



## REVIEW ARTICLE

# Oral manifestations and their treatment in Sjögren's syndrome

S González<sup>1</sup>, H Sung<sup>2</sup>, D Sepúlveda<sup>2</sup>, MJ González<sup>2</sup>, C Molina<sup>1</sup>

<sup>1</sup>Oral Pathology Department, Faculty of Dentistry, Mayor University, Santiago, ; <sup>2</sup>Faculty of Medicine, Institute of Biomedical Sciences (ICBM), University of Chile, Santiago, Chile

**Sjögren's syndrome (SS) is a complex, chronic, systemic, autoimmune disease that mainly affects the exocrine glands, especially the salivary and lacrimal glands, leading to dryness of the oral and ocular mucosae. Several factors have been studied that could explain the glandular hypofunction primarily related to water transport. Recent reports have shown alterations in secretory route and trafficking in labial salivary glands, explaining alterations in the saliva quality. The decrease in salivary flow and qualitative alterations in saliva could explain many of the oral manifestations. The exocrine manifestations and systemic involvement significantly impact the patient's perception of health-related quality of life. For this reason and given its systemic nature, the treatment of these patients should be multidisciplinary. This review addresses some particular oral health aspects of SS patients and focuses on relevant topics concerning the treatment and prevention of common oral disorders associated with this disease.**

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Sjögren's syndrome (SS) is a complex autoimmune, chronic, and systemic disease (Mathews *et al*, 2008; Ramos-Casals *et al*, 2012). It affects mainly the exocrine glands, such as the lacrimal and salivary glands. The patient complains of dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca) (Mathews *et al*, 2008; Ramos-Casals *et al*, 2012). Several factors including immunologic, inflammatory, genetic, epigenetic, environmental, hormonal, and infectious agents have been postulated to explain the pathogenesis of the disease (Mavragani and Moutsopoulos, 2010).

Primary SS occurs in people with no other rheumatologic disease. Secondary SS occurs in people who have another rheumatologic disease, most often systemic lupus erythematosus or rheumatoid arthritis (Mathews *et al*,

2008). Population prevalence is 0.5–2% with a female to male ratio of 9:1, being mainly diagnosed during the fourth and fifth decade of life (Kassan and Moutsopoulos, 2004; Carr *et al*, 2012).

The autoimmune features of the disease are characterized by circulating autoantibodies (anti-Ro, anti-La, ANA, etc.) and lymphocytic infiltrates in exocrine glands. Both findings are considered in the diagnostic criteria (Vitali *et al*, 2002). In this context, the inflammatory cells play a major role in the pathogenesis, attacking the epithelial cells (Manoussakis and Kapsogeorgou, 2010). However, an important body of evidence suggests that other factors promote the loss of epithelial cell homeostasis, occurring in the pre-autoimmune phase or independent of inflammatory cells (Perez *et al*, 2000; Ewert *et al*, 2010; Delaleu *et al*, 2011).

The SS patient presents with a variety of signs and symptoms, with ocular and oral dryness subsequent to salivary and lacrimal gland damage constituting the most common complaints. Several factors related to water transport could explain the glandular hypofunction (Castro *et al*, 2012). Recent reports have also shown alterations in secretory route and trafficking of secretory products in labial salivary glands (LSG) (Bahamondes *et al*, 2011; Barrera *et al*, 2012). Additionally, changes in protein expression involved in maintaining cell–cell and cell–extracellular matrix relationships have been described in murine models and SS patients (Perez *et al*, 2000; Ewert *et al*, 2010; Delaleu *et al*, 2011; Gonzalez *et al*, 2011). These alterations would produce changes in quality of secretion and may even contribute to inflammatory process (Barrera *et al*, 2012).

The sicca symptoms, in addition to non-exocrine epithelial manifestations, significantly impact the patient's perception of health-related quality of life (HRQoL) (Lopez-Jornet and Camacho-Alonso, 2008; Stewart *et al*, 2008). Using the Medical Outcome Short Form Health Survey questionnaire, a marked reduction in HRQoL was measured in SS patients. Parameters affected included impaired perception of physical, emotional, and social function as well as symptoms related to disease and treatment. These results were more marked in patients with primary SS (Rostron *et al*, 2002; Belenguer *et al*, 2005).

