



Oral Complications of Congestive Heart Failure Drugs in Patients Referred to Heart Clinics in Birjand (Iran) in 2016

Narjes Akbari ¹, Toba Kazemi ², Vajihollah Raeesi ³, Negin Samiee ^{4,*} and Mohsen Saadati ⁵

¹Oral and Maxillofacial Medicine, Birjand Dental School, Birjand University of Medical Sciences, Birjand, Iran

²Atherosclerosis and Coronary Artery Research Center, Department of Cardiology, Birjand University of Medical Sciences, Birjand, Iran

³Cardiovascular Diseases Research Center, Department of Internal Medicine, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran

⁴Department of Oral and Maxillofacial Medicine, Faculty of Dentistry, Kurdistan University of Medical Sciences, Sanandaj, Iran

⁵Birjand Dental School, Birjand University of Medical Sciences, Birjand, Iran

*Corresponding author: Department of Oral and Maxillofacial Medicine, Faculty of Dentistry, Kurdistan University of Medical Sciences, Sanandaj, Iran. Email: negin.samiee@gmail.com

Received 2020 April 21; Revised 2021 February 24; Accepted 2021 June 01.

Abstract

Background: Cardiovascular diseases (CVDs) are the most common medical disorder, and the number of medicines available to address CVDs is on the rise; meanwhile, complications and drug interactions are major concerns. CVD patients' medications include hypertension, ischemic heart disease, arrhythmias, and congestive heart failure. However, their administration is associated with side effects such as oral dryness, change in taste, and a burning sensation in the mouth.

Objectives: This study aimed to evaluate medicine-related oral complications of patients with heart failure.

Methods: Following a cross-sectional design, 340 patients (146 men and 194 women) referring to heart clinics in Birjand (Iran) from March to September 2016 were evaluated. The mean age of participants was 60.13 ± 9.35 . Participants were interviewed using standard checklists, and a complete clinical examination of the oral cavity for the presence of any oral mucosal lesions was performed using a mirror and dental probe. Data were analyzed using SPSS v. 22.

Results: The most common side effect of heart failure medications was oral dryness (28.8%), followed by bitter taste (11.2%) in the mouth. The side effects were proportional to the patient's age and the time since receiving the medication.

Conclusions: Educational pamphlets are suggested to be separately prepared for patients and cardiologists about ways to prevent oral side effects of medications and oral considerations. Dentists can use supportive treatments and sialagogue medications to improve oral complications upon appropriate referrals.

Keywords: Adverse Drug Reactions, Cardiovascular Agents, Oral Diagnosis, Xerostomia

1. Background

The increasing prevalence of chronic diseases has become a major problem in developed as well as developing countries (1). Chronic diseases, with cardiovascular diseases (CVDs), cancer, diabetes, and chronic respiratory diseases as the major ones, claimed more than 30 million lives worldwide in 2008 (2) and have become the leading cause of death in many countries. While CVDs are declining in developed countries, they are not only a major cause of death in developing countries but also have become a significant public health concern due to their rising trend. Today, coronary heart disease is the most common cause of mortality worldwide and is predicted to be the most important cause of global death by 2030 (3, 4). Cardiovascular mortality is also the most common cause of death in Iran, with the highest mortality rate (3, 5).

Congestive heart failure often referred simply to as heart failure, is the underlying cause of more than 55,000 deaths each year, with one out of every nine deaths occurring annually (3, 6). Heart failure is a debilitating condition caused by an inherited or acquired disorder in the structure or function of the heart and has profound effects on patients' functional conditions and quality of life (6, 7). The disease is often progressive, in which the heart is unable to supply sufficient blood to meet the metabolic needs of organs and tissues. It also reduces the capacity for physical activities and causes short breathing (8). About half of patients with heart failure die after being hospitalized or are at increased risk of re-admission (9). The disease and its consequences cost the health care sector a great deal. In the United States, for example, such cost is estimated at more than 20 billion dollars (10). The cost was estimated to be 400 million dollars in Iran in 2007 (11). The prevalence

of CVDs is 2 - 3%, increases with age, and is higher in men than women (12, 13).

Cardiovascular drugs lead to oral complications in 14% (14) to 67.4% (15) of patients. Angiotensin-converting enzyme inhibitors (aceis) can cause oral lichen planus, burning mouth sensation, and ageusia (16). Lichenoid reactions have also been described in association with alpha- and beta-adrenergic blockers. Taste perception abnormalities may also be caused by aspirin, statins, and diuretics (17).

