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Original Article

Xerostomia and dysgeusia in the elderly: prevalence of and association with polypharmacy

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Xerostomia is defined as the perception of dry mouth, and dysgeusia, as a change in taste. Both are common complaints in the elderly, especially among those making use of polypharmacy drug combinations. **Aim:** This study aimed to determine the prevalence of xerostomia and dysgeusia and to investigate their association with polypharmacy in the elderly. **Methods:** older people under follow-up at the Multidisciplinary Elderly Center of the University Hospital of Brasília were interviewed and asked about health problems, medications used, presence of xerostomia and dysgeusia. Descriptive statistics were used to determine the prevalence of the symptoms surveyed. The chi-square test was used to investigate the relationship between xerostomia and dysgeusia and polypharmacy. Secondary associations were performed using binomial logistic regression. **Results:** Ninety-six older people were evaluated and of these, 62.5% had xerostomia and 21.1%, had dysgeusia. The average number of medications used was 4±3 medications per individual. Polypharmacy was associated with xerostomia but not dysgeusia. It was possible to associate xerostomia with the use of antihypertensive drugs. **Conclusion:** Xerostomia was a frequent complaint among elderly people making use of polypharmacy, especially those using antihypertensives. Antihypertensives and antidepressants were used most drugs by the elderly and exhibited interactions with drugs most prescribed in Dentistry. Two contraindications were found between fluconazole and mirtazapine; and between erythromycin and simvastatin.

Keywords: Xerostomia. Dysgeusia. Drug interactions. Dental care for aged.

Introduction

Elderly Brazilians represent about 15% of the country's population[1], and the number is expected to increase due to the demographic transition[2]. In view of this reality, the aging process requires multidisciplinary attention, especially from health professionals. Older people are often affected by mutimorbidies and are exposed to polypharmacy[3], predisposing to drug interactions and adverse reactions[4]. The concept of polypharmacy is variable in the literature, and it can be considered to be the simultaneous continuous long-term use of 3 or more different drugs, in addition to those inappropriate for the clinical conditions[5], such as medications that meet the Beers criteria, in the case of the elderly[5]. Among the common adverse effects of polypharmacy, xerostomia and dysgeusia have been found[4,6]. Xerostomia is a symptom defined as a perception of dry mouth[7] and may or may not be associated with hyposalivation, characterized by decreased salivary flow[8]. The sensation of dry mouth affects about 50% of the elderly over 60 years[9], and it can occur due to salivary gland agenesis[7], in patients undergoing radiotherapy treatment of the head and neck region, those with Sjogren's syndrome, and metabolic disorders such as diabetes mellitus and rheumatoid arthritis[10]. In addition, certain classes of drugs have been related to xerostomia, such as antidepressant, anxiolytic, opioid, antihypertensive, diuretic, and antihistamine drugs[11].

Dysgeusia is characterized as a change in the sense of taste. It can be qualitative when the change occurs in the altered perception of the taste of food or quantitative when the change refers to the lack of taste in the food[4]. This condition can be caused by using some groups of drugs, such as antineoplastic agents, systemic antibiotics, and drugs indicated for the treatment of nervous system diseases and the result of drug interactions[12]. Infection with the new coronavirus (SARS-CoV-2) also drew attention to dysgeusia, as it has been reported by approximately 43% of patients affected by COVID-19[13].

Both xerostomia and dysgeusia significantly impact the quality of life[12,14]. Xerostomia affects the perception of oral health and is related to a burning sensation in the mouth and halitosis[15]. It can also induce caries lesions and periodontal disease, taste disorders, candidiasis, dysphagia, and speech difficulties[14]. Dysgeusia can cause feeding difficulties, leading to malnutrition and sarcopenia in the elderly[12]. In addition, it reduces the ability to differentiate excessive concentrations of salt and sugar, which can worsen the clinical condition associated with chronic diseases such as diabetes and high blood pressure[12].