Correspondence: Sergio González, Avenida Libertador Bernardo O'Higgins 2013, Santiago 8340585, Chile. Tel: 5623281771, Fax: 5623281737, E-mail: sergiogprovidell@yahoo.com

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Xerostomia and hyposalivation are important in the diagnosis of SS. They are the result of alterations in salivary gland secretion and result in several subjective and clinical manifestations because of the loss of secretion and the products therein (Soto-Rojas and Kraus, 2002). Their impact on patients' quality of life (QoL) perception has been poorly studied. SS patients with a high level of oral distress yielded low scores in their perception of QoL, with regard to both physical and mental components (Enger *et al*, 2011). Salivary gland dysfunction can affect self-esteem with regard to esthetics, social interaction, and personal comfort (Soto-Rojas and Kraus, 2002). Therefore, the oral health issue constitutes a relevant aspect from the clinical and practical point of view. Interestingly, SS patients were found to visit their dentist more frequently than control subjects (Christensen *et al*, 2001), but many of their needs were not addressed (Enger *et al*, 2011).

## Saliva

Saliva is composed mainly of water plus small but essential levels of electrolytes and a complex mixture of proteins, glycoproteins, enzymes, and many other molecules with biological and biochemical properties essential to maintaining stomatognathic system physiology (Turner and Sugiya, 2002). Saliva forms a thin layer that covers both hard and soft tissues, while also providing protection and humectation to the mucosal structures; not only oral, but also oropharyngeal and esophageal. Moreover, its organic and inorganic components can buffer pH changes, and salivary proteins can be adsorbed over tooth surfaces (Bernardi and Kawasaki, 1968; Sonju and Rolla, 1973; Lamanda *et al*, 2007) forming an organic film called the pellicle. The interface between the dental surface and pellicle is where demineralization and remineralization of hard dental tissues take place.

Saliva secretion is a regulated process. The major output is released under stimulation, with that of a mechanical and chemical nature being the most effective. The average daily production of saliva is about 1.0–1.5 l (Tschoppe *et al*, 2010). Food and chewing are the main stimulants to salivary flow. Between meals, salivation occurs slowly and diminishes to almost zero during sleep. The composition of saliva varies depending on the origin of the stimulation and the type of salivary gland. Mechanical and chemical afferent signals are transmitted from sensory receptors in the periodontal ligament and taste buds via the trigeminal, facial, and glossopharyngeal nerves to the salivary nuclei in the medulla oblongata of the brain. Efferent impulses to the salivary glands are transmitted via sympathetic and parasympathetic autonomic nerves, the former following the blood vessels supplying the glands and the latter following the efferent facial or glossopharyngeal nerves.

Hyposalivation is a consequence of diverse conditions, including dehydration, denervation, trauma, chronic inflammation of the salivary glands (immune and non-immune mediated), head and neck irradiation therapy, psychologic factors, and medications (Bergdahl and Bergdahl, 2000; Nederfors, 2000; von Bultzingslowen *et al*, 2007; Mese and Matsuo, 2007; Moore and Guggenheimer, 2008; Albuquerque *et al*, 2010; Smidt *et al*, 2010; Nava-

zesh, 2011). Xerostomia, the symptom of dry mouth, is often related to low salivary rate, primarily when unstimulated salivary flow falls below 50% of the normal (Dawes, 1987; Bergdahl, 2000). However, in SS patients, xerostomia has been associated with changes in the quality of salivary mucins rather than with decreased salivary flow (Alliende *et al*, 2008).

Patients with low salivary flow are susceptible to experiencing alterations in soft and (chiefly) hard tissues. In such individuals, caries are established in sites supporting the retention of dental plaque, especially along the gingival margin of root surfaces and surfaces adjacent to dental fillings. Also, salivary deficiency can lead to the rapid development of caries in abnormal sites (lingual, incisal, and cuspal tooth surfaces). Diminished salivation has been associated with slow sugar clearance, and thus, with increased levels of caries (Leone and Oppenheim, 2001). In this regard, Bardow *et al* (2003) suggested that unstimulated salivary flow seems to be of greater relevance than stimulated flow.

