# 6

# Antidepressants: Side Effects in the Mouth

Patrícia Del Vigna de Ameida, Aline Cristina Batista Rodrigues Johann, Luciana Reis de Azevedo Alanis, Antônio Adilson Soares de Lima and Ana Maria Trindade Grégio
*Pontifícia Universidade Católica do Paraná & Universidade Federal do Paraná*
*Brazil*

## 1. Introduction

Oral reactions to medications are common and affect patients' quality of life. Almost all classes of drugs, particularly those used continuously, such as antidepressants, anti-hypertensives, anxiolytics, hypnotics, diuretics, antipsychotics among others, including vitamins, minerals and phyto-pharmaceuticals, may cause oral alterations. If not suitably treated, these may aggravate the patient's general state of health and affect his/her oral health (Lamy, 1984; Smith & Burtner, 1994; Rees, 1998; Ciancio, 2004; American Dental Association [ADA], 2005; Scelza et al., 2010).

Prescribed and over-the-counter medications are frequently used in large quantities and by many adults, particularly by those over the age of 65 years. The abusive use of drugs, mainly by elderly patients, may generate oral side effects (Lamy, 1984; Ciancio, 2004; ADA, 2005).

The number of prescriptions in the USA is mainly due to the therapeutic advances in the treatment of various medical conditions and the increase in the geriatric population. Josephe et al. (2003) observed that 21% of the 1,800 patient dental records reviewed showed antidepressant use. It is suspected that the prevalence of oral lesions increases in direct relation to the increase in the use of necessary drugs, mainly to control chronic diseases. Over 200 drugs are involved in adverse reactions and side effects on oral tissues. Smith & Burtner (1994) founded as oral side-effects of the most frequently prescribed drugs: dry mouth (80.5%), dysgeusia (47.5%) and stomatitis (33.9%).

Xerostomia, a subjective dry mouth sensation, is a side effect of around 400 medications. Moreover, it is one of the major problems in the USA at present, affecting millions of persons. Diminishment or absence of saliva may affect the emotional well being, cause significant morbidity and a reduction in the patient's quality of life (Ciancio, 2004; Fox et al., 1985; Sreebny & Schwartz, 1986; Sreebny & Valdini, 1987; Butt, 1991; Guggenheimer & Moore, 2003). Thus, a dental and medical record of the patient is necessary, with regular updating of the prescribed medications, because of the potential side effects of drugs and interactions among them. It is also important for dentists to know about the problems related to medication and the impact of this on diagnosis and the treatment plan (Keene et al., 2003).

## 2. Antidepressant

Psychotropic drugs are those that act on the central nervous system (SNC) producing alterations in behaviour, mood and cognition, and that may lead to dependence.

The use of psychotropic has increased over the last few decades in several countries. This growth has been attributed to the increased frequency of psychiatric disturbance diagnoses in the population, the introduction of new psycho pharmaceuticals on the pharmaceutical market and the new therapeutic indications of existent psychotropics (Rodrigues, 2006).

Patients that take psychotropic medications for long periods may experience behaviours that have a negative impact on oral health. These medications may cause lethargy, fatigue and lack of motor control and memory that may impair the individual's ability to practice a good oral hygiene technique (McClain et al., 1991). Furthermore, a large number of medications used for the treatment of psychiatric diseases, have the side effects of dry mouth, diminished salivary flow speed and/or alteration in saliva composition (Sreebny & Schwartz, 1997; Loesche et al., 1995; Bardow et al., 2001). Zaclikevis et al. (2009) observed that psychotropic drugs caused hyposalivation in rats and acinar hypertrophy in their parotid glands. De Almeida et al. (2009) observed that psychotropic users presented a significant decrease in the stimulated salivary flow rate compared with the control group.

Antidepressants are medications prescribed to patients of all ages (Von Knorring & Wahlin, 1986; Meskin & Berg, 2000), for the treatment of a variety of psychiatric diseases (depression, affective disease, insomnia, anxiety, the panic syndrome and bipolar disorder). In addition, they are also prescribed for the treatment of some medical conditions, such as rheumatoid arthritis, dietary disorders, fibromyalgia, migraine, trigeminal neuralgia, pre-menstrual tension (Keene et al., 2003).

Antidepressant drugs were discovered in the early 1950s, with the development of the monoamine-oxidase inhibitors (MAOIs). MAO is the enzyme responsible for the degradation of various neurotransmitters, including adrenalin, serotonin, noradrenalin and dopamine. It is believed that MAO inhibition alleviates depression, allowing serotonin and noradrenalin to accumulate at the synaptic junction, in the storage locations, in the SNC and the independent sympathetic system (Perry et al., 1997). The following are examples of this class of antidepressants: tranylcypromine, moclobemide and selegiline.

In addition to the MAOIs, there are tricyclic antidepressants (TCAs) that are relatively non selective, acting not only on the serotonergic and noradrenergic systems, but also on the muscarinic, histaminergic and α- adrenergic systems (Messer et al., 1997). Their efficiency appears to be related to the increase in serotonin and noradrenalin, and to a lesser extent, of dopamine, at the synaptic gap (Stahl, 1992). Amitriptyline, imipramine, clomipramine and nortriptyline are some examples of tricyclic antidepressants.

The selective serotonin recapture inhibitors (SSRIs), such as: citalopram, fluoxetine, fluvoxamine, paroxetine and sertraline, represent another class of antidepressants that increase the availability of serotonin at the post-synaptic terminals by means of blocking recapture at the pre-synaptic terminal (Coccaro & Siever, 1985; Friedlander et al., 2002; Preskorn et al., 2004). The SSRIs appear to have fewer side effects than the TCAs, which present significant anticolinergic and cardiovascular effects (Keene et al., 2003).

The serotonin-noradrenalin recapture inhibitors are a new class of antidepressants, of which the venlafaxine, mirtazapine, trazodone and nefazodone form part (Feighner, 1999). Venlafaxine, especially, is a potent pre-synaptic inhibitor of serotonin and noradrenalin recapture, and a moderate inhibitor of dopamine recapture (Feighner, 1999; Barman Balfour & Jarvis, 2000; Wellington K, Perry, 2001).