2. Objectives

The goal of treating heart failure is to alleviate symptoms, improve patients' functional conditions and quality of life, increase survival, and achieve disease adaptation. There are many medications prescribed for heart failure, including angiotensin-converting enzyme inhibitors, beta-blockers, diuretics, and digitalis. Due to the increasing trend of using heart failure medications, the side effects of these drugs are expected to increase further. Therefore, specialized preventive and therapeutic care are necessary today more than ever. The aim of this study was to evaluate the oral side effects of heart failure drugs in patients with congestive heart failure.

3. Methods

In this cross-sectional study, 340 patients referring to heart clinics in the city of Birjand, Iran, from March to September 2016, who had heart failure treated with heart failure medication were included. Those receiving concomitant medications for diabetes, hypothyroidism, and hyperthyroidism, as well as patients with dementia, confusion, and physical disabilities, were excluded (14).

Written informed consent was obtained from all participants before entering the study and after a comprehensive introduction to the study protocol. Patients were divided into four groups according to the type of medication used to treat heart failure, as follows: (1) Angiotensin receptor blockers (ARB), (2) angiotensin receptor blockers + beta blockers (ARB + BAB), (3) beta-blockers + nitrates + antiplatelet + angiotensin receptor blockers or angiotensin-converting enzyme inhibitors (BAB + Nitrate + Anti Plt + ARB or ACEI), (4) digoxin + diuretics + angiotensin receptor blockers or angiotensin-converting enzyme inhibitors (Digital + dieuretics + ACEI or ARB).

Data on demographic characteristics, number of medications and duration of use, hospitalization, and medical records were collected. A complete history of oral symptoms, such as oral dryness, changes in taste or burning sensation in the mouth, and other symptoms, were also

asked orally according to a standard checklist by the examiner. Moreover, a full clinical examination of the oral cavity for the presence of any oral mucosal lesions was performed using a mirror and dental probe. Data analysis was administered using SPSS version 22 by the chi-squared and the ANOVA. Descriptive information are provided using frequency tables. Statistical significance was considered when the P-value < 0.05.

4. Results

This study was performed on 340 patients (146 men (42.9%) and 194 women (57.1%)) with heart failure referring to heart clinics in the city of Birjand in Iran in 2016. The youngest and oldest participants were 32 and 86 years old, respectively, with a mean age of 60.13 ± 9.35 years. Most patients were using angiotensin receptor blocking drugs (n = 116; 34.1%). The frequency distribution of patients according to their education level were as follows; 19.7% were illiterate (67 patients), 42.05% had lower secondary education (143 patients), 23.5% with high school diploma (80 patients), and 14.7% with higher educations (50 patients). Oral complications of heart failure medications were evaluated, including oral dryness, bitter taste in the mouth, lichenoid reaction, gingival enlargement, burning sensation, oral aphthous, angioedema, facial lupus, lymphadenopathy, petechia, oral ulcer, and high salivation. According to Table 1, the highest frequency of oral complications was observed in patients taking beta-blocker + antiplatelet + angiotensin-blocking drug or angiotensin enzyme inhibition. The most common complication was oral dryness, followed by bitter taste in the mouth. There was also a significant relationship between oral dryness, bitter taste in the mouth, and the type of medication used (P < 0.05).

There was also a significant relationship between oral dryness, bitter taste in the mouth, and the duration of drug use (P < 0.05). On the other hand, there was no significant relationship between lichenoid reaction time and the duration of drug use (P > 0.05). The most common complication was in patients with a history of over 5 drug use. Oral dryness was more common in females than males, and no significant relationship was found between complications and gender (P > 0.05).