Reduction in chronic salivary flow has an important impact on oral physiology: mucosal dryness causes the patient oral discomfort and a burning sensation in the mouth, and difficulty in speaking and swallowing food, the latter often requiring extra water intake. Moreover, hyposalivation increases susceptibility to bacterial and fungal diseases (van der Reijden *et al*, 1999).

## Oral microbiota changes in SS patients

Saliva plays an important role in oral microbiota composition and is associated mainly with the different salivary components including defensins, proteases, histatins, and lysozyme among others. Although bacterial composition remains relatively stable after environmental change, several studies have shown that subjects with diminished salivary flow have a modified oral microbial plaque composition (van Houte, 1994; Marsh, 1994).

Salivary protein precipitation and biofilm formation on both soft and hard tissues is a continuous process and cannot be prevented (except in natural, self-cleaning surfaces such as sites with occlusal function or friction). Bacterial species that establish dental plaque rapidly colonize these pellicles, which independently of their stage of maturation are metabolically active. The interface between the plaque and tooth surface is essential for demineralization and remineralization, and considering that pellicle formation occurs at random, this cannot be prevented. Since the integrity and metabolic activity of dental plaque can be modified, therapies designed to promote mineralization are the basis of preventive caries treatment.

Total salivary bacterial count was found to be similar between SS patients and controls (Lundstrom and Lindstrom, 1995). However, it has also been shown that low salivary flow is associated with a high bacterial count of species such as *Lactobacillus acidophilus*, *Streptococcus mutans*, and *Candida albicans*, which may explain the occurrence of caries and candidiasis, infections common in SS patients (Lundstrom and Lindstrom, 1995; Kolavic *et al*, 1997). Similar findings have been encountered in patients with other causes of hyposalivation (Bardow *et al*, 2001; Almstah *et al*, 2003).

Interestingly, periodontopathogenic micro-organism numbers were not increased in SS (Pedersen *et al*, 2005). Almstahl *et al* demonstrated that salivary counts of *Fusobacterium nucleatum* and *Prevotella intermedia/nigriscens* were similar in SS patients and controls (Almstahl *et al*, 1999, 2001), although these bacteria were detected at lower levels in the gingival crevice (Leung *et al*, 2007).

The evaluation of microbiota in different sites of the oral cavity has indicated increased number and frequency of *Lactobacillus* spp., *S. mutans*, and *C. albicans* in supragingival plaque (Leung *et al*, 2007). Distinctively, the mucosa and tongue harbor higher levels of *C. albicans*, *Staphylococcus aureus*, enteric bacteria, and enterococci (Leung *et al*, 2007). Concomitantly, in SS patients, a higher number of retention sites generated by dental restorations (fillings, crowns, bridges, etc.) contribute to changes in the oral environment and subsequent alteration in microbiota.

These results correlate with a higher incidence of infectious diseases such as caries and candidiasis in SS patients. Nevertheless, an increased prevalence of periodontal diseases has not been established consistently in these patients (Kuru *et al*, 2002). In summary, the plaque present in SS patients has a profile more cariogenic and acidophilic than that in controls, thereby elevating the risk of caries and candidiasis.

## Caries

Caries is a multifactorial disease described as the dissolution of hard dental tissues (specifically hydroxyapatite crystal dissolution) caused by acids produced by dental plaque covering the site involved. Enamel, dentin, and cementum may be affected, and any tooth surface where the biofilm has settled and remains undisturbed for a long period of time should be considered as susceptible. For the development of caries, several factors must converge in concert (e.g., the presence of dental plaque capable of metabolizing fermentable carbohydrates to organic acids such as lactic acid). Individual factors such as diet (composition and frequency), hygiene, education and knowledge about the disease, health expectations, and characteristics of saliva (flow, composition, buffer and sugar clearance capacities, fluoride concentration, etc.) are also important. Finally, as mentioned previously, the imbalance supporting the caries process must be maintained for a long period of time to produce a net loss of minerals from the tooth.