Bupropion, an atypical antidepressant, exercises its effect by preventing the reuptake of noradrenalin and dopamine at the synaptic gap, thus facilitating neural transmission

(Goodnick PJ, Dominguez, 1998). The antidepressant effect of lithium, a mood stabilizing agent used to treat the depressive phase of bipolar disorder, may derive from its ability to increase the serotonin levels in the SNC (Schou, 1999).

The majority of antidepressant medications prescribed is associated with a number of significant oral reactions (Friedlander & Mahler, 2001). These complications, including xerostomia, sialoadenitis, gingivitis, dysgeusia, glossitis, tongue edema and discoloration and stomatitis, almost always appear due to dysfunction of the salivary gland induced by the medication. But in patients that make use of mirtazapine, the development of stomatitis may represent the initial signs of bone marrow suppression induced by the medication, such as: agranulocytosis, leukopenia or granulocytosis, a potentially fatal event (Friedlander & Norman, 2002). Bertini et al. (2009) reports a case of ulceration of the oral mucosa induced by antidepressant medication.

Rindal et al. (2005) suggest that antidepressant drugs do not generate a raise in the overall restoration risk level when compared with a group on non-xerogenic drug. Instead, that antidepressant medication raises the quantity of disease for persons already at risk. The non-xerogenic group had a superior restoration rate than the no medication group but not as high as the antidepressant group rate.

Studies that assessed the oral health of patients that use antidepressants observed extensive tooth losses. This may occur because of various factors: lack of interest in oral hygiene, preference for carbohydrates (probably because of the reduction of serotonin in the SNC), preference for sweetened foods because of alterations in the sense of taste (dysgeusia), by the diminishment of saliva release and by the high lactobacillus counts (Rundegren et al., 1985; Christensen & Somers, 1996; Anttila et al., 1999).

Persons with depression are also at high risk of developing periodontal disease, because neglected oral hygiene, increased smoking and altered immune response, associated with xerostomia facilitate increased colonization by pathologic bacteria in the mouth, leading to collapse of the periodontium (Moss et al., 1996; Elter et al., 1999). Patients that receive SSRIs or atypical antidepressants may sometimes develop movement disorders that include bruxism or tooth-grinding, which may aggravate the patient's periodontal status (Brow & Hong, 1999). These drugs raise the extrapyramidal serotonin levels, thus inhibiting the dopaminergic pathways that control the movements (Bostwick & Jaffee, 1999).

There is consensus among various authors that xerostomia is the main and the commonest side effect of antidepressant drugs (Smith & Burtner, 1994; Pajukoski et al., 2001; Ciancio, 2004; Scully, 2003; Josephe et al., 2003; Thomson et al., 2006; Uher et al., 2009), in addition to this, patients that receive antidepressant therapy frequently complain about diminished salivation and changes in salivary viscosity (Astor et al., 1999).

### 2.1 Role of saliva in oral health

Saliva is a true mirror of the body that contains a large number of organic and inorganic compounds, and can be seen as a very important health indicator. Salivary secretion is controlled by the autonomic nervous system through receptors present in the salivary gland. Many studies show that medicine and diseases can affect the function of salivary glands as regards the quality and quantity of saliva secreted (Greabu et al. 2009; Gregio et al., 2006).

Salivary secretion is complex and occurs subsequent to neurotransmitter stimuli. The principal control of secretion is derived from sympathetic and parasymphatetic innervation

which regulates the secretory function on the acinar cell level and controls the reabsorption process in the striated ducts of salivary glands. Parasympathetic stimulation increases the volume of secreted saliva, whereas sympathetic stimulation mainly affects protein content and composition. The salivary gland may serve as a model to determine the peripheral effects of different antidepressants on the monoaminergic and the cholinergic systems. Salivary gland function depends on the integrity of both parasympathetic and sympathetic innervation. Normal salivation is an essential demand for oral health, due to its important contributions to the oral defense mechanisms. Diminished salivary secretion could lead to serious disease and deterioration of the mucosa (Von Knorring & Mornstad, 1986; Hunter& Wilson, 1995) The saliva has several important functions in the mouth, including protection of the oral mucosa, chemical buffering, digestion, taste, antimicrobial action, and maintaining the integrity of the teeth. Due to its glycoprotein contents saliva has a viscous aspect that protects the oral mucosa by the formation of a barrier against noxious stimuli, microbial toxins, and minor trauma. Its fluid nature facilitates the removal of cell debris and non-adherent bacteria (Edgar, 1992).

### 2.2 Antidepressant and xerostomia

Xerostomia means a subjective dry mouth sensation and represents a symptom related by the patient. It may occur in the presence of systemic diseases or conditions, such as displayed on Table 1, or as consequence of use of drugs (Table 2) (Lamy, 1984; Sreebny & Schwartz, 1997; Stack & Papas, 2001; Scully, 2003; Guggenheimer & Moore, 2003). Between the drugs stands out the antidepressants (Table 3). Patients with xerostomia displayed various degrees of discomfort related to the quality of life according to the aetiology of their conditions (Cho et al., 2010). Around 1 in 5 people complain of dry mouth, and a rising occurrence in the elderly, it is essential to have a complete understanding of this subject (Hopcraft & Tan, 2010).

Of the conditions mentioned above, salivary hypofunction secondary to the use of medications is the commonest (Nederfors, 1996; Fox, 1998). They inhibit the cholinergic signals in the salivary tissues and thus diminish the excretion of fluids by the glands, and interferences in central pathways (serotoninergics and dopaminergics) may also alter salivary composition (Atkinson & Baum, 2001). The normal stimulated salivary flow rate is between 0.7 to 1 mL/min, whereas hyposalivation is considered when the salivar production is under 0.7 mL/min (Tenovuo & Lagerlöf, 1994).

Aging has a minimum impact on salivary flow, but the advance of age and the appearance of chronic diseases lead to the use of drugs that may diminish the salivary flow by up to 40% (Sreebny & Schwartz, 1997; Ben-Aryeh et al., 2001). Complaints of xerostomia may increase three-fold in elderly patients that receive xerogenic medication (Osterberg et al., 1984).

