"Literature Review"

Correlation of Antihypertensive Drugs Ca-Antagonist Amlodipine with Xerostomia

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Abstract

Xerostomia is defined as a subjective complaint of dry mouth. Interestingly, patients complaining of dry mouth often have no objective signs of decreased salivation and their symptoms vary. May be secondary to qualitative and/or quantitative factors. changes in the composition of saliva. Normal stimulated salivary flow averages 1.5-2.0 ml/min while unstimulated salivary flow is about 0.3-0.4 ml/min. This review aimed to determine the correlation between the Ca antagonist of the antihypertensive drug (Amlodipine) and xerostomia through a literature review conducted by researchers which was used as a reference for making this literature review. Data were obtained by data collection methods related to the study being studied and analyzed descriptively. Several studies show that there are differences in prevalence between genders and xerostomia appears to increase with age. A possible explanation is that older people are at risk due to some xerogenic medications for their chronic conditions and this may cause an overall decrease in the rate of unstimulated saliva flow. Xerostomia remains a common unresolved complaint especially among the geriatric population, despite efforts for medical or dental consultation. It was concluded that Ca-Antagonist antihypertensive drugs (amlodipine) were associated with xerostomia.

Keywords: Xerostomia; Antihypertensives; Hyposalivation; Salivary Flow; Hypertension

INTRODUCTION

Xerostomia (dry mouth) is a dryness in the mouth due to sufficient saliva secretion or a lack of saliva1. Xerostomia is a subjective complaint of dry mouth, while hyposalivation is an objectively reduced salivary flow2. The diagnosis of xerostomia and hypofunction of the salivary gland requires a thorough medical history. Special attention should be paid to symptoms, drug use, and past medical history. Patients with salivary hypofunction usually complain of dry mouth, difficulty swallowing, and/or speaking; they have difficulty tolerating spicy, sour, and roasted foods, and they often report changes in taste or difficulty wearing fake teeth. Several questionnaires have been submitted to identify patients with xerostomia and hyposalivation2.

Fox et al. developed a questionnaire on the severity of dry mouth that could predict the actual hyposalivation. A positive answer to all the questions was associated with a low rate of salivary flow3. Saliva plays an important role in keeping your mouth healthy. Water is the main component of saliva, which accounts for 99% of its volume. Other components, consisting of the remaining 1%, include the inorganic salts of sodium, potassium, calcium, and magnesium, as well as organic compounds such as cholesterol, uric acid, and protein (enzymes)1.

Hypertension (HT) is a chronic medical condition in which the arterial blood pressure is elevated. HT is currently defined as systolic blood pressure > 140 mmHg and/or diastolic blood pressure > 90 mmHg. Non-pharmacological therapy with appropriate lifestyle modifications is recommended for all HT patients. Additionally, antihypertensive drugs are
recommended in many cases and should be considered in other cases where blood pressure has not reached its target despite having been given non-pharm therapy.4

Signs of hyposalivation and xerostomia include: smooth and smooth gums; loss of papillae in the dorsal part of the tongue; broken or fuzzy tongues; foaming saliva; no or little accumulation of saliva in the bottom of the mouth; more than two cervix caries; slime fragments in the ceiling of the oral cavity; and the sticking of a dental mirror to a tongue or mucous mucosa.5 Xerostomia and hyposalivation can have a negative impact on the quality of life of the patient, causing situations such as stress or anxiety. In addition, a decrease in saliva flow can increase susceptibility to tooth decay or fungal infections of the mouth, so this condition should be considered critical.6 More than a thousand drugs have been linked to xerostomia. Tricyclic antidepressants, muscarinic receptor antagonists, antipsychotics, opioids, benzodiazepines, antihypertensives, and antihistamines are the main drugs that produce these effects.7

METHOD

This research is a literature review. The data search was done in three databases: PubMed, Science Direct, and Google Scholar. Additional literature is taken from the bibliography of the entire relevant article. A comprehensive literature search was conducted from 1987 to 2022. The literature used is English and Indonesian.

RESULTS

DIAGNOSIS OF XEROSTOMIA AND SALIVA HYPOSALIVATION

Xerostomia occurs in 5.5% to 46% of the population and is most common in older adults. Xerostomia is also more common in women than in men. It can occur due to inadequate salivary secretion due to abnormal spleen gland function. Most patients with xerostomia often have no objective signs of hyposalivation.8 A xerostomia, or dry mouth, is diagnosed based on several questions:

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<thead>
<tr>
<th>No</th>
<th>Questions</th>
<th>Yes</th>
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<tbody>
<tr>
<td>1.</td>
<td>Does your mouth usually feel dry?</td>
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<td>2.</td>
<td>Does your mouth feel dry while eating?</td>
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<td>3.</td>
<td>Do you have trouble swallowing dried food?</td>
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<td>4.</td>
<td>Do you drink liquids to help swell dry food?</td>
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<td>5.</td>
<td>Is the amount of saliva in your mouth too little?</td>
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<td>6.</td>
<td>Does your mouth feel dry right now?</td>
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<td>7.</td>
<td>Do you wake up at night to drink water?</td>
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A positive answer to one of these questions is enough to make a diagnosis of xerostomia.9

The normal salivation rate when stimulated is between 1.5 and 2.0 mL/min, and if not stimulated, the flow rate is between 0.3 and 0.4 mL/min. Hyposalivation refers to the rate of stimulated saliva flow of <0.5 to 0.7 mL/min and the unstimulated salivary flow rate of <0.1 mL/min, measured when the patient is sitting upright.5

Subjective sensations of xerostomia can occur in patients taking blood pressure-regulating drugs, antidepressants, or immunosuppressive drugs that cause a decrease in blood flow through the salivary glands, which can lead to reduced saliva production. It is quite common in patients with arterial hypertension, coronary thrombosis, diabetes, and thyroid disease at the same time, so it requires the use of different drugs. The occurrence of dry mouth in this case is related to the fact that...
the salivary glands have some kind of target receptor for various different drugs. The most important of these are the anticholinergic drugs that are the main cause of dry mouth. The activation of α-1A, β-1, M3, and H2 receptors occurs in the protein kinase A pathway that depends on cAMP, while NK-1 and M3R activation is induced in the protein kinase C pathway. GABA and benzodiazepines cause a decrease in salivary production.

**MEASUREMENT OF SALIVA RATE**

Most methods to measure salivary flow are easy to do and only take a little time. The rate of salivary flow is usually measured at least 5 minutes after fasting during the night or 2 hours after a meal. The overall rate of unstimulated saliva flow is assessed with the patient sitting upright. The patient was asked to keep the saliva flowing from the lower lip into the measuring container for 15 minutes. The saliva can also be collected using a layered absorbent strip placed at the bottom of the mouth (reading at the first, second, and third minutes. The overall rate of unstimulated saliva flow is assessed with the patient sitting upright. The patient was asked to keep the saliva flowing from the lower lip into the measuring container for 15 minutes. The saliva can also be collected using a layered absorbent strip placed at the bottom of the mouth (reading at the first, second, and third minutes.

Other methods for assessing the overall rate of non-stimulated saliva flow include the spraying method and the suction method. The rate of stimulated saliva flow was measured after the patient chewed unflavored rubber candles or paraffin candles (1-2 g) for 1 minute. The salivary flow (whether stimulated or not) can also be measured selectively from a single major spleen or minor spleen gland. Parotid gland secretions are usually collected by using a sucker and putting a cup (a Lashley cup or a Carlson Crittenden cup) over the Stensen canal. A similar system for measuring the rate of salivary flow in the sublingual and submandibular glands has been developed by Wolff et al. The salivary flow of the minor spleen glands can be measured with a micropipet and absorbent filter paper. The flow rate can be measured in μL/min/cm² of mucous membrane.

**MECHANISMS OF ACTION OF ANTIHYPERTENSIVE DRUGS**

In some cases, the antihypertensive drug amlodipine can cause the user to experience a decrease in the rate of saliva flow, both directly and indirectly. When directly applied, it will affect the flow of the saliva by imitating the action of the autonomic nervous system or by reacting to the cellular processes that require saliva, while indirectly, it will affect the saliva by altering the balance of fluids and electrolytes or by affecting blood flow to the glands.

This is in line with a study by Wotulo et al. that suggests that both antihypertensive drugs, amlodipine and captopril, cause a decrease in the rate of salivary flow that directly or indirectly results in the occurrence of xerostomia, but there are no significant differences between the two groups of drug users.

The mechanism of action of amlodipine is to inhibit the inflow of calcium ions into the cells of the heart muscle and the plain muscle of the blood vessels. Amlodipin has a relaxing effect on the muscles, resulting in a decrease in blood pressure. In the salivary glands, this drug suppresses the secretion of water by closing the Ca²⁺ channel so that the Cl⁻ door can't be opened. Unopened Cl-doors cause Cl⁻ from the intracellular cells not to come out through the apical membrane of the axial cells, and water cannot enter the lumen. The mechanism affects the whole saliva, which consists of 99% water, and eventually leads to xerostomia.
MANAGEMENT AND TREATMENT OF XEROSTOMIA

Precautionary measures are key to managing xerostomia. Patients should be advised to keep hydrated with adequate water intake. Good oral hygiene with regular visits to the dentist and topical fluoride is also necessary for the identification of signs of xerostomia and for the prevention of tooth damage. Quitting treatment that causes dry mouth or replacing it with alternative medicine should be considered if it is safe and necessary for the patient. Patient education aimed at the implementation of systematic and correct oral hygiene is a priority in the prevention and treatment of dry mouth. It is recommended to avoid dry, sour, and salty foods. In an effort to improve the quality of life of xerostomia patients, various forms of salivary substitution have been introduced: gels (Biotene), aerosols (Glandosane spray), suction tablets (Saliva Orthana sucking tablets), pimples, and rubber sweets.

CONCLUSION

It was concluded that the antihypertensive drug Ca-Antagonis (amlodipine) was associated with xerostomia.

REFERENCES