Given the above, this study aimed to determine the prevalence of xerostomia and dysgeusia in the elderly and to associate it with polypharmacy. An additional purpose was to determine the prevalence of medications used by the participants and map possible interactions between the medications used with those most prescribed in Dentistry.

Material and Methods

Study design and location

A cross-sectional study was conducted at the Geriatric Outpatient Clinic of the Multidisciplinary Center of the Elderly Hospital Universitário de Brasília, from July to

August 2018. The Ethics Committee approved the study for Research with Human Beings of the Faculty of Sciences of the Health of the University of Brasília (Opinion No. 3,033,121; CAAE 818897177.7.0000.0030).

Participants

All the participants who attended the "Centro Multidisciplinar do Idoso" (multidisciplinary center for the elderly) aged 60 years or over, between July and August 2018 were interviewed. The exclusion criterion was patients with cognitive deficit or dementia. The interview was conducted after the objective of the research had been explained to the participants and they had signed the Term of Free and Informed Consent (TFIC). The sample calculation was based on the elderly population in Brazil in 2017, with a 95% confidence level and a 10% margin of error.

Assessment

The assessment consisted of data collection from the personal interview, such as age and gender, clinical history (comorbidities and continuous use of medications), and evaluation of the participants' clinical records.

Participants were asked about the number of drugs they used continuously, and their generic or trade names. In case the elderly had difficulty in providing this information, the medical record was consulted. In addition, the participants were asked about their self-perception of dry mouth (xerostomia) and taste alteration (dysgeusia).

Mapping of drug interactions

The drugs listed by the participants were grouped according to their drug class into hypoglycemic, antihypertensive, antiplatelet and anticoagulant, antilipidemic, analgesic, and non-steroidal anti-inflammatory (NSAID), muscle relaxant, benzodiazepine, and others. The medications most used by the participants (those mentioned more than five times in the formatted form) were selected, and their possible association with xerostomia and dysgeusia was verified.

The Micromedex Drug Interactions® and Dynamed® database was used to verify the possibility of interaction with the drugs most frequently prescribed in Dentistry, such as non-opioid analgesics and non-steroidal anti-inflammatory drugs (NSAIDs), antibiotics, steroidal anti-inflammatory drugs (AIES), anxiolytic and antifungal agents, and local anesthetics[16]. Drug interaction was selected and classified according to its severity in minor, moderate, major, and contraindicated use.

Statistical analysis

General and sociodemographic data were provided in the form of descriptive statistics. The chi-square test with the calculation of the prevalence ratio (PR) was performed to assess an association between xerostomia and dysgeusia (dependent variables) with polypharmacy (independent variable), defined as the use of 3 or more medications[17]. The binomial logistic regression was performed to verify the association between the medications most used by the participants and the presence of xerostomia and dysgeusia. The level of significance adopted was for $p < 0.05$

Results

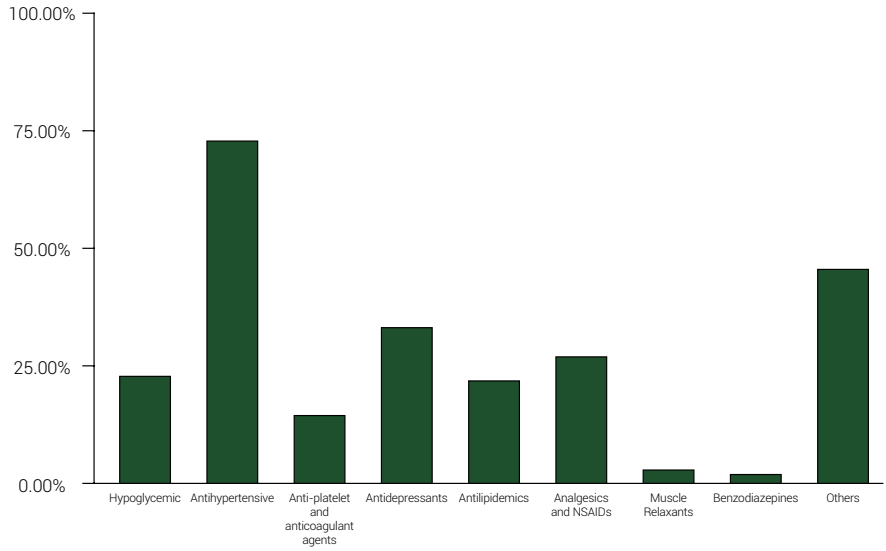
A total of 96 older people were interviewed, all of whom were being monitored at the Multidisciplinary Center of the University Hospital of Brasília (HUB), between July and August 2018. The characteristics of the research participants are shown in Table 1.