In a study comparing the use of escitalopram and nortriptyline, Uher et al. (2009) observed that dry mouth was the most commonly reported adverse effect, and that it was more common during treatment with either nortriptyline or escitalopram than in the medication-free state. The authors also demonstrated a positive correlation with the dose of both antidepressants.

There is evidence that the prevalence of dry mouth is correlated to polymedication (Locker, 1995; Nederfors et al., 1997). But, Persson et al. (1991) verified that the use of up to 4

different xerogenic medications did not result in significantly additional reduction in the salivary flow speed in his patients.

| **Diseases/Conditions** |
|---|
| Salivary aplasia |
| Dehydration |
| Sarcoidosis |
| Cystic fibrosis |
| Psycogenic |
| Sjögren´s syndrome |
| Primary biliary cirrhosis |
| Infections (HIV, HTLV-1, Hepatitis C) |
| Radiation therapy |
| Renal dialysis |
| Vasculits |
| Bone marrow transplantation |
| Anxiety |
| Depression |
| Graft vs host disease |
| Diabetes type 1 or 2 |
| Diabetes insipidus |
| Haemorrhage |
| Chemotherapy |
| Tabagism |
| Oral respiration |

Table 1. Systemic diseases or conditions related with xerostomia

The subjective dry mouth sensation may occur even in the presence of a normal salivary flow that is, not necessarily being associated with a diminution in the amount of saliva (Fox et al., 1985; Närhi, 1994). According to Mandel & Wotman (1994) the quality of salivary secretion (especially the mucin content) is more important than the quantity in the dry mouth sensation. The type of saliva (rest or stimulated), procedures and time of collection, composition and source (larger or smaller salivary glands) are factors that can contribute to the patient's report of dry mouth and it relationship with hyposalivation (Mandel & Wotman, 1994; Von Knorring & Mörnstad, 1981). According to Nagler (2004), in up to one third of cases, xerostomia does not reflect a real reduction in salivary flow speed.

As regards dry mouth, it is due to the reduction in saliva secretion or when its composition is altered, and it may cause various clinical problems (Table 4) (Nagler, 2004; Ursache et al., 2006; Tuner et al., 2007).

| **Drugs** |
|---|
| Skeletal muscle relaxants |
| Antihypertensive agents |
| Anti-Parkison agents |
| Antihistamines |
| Antipsychotics |
| Diuretics |
| Antispasmodics - Scopolamine |
| Atropine |
| Muscarinic receptor antagonists for treatment of overactive bladder |
| Barbiturates |
| Clonidine |
| Lithium carbonate |
| Phenylbutazone |
| Psychotropics |
| Tri-iodothyronine |
| Anticonvulsivants |
| Antidysrhythimic |
| Anti-incontinence agent |
| Ophtalmic formulation |
| Smoking cessation agent |
| Appetite suppressants |
| Antimigraine agents |
| Antidepressants |
| Descongestionants |
| Bronchodilators |
| Alfa receptor antagonist for treatment of urinary retention |
| Benzodiazepines- Lorazepam |
| Opioids- morphine |
| Hypnotics |
| Retinoids |
| Cytokines |
| Anti-HIV drugs |
| H2 antagonists and proton pump inhibitors |
| Cytotoxic agents |
| Drugs of abuse |
| Anxiolytics |

Table 2. Drugs related with xerostomia

| **Antidepressant** |
|---|
| Serotonin agonists |
| Noradrenalin re-uptake blockers |
| Serotonin re-uptake inhibitors |
| Noradrenalin and Serotonin re-uptake blockers |
| Atipical antidepressants |
| Tricyclic antidepressants |
| Heterocyclic antidepressants |
| Monoamine oxidase inhibitors |
| Venlafaxine |
| Buspirone |
| Alprazolan |

Table 3. Antidepressant related with xerostomia

| |
|---|
| Dental caries |
| Dry lips (Fig.1) |
| Colourless oral mucosa |
| Dry mouth (Fig.2) |
| Dysgeusia |
| Partially no papilla tongue |
| Atrophied papilla and deep fissures (Fig.3) |
| Dysphagia |
| Gingivitis |
| Halitosis |
| Mastication problems |
| Burning sensation in the mouth |
| Mucositis |
| Candidiasis |
| Poorly fitting prostheses |
| Sleeping difficulty |
| Difficulty with speech |
| Traumatic oral lesions |
| Halitosis |
| Ulceration |
| Periodontal disease |
| Saliva composition changes |

Table 4. Oral effects of hipossalivation

A variety of technique have used to evaluate xerostomia: questionnaire; visual analogue-scale; clinical inspection if a tongue blade adheres to the buccal mucosa or if a patient can

chew and swallow dried food without water; by quantifying the volume of residual saliva on mucosal surfaces using filter paper and micro-moisture meter and calculating thickness; and mucosal wetness devices (Osailan et al., 2011). Also, sialometry (salivary flow rate measurement) is indicated as part of the diagnostic procedures for hyposalivation (Tenovuo & Lagerlöf, 1994), and the composition of saliva can be verified by means of biochemical salivary exams.

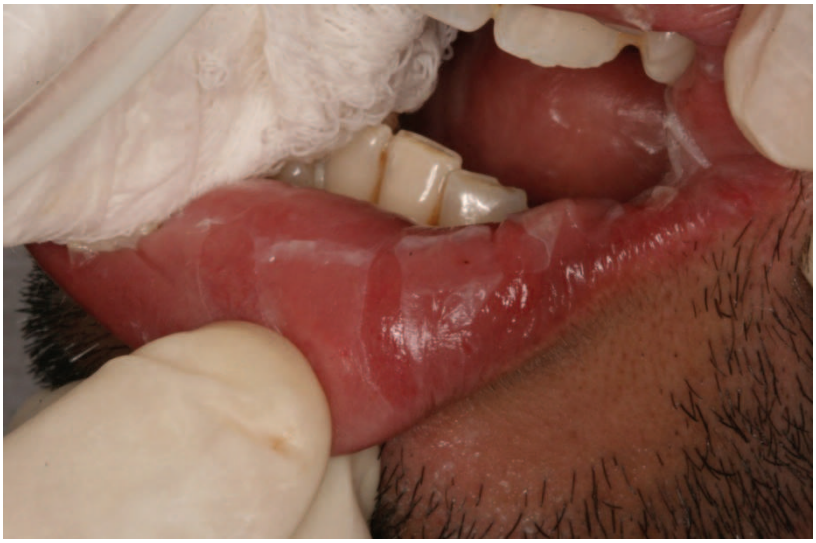


Fig. 1. Clinical presentation: A patient in a coma state showing intense dry lip mucosa