According to Table 2, the mean age and the duration of drug use in patients with drug side effects were significantly higher than that of those receiving heart failure medications (P < 0.001). As shown in Table 3, there was a significant difference between the prevalence of side effects depending on the duration of drug use and age. The prevalence of drug side effects was significantly enhanced

Table 1. Frequency Distribution of Oral Complications of Heart Failure Drugs in Patients Referred to Birjand Heart Clinics in 2016 by Medication Group ^a

Study Group and Type of Oral Complication	1st Group	2nd Group	3rd Group	4th Group	Total	Statistical Test Results	
						P	χ^2
Symptom							
Oral dryness	24 (20.7)	28 (24.3)	43 (47.3)	3 (16.7)	98 (28.8)	< 0.001	21.2
Bitter taste	6 (5.2)	11 (9.6)	20 (22)	6 (5.6)	38 (11.2)	< 0.001	10.8
Sign							
Oral dryness	2 (1.7)	9 (7.8)	14 (15.4)	2 (11.1)	27 (7.9)	0.004	13.3
Lichenoid reaction	0 (0)	2 (1.7)	4 (4.4)	0 (0)	6 (1.8)	0.11	5.11

^a Values are expressed as No. (%).

with the increase in the duration of drug use and age ($P < 0.001$).

5. Discussion

The most common drug side effect was observed in those older than 65, which was not unexpected due to the high prevalence of CVDs in these ages. Moreover, the most common complications and manifestations were observed in female patients. It could probably be due to the fact that women, in general, undertake more medical visits than men, leading to higher rates of reporting hypertension in women in most studies. Thirty percent (103 out of 340) of patients with heart failure taking medications had oral manifestations and complications.

Habbab et al. reported a prevalence of 14.1% for these complications (14). In another study by Arunkumar et al., 382 (out of 603) patients with hypertension (63.3%) had at least one manifestation and oral side effects of antihypertensive drugs (15). The most common complication observed in this study was oral dryness ($n = 98$; 28.8%), which is in agreement Shinkai et al. and Smith and Burtner (18, 19).

Mohan et al. reported a prevalence of 50% for oral dryness (20). Bitter taste in the mouth ($n = 20$; 7.9%) has also been reported as the second common oral manifestation (after oral dryness), with the highest prevalence in the third group of drug users (BAB + Nitrate + anti-Plt + ARB or ACEI) ($n = 14$; 15.4%). Luzardo and Raad Bassil (21) reported that 80.53% of patients using antihypertensive drugs had oral manifestations. The most common manifestation was dysgeusia (60%), followed by hyposalivation (58%) and gingival enlargement (12%), which is not consistent with our study. The results of this study are consistent with Arunkumar et al., who reported oral dryness as the most common oral complication ($n = 10$; 6.6%), followed by bitter taste in the mouth ($n = 3$; 2.8%) (15).

In the present study, the frequency of lichenoid reaction in patients was 1.8% (6 cases). The results are consistent with Arunkumar et al., which stated that the most common oral complication in patients taking the calcium channel blocker drug was oral dryness ($n = 29$; 19.1%). However, our findings are not consistent with respect to the frequency of gingival enlargement, which was 18 cases (33.3%) (15). According to Mohan et al., the most common complication next to oral dryness is oral hyperpigmentation (23.3%) (18). Arunkumar et al. reported that the most common complications in this group of patients were oral dryness ($n = 19$) and oral bitterness ($n = 18$; 16.8%) (15).

In the present study, gingival enlargement was observed in six cases (1.8%), four of which (4.4%) were in patients taking the third drug (BAB + Nitrate + anti-Plt + ARB or ACEI). It is consistent with Arunkumar et al. (15), stating that the most common complication in this group was oral dryness, bitter taste in the mouth, and lichenoid reaction with a frequency of four (14.8%), respectively.

The oral dryness complication of the drugs used in CVDs roots in their anticholinergic effects. Many studies showed that the prevalence and incidence of oral dryness increase with age. Other causes may include aging, gender, dehydration, habits such as oral breathing, smoking, alcohol consumption, decreased salivary gland function, salivary gland diseases (e.g., sialolite, sialadenitis, and sjogren's syndrome), stress, depression, and systemic diseases such as diabetes and hypertension (22). The bitter taste in the mouth may be due to decreased salivary flow or the secretion of drugs into the saliva, leading to a change in the taste.

Some studies suggested that certain drugs used to treat heart disease lead to changes in the perception of food taste (15). There is evidence that drugs can influence the taste of foods by affecting the metal ions associated with cell membranes. In the present study, some complications and lesions, such as gingival enlargement,

Table 2. Comparison of Mean Age and Duration of Drug Use According to Different Oral Drug Complications in Patients^a

Drug Complication Status/Variable	Present (n = 188)	Absent (n = 188)	Independent t-Test Results
Age (y)	66.0 ± 8.61	57.6 ± 8.5	t = 8.381; df = 338; P < 0.001
Duration of drug use (y)	7.29 ± 3.1	3.72 ± 1.62	t = 14.016; df = 338; P < 0.001

^a Values are expressed as mean ± SD.

