morning after breakfast, when showering and at night before bed. Patients have admitted that they clean the oral cavity only with their fingers smeared with toothpaste. Then clean the dentures with a toothbrush that has soft bristles.

The patient has a history of hypertension which was diagnosed 1 year ago. The patient has been taking antihypertensive medication in the form of candesartan cilexetil 8 mg once a day since being diagnosed with hypertension until now. The patient admitted that he had reduced eating oily and sweet foods. The patient routinely consumes approximately 3 liters of mineral water every day. The patient also routinely exercises every Saturday morning as an active elderly person.

Objective examination showed that blood pressure at the time of examination was 128/83 mmHg and pulse 70x/minute.
Intraoral examination showed edentulous areas throughout the upper and lower jaw (Figure 1). The patient's oral mucosa is dry with thick, sticky and foamy saliva. The provisional diagnosis in this case is xerostomia with a treatment plan consisting of administering a questionnaire and examining the unstimulated salivary flow rate.

![Intraoral clinical photo of the patient](image1)

### MANAGEMENT

**First Visit**

After carrying out subjective and objective examinations, establishing a diagnosis and treatment plans, the patient is given several questionnaires and an unstimulated salivary flow rate examination. Questionnaire indicators according to Fox., et al (1987) used with patients are as follows:

<table>
<thead>
<tr>
<th>No</th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is the amount of saliva in your mouth too little most of the time?</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Do you have difficulty swallowing dry food?</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>3</td>
<td>Does your mouth feel dry when eating a meal?</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Do you sip liquid to aid in swallowing dry food?</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

Then an Unstimulated Salivary Flow Rate examination is carried out (Figure 2). Based on examination of the unstimulated saliva flow rate, the results were 0.8 mL/5 minutes or 0.16 mL/minute (Figure 3). The diagnosis was made again after examining the patient, namely xerostomia accompanied by hyposalivation. The prognosis for this condition is good if the patient is given dry mouth gel which is applied to the oral cavity in the edentulous area, right and left inner cheeks and upper and lower inner lip areas. The dry mouth gel was given for 3 weeks, then the patient underwent control and evaluation.

![Observation stage](image2)

**Observation stage**

GC Dry Mouth Gel is given 6 times a day at the following times: (1) in the morning when you wake up, (2) at 09.00, (3) at 12.00, (4) at 15.00, (5) at 18.00, (6) before sleep. The gel application is taken the size of a red bean and then rubbed throughout the oral cavity, namely on the
edentulous area, right and left inner cheeks and upper and lower inner lip areas.

One week and two weeks after using the dry mouth gel, the patient's unstimulated saliva flow rate was measured using the same method and technique as during the first visit. The results of measurements in the first week of use, the unstimulated saliva flow rate showed results of 1 mL/5 minutes or 0.2 mL/minute. Two weeks after use, unstimulated saliva flow rate measurements showed results of 1.4 mL/5 minutes or 0.28 mL/minute.

**Second Visit**

The patient came after 3 weeks for control after three weeks ago the patient complained of dry mouth. The patient has felt that his oral cavity is moist and there is more saliva. The patient has smeared his oral cavity according to the instructions. The patient felt more comfortable after being smeared with the gel provided. At this visit, a questionnaire was given again and an Unstimulated Salivary Flow Rate examination was carried out (Figure 4) for evaluation with results of 1.8 mL/5 minutes or 0.38 mL/minute. The questionnaire indicators given to patients are as follows:

<table>
<thead>
<tr>
<th>No</th>
<th>Question</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is the amount of saliva in your mouth too little most of the time?</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>2</td>
<td>Do you have difficulty swallowing dry food?</td>
<td></td>
<td>√</td>
</tr>
<tr>
<td>3</td>
<td>Does your mouth feel dry when eating a meal?</td>
<td></td>
<td>√</td>
</tr>
</tbody>
</table>

Objective examination showed the patient's blood pressure was 124/79 mmHg and pulse 87 x/minute. Intraoral examination showed that the patient's oral mucosa was much moister, the saliva was clearer and thinner than before (Figure 5).

Figure 4. First visit saliva rate examination placed into the syringe

Figure 5. Intra-oral clinical photos during control

The diagnosis of this condition is hyposalivation with treatment plans in the form of IEC and evaluation. At this visit, the patient is instructed to continue applying dry mouth gel according to the previously scheduled time to keep the oral cavity moist because the patient continues to consume xerogenic drugs.

**DISCUSSION**

Hypertension is a condition where blood pressure in the arteries increases. Hypertension has a systolic blood pressure value > 140mmHg and/or diastolic blood pressure > 90mmHg. With regard to the current management of hypertension, among the antihypertensive drugs used are angiotensin-converting enzyme (ACE) inhibitors.
inhibitors, angiotensin inhibitors, beta blockers, calcium channel blockers and diuretics. Antihypertensive drugs are a type of drug that elderly people often take to lower blood pressure.

The antihypertensive drug consumed by the patient in this case was candesartan cilexetil. Candesartan cilexetil is a drug with a high level of popularity on the market. This hypertension drug is very selective, has high potency and has a long duration of action. Several clinical trials have stated that the drug is effective in reducing the risk of death, stroke, kidney failure, heart failure, arterial stiffness, retinopathy and migraines.

