



**Ministry of Higher Education
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University of Diyala
College of Medicine**



The association between oral ulcers and the usage of Anti-hypertensive drugs

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(أَمْ مَنْ هُوَ قَانِتٌ أَنْاءَ اللَّيْلِ سَاجِدًا وَقَانِمًا يَحْذَرُ الْآخِرَةَ وَيَرْجُو رَحْمَةَ رَبِّهِ قُلْ هَلْ

يَسْتَوِي الَّذِينَ يَعْلَمُونَ وَالَّذِينَ لَا يَعْلَمُونَ إِنَّمَا يَتَذَكَّرُ أُولُو الْأَلْبَابِ)

سورة النمر: الآية ٩



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Dedication

This project is especially dedicated to the doctors who helped and guided us to successfully complete this project work. Also I would like to dedicate this project to my dear father, who has been a wonderful supporter until my research was completed, and to my beloved mother, who has been encouraging me for months.



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1. Abstract

Anti-hypertensive drugs are an effective treatment choice for half of hypertensive patients. These medications can cause oral side effects within a few weeks of starting the drug intake. Oral mucosal lesions are usually detectable by taking a history and clinical examination. However, due to the clinical similarity of the lesions, they may be missed in some cases.

Aim of study: In this study, we will highlight the association between antihypertensive drugs and the oral ulcer in patients attending Baquba teaching hospital in Diyala province, Iraq.

Patients and methods: This cross-sectional study included analysis of the reported cases of oral ulcer among the hypertensive patients Data have been collected from the cases attended the Baquba teaching hospital from December 2022- February 2023 in which the cases suffered from oral ulceration and take antihypertensive drug without other disease .The data analyzed using SPSS program.

Results: 40 patients were enrolled in our survey. 24 males and 16 females. 42.5% of them took CCBs, 25% took ACEI, 20% took BBs and 12.5% took ARBs. There was no significant association between the usage of antihypertensive drugs and the incidence of oral ulceration.

Conclusion: We found no significant difference between the usage of antihypertensive drugs and the incidence of oral ulcers.

Keywords: antihypertensive, oral ulcers.



2. Introduction

Several systemic factors are known to contribute to oral diseases or conditions and among those are the intake of drugs. An adverse drug reaction is defined by WHO as ‘a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, therapy of diseases or for the modification of physiological function [1].

The World Health Organization attributes hypertension, or high blood pressure, as the leading cause of cardiovascular mortality. An elevated arterial pressure is probably the most important public health problem in developed countries. It is common, asymptomatic readily detectable and easily treatable, and if untreated, often leads to complications. Although our understanding of the pathophysiology of elevated arterial pressure has increased, in 90 to 95% of cases the etiology is still largely unknown. As a consequence, in most cases hypertension is treated non-specifically, resulting in the large number of minor side effects and relatively high non-compliance rate. The ratio of hypertension frequency in women versus men increases from 0.6 to 0.7 at age 30 to 1.1 to 1.2 at age 65 [2].

Anti-hypertensive drugs are an effective treatment choice for half of hypertensive patients. These medications can cause oral side effects within a few weeks of starting the drug intake. Oral mucosal lesions are usually detectable by taking a history and clinical examination. However, due to the clinical similarity of the lesions, they may be missed in some cases [3].



The side effects of anti-hypertensive drugs include xerostomia, lichenoid reactions, mucosal burning, dysgeusia, gingival hypertrophy, angioedema, and bleeding [4].

Ulceration is a breach in the oral epithelium, which typically exposes nerve endings in the underlying lamina propria, resulting in pain or soreness especially when eating spicy foods or citrus fruits. Oral Ulcers are Inflammatory lesions of the oral mucosa that affect approximately 20% of the population. Numerous causes of these ulcers include, immunological alterations, infections, nutritional deficiencies, repetitive trauma to the mucosa, food and contact allergies, autoimmune diseases and neoplasms, as well as psychosomatic, genetic and environmental factors [5,6].

Typical oral ulcers due to drugs are clinically classified into two types [7]; -

- The first is widespread mucositis and ulceration, which is caused predominantly by cytotoxic anti-tumor chemotherapy drugs. Sloughing and ulceration appear within days of starting treatment, and the discomfort frequently necessitates the use of opioids and the modification or termination of chemotherapy. 5-fluorouracil, methotrexate, bleomycin, and cisplatin are examples of cytotoxic drugs. Immunosuppressive drugs can also lead to oral ulcers by causing opportunistic secondary infections with Gram-negative bacteria and fungi.
- The second form is known as a fixed drug eruption, which is characterized by the development of treatment-resistant ulcers on a regular basis. On any site of the oral mucosa, single or multiple large ulcerations can be seen.



Hypertensive Drug-induced oral ulcerations, erosions, or necrosis of oral mucous membrane tissue can be triggered by systemic or locally delivered medications. Pathogenic mechanisms include focal irritation due to low pH, allergic hypersensitivity, and cytotoxicity. Hypertensive medications with strong evidence for injury of oral mucosal epithelium include chemotherapeutic agents. Hypertensive medication mediated the oral ulceration resulting in an ulcerative lichenoid reaction in the buccal or lingual mucosa [8].