## Caries control in patients with hyposalivation

Prior to treating caries in patients with hyposalivation, it is important to assess their current oral status and the risk of future caries progression. Identifying these risk factors will help focus the appropriate operative, non-operative, and preventive measures, since dental care neither begins nor ends with a single therapy. In particular, patients should be aware of their relative caries risk and become involved in their own care. (Table 1).

Evaluation of the caries risk must consider the medical history of the patient; past and current diseases and their respective treatments (Moore and Guggenheimer, 2008;

Smidt *et al*, 2010); dietary pattern (particularly amount and frequency of sugar intake); salivary flow rate and dental history; activity level of carious lesions; hygiene practices; and the use of preventive measures (fluorides). Some of these factors can be modified and others not.

## Oral hygiene

It is currently recognized that the presence of dental plaque is necessary for the development of caries. However, there are other key factors that may have a role to play in this disease—it is the combined effect of positive and negative determinants, rather than the amount of biofilm itself, that determines whether a carious lesion will develop and progress (Nyvad and Fejerskov, 1997). The removal of dental plaque reduces acid production after a sucrose rinse and avoids a drop in salivary pH and subsequent tooth demineralization (Firestone and Muhlemann, 1985). However, it is important to keep in mind that oral hygiene depends almost totally on the individual's ability to maintain good plaque control. Many studies have shown that careful oral hygiene in addition to the regular use of fluoride toothpaste can be very effective in controlling the development and progression of caries (Dijkman *et al*, 1990; Nyvad and Fejerskov, 1997). The use of fluorides without good plaque control has not been reported to yield any benefits (Mathiesen *et al*, 1996).

## Diet

While there is no doubt about the influence of diet on the development of caries, additional factors must be considered. These include total food intake, intake pattern, plaque composition, salivary secretion, use of fluoride, and socioeconomic variables among others (Table 1). The Vipeholm study (Gustafsson *et al*, 1954) indicated that caries incidence is low with a virtually sugar-free diet. The addition of sugars to the diet increases the caries rate depending on the manner of consumption. Sugars consumed between meals produce more caries than those ingested with regular meals, while those consumed between meals in a highly retentive (sticky) form result in the highest caries activity.

Sugar-rich soft drinks have been associated with high rates of caries in different risk groups such as infants and toddlers, younger children, and individuals of low socioeconomic status. Subjects affected by different diseases and elderly people show increased risk of caries related to hyposalivation.

Monosaccharides and disaccharides (sucrose, maltose, and lactose) can be readily metabolized by many bacteria involved in dental biofilm formation, generating acid by-products that can lead to demineralization of the tooth structure. The consumption of some monosaccharides and starch-refined compounds is directly related with the development of caries (Sreebny, 1982; Lingstrom *et al*, 2000; Burt and Pai, 2001). Sucrose is the most cariogenic, while starch-derived foods have low cariogenic potential.

Non-caloric sweeteners (aspartame, acesulfame-K, cyclamate, and saccharin) are not metabolized to acids by oral micro-organisms, and thus, cannot cause dental caries.

156 **Table 1** Guidelines in the treatment of oral manifestations in Sjögren's syndrome patients