Angiotensin receptor blocker drugs such as candesartan cilexetil work selectively and non-competitively on angiotensin type 1 (AT1) receptors. Angiotensin receptor blockers (ARB) are a class of hypertension drugs that inhibit the specific angiotensin II-AT1 receptor. The clinical effect of ARB is the ability to block the interaction of angiotensin II with the AT1 receptor in the target tissue. The tissues targeted are the afferent and afferent arterioles of the kidney, vascular smooth muscle, and the zona glomerulosa of the adrenal glands.

Prototype drugs targeting ACE1 (ACE inhibitors) and Ang II receptor blockers (ARBs) stimulate Ang II receptors in various end organs, including the vasculature, adrenal cortex, and central nervous system. The results of this action can cause vasoconstriction of blood vessels, the release of aldosterone from the adrenal cortex, which binds to receptors in the kidneys and increases sodium and water retention. The release of vasopressin from the posterior pituitary, causes further vasoconstriction and can cause water retention. In addition, it can also cause inflammation with possible alveolar bone resorption as well as stimulation of the sympathetic nervous system in the brain and spinal cord. ACE inhibitors block the synthesis of Ang II, which explains many of the beneficial effects of these drugs in the treatment of cardiovascular diseases. The ability of ACE inhibitors to block bradykinin inactivation causes additional vasodilation but explains many of the potential side effects of these drugs, including dry cough and rare cases of angioedema. In contrast to ACE inhibitors, ARBs do not increase bradykinin levels. The ACE2 products angiotensin 1–7 are breakdown products of bradykinin and oppose the vasoconstrictive action of Ang II. It also has cytoprotective and anti-inflammatory actions. Directly, the drug can influence the rate of saliva and can mimic the action of the autonomic nervous system by interacting with the cellular processes required by saliva. Meanwhile, indirectly, the drug can affect fluid and electrolyte balance by affecting blood flow to the glands.

Xerostomia or dry mouth sensation is a subjective symptom that is related or not related to reduced saliva production. Complaints of xerostomia are often experienced by 50% of elderly people aged over 60 years. Xerostomia affects the perception of oral health and is associated with a burning sensation in the mouth and halitosis. It can also cause carious lesions and periodontal disease, taste disorders, candidiasis, dysphagia, and speech difficulties. Xerostomia that occurs in the elderly can occur due to consumption of drugs such as anticoagulants, antidepressants, antihypertensives, anti-inflammatory drugs, hypoglycemics, levothyroxine, supplements and vitamins and steroid inhalers.

Making a diagnosis related to xerostomia in patients is based on a questionnaire proposed by Fox et al (1987) with several questions including: (1) Is the
amount of saliva in your mouth too little? (2) Do you have difficulty swallowing? (3) Does your mouth feel dry when eating? (4) Do you drink fluids to help swallow dry food? An affirmative answer to any of these questions is sufficient to make a diagnosis of xerostomia.

Xerostomia is still a heavy burden for some people who experience it. In particular, this can affect the function of speaking, mastication, swallowing, wearing dentures, and the sufferer's daily activities. Xerostomia is closely related to low saliva rate (hyposalivation), so saliva rate measurements can be carried out to determine saliva production in the patient's oral cavity. Salivary rate measurements are usually measured at least 5 minutes after not eating or drinking overnight or 2 hours after eating. The rate of unstimulated saliva is assessed with the patient sitting in an upright position and then the patient is instructed to collect it in the oral cavity. After 5 minutes, the patient can collect his saliva into the container provided.

Dry mouth gel is a synthetic saliva replacement product which functions to moisten the oral cavity area. This gel has a neutral pH and contains carboxymethyl cellulose which has a viscosity like saliva. Dry mouth gel also has a polymer base of glycerate and mucopolysaccharide which can cause the oral mucosa to become moist. In this patient's case, there was an increase in saliva rate from 0.16 mL/minute, then intervention was given with dry mouth gel for three weeks when the control level became 0.38 mL/minute. In accordance with the literature, artificial saliva can improve signs and symptoms of dry mouth and increase the patient's ability to swallow.

CONCLUSION

Patients who take antihypertensive drugs are at risk of manifestation in the form of xerostomia, which is characterized by a decrease in salivary flow rate. Treatment that can be done to improve the condition of the patient's oral cavity so that it doesn’t cause complications is to provide education to maintain healthy teeth and mouth. In addition, patients are instructed to wear dry mouth gel which is applied to the entire oral mucosa. In this case, there was an increase in saliva rate from 0.16 mL/minute to 0.38 mL/minute during the three weeks of intervention. So it can be concluded that the use of dry mouth gel is effective in treating xerostomia and can increase the rate of saliva in the oral cavity.

ACKNOWLEDGEMENT

Researchers would like to thanks for drg. Dwi Suhartiningtyas, MDSc, Dentist Professional Education Study Program, Faculty of Dentistry, Muhammadiyah University of Yogyakarta for the guidance in solving this clinical case.

REFERENCE

4. de Mendonça Guimarães, D. et al.