Ulceration reaction is a delayed hypersensitivity reaction to a drug. Clinically, this condition is often confused with lichen planus, an autoimmune disease. Patients may or may not be symptomatic. Clinicians should assess a “new” presentation of ulceration and correlate onset with the timing of the introduction of a antihypertensive medication since the last dental visit. Although many other drugs have also been implicated, common medications associated with lichenoid drug reaction include nonsteroidal anti-inflammatory drugs [9].

3. Aim of study

The aim of this study was to evaluate the effect of antihypertensive drug on the oral ulceration



4. Patients and methods

This cross-sectional study included analysis of the reported cases of oral ulcer among the hypertensive patients Data have been collected from the cases attended the Baquba teaching hospital from December 2022- February 2023 in which the cases suffered from oral ulceration and take antihypertensive drug without other disease .The data analyzed using SPSS program.

5. Results

In this study, 40 patients were involved. The age groups and gender are described in Table (1).

Table 1. Frequency distribution of cases group by selected variables

Age Groups	Gender		Total
	Male	Female	
Less than 40 years	1	0	1
40-60 years	12	11	23
More than 60 years	11	5	16
Total	24	16	40

The drugs they using is enlisted in table 2.

Table 2. frequency of distribution of anti-hypertensive drugs

Drugs	Frequency	Percent%
Angiotensin converting enzyme inhibitors	10	25
Angiotensin receptor blockers	5	12.5
Calcium channel blockers	17	42.5

Beta blockers	8	20
Total	40	100

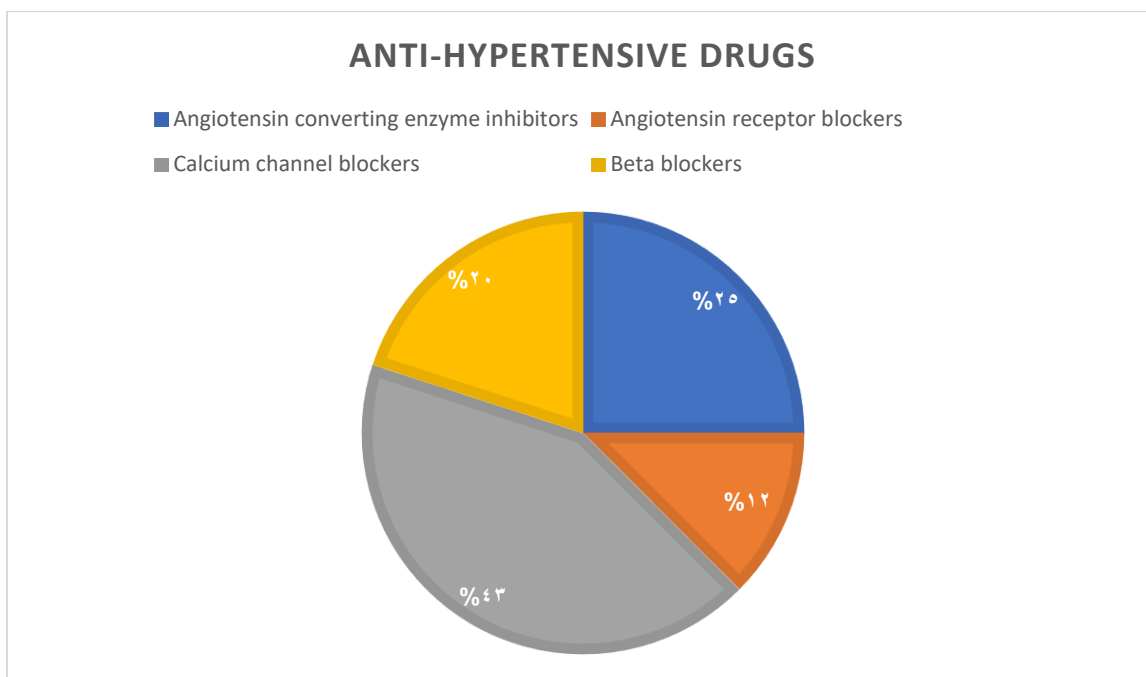


Figure 1. Pie chart for the anti-hypertensive drugs in our survey

Table 3. distribution of age groups and drugs

Age Groups	Type of anti-hypertensive drugs				Total
	ACEI	ARBs	CCBs	BB	
Less than 40 years	0	0	0	1	1
40-60 years	5	2	12	4	23
More than 60 years	5	3	5	3	16

Total	10	5	17	8	40
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62.5% of them had family history of hypertension and 37.5% don't have.

The shape and site of the ulcers are enlisted in table 3.