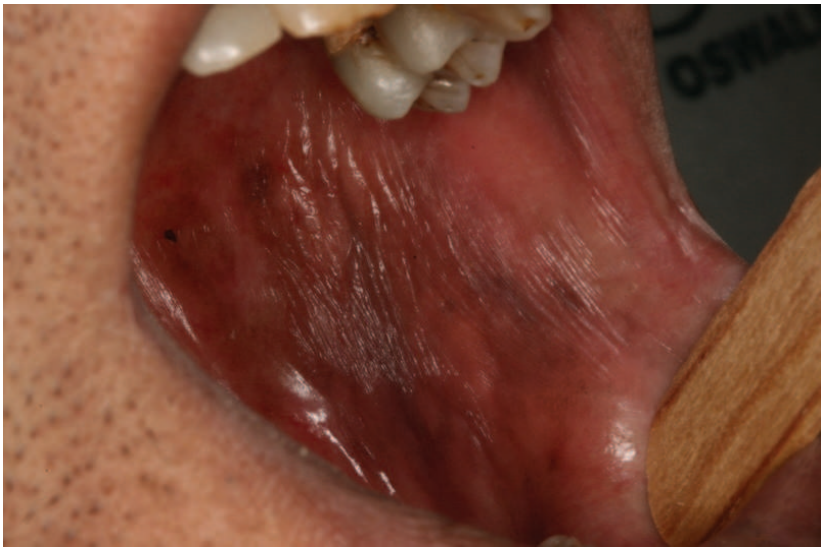


Fig. 2. Clinical presentation: A patient showing dry mucosae after use of medications

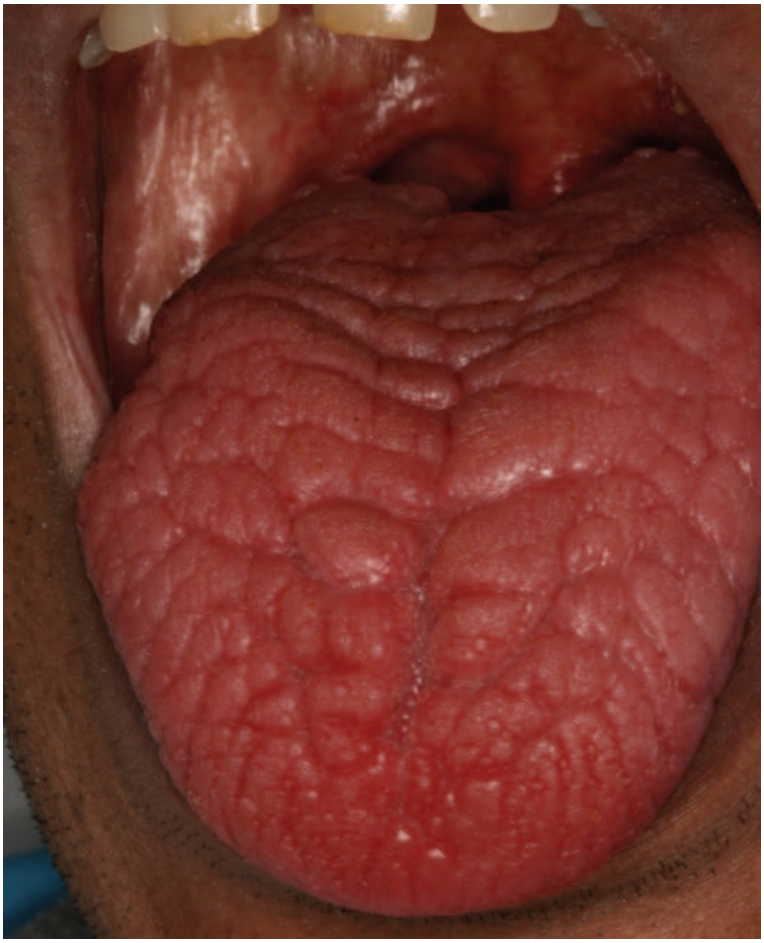


Fig. 3. Clinical presentation: A patient treated with medication showing tongue with atrophied papilla and deep fissures

Antidepressants have anticolinergic or antimuscarinic action, which acts to block the actions of the parasympathetic system by inhibiting the effects of acetylcholine on the salivary gland receptors. This results in a dry mouth sensation, probably because the sympathetic portion of the independent nervous system predominates over the "blocked" parasympathetic system (Wynn et al., 2001). According to Schubert & Izutsu (1987), the drugs may affect the salivary flow and its composition by interferences in the acinary and duct functions, and by means of alterations in the blood flow of the salivary glands. According to Douglas (2002) diminishment of the salivary flow is due to the reduction in the blood flow of the gland, produced by adrenergic sympathetic vasoconstriction. Therefore, when there is sympathetic hyperactivity the mouth presents dry.

It is important to emphasize that the dry mouth sensation and alteration in salivary composition may occur during periods of stress and/or acute anxiety, frequently present in depressive disorders, due to predominant stimulation of the sympathetic system,

irrespective of the use of anxiolytic and/or antidepressant medication (Guggenheimer & Moore, 2003). Isolated depression is related to diminishment of salivary secretion and to xerostomia, due an anticolinergic action (Stack & Papas, 2001; Brown, 1970). Therefore, it may be difficult to determine whether these side effects and their intensity arise from the medical condition that led to the treatment, or from the medication prescribed for it (Smith & Burtner, 1994), it probably is as a result of both.