Manifestation	Comments	Recommendations
Xerostomia	Dry mouth is a very common complaint in SS patients	Local measures to relieve symptoms/stimulate salivation: sip water frequently (with sodium bicarbonate optional), mechanical/gustatory stimulation of salivary flow (sugarless candies, chewing gums, tablets, lozenges). Use a saliva substitute spray, liquid or gel. Systemic salivary stimulation with pilocarpine hydrochloride (5 mg per 3 times a day), Cevimeline, a more specific muscarinic agonist, had less side reactions and with a longer-lasting effect
Tooth decay	Caries is one of the most prevalent oral diseases in SS patients	Sites promoting dental plaque accumulation (i.e. defective restorations) should be detected, replaced or removed. Carefully assess the patient's caries risk. Support the patient's commitment to self-care. Reinforce oral hygiene: brushing and flossing after every meal and especially before sleep. Diet modification: Reduce the total sugar intake; restrict the intake of sugary and sticky foods between meals and/or sugar containing drinks. Favoring the use of non-cariogenic sweeteners. Take the adequate measures to increase salivary flow (see above). Fluoride therapy at dental office: an application of a high concentration fluoride agent (gel or varnish) every 3 months. Fluoride therapy at home: Neutral fluoride gel in a custom fitted tray (once a week), fluoride rinses (0.05% daily or 0.2% weekly), high fluoride toothpaste. Chlorhexidine therapy: Chlorhexidine Gel (1%) or high concentration varnishes can be used in high risk caries patients at dental office, domestic use of chlorhexidine is considered optional and indicated in high-risk caries patients. Close and periodical follow-up of the patient is essential
Candidiasis	Fungal infection frequently observed in SS patients, recurrence is expected	Elimination of relevant local factors, particularly in patients with poor hygiene. Dentures or prostheses should be disinfected regularly and their use during night-time should be avoided. Topical use of nystatin, clotrimazole or miconazole (oral troches, gels, ointments, creams, suspensions, or vaginal ovules), for at least 14–21 days. Chlorhexidine mouthwashes are optional
Others		Ointments, creams, and oils could be useful for dry and cracked lips. Avoid mouthwashes containing alcohol, acidic or spicy foods, smoking or tobacco products, and alcohol-containing drinks

SS, Sjögren's syndrome.

Sugar alcohol sweeteners such as sorbitol and xylitol have been evaluated for their cariogenic potential. Sorbitol is fermentable by oral bacteria, but at a low rate and with reduced acid production. Xylitol is not fermentable by oral streptococci and appears to exert a bacteriostatic effect on *S. mutans* due to the accumulation of xylitol 5-phosphate within the bacterial cell. Xylitol also does not reduce the pH of dental plaque (Muhlemann *et al*, 1977). The low cariogenic effects of xylitol have been demonstrated both *in vivo* and *in vitro* (Scheinin *et al*, 1975; Muhlemann *et al*, 1977).

### Salivary flow stimulation

Since reduced salivary flow is one of the key features of SS, efforts to restore salivary output to normal levels would seem an appropriate therapy.

*Local salivary stimulation:* It has been reported that salivary stimulation with sugar-free chewing gum promotes salivary flow, increasing pH and buffer capacity (Dodds *et al*, 1991; Dawes and Kubieniec, 2004). The addition of substances such as polyols and carbamide apparently does not improve the caries-preventive effect of the chewing process itself (Machiulskiene *et al*, 2001). Other sugar-free products (tablets and lozenges) can improve salivary flow by stimulation of taste buds.

*Systemic salivary stimulation:* Cholinergic agonists have been used to improve xerostomia in SS patients, with pilocarpine being the most studied and the most successful in treatment (Vivino *et al*, 1999), but not in all patients (Jorkjend *et al*, 2008). Cevimeline is also

used for xerostomia in SS patients (Fox *et al*, 2000; Fife *et al*, 2002; Suzuki *et al*, 2005) and shares similar mechanisms of action and side effects with pilocarpine (Fox, 2004). To date, no long-term clinical trials regarding the use of secretagogues in caries prevention or reduction are underway.

*Salivary substitutes:* A wide variety of products are currently available for the amelioration of xerostomia in SS patients. Since these are supplemented with calcium, phosphate, and fluoride ions, such products prevent demineralization and can be used in different ways, from mouthwashes to intraoral devices. Although it is expected that the addition of fluorides helps to prevent caries, most saliva substitutes are formulated to alleviate xerostomia. However, as stated in a comprehensive review by Furness *et al* (2011) there is no conclusive evidence about their effectiveness for caries prevention.

### Chemical control

The chemical control of dental plaque is aimed at altering different aspects of micro-organism adhesion and growth. Since the development of caries depends on dental plaque adhesion to the tooth surface, many strategies to prevent bacterial colonization have been developed. As mentioned previously, since the pellicle is deposited spontaneously on the dental surface, targeting surface-associated proteins may be a logical strategy in controlling biofilm formation/activity. Caries immunization is a good example of this strategy, but such approaches are directed against single microbial species, particularly *S. mutans* that metabolize sugars to



produce the adhesive extracellular polymers necessary for bacterial colonization. Unfortunately, these products are still in the early stages of testing and have not shown sound clinical efficiency to date (Shivakumar *et al*, 2009).