Table 3. frequency of distribution of shape and sites of the ulcers

Shape	Site					Total
	Tongue	Lips	Floor of mouth	Buccal mucosa	Palate	
Rounded	6	5	3	7	3	24
Irregular	1	3	0	2	1	7
Punched	1	1	0	4	3	9
Total	8	9	3	13	7	40

Ulcers were more common in middle age group as in table 4.

Table 4. frequency of distribution of ulcers in age groups

Age Groups	Site					Total
	Tongue	Lips	Floor of mouth	Buccal mucosa	Palate	
Less than 40 years	1	0	0	0	0	1
40-60 years	5	3	1	11	3	23

More than 60 years	2	6	2	2	4	16
Total	8	9	3	13	7	40

Ulcers were more common in the positive family history patients as in table 5.

Table 5. family history and ulcers

Family history	Shape			Total
	Rounded	Irregular	Punched	
Positive	16	4	5	25
Negative	8	3	4	15
Total	24	7	9	40

We found significant difference between gender and the shape of ulcers as in table 6.

Table 6. association between gender and shape variables

Gender	Shape			Total	Sig.
	Rounded	Irregular	Punched		
Male	13	7	4	24	$P < 0.05$
Female	11	0	5	16	$P = 0.45$
Total	24	7	9	40	

6. Discussion

Hypertension (HTN) or high blood pressure, sometimes arterial hypertension, is a chronic medical condition in which the blood pressure in the arteries is elevated. This requires the heart to work harder than normal to circulate blood through the blood vessels.

Considering the aging of the population along with widespread and increased use of prescription, over-the-counter, and herbal remedies, dentists can expect to encounter oral side effects from medication use among their patients. A survey of 3302 patients visiting the Stomatology Center at Baylor College of Dentistry revealed 66% were taking prescription drugs and 42% were taking two or more prescription medications daily. Since many patients regularly take prescription and nonprescription medications, dentists always should take thorough medical histories and be aware of medication-related problems and their potential effects on diagnosis and treatment planning [10].

No statistically significant difference was detected between patients with and the oral manifestations and the number of antihypertensive drugs, as we found tendency to have rounded ulcers in CCBs user but with no statistical difference. And this is consistent with the findings of Habbab et al [11].

We found significant difference between the gender and the type of ulcer as it tend to happen in males more than females ($P < 0.05$) and this is probably due to less mouth care in males compared to females.

We also found that oral ulcers tend to happen in patients with positive family history of hypertension than the patients without history but with no statistical significant.

Up to our knowledge, this is the first study about the association of antihypertensive drugs and the oral ulceration, the main limitations were the size of the sample and the wide diversity in the types of anti-hypertensive drugs.

7. Conclusion

We found no significant difference between the usage of antihypertensive drugs and the incidence of oral ulcers.

8. References

1. Torpet LA, Kragelund C, Reibel J, Nauntofte B. Oral adverse drug reactions to cardiovascular drugs. *Critical reviews in oral biology & medicine*. 2004 Jan;15(1):28-46.
2. Kumar P, Mastan K, Chowdhary R, Shanmugam K. Oral manifestations in hypertensive patients: A clinical study. *J Oral Maxillofac Pathol*. 2012 May;16(2):215-21
3. Elmi Rankohi Z, Shabaniyan M, Maleki D. Oral Manifestations of Patients Taking Anti-Hypertensive Medications. *Journal of Iranian Dental Association*. 2020 Oct 10;32(3):83-8.
4. Pamplona MC, Soriano YJ, Perez MGS. Dental considerations in patients with heart disease. *J clin Exp Dent*. 2011 Dec;3(2):e97-105.
5. O'Neill A, De Leon J. Two case reports of oral ulcers with lamotrigine several weeks after oxcarbazepine withdrawal. *Bipolar disorders*. 2007 May;9(3):310-3.
6. Jayakaran TG. The effect of drugs in the oral cavity-A review. *Journal of pharmaceutical sciences and research*. 2014 Feb 1;6(2):89.

7. Özkaya E. Oral mucosal fixed drug eruption: characteristics and differential diagnosis. *Journal of the American Academy of Dermatology*. 2013 Aug 1;69(2):e51-8.
8. Aliko A, Wolff A, Dawes C, Aframian D, Proctor G, Ekström J, Narayana N, Villa A, Sia YW, Joshi RK, McGowan R. World Workshop on Oral Medicine VI: clinical implications of medication-induced salivary gland dysfunction. *Oral surgery, oral medicine, oral pathology and oral radiology*. 2015 Aug 1;120(2):185-206.
9. Fortuna G, Aria M, Schiavo JH. Drug-induced oral lichenoid reactions: a real clinical entity? A systematic review. *European Journal of Clinical Pharmacology*. 2017 Dec;73:1523-37.
10. Abdollahi M, Rahimi R, Radfar M. Current opinion on drug-induced oral reactions: a comprehensive review. *J Contemp Dent Pract*. 2008 Mar 1;9(3):1-5.
11. Habbab KM, Moles DR, Porter SR. Potential oral manifestations of cardiovascular drugs. *Oral diseases*. 2010 Nov;16(8):769-73.