### 2.3 Treatment of hyposalivation

Various treatments are proposed for enhanced salivary secretion, among them, the use of a salivary flow stimulating drug pilocarpine chloride which acts by stimulating the parasympathetic ANS (Vivino et al., 1999). This drug has been used because it stimulates the cholinergic receptors, among them the muscarinicM3 receptor present in the salivary glands, resulting in the expulsion of the stored salivary contents (Ferguson, 1993), thus an increase in saliva production and release was observed with the use of cholinergic drugs.
The next table shows the types of hyposalivation treatment according to Turner & Ship (2007), treatment strategies include salivary replacement therapies, as well as use of statory, masticatory and pharmacological stimulants.

| |
|---|
| Gustatory and tactile sialogogues |
| Acid-tasting substances |
| Acidic (sugar-free) sweets |
| Acidic or effervescent drinks (lemon juice, citric acid, buttermilk) |
| Citric acid crystals |
| Cotton-wool gauze soaked in a citric acid and glycerine solution |
| Lemon pastilles |
| Lemon slices |
| Vitamin C tablets |
| Miscellaneous substances |
| Dried pieces of reed root (calami rhizome) |
| Sugar-free chewing gum |
| Sugar-free sweets |
| Vegetables or fruits |
| Anetholetrithione |
| Benzapyrone |
| Betanechol chloride |
| Carbachol |
| Cevimeline |
| Folia Jaborandi and tinctura Jaborandi |
| Neostigmine, neostigmine bromide, pyridostigmine bromide |
| Destigmine bromide |
| Nicotinamide and nicotine acid |
| Pilocarpine hydrochloridey, pilocarpine nitrate |
| Potassium iodide |
| Trithioparamethoxyphenylpropene |

Table 5. Treatment of hiposalivation

## 3. Conclusion

Xerostomia is the main oral side effect associated with the various classes of drugs, particularly those used continuously. There is, however, not always a positive correlation between hyposalivation and xerostomia. This symptom may be the result of both diminished salivary secretion and an alteration in saliva composition. Nevertheless, when present, xerostomia may affect the patient's emotional well being, aggravate his/her general state of health, as well as affect his/her oral health, as other reactions such as dygeusia, candidosis, caries and stomatitis are reported as being the consequence of xerostomia. It is important to emphasize the dentists' role as regards patients that make use of medications, mainly for treating chronic diseases. It is their obligation to keep a detailed and updated medical history of their patients, in order to be alert to problems related to medication, and the impact of this on the diagnosis and treatment plan, as well as to prepare the most adequate and effective preventive programs possible. In order to determine whether or not the patient presents hyposalivation, the dentist can have a complementary exam, called sialometry (salivary flow speed measurement), may be performed. If there is any doubt about the composition of the saliva, there are biochemical tests that can reveal alteration in its composition. Communication between the doctor and dentist is extremely important, so that together, they re-establish the patient's general and oral health as far as possible.

## 4. Acknowledgment

The authors thank to Sonia Maria Del Vigna for technical support, and to Pontifícia Universidade Católica do Paraná for financial support.

## 5. References

American Dental Association [ADA]- Division of Communications. (2005). For the dental patient. How medications can affect your oral health. *Journal of the American Dental Association*, Vol.136, No.6, (June 2005), pp.831, ISSN 0002-8177

Anttila, S.; Knuuttila, M. & Sakki, T. (1999). Depressive symptoms favor abundant growth of salivary lactobacilli. *Psychosomatic Medicine*, Vol.61, No.4, (July-August 1999), pp.508-512, ISSN 0033-3174

Astor, F.; Hanft, K. & Ciocon, J. (1999). Xerostomia: a prevalent condition in the elderly. *Ear, nose, & throat journal*, Vol.78, No.7, (July 1999). pp.476-479, ISSN 0145-5613

Atkinson, J. & Baum, B. (2001). Salivary enhancement: current status and future therapies. *Journal of dental education*, Vol.65, No.10, (October 2001), pp.1096-1101, ISSN 0022-0337

Bardow, A.; Nyvad, B. & Nauntofte, B. (2001). Relationships between medication intake, complaints of dry mouth, salivary flow rate and composition, and the rate of tooth demineralization in situ. *Archives of oral biology*, Vol. 46, No.5, (May 2001), pp.413-423, ISSN 0003-9969

Barman Balfour, J. & Jarvis, B. (2000). Venlafaxine extended-release: a review of its clinical potential in the management of generalized anxiety disorder. *CNS Drugs*, Vol.14, No.6, (December 2000), pp.483-503, ISSN 1172-7047

Ben-Aryeh, H.; Miron, D.; Szargel, R. & Gutman, D. (1984). Whole-saliva secretion rates in old and young healthy subjects. *Journal of dental research*, Vol. 63, No.9, (September 1984), pp.1147-1148, ISSN 0022-0345

Bertini, F.; Costa, N.; Brandão, A.; Cavalcante, A. & Almeida, J. (2009). Ulceration of the oral mucosa induced by antidepressant medication: a case report. *Journal of medical case reports,* Vol.3, No.3, (November 2009), pp.98, ISSN 1752-1947

Bostwick, J. & Jaffee, M. (1999). Buspirone as an antidote to SSRI-induced bruxism in 4 cases. *The Journal of clinical psychiatry*, Vol. 60, No.12, (December 1999), pp.857-860, ISSN 0160-6689

Brow, E. & Hong, S. (1999). Antidepressant-induced bruxism successfully treated whith gabapentin. *Journal of the American Dental Association*, Vol.130, No.10, (October 1999), pp.1467-1469, ISSN 0002-8177

Brown, C. (1970). The parotid puzzle: a review of the literature on human salivation and its applications to psychophysiology. *Psychophysiology*, Vol. 7, No.1, (July 1970), pp.65-85, ISSN 0048-5772

Butt, G. (1991). Drug-induced xerostomia. *Journal of the Canadian Dental Association*, Vol.57, No5., (May 1991), pp.391-393, ISSN 0008-3372

Cho, M.; Ko, J.; Kim, Y. & Kho, H. (2010). Salivary flow rate and clinical characteristics of patients with xerostomia according to its aetiology. *Journal of oral rehabilitation*, Vol.37, No. 3, (March 2010), pp.185-193, ISSN 0305-182X

Christensen, L. & Somers, S. (1996). Comparison of nutrient intake among depressed and nondepressed individuals. *The International journal of eating disorders*, Vol.20, No.1, (July 1996), pp.105-109, INSS 0276-3478.