Table 1. General characteristics and oral health conditions, and several medications used by elderly people followed-up at the Geriatric Outpatient Clinic (University Hospital of Brasília) between July and August 2018. Data expressed in the form of mean and standard deviation or absolute number and percentage (n = 96)

Age (years)	74 ± 8
Gender	M - 17(17.7%)
	F - 79 (82.3%)
Number of drugs used by participants	4.4 ± 3.1
Xerostomia	60 (62.5%)
Dysgeusia	50 (21.1%)
Total	96 (100%)

Among the drug classes most used by the participants, antihypertensives (72.9%) and antidepressants (33%) were outstanding (Graph 1). Medicines included in "others" are food supplements like calcium, glucosamine, omega 3, cholecalciferol, melatonin, lactulose, lithium carbonate, and folic acid; thyroid treatment agents such as levothyroxine; hormone therapy medications such as tibolone; Parkinson's treatment agents such as levodopa and benserazide hydrochloride; gastric protectors such as omeprazole and pantoprazole; medications for cardiac arrhythmias such as propafenone, amiodarone; for treatment of benign prostatic hyperplasias such as tamsulosin and dutasteride; for treating glaucomas such as latanoprost and timolol maleate; nasal decongestant such as sodium chloride; and anti-vertigo drugs such as bestatin.

Graph 1. Percentage distribution of drug classes used by older people followed-up at the Geriatric Outpatient Clinic (University Hospital of Brasília) between July and August 2018



The medications most used by research participants are listed in Table 2. The use of Losartan (51%), Amlodipine (22.9%), and Metformin (16.6%) were outstanding. Medicines mentioned five times or more by the elderly were considered.

Table 2. Prevalence of medication use by older people monitored at the Geriatric Clinic between July and August 2018

Medication	Prevalence of use among participants
Losartan	51%
Amlodipine	22.9%
Metformin	16.6%
Hydrochlorothiazide (HCTZ)	15.6%
Simvastatin	13.5%
Acetylsalicylic Acid(ASA)	12.5%
Calcium	12.5%
Levothyroxine	11.4%
Dipyrone	11.4%
Atenolol	10.4%
Indapamide	10.4%
Omeprazole	10.4%
Acetaminophen	7.2%
Rosuvastatin	7.2%
Mirtazapine	6.2%
Gliclazide	5.2%
Duloxetine	5.2%

The interactions between the drugs used with those most prescribed in dentistry[16] were described in Chart 1. No relevant drug interactions with local anesthetics used in dental practice were found.

There was an association between polypharmacy and xerostomia (PR = 1.57, 95%CI, 1.10-2.23, p = 0.004), but there was no association between polypharmacy and dysgeusia (PR = 1.14, 95%CI, 0.862-1 .51, p=0.348).

Table 3 shows the result of the binomial logistic regression. The use of antihypertensive drugs was associated with the occurrence of xerostomia. There was no association between the use of the drugs listed and the presence of dysgeusia.

Chart 1. Interactions between the drugs most used by study participants and those frequently prescribed in Dentistry, according to the severity of the interaction described by Micromedex Drug Interactions® and Dynamed®

Drug Classes	Medicines often prescribed in dentistry	Medicines most used by the older people											
		ASA	Atenolol	Duloxetine	Dipyrone	HCTZ	Indapamide	Losartan	Mirtazapine	Omeprazole	Acetaminophen	Prednisone	Rosuvastatin	Simvastatin
Non-Opioid Analgesics / NSAIDs/ Opioid Analgesics	Dipyrone		++	+++		+++	+++							
	ASA		++					+++			+++	++		
	Diclofenac Sodium	+++	++	+++		+++	+++	++				+++		
	Ibuprofen	+++	++	+++		+++	+++	++				+++		
	Codeine			+++										+++
Antibiotics	Erythromycin													X
	Azithromycin													+++
EIA	Dexamethasone	++			+++									
Anxiolytics (Benzodiazepines)	Diazepam								+++	+				
Antifungals	Fluconazole								X	++		++	++	

Severity of drug interaction: X: contraindicated; +++: major; ++: moderate; +:minor.

Chart 2. Details about the interactions between the drugs most used by study participants and those frequently prescribed in Dentistry described by Micromedex Drug Interactions® and Dynamed®

Medicines most used by the older people	Medicines often prescribed in dentistry	Interactions
ASA	1. Diclofenac Sodium	1. May result in an increased risk of bleeding and cardiovascular events
	2. Ibuprofen	2. May result in decreased antiplatelet effect of acetylsalicylic acid, an additive risk of bleeding, and risk of cardiovascular events
	3. Dexamethasone	3. May result in an increased risk of gastrointestinal ulceration and lower aspirin serum concentrations
Atenolol	1. Dipyrone	1. May result in decreased antihypertensive activities
	2. ASA	2-4. Concurrent use of them may result in an increased blood pressure
	3. Diclofenac Sodium	
	4. Ibuprofen	
Duloxetine	1. Dipyrone	1. May result in increased risk or severity of gastrointestinal bleeding
	2. ASA	2-4. May result in an increased risk of bleeding
	3. Diclofenac Sodium	
	4. Ibuprofen	
	5. Codeine	5. May result in an increased risk of serotonin syndrome increased codeine plasma concentrations and reduces plasma concentrations of the active metabolite
Dipyrone	1. Dexamethasone	1. May result in increased risk or severity of gastrointestinal irritation
HCTZ	1. Dipyrone	1. May result in decreased Hydrochlorothiazide therapeutic efficacy
	2. ASA	2-4. May result in reduced diuretic effectiveness and possible nephrotoxicity
	3. Diclofenac Sodium	
	4. Ibuprofen	
Indapamide	1. Dipyrone	1. May result in decreased Indapamide therapeutic efficacy
	2. ASA	2-4. May result in reduced diuretic effectiveness and possible nephrotoxicity
	3. Diclofenac Sodium	
	4. Ibuprofen	
Losartan	1. ASA	1-3. May result in renal dysfunction and/or increased blood pressure
	2. Diclofenac Sodium	
	3. Ibuprofen	
Mirtazapine	1. Diazepam	1. May result in an increased risk of somnolence
	2. Fluconazole	2. May result in increased mirtazapine plasma concentrations and increased risk of QT-interval prolongation and ventricular arrhythmias
Omeprazole	1. Diazepam	1. May result in enhanced and prolonged diazepam effects
	2. Fluconazole	2. May result in increased plasma concentrations of omeprazole
Acetaminophen	1. ASA	1. May result in an increased risk of bleeding

Continue

Continuation

Prednisone	1. ASA	1. May result in an increased risk of gastrointestinal ulceration and lower aspirin serum concentrations
	2. Diclofenac Sodium	2-3. May result in an increased risk of a gastrointestinal ulcer or bleeding
	3. Ibuprofen	
	4. Fluconazole	4. May result in a decrease in the metabolic degradation of prednisone and an increase in prednisone efficacy
Rosuvastatin	1. Fluconazole	1. May result in increased rosuvastatin exposure and an increased risk of myopathy or rhabdomyolysis
Simvastatin	1. Codeine	1. May result in decreased Simvastatin metabolism
	2. Erythromycin	2. May result in an increased risk of myopathy or rhabdomyolysis
	3. Azithromycin	3. May result in an increased risk of rhabdomyolysis

Table 3. Binomial Logistic Regression Model between xerostomia and the drugs most used by the participants.

Drugs Classes	Estimate	Standard Error	Z[1]	p value
Hypoglycemic	0.188	0.597	0.31484	0.753
Antihypertensives	1.397	0.536	2.60448	0.009
Platelet antiaggregants and anticoagulants	-1.414	0.777	-1.82012	0.069
Antidepressants	0.600	0.597	1.00482	0.315
Antilipidemics	-0.177	0.676	-0.26170	0.794
Analgesics and NSAIDs	0.517	0.608	0.85171	0.394
Benzodiazepines	-18.991	2452.989	-0.00774	0.994
Others	0.919	0.588	1.56239	0.118

1- Z-score

Discussion

The majority of study participants reported having xerostomia, which was statistically associated with polypharmacy. Therefore, the prevalence of xerostomia was high (62.5%) compared with that of another study, also conducted in Brazil, in which it was prevalent in 49% of non-institutionalized elderly[18]. A systematic review with meta-analysis showed a prevalence of xerostomia of 22% in adults, and that this percentage was higher in the elderly[19] due to the aging process predisposed to salivary gland agenesis, immunological disorders such as Sjogren's syndrome, metabolic disorders such as diabetes mellitus and rheumatoid arthritis, and use a lot of medications[7].

Xerostomia is a subjective measure, and its diagnosis is often the patient's report[10]. Methods to assess the quantity and quality of saliva can be used simultaneously,

such as chewing gum test, paraffin, or Saxon test[7]. In addition, scintigraphy, sialography, and minor salivary gland biopsy can help gland dysfunctions diagnosis[7,8].

It is essential to emphasize the importance of a multidisciplinary approach to the elderly with xerostomia with the purpose of verifying the etiology and implementing the most appropriate treatment for this situation[10,11]. The doctor and the pharmaceutical responsible can help in the alternative medications to improve the dry mouth sensation; use of chewing gums and substitutes of saliva are non-pharmacological alternatives that can relieve the xerostomia[8].

Our study showed a low prevalence of dysgeusia (21.1%), similar to rates in another Brazilian study, which found a prevalence of 19.4% in the elderly[20]. Dysgeusia has a multifactorial etiology and may result from sensory and nutritional disorders, medications, and polypharmacy. Furthermore, it may be related to infections since half of those infected with SARS-CoV-2 have experienced a loss of taste[21]. Dysgeusia interferes with the quality of life of the elderly, as it can cause feeding difficulties related to the lack of perception and taste distinction and consequently lead to weight loss[12].

In both xerostomia and dysgeusia, polypharmacy and drug use are common causes[4,6]. In the present study, there was an association between xerostomia and polypharmacy (particularly the use of antihypertensive drugs), but not between dysgeusia and polypharmacy. Previous studies have shown elevated rates of xerostomia associated with polypharmacy that included use of antihypertensives, anticholinergic, adrenergic, Thyroid-stimulating hormones, sedative, hypoglycemic, nonsteroidal anti-inflammatory, corticosteroid, and antiulcerogenic hormones[18]. Although the literature has previously included the association of dysgeusia with various medications, such as antimicrobials, angiotensin-converting enzyme inhibitors, chemotherapeutic agents, among others[12], in this study, no drug classes were found to be associated with dysgeusia.