Table 3. Comparison of Prevalence of Drug Side Effects According to Age, Gender and Duration of Drug Use^a

Drug Complication Status/Variable	Present	Absent	χ ² -Test Results
Duration of drug use (y)			χ ² = 108.5; df = 2; P < 0.001
< 4	11 (8.5)	119 (91.5)	
4 - 6	20 (19)	85 (81)	
> 6	72 (68.8)	33 (31.4)	
Gender			χ ² = 1.29; df = 1; P < 0.26
Male	49 (33.6)	97 (66.4)	
Female	54 (27.8)	140 (72.2)	
Age (y)			χ ² = 73.4; df = 2; P < 0.001
< 50	4 (10.8)	33 (89.2)	
50 - 65	33 (16.8)	163 (83.2)	
> 65	66 (61.7)	41 (38.3)	

^a Values are expressed as No. (%).

oral aphthous ulcer, oral ulcer, high salivation, petechia, lymphadenopathy, lupus lesions, and facial angioedema, were not observed in any patient. In the study by Habbab et al., the prevalence of any of the complications ulcers, lichenoid reaction, oral aphthous, and burning sensation was less than 1% (14).

5.1. Conclusions

This study demonstrated an increased prevalence of side effects related to CVD drugs. It can be attributed to factors like increased life expectancy, resulting in prolonged consumption of drugs, and increased prevalence of the diseases. These complications could also be oral, and dentists might, therefore, play a crucial role in reducing such complications. It appears that defining protocols to visit dentists as well as informing cardiologists and patients about the beneficial role of the dentist in reducing oral complications can be highly advantageous.

5.2. Limitations

We did not consider the personal dental hygiene of patients (as an interfering factor) in the study.

Footnotes

Authors' Contribution: Study concept and design: N. A. and V. R.; abstract and analyzing data, writing the

manuscript: M. S.; study supervision: T. K. and N. A.; manuscript preparation: N. S.

Conflict of Interests: The authors declare no conflicts of interest.

Data Reproducibility: It was not declared by the authors.

Ethical Approval: IR.bums.REC.1395.72.

Funding/Support: This study was supported by grants from Birjand University of Medical Sciences.

Informed Consent: Written informed consent was obtained from all participants before entering the study and after a comprehensive introduction to the study protocol.

References

- Rafii F, Soleimani M, Seyedfatemi N. A model of patient participation with chronic disease in nursing care. *Koomesh*. 2011;12(3):293-304. Persian.
- Paradis G, Chioloro A. The cardiovascular and chronic diseases epidemic in low- and middle-income countries: a global health challenge. *J Am Coll Cardiol*. 2011;57(17):1775-7. doi: 10.1016/j.jacc.2010.11.047. [PubMed: 21511114].
- Mohammadzadeh N, Safdari R. [Chronic Heart Failure (CHF) Management through Agent Technology]. *Payavard-Salamat*. 2017;11(2):181-8. Persian.
- Kadkhodaei Khalafi M, Dabidi Roshan V, Beyranvand MR. [Response of the cardiovascular physiological and functional markers following the short term taurine supplementation and burce protocol in