Ciancio, S. (2004). Medications' impact on oral health. *Journal of the American Dental Association*, Vol.,135, No.10, (October 2004), pp.1440-1448, ISSN 0002-8177

Coccaro EF, & Siever LJ (1985) Second generation antidepressants: a comparative review. *Journal of clinical pharmacology*, Vol.25, No.4, (May-June 1985), pp.241-260, ISSN 0091-2700

de Almeida, P.; Grégio, A.; Brancher, J.; Ignácio, S.; Machado, M.; de Lima, A. & Azevedo L,. (2008). Effects of antidepressants and benzodiazepines on stimulated salivary flow rate and biochemistry composition of the saliva. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics,* Vol.106, No.1, (July 2008), pp.58-65, ISSN 1079-2104

Douglas, C. (2002) *Tratado de fisiologia aplicada à saúde* (5th ed), Robe Editorial, ISBN 8573630256, São Paulo, Brazil

Edgar, W. M. (1992) Saliva: its secretion, composition and functions. British dental journal Vol.172, No.8, (April 1992), pp. 305-312, ISSN 0007-0610

Elter, J.; Beck, J.; Slade, G. & Offenbacher, S. (1999). Etiologic models for incident periodontal attachment loss in older adults. *Journal of clinical periodontology*, Vol.26, No.2, (February 1999), pp.113-123, ISSN 0303-6979

Feighner, J. (1999). Mechanism of action of antidepressant medications. *The Journal of clinical psychiatry*, Vol.60, Suppl.4, (1999), pp.4-11, ISSN 0160-6689

Ferguson, M. (1993). Pilocarpine and other cholinergic drugs in the management of salivary gland dysfunction. *Oral surgery, oral medicine, oral pathology*,Vol.75, No.2, (Feburary 1993), pp.186-191, ISSN 0030-4220

Fox, P. (1998). Acquired salivary dysfunction. Drugs and radiation. *Annals of the New York Academy of Sciences,* Vol.842, (April 1998), pp.132-137, ISSN 0077-8923

Fox, P.; van der Ven, P.; Sonies, B.; Weiffenbach, J. & Baum, B. (1985). Xerostomia: evaluation of a symptom with increasing significance. *Journal of the American Dental Association*, Vol.110, No.4, (April 1985), pp.519-525, ISSN 0002-8177

Friedlander, A.; Friedlander, I. & Marder, S. (2002). Bipolar I disorder: psychopathology, medical management and dental implications. *Journal of the American Dental Association,* Vol.133, No.9, (September 2002), pp.1209-1217, ISSN 0002-8177

Friedlander, A. & Mahler, M. (2001). Major depressive disorder: psychopathology, medical management and dental implications. *Journal of the American Dental Association*, Vol.132, No.5, (May 2001), pp.629-638, ISSN 0002-8177

Friedlander, A. & Norman, D. (2002). Late-life depression: psychopathology, medical interventions and dental implications. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics*, Vol.94, No.4, (October 2002), pp.404-412, ISSN 1079-2104

Goodnick, P.; Dominguez, R.; DeVane, C. & Bowden, C. (1998). Bupropion slow-release response in depression: diagnosis and biochemistry. *Biological psychiatry*, Vol.44, No.7, (October 1998), pp.629-632, ISSN 0006-3223

Greabu, M.; Battino, M.; Mohora, M.,; Totan, A.; Didilescu, A.; Spinu, T.; Totan, C.; Miricescu, D. & Radulescu, R. Saliva--a diagnostic window to the body, both in health and in disease. *Journal of medicine and life*. Vol.2, No.2 (April-June 2009), pp.124-132, ISSN 1844-122X.

Grégio, A.; Durscki, J.; Lima, A.; Machado, M.; Ignácio, S. & Azevedo, L (2006). Association of amitryptiline and Diazepam on histomorphometry of rat parotid glands. *Pharmacologyonline,* Vol.2, (2006), pp.96-108, ISSN, 1827-8620.

Guggenheimer, J. & Moore, P. (2003). Xerostomia: etiology, recognition and treatment. *Journal of the American Dental Association*, Vol.134, No.1, (January 2003), pp.61-69, ISSN 0002-8177

Hopcraft, M. & Tan, C. (2010). Xerostomia: an update for clinicians. *Australian Dental Journal*, Vol.55, No.3, (September 2010), pp.238-44, ISSN 0045-0421

Hunter, K. & Wilson, W. (1995). The effects of antidepressant drugs on salivary flow and content of sodium and potassium ions in human parotid saliva. *Archives of oral biology,* , Vol.40, No.11, (November 1995), pp. 983-989, ISSN:0003-9969

Keene, J.; Galasko, G. & Land, M. (2003). Antidepressant use in psychiatry and medicine: importance for dental practice. *Journal of the American Dental Association*, Vol.134, No.1, (January 2003), pp.71-79, ISSN 0002-8177

Lamy, M. (1984). Drugs and oral health. *Journal of the Maryland State Dental Association*, Vol.27, No.3, (December 1984), pp.125-130, ISSN 0025-4355

Locker, D. (1995). Xerostomia in older adults: a longitudinal study. *Gerodontology*, Vol.12, No.1, (July 1995), pp.18-25, ISSN 0734-0664

Loesche, W.; Bromberg, J.; Terpenning, M.; Bretz, W.; Dominguez, B.; Grossman, N. & Langmore, S. (1995). Xerostomia, xerogenic medications and food avoidances in selected geriatric groups. *Journal of the American Geriatrics Society*, Vol.43, No.4, (April 1995), pp.401-407, ISSN 0002-8614

Mandel, I. & Wotman, S. (1976). The salivary secretions in health and disease. *Oral sciences reviews*, Vol.8, (1976), pp.25-47, ISSN 0300-4759

McClain, D.; Bader, J.; Daniel, S. & Sams, D. (1991). Gingival effects of prescription medications among adult dental patients. *Special care in dentistry*, Vol.11, No.1, (January-February 1991), pp.15-18, ISSN 0275-1879

Meskin, L. & Berg, R. (2000). Impact of older adults on private dental practices, 1988-1998. *Journal of the American Dental Association,* Vol.131, No.8, (August 2000), pp.1188-1195, ISSN 0002-8177

Messer, T.; Schmauss, M. & Lambert-Baumann, J. (2005). Efficacy and tolerability of reboxetine in depressive patients treated in routine clinical practice. *CNS Drugs,* Vol.19, No.1, (2005), pp.43-54, ISSN 1172-7047

Moss, M.; Beck, J.; Kaplan, B.; Offenbacher, S.; Weintraub, J.; Koch, G.; Genco, R.; Machtei, E. & Tedesco, L. (1996). Exploratory case-control analysis of psychosocial factors and adult periodontitis. *Journal of periodontology,* Vol.67, 10 Suppl, (October 1996), pp.1060-1069, ISSN 0022-3492

Murray Thomson, W.; Poulton, R.; Mark Broadbent, J. & Al-Kubaisy, S. (2006) Xerostomia and medications among 32-year-olds. *Acta odontologica Scandinavica*, Vol.64, No.4, (August 2006), pp.249-254, ISSN 0001-6357

Nagler, R. (2004). Salivary glands and the aging process: mechanistic aspects, health-status and medicinal-efficacy monitoring. *Biogerontology*, Vol.5, No.4, (2004), pp.223-233, ISSN 1389-5729

Närhi, T. (1994). Prevalence of subjective feelings of dry mouth in the elderly. *Journal of dental research,* Vol.73, No.1, (January 1994), pp.20-25, ISSN 0022-0345

Nederfors, T. (1996). Xerostomia: prevalence and pharmacotherapy. With special reference to beta-adrenoceptor antagonists. *Swedish dental journal*. Supplement, Vol.116, pp.1-70, ISSN:0348-6672

Nederfors, T.; Isaksson, R.; Mörnstad, H. & Dahlöf, C. (1997). Prevalence of perceived symptoms of dry mouth in an adult Swedish population – relation to age, sex, and pharmacotherapy. *Community dentistry and oral epidemiology,* Vol.25, No.3, (June 1997), pp.211-216, ISSN 0301-5661

Osailan, S.; Pramanik, R.; Shirodaria, S.; Challacombe, S. & Proctor, G. (2011). Investigating the relationship between hyposalivation and mucosal wetness. *Oral diseases*, Vol.17, No.1, (January 2011), pp.109-114, ISSN 1354-523X

Osterberg, T.; Landahl, S. & Hedegard, B. (1984). Salivary flow, saliva, pH and buffering capacity in 70-year-old men and women. Correlation to dental health, dryness in the mouth, disease and drug treatment. *Journal of oral rehabilitation*, Vol.11, No.2, (March 1984), pp.157-170, ISSN 0305-182X

Pajukoski, H.; Meurman, J.; Halonen, P. & Sulkava, R. (2001). Prevalence of subjective dry mouth and burning mouth in hospitalized elderly patients and outpatients in relation to saliva, medication, and systemic disease. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics,* Vol.92, No.6, (December 2001), pp.641-649, ISSN 1079-2104

Perry, P.; Alexander, B. & Liskow, B. (1997). *Psychotropic drug handbook.* 7th ed, American Psychiatric Press, ISBN 0-88048-851-4, Washington, USA

Persson, R.; Izutsu, K.; Truelove, E. & Persson, R. (1991). Differences in salivary flow rates in elderly subjects using xerostomatic medications. *Oral surgery, Oral Medicine, and Oral Pathology,* Vol.72, No.1, (July 1991), pp.42-46, ISSN 0030-4220

Preskorn, S.; Ross, R. & Stanga, C. (2004). Antidepressants: past, present and future. Springer Verlag, ISBN 3-540-43054-7, Berlim, Germany

Rees, T. (1998). Drugs and oral disorders. *Periodontology 2000,* Vol.18, (October 1998), pp.21-36 ISSN 0906-6713

Rindal, D.; Rush, W.; Peters, D. & Maupomé, G. (2005). Antidepressant xerogenic medications and restoration rates. *Community dentistry and oral epidemiology*, Vol.33, No.1, (February 2005), pp.74-80, ISSN 0301-5661

Rodrigues, M.; Facchini, L. & Lima, M. (2006). Modifications in psychotropic drug use patterns in a Southern Brazilian city. *Revista de Saúde Pública*, Vol.40, No.1, (Feburary 2006), pp.107-114, ISSN 0034-8910

Rundegren, J.; Van Dijken, J.; Mörnstad, H. & Von Knorring, L. (1985). Oral conditions in patient receiving long-term treatment with cyclic antidepressant drugs. *Swedish dental journal,* Vol.9, No.2, (1985), pp.55-64, ISSN 0347-9994

Schou, M. (1999). Perspectives on lithium treatment of bipolar disorder: action, efficacy, effect on suicidal behavior. *Bipolar disorders*, Vol.1, No.1, (September 1999), pp.5-10, ISSN 1398-5647

Schubert, M. & Izutsu, K. (1987). Iatrogenic causes of salivary gland dysfunction. Journal of dental research, Vol.66, Spec No., (Feburary 1987), pp.680-688, ISSN 0022-0345

Scully, C. (2003). Drug effects on salivary glands: dry mouth. *Oral diseases*, Vol.9, No.4, (July 2003), pp.165-176, ISSN 1354-523X

Smith, R. & Burtner, A. (1994). Oral side-effects of the most frequently prescribed drugs. *Special care in dentistry*, Vol.14, No.3, (May-June 1994), pp.96-102, ISSN 0275-1879

Sreebny, L. & Schwartz, S. (1986). A reference guide to drugs and dry mouth. *Gerodontology*, Vol.5, No.2, (Autumn 1986), pp.75-99, ISSN 0734-0664

Sreebny, L. & Schwartz, S. (1997). A reference guide to drugs and dry mouth: 2nd edition. *Gerodontology*, Vol.14, No.1, (July 1997), pp.33-47, ISSN 0734-0664

Sreebny, L. & Valdini, A. (1987). Xerostomia: a neglected symptom. *Archives of internal medicine*, Vol.147, No.7, (July 1987), pp.1333-1337, ISSN 0003-9926

Stack, K. & Papas, A. (2001). Xerostomia: etiology and clinical management. *Nutrition in clinical care*, Vol.4, No.1, (March-April 2001), pp.15-21, ISSN: 1523-5408

Stahl, S. (1992). Neuroendocrine markers of serotonin responsivity in depression. *Progress in neuro-psychopharmacology & biological psychiatry*, Vol.16, No.5, (September 1992), pp.655-659, ISSN 0278-5846

Tenovuo, J. & Lagerlöf, F. (1994). Saliva. In: Textbook of clinical cariology, 2nd ed. Thylstrup, A. & Fejerskov, O. (Ed.), Munksgaard, ISBN 8716109163, Copenhagen, Denmark

Turner, M. ; Ship, J. (2007). Dry mouth and its effects on the oral health of elderly people. *Journal of the American Dental Association*, Vol.138, Suppl., (September 2007), pp. 15S-20S, ISSN 0002-8177.