The medications most used by the participants were antihypertensives (losartan and amlodipine) and hypoglycemic agents (metformin), followed by antidepressants. A cohort conducted in the United States showed that the drug classes most used among the population were antihypertensives, analgesics, statins, anticholinergics, psychiatric drugs, and antibiotics[6]. A Brazilian study also highlighted antihypertensives, used by 70.9% of the elderly, followed by antilipemic agents, antacids, hypoglycemic agents, antiplatelet agents, thyroid hormone, antidepressants, and benzodiazepines[22] . These data reflect the epidemiological transition experienced in Brazil. There is an increase in the prevalence of chronic and mental diseases when compared with the high number of infectious diseases reported in the past[23].

Drug therapy in dentistry includes infection, inflammation, pain, and anxiety[24]. Therefore, it is necessary to use non-opioid and opioid analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), antimicrobials, anxiolytics, in addition to local anesthetics[16]. We considered the medications used by the participants in our study, and drug interactions relevant to dental practice were found. The concomitant use of simvastatin and erythromycin is contraindicated, as it can reduce the effect of simvastatin. Consequently, it can lead to myopathy, as erythromycin contains an inhibitory effect on a CYP3A4 enzyme, which metabolizes simvastatin[25]. Another

relevant contraindication is between fluconazole and mirtazapine because the CYP3A enzyme metabolizes mirtazapine, and fluconazole initiates its activity. The concomitant use of these two drugs increases the plasma concentration of mirtazapine, therefore, increases the risk of prolongation of the QT interval and episodes of ventricular arrhythmia[26] .

Furthermore, healthcare professionals should be aware of the contraindication between NSAIDs and thiazide diuretics since this combination is associated with diuretic efficacy and can lead to nephrotoxicity[26]. Increased risk of gastrointestinal ulcers can occur when there is concomitant use of NSAIDs and corticosteroids[26]. The use of duloxetine may cause a relevant interaction with NSAIDs, which may increase the risk of bleeding[26]. The use of fluconazole is also considered a risk for simultaneous use with simvastatin due to the possibility of [leading to] myopathy and rhabdomyolysis[26].

Drug interactions may occur due to drugs that have a high rate of binding to plasma proteins, a long half-life, and a narrow therapeutic window. Furthermore, they are more common in patients with chronic diseases, making use of polypharmacy and self-medication, including herbal medicines[16].

Given the above, health professionals who prescribe medications, such as physicians and dentists, should know about possible drug interactions and adverse reactions[27]. Therefore, it is necessary to carry out a detailed anamnesis that will allow the professional to recognize the possibility of drug interactions occurring, thus preventing adverse effects and even providing treatment when necessary[28].

Among the study limitations, the use of a non-probabilistic sample, limited to a research center can be mentioned. The discrepancy between men and women is due to the study location and the trend towards greater self-care in women[29]. This fact may have influenced the prevalence of xerostomia and dysgeusia, as hormonal changes are frequent in elderly women and predispose to changes in taste and dry mouth[4,11]. Furthermore, the dose and frequency of medications used by the participants were not evaluated.

In conclusion, xerostomia is a frequent complaint among older people using polypharmacy, especially those using antihypertensives. Antihypertensives and antidepressants were used most drugs by the elderly and exhibited interactions with drugs most prescribed in Dentistry. Two contraindications were found between fluconazole and mirtazapine; and between erythromycin and simvastatin.

Author Contribution

Danielly de Mendonça Guimarães: assisted in collecting and tabulating data, carried out the article's writing, and carried out the final review.

Yeda Maria Parro: responsible for collecting the data, helping with the study design and reviewing the final version of the article.

Herick Sampaio Muller: responsible for assisting in data interpretation and reviewing the final version of the article.

Eduardo Barbosa Coelho: responsible for assisting in the elaboration of the work methodology, statistical calculations, and reviewing the final version of the article.

Vicente de Paulo Martins: responsible for assisting in data interpretation and reviewing the end of the article.

Rafael Santana: responsible for assisting in the interpretation and organization of data, guiding the discussion about pharmacology, and reviewing the final version of the article.

Érica Negrini Lia: responsible for outlining the study and guiding and reviewing the final version of the article.

All authors actively participated and revised and approved the final version of the manuscript.

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