Prophylactic agents to prevent caries can be delivered in many vehicles, such as sprays, gels, varnishes, chewing gums, toothpastes, and mouth rinses, the latter two being the most frequently used. Only a few prophylactic agents will be mentioned here.

**Chlorhexidine:** Chlorhexidine (CLX) is a bisbiguanide that disrupts the microbial membrane. In clinical concentrations, it is bacteriostatic by virtue of its interference with normal membrane function (McDonnell and Russell, 1999). It may also inhibit essential enzymes such as glucosyltransferase and phosphoenolpyruvate phosphotransferase, which interfere with microbial accumulation on the tooth surface and the transmembrane phosphorylation of glucose, respectively (Marsh *et al*, 1983; Scheie *et al*, 1987). CLX has a broad antibacterial spectrum, with Gram-positive micro-organisms being more sensitive than Gram-negative organisms (Emilson, 1977). CLX sustains its activity even when adsorbed to biofilms (substantivity). It appears that the professional application of CLX yields better results than non-supervised home usage. The combination of fluoride and CLX decreased lesion progression more effectively compared with a control condition (Schaecken *et al*, 1991).

**Xylitol:** As mentioned previously, this sugar alcohol does not promote dental caries. Xylitol was found to reduce the bacterial count of *S. mutans* in saliva and dental films (Soderling *et al*, 2011) and appears to inhibit glycolysis in this species (Soderling, 2009). Xylitol has now been incorporated in dental hygiene products, but its additive effects with fluoride are not supported by all studies (Cutress *et al*, 1992; Sintes *et al*, 1995).

**Fluorides:** Fluoride has been widely used in the prevention of caries. This element is found naturally in water, is voided by the kidneys, and its concentration in the body depends essentially on its intake. Topical activity on the tooth surface is the most important mode of action. Dissolution of hydroxyapatite takes place when pH drops below 5.5, following which fluoride can be incorporated with hydroxyapatite crystals, forming fluorhydroxyapatite on the surface layers. The latter compound is more resistant to acid attack, thus reducing dental demineralization. Also, when the pH rises again above 5.5, fluoride enhances remineralization of dental tissues. Fluorides are delivered by different means—systemic (water, supplements, milk, and salt) and topical (toothpaste, gels, varnishes, and mouth rinses). Fluoride toothpaste has been by far the most successful fluoride delivery system developed to date (Cury *et al*, 2004), with sodium fluoride and sodium monofluorophosphate the most frequently used fluoride derivatives. Fluorides inhibit bacterial metabolism, and when plaque pH drops, hydrofluoric acid is formed and diffuses into the cell inhibiting enolase, a glycolytic enzyme necessary for carbohydrate metabolism (Featherstone, 2000). Fluorides applied in the dental office and at home are very important in complementing basic dietary and hygiene control measures (van der Reijden *et al*, 1999).

## Some novel strategies

**Probiotics:** Probiotics (e.g., *Lactobacillus* and *Bifidobacterium* spp.) are live micro-organisms that when administered at sufficient levels confer a health benefit to the host, and these can be delivered in many ways (lozenges, mouth rinses, capsules, etc.). The hypothetical mechanisms of probiotic action in the oral cavity include (i) interference in the formation of acquired pellicle; (ii) disturbance of the complex plaque ecosystem by competing with bacterial attachments; (iii) involvement in substrate metabolism and the production of chemicals that inhibit oral bacteria; and (iv) indirect probiotic actions to modulate/stimulate the host's immune function (Twetman and Keller, 2012).

Probiotics have therapeutic applications against caries, periodontal disease, and candidiasis, among others, but long-term clinical trials are still awaited.