- patients with cardiac heart failure]. *Razi Journal of Medical Sciences*. 2011;**18**(84):28-37. Persian.
5. Kazemi T, Sharifzadeh GR, Zarban A, Fesharakinia A, Rezvani MR, Moezy SA. Risk factors for premature myocardial infarction: a matched case-control study. *J Res Health Sci*. 2011;**11**(2):77-82. [PubMed: 22911956].
 6. Stavem K, Lossius MI, Kvien TK, Guldvog B. The health-related quality of life of patients with epilepsy compared with angina pectoris, rheumatoid arthritis, asthma and chronic obstructive pulmonary disease. *Qual Life Res*. 2000;**9**(7):865-71. doi: 10.1023/a:1008993821253. [PubMed: 11297029].
 7. Juenger J, Schellberg D, Kraemer S, Haunstetter A, Zugck C, Herzog W, et al. Health related quality of life in patients with congestive heart failure: comparison with other chronic diseases and relation to functional variables. *Heart*. 2002;**87**(3):235-41. doi: 10.1136/heart.87.3.235. [PubMed: 11847161]. [PubMed Central: PMC1767036].
 8. Hamilton AL, Killian KJ, Summers E, Jones NL. Muscle strength, symptom intensity, and exercise capacity in patients with cardiorespiratory disorders. *Am J Respir Crit Care Med*. 1995;**152**(6 Pt 1):2021-31. doi: 10.1164/ajrccm.152.6.8520771. [PubMed: 8520771].
 9. Lofvenmark C, Karlsson MR, Edner M, Billing E, Mattiasson AC. A group-based multi-professional education programme for family members of patients with chronic heart failure: effects on knowledge and patients' health care utilization. *Patient Educ Couns*. 2011;**85**(2):e162-8. doi: 10.1016/j.pec.2010.09.026. [PubMed: 21050694].
 10. Soundarraj D, Singh V, Satija V, Thakur RK. Containing the Cost of Heart Failure Management: A Focus on Reducing Readmissions. *Card Electrophysiol Clin*. 2015;**7**(4):577-84. doi: 10.1016/j.ccep.2015.08.002. [PubMed: 26596803].
 11. Hekmatpou D, Mohammadi E, Ahmadi F, Arefi S, Rafie M. [The Effectiveness of Applying "Making Sensitivity to Re-admission Caring Model"]. *Razi Journal of Medical Sciences*. 2010;**17**(75):33-50. Persian.
 12. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail*. 2012;**14**(8):803-69. doi: 10.1093/eurjhf/hfs105. [PubMed: 22828712].
 13. Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the diagnosis and treatment of acute and chronic heart failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). *Eur J Heart Fail*. 2008;**10**(10):933-89. doi: 10.1016/j.ejheart.2008.08.005. [PubMed: 18826876].
 14. Habbab KM, Moles DR, Porter SR. Potential oral manifestations of cardiovascular drugs. *Oral Dis*. 2010;**16**(8):769-73. doi: 10.1111/j.1601-0825.2010.01686.x. [PubMed: 20604876].
 15. Arunkumar S, Kalappanavar AN, Annigeri RG, Shakunthala GK. Adverse Oral Manifestations of Cardiovascular Drugs. *IOSR J. Dent. Med. Sci*. 2013;**7**(5):64-71. doi: 10.9790/0853-0756471.
 16. Cruz Pamplona M, Jiménez Soriano Y, Sarrión Pérez MG. Dental considerations in patients with heart disease. *J. Clin. Exp. Dent*. 2011;**3**(2):97-105. doi: 10.4317/jced.3.e97.
 17. Moisa SM, Miron I, Lupu A, Pertea IL, Padurarau G, Lupu VV. Oral Manifestations Linked to Cardiovascular Pathology or Medication. *Romanian J. Oral Rehabil*. 2019;**11**(3):79-82.
 18. Shinkai RS, Hatch JP, Schmidt CB, Sartori EA. Exposure to the oral side effects of medication in a community-based sample. *Spec Care Dentist*. 2006;**26**(3):116-20. doi: 10.1111/j.1754-4505.2006.tb01434.x. [PubMed: 16774189].
 19. Smith RG, Burtner AP. Oral side-effects of the most frequently prescribed drugs. *Spec Care Dentist*. 1994;**14**(3):96-102. doi: 10.1111/j.1754-4505.1994.tb01112.x. [PubMed: 7871475].
 20. Mohan N, Fenn SM, Jacob M. Oral Adverse Reactions to Cardiovascular Drugs. *Journal of Integrated Dentistry*. 2017;**1**(3):1-4.
 21. Luzardo G, Raad Bassil N. Prevalence of oral manifestations in hypertensive patients with continuous medication at the Hospital of the day Jacobo and María Elena Ratinoff in 2014. *J. Am. Health*. 2019;**2**(2):23-33. doi: 10.37958/jah.v2i2.19.
 22. Prasanthi B, Kannan N, Patil R. Effect of Diuretics on Salivary Flow, Composition and Oral Health Status: A Clinico-biochemical Study. *Ann Med Health Sci Res*. 2014;**4**(4):549-53. doi: 10.4103/2141-9248.139311. [PubMed: 25221702]. [PubMed Central: PMC4160678].