Uher, R.; Farmer, A.; Henigsberg, N.; Rietschel, M.; Mors, O.; Maier, W.; Kozel, D.; Hauser, J.; Souery, D.; Placentino, A.; Strohmaier, J.; Perroud, N.; Zobel, A.; Rajewska-Rager, A.; Dernovsek, M.; Larsen, E.; Kalember, P.; Giovannini, C.; Barreto, M.; McGuffin, P. & Aitchison, K. (2009). Adverse reactions to antidepressants. *The British journal of psychiatry : the journal of mental science,* Vol.195, No.3, (September 2009), pp.202-210, ISSN:1472-1465

Ursache, M.; Grădinaru, I.; Nechifor, M. & Cherciu-Ciubotaru, B. (2006). Implications of xerostomia in oral dis-homeostasis. *Revista medico-chirurgicală a Societăţii de Medici şi Naturalişti din Iaşi*, Vol.110, No.2, (April-June 2006) pp.432-437, ISSN: 0048-7848

Vivino, F.B., Al-Hasshimi, I.; Khan, Z.; Leveque, F.G.; Salisbury, P.L.; Tran-Johson, T.K.; Muscoplat, C.C.; Trivedi, M.; Goldlust, B.; Gallagher, S.C. Pilocarpine Tablets for the treatment of dry mouth and dry eye symptoms in patients with Sjogren syndrome: a randomized, placebo-controlled, fixed-dose, multicenter trial. P92-01 Study Group. *Archives of internal medicine,* Vol.159, No.2, (January 1999), pp.174-181, ISSN 0003-9926

Von Knorring, A. & Wahlin, Y. (1986). Tricyclic antidepressants and dental caries in children. *Neuropsychobiology,* Vol.15, No.3-4, (1986), pp.143-145, ISSN 0302-282X

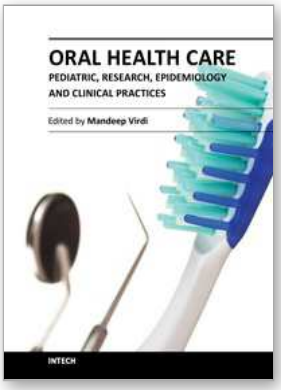
Von Knorring, L. & Mörnstad, H. (1981). Qualitative changes in saliva composition after short-term administration of imipramine and zimelidine in healthy volunteers. *Scandinavian journal of dental research*, Vol.89, No.4, (August 1981), pp.313-320, ISSN 0022-0345

Von Knorring, L. & Mornstad, H. Saliva secretion rate and saliva composition as a model to determine the effect of antidepressant drugs on cholinergic and noradrenergic transmission. *Neuropsychobiology*, Vol.15, No.3-4, (1986), pp. 146-54, ISSN 0302-282X

Wellington, K. & Perry, C. (2001) Venlafaxine extended-release: a review of its use in the management of major depression. *CNS Drugs*, Vol.15, No.8, (2001), pp.643-669, ISSN 1172-7047

Wynn, R. & Meiller, T. (2001). Drugs and dry mouth. *General dentistry,* Vol.49, No.1, (January- Feburary 2001), pp.10-14, ISSN 0363-6771

Zaclikevis, M.; D'Agulham, A.; Bertassoni, L.; Machado, M.; de Lima, A.; Grégio, A. & Azevedo-Alanis, L. (2009). Effects of benzodiazepine and pilocarpine on rat parotid glands: histomorphometric and sialometric study. *Medicinal Chemistry*, Vol.5, No.1, (January 2009), pp.74-78, ISSN 1573-4064




**Oral Health Care - Pediatric, Research, Epidemiology and Clinical Practices**

Edited by Prof. Mandeep Virdi

ISBN 978-953-51-0133-8
Hard cover, 302 pages
**Publisher** InTech
**Published online** 29, February, 2012
**Published in print edition** February, 2012

Oral health care in pediatric dentistry deals with complete oral health, including preventive aspects for children right from their conception to adolescence, encompassing all the spheres of dentistry including various specialties. It also includes planning a preventive program at individual and community levels. The current research interests in oral health care include studies regarding the role of stem cells, tissue culture, and other ground-breaking technologies available to the scientific community in addition to traditional fields such as anatomy, physiology, and pharmaceuticals etc of the oral cavity. Public health and epidemiology in oral health care is about the monitoring of the general oral health of a community, general afflictions they are suffering from, and an overall approach for care and correction of the same. The oral health care-giver undertakes evaluation of conditions affecting individuals for infections, developmental anomalies, habits, etc. and provides corrective action in clinical conditions. The present work is a compendium of articles by internationally renowned and reputed specialists about the current developments in various fields of oral health care.

**How to reference**

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Patrícia Del Vigna de Ameida, Aline Cristina Batista Rodrigues Johann, Luciana Reis de Azevedo Alanis, Antônio Adilson Soares de Lima and Ana Maria Trindade Grégio (2012). Antidepressants: Side Effects in the Mouth, Oral Health Care - Pediatric, Research, Epidemiology and Clinical Practices, Prof. Mandeep Virdi (Ed.), ISBN: 978-953-51-0133-8, InTech, Available from: http://www.intechopen.com/books/oral-health-care-pediatric-research-epidemiology-and-clinical-practices/antidepressants-side-effects-in-the-mouth-

INTECH
open science | open minds

**InTech Europe**
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

**InTech China**
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821