**Phosphoproteins/phosphopeptides:** These compounds are found in nature and stabilize calcium and phosphates, preventing precipitation. Saliva and milk are examples of biological fluids that contain phosphoprotein/phosphopeptide-stabilized calcium phosphate. Milk-derived phosphopeptides can stabilize high levels of calcium and phosphate. Cochrane and Reynolds stated that 'casein phosphopeptide-stabilized amorphous calcium phosphate nanocomplexes (CPP-ACP) deliver high concentrations of bioavailable calcium and phosphate ions intraorally to inhibit demineralization and promote remineralization' (Cochrane and Reynolds, 2012). CPP-ACP added to fluoride-containing toothpaste could aid in remineralization (Cochrane and Reynolds, 2012). Rinses with these compounds have been used in primary SS patients, showing low efficacy (Hay and Thomson, 2002). More clinical trials are necessary to determine its usefulness in the prevention and control of caries.

## Others

**Light therapy:** the effects of non-coherent blue light and CO<sub>2</sub> laser action on bacteria present in biofilms and dental plaques are currently under investigation (Feuerstein, 2012).

**Nanotechnology:** has many potential applications in dentistry, and with regard to caries therapy, efforts have been directed toward remineralization of early lesions (e.g., nano-sized hydroxyapatite or the above-mentioned CPP-ACP); supplementation of restorative materials with calcium-, phosphate-, or fluoride-containing nanoparticles; and enamel-like nanomaterials intended to repair incipient lesions. However, many of these therapies are still awaiting clinical implementation (Hannig and Hannig, 2012).

## Restorative treatment

Despite visiting their dentist frequently and demonstrating excellent levels of oral hygiene, some studies have shown that SS patients have higher DMFT (decayed-missing-filled teeth) scores. They present with new, recurrent, and atypical caries lesions. Therefore, it is

necessary that dentist diagnosis and intervene early, considering the individual patient's caries risk. The dentist must be careful in the selection of technique and restorative materials. Today, there are a variety of dental materials, such as dental amalgam, composite resins, resin-modified glass ionomer, and conventional ionomers, (direct materials); and indirect composite inlays, veneer, ceramic, and porcelain (indirect materials). Some authors have recommended direct plastic restorative material for small and moderate sized lesion, avoiding removal of sound tooth structure (Atkinson *et al*, 2005), but this opinion is not supported by rigorous clinical trials. Long-term clinical trials comparing different techniques and restorative materials in SS patients are needed.

### Periodontal disease

Periodontal disease is defined by the American Academy of Periodontology as a pathological process affecting periodontal tissues. It is an infectious disease resulting in inflammation that can destroy periodontal tissues, with progressive attachment and bone loss. This destruction results in breakdown of collagen fibers in the periodontal ligament, resulting in the formation of a periodontal pocket between the gingiva and tooth.

As mentioned previously, since low salivary flow promotes plaque formation, the development of periodontal disease may be expected. Despite this, evidence of increased prevalence of periodontal disease in SS patients is controversial. Some studies have demonstrated higher plaque index, gingival bleeding, probing depth, and periodontal index in SS patients with elevated risk of periodontal disease (Najera *et al*, 1997; Celenligil *et al*, 1998; Rhodus and Michalowicz, 2005; Ergun *et al*, 2010). While others have shown non-significant differences between SS patients and control groups regarding clinical parameters and periodontal status (Tseng *et al*, 1990; Tseng, 1991; Mutlu *et al*, 1993; Lundstrom and Lindstrom, 1995; Tervahartiala *et al*, 1995; Kolavic *et al*, 1997; Boutsis *et al*, 2000; Kuru *et al*, 2002; Jorkjend *et al*, 2003; Leung *et al*, 2007). In addition, no increased risk of periodontal disease has been detected in some of the above-mentioned studies (Pedersen *et al*, 1999). These conflicting results may be due to the gingival crevicular fluid remaining unaffected by low salivary flow (Celenligil *et al*, 1998).

Furthermore, these studies may not be comparable due to differences in experimental design (e.g. SS diagnostic criteria used and the type and quality of control groups). In addition, the use of non-steroidal anti-inflammatory drugs, corticosteroids, and disease-modifying antirheumatic drugs (hydroxychloroquine or methotrexate) might possibly affect the inflammatory response in periodontal disease (Antoniazzi *et al*, 2009).

In brief, the evidence suggests that SS patients do not require special periodontal care, since their periodontal status is similar to that of systemically healthy people. Although SS is a systemic disease, it is not apparently associated with increased risk of periodontal disease (Schiodt *et al*, 2001).

### Candidiasis

Candidiasis is a fungal infection frequently observed in SS patients, with the most common forms being erythematous (atrophic) and angular cheilitis (Tapper-Jones *et al*, 1980; Rhodus *et al*, 1997). As in non-SS patients, the risk is higher in subjects who wear removable dentures. Treatment strategies should include the elimination of relevant local factors, particularly in patients with poor hygiene. Dentures or prostheses should be disinfected regularly and their use during nighttime should be avoided (van der Reijden *et al*, 1999; Soto-Rojas and Kraus, 2002). The optimal treatment choice in oral candidiasis is the topical use of antifungal drugs such as nystatin, clotrimazole or miconazole in the form of either oral troches, 1.6 gels, ointments, creams, suspensions, or vaginal ovules. Treatment should be continued for at least 2–3 weeks, since recurrence not uncommon (Soto-Rojas and Kraus, 2002). CLX mouthwashes are sometimes recommended (van der Reijden *et al*, 1999). See Table 1.

### Dental implants in SS patients

Several studies have shown a higher incidence of caries in SS patients. Furthermore, SS patients experience greater loss of teeth due to caries (Baudet-Pommel *et al*, 1994; Christensen *et al*, 2001). Even though preventive dental care is the principal focus in SS patients, they need alternatives to replacement of teeth and improvement in stomatognathic function.

Partially removable dentures are an adequate alternative to replacing lost teeth. However, since patients with xerostomia have reduced retention and poor acceptance of dentures, the wearing of dentures is usually a difficult and unpleasant experience for SS patients (Isidor *et al*, 1999). The use of complete dentures with reservoirs for artificial saliva has been proposed (Frost *et al*, 2006), but results are conflicting. Their apparent usefulness would be restricted to night-time use, when salivary flow diminishes (Frost *et al*, 2006). Additionally, this prosthetic device was found to augment the bacterial count of both *L. acidophilus* and *S. mutans*, leading to slurred speech and frequent refilling of the reservoir (Frost *et al*, 2006; Agrawal *et al*, 2011).

Even though removable dentures are an excellent therapeutic alternative in SS patients, their use can result in dental abrasions, sore spots, ulceration, irritation, and mucosal pain (Binon and Fowler, 1993). Therefore, dental implants appear to be the ideal treatment, although few studies have investigated their use in SS.

Dental implants require continual bone remodeling to maintain a rigid implant–bone interface (Oczakir *et al*, 2005). Furthermore, appropriate osseous integration depends on specific systemic and local oral factors (Sugerman and Barber, 2002). Clinical reports have shown that rehabilitation of implant-supported SS patients is successful (Binon and Fowler, 1993; Payne *et al*, 1997; Isidor *et al*, 1999; Binon, 2005; Oczakir *et al*, 2005). However, since these results were obtained with low patient numbers and under short periods of observation, additional studies with a larger number of patients are necessary. Despite

this, dental implants can be recommended in the rehabilitation of SS patients, since the disease would not affect bone healing and osseous integration. While Binon and Fowler found no radiological or clinical differences between SS patients and healthy individuals treated with implants (Binon and Fowler, 1993), the drugs used in SS patients could complicate dental implant treatment. In some instances, SS patients need corticoids to control their symptoms, and these may contraindicate the use of dental implants. Regardless, the dentist must maintain a close communication with the rheumatologist.

## Conclusions

Dental treatment of SS patients is a challenging task. It is important to bear in mind that many of the oral pathologies observed should be treated based on the patient's systemic condition. Many drugs taken by the patient can modify the course or the treatment of associated oral diseases, and thus, knowledge of the nature of the relevant pathologies is fundamental to gaining an understanding of the basis of different current and future therapeutic strategies. It is very important to realize that oral treatment does not end when the operative procedures have been completed. Other relevant aspects are the preventive measures taken and performed at home and at the dental office. Last but not least is the commitment of the patient to her/his own dental care.

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## Author contributions

We apologize to the authors whose work we did not cite due to space constraints. All authors contributed equally to the literature review and writing of individual sections.

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