



## **Sjogren Syndrome: A Review on Diagnostic Methods and Treatment Strategies**

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### **ABSTRACT**

Sjogren syndrome is a chronic autoimmune disease in which white blood cells attack and destroy moisture producing glands and causing reduced production of saliva (xerostomia) and tear (xerophthalmia). The treatment of sjogren syndrome focuses on symptomatic management like administration of artificial tears, cholinergic agents such as Pilocarpine and Cevemeline to stimulate the production of saliva and tears, Hydroxychloroquine for arthritis and myalgias. The present study focuses about clinical features, diagnostic methods and detailed treatment strategies of sjogren syndrome.

**KEYWORDS:** Sjogren Syndrome, Xerostomia, Xerophthalmia.

### **INTRODUCTION**

Sjogren syndrome is a chronic systemic autoimmune disease characterized by polyglandular tissue destruction, which causes diminished lachrymal and salivary gland function [1,2,3]. Most common symptoms of the disease are dry eyes (kerato conjunctivitis sicca) dry mouth and parotid enlargement. Oral symptoms like difficulty in speaking, eating or swallowing so that there is a need of frequent sip of water may be needed. Eye symptoms include dryness, grittiness, pruritus and foreign body sensation [4]. Various autoimmune disease such as rheumatoid arthritis, Systemic Lupus Erythematosus (SLE), or myositis may associate with Sjogren Syndrome [5].

Generally there are two types of sjogren syndrome primary sjogren syndrome and secondary sjogren syndrome. Primary sjogren syndrome characterized by sicca complex and extraglandular symptoms without any connective tissue disorder. Secondary sjogren syndrome associated with autoimmune disease such as rheumatoid arthritis and systemic lupus erthematosus.

In general population, prevalence of about 1 to 3 % of patients was affected by primary Sjogren syndrome whereas secondary has been observed in approximately 10-20% of patients with rheumatoid arthritis, systemic lupus erthematosus and

scleroderma [6,7]. The prevalence is more in females compared to males due to immunoregulatory properties of sex hormones [8,9,10]. Our review article aimed at focusing on the diagnosis and management of sjogren syndrome.

### **DISCUSSION:**

#### **DIAGNOSIS:**

Sjogren syndrome initial manifestations may be mild and gradually it progresses so that it may take years to identify the syndrome. The diagnosis is based on various criteria's (eg: AECG-American European Consensus Group) and tests like serologic testing, lip biopsies, evaluation of xerostomia, xerophthalmia, schirmer's test, Rose Bengal staining and Tear break up time.

**Serological Testing:** Anti RO/SSA and anti La/SSB) are usually present in patients with sjogren syndrome. Anti-Nuclear Antibody (ANA) and Rheumatoid Factor (RF) levels are elevated. Various autoantibodies like thyroglobulin, thyroid microsomal mitochondrial, smooth muscle, parietal, peroxisomal and muscarnic receptors are present [11,12].

**Sialometry And Sialochemistry:** Salivary flow rates can be measured clinically for whole saliva or for separate secretions from the parotid or

submandibular and sublingual glands with or without stimulation. Patients having sjogren syndrome have lower submandibular flow rates and reduced flow. It varies based on many factors like age, medication, sex and time of the day.

Sialochemistry of collected glandular saliva samples may shows several characterstic changes in electrolytes and proteins in Sjogren syndrome. The sodium concentration level in the parotid glandular saliva is six fold higher in sjogren syndrome patients as compared to healthy volunteers[13].

**Sialography And Scintigraphy:** Sialography is the radiography of the salivary gland and its associated ducts, following the injection of a contrast radioopaque substance. This technique assess the anatomical changes of salivary gland ductal system. In this technique, two types of radiocontrast substance is used: fat soluble and water soluble compounds. Water soluble contrast media are usually preferred, they induce less localized inflammation in contrast to fat soluble compounds, which provide better radiographic imaging. Water soluble contrast media can cause chronic inflammatory changes if leakage of the product occurs. The major changes observed in sjogren syndrome consists of salivary gland duct dilations, duct strictures, sialectasis and occasionally peripheral duct narrowing occurs. Salivary scintigraphy is to assess the involvement of salivary gland in sjogren syndrome. In this technique  $Tc^{99}$  (technetium 99) administered intravenously, then take sequential images of head. The people with sjogren syndrome shows delayed uptake of technetium 99( $Tc^{99}$ ) [14].

**Schirmer's Test:** This test assess the functions of lachrymal gland, a small piece of filter paper placed in the lower eyelid over 5 minutes. In the normal non-anesthetized eye atleast 15mm of wetting is expected in patient's younger than 40 years old, and atleast 10mm of wetting is expected in elderly patients. The test is considered to be abnormal when the results of wetting is less than 5mm, confirms the sjogren syndrome or dry eye syndrome.

**Tear Break Up Time:** A drop of fluorescence dye is instilled and the time interval measured between a complete blink and appearance of dark, non-fluorescent areas in the tear film is measured. Rapid tear break up indicates an abnormality of the either the mucin or the lipid layer. Tear break up time shorter than the blink interval of 5 second would implies ocular surface damage, while very short tear break up time (less than 2 sec) indicates keratoconjunctivitis sicca.

**Rose Bengal Staining Test:** This test is conducted by application of 1% solution of Rose Bengal stain to the inferior fornix of both eyes and ask the patient to make one or two full blinks. The examiner use white light to assess the staining amount, in the two exposed conjunctival zones and cornea. Each section is scored upto 3 points, sparsely scattered spot, densely scattered spot and confluent spot based on Van Bijsterveld score. The maximum score is 9, a score of 4 or more, or 3 or more was considered as the conformation of Sjogren Syndrome[15].

#### MANAGEMENT:

Xerophthalmia: Management of dry eyes include three basic strategies

1. Conservative of available tears
2. Replacement with artificial tears
3. Stimulating the production of tears.

The conservation of available tears comprises the use of moisturized chamber panels and glasses, both of them which protect the eye from wind and reducing evaporation of tears[16,17]. Ocular treatment starts with non-preservative artificial tears in the form of ointments, eyedrops and gels. Bicarbonate buffered electrolyte solution shows useful effects in human tear composition. If the non-preservative artificial tears are not beneficial, the next step is to increase the tear production by stimulating  $M_1$  and  $M_3$  receptors by muscarnic agonists which exerts the pharmacological stimulation of exocrine glands. The major drugs in this category are Pilocarpine and Cevemeline[18]. Pilocarpine increases lachrymal responses and thereby reduces dry eyes. Oral Pilocarpine 10 mg/day is the recommended dose and it shows improve result in Rose Bengal staining test. If the patient is not respond the dose is increased to 15 or 20 mg/day, in some cases increased upto 30 mg/day. Pilocarpine is contraindicated in acute narrow angle glaucoma, uncontrolled asthma and acute iritic [19,20]. The other drug, Cevemeline which may have longer duration of action than pilocarpine and the recommended dose is 30mg three times daily. It increase tear flow rate and improve sicca symptoms [21]. In addition, warm ocular compress and massage reduce meibomian inflammation. The patients who are having severe ocular symptoms favours temporary and permanent puncture occlusion. In some studies systemic administration of anhydrous Methyl testosterone or Mesterolone and Cyclosporine shows beneficial effects on lacrimal and meibomian function.

**Xerostomias:** The treatment of xerostomia is difficult, most of this aimed at palliation and stimulation of the residual capacity of the salivary

glands or substitution of saliva with mouth rinsers or saliva substitutes and thus prevents oral complications[22,23]. Adequate hydration is the most prominent method to treat xerostomia. Frequent small sips of water rehydrate the oral cavity along with cleanses and thus reduce microbial load.

Xerostomia increases the progression of hyposalivation, dental caries and oral infection. The most suitable formula of topical fluoride gel contains 0.4-1.25% fluoride which can be used at least once a week. If the hyposalivation is severe, application should be increased two times per day[24,25].

Pilocarpine and Cevimeline, is beneficial in xerostomia. Pilocarpine at a dose of 5mg four times daily will improve xerostomia and Cevimeline 30 mg three times daily increase salivary flow and improve the symptoms of xerostomia[26]. Anethole trithione 25 mg three times per day also a potential drug for the treatment of xerostomia in Sjogren syndrome. It includes less side effect than Pilocarpine[27]. Studies show that, interferon  $\alpha$  is an immunomodulator which improves increased activation and reduced salivary gland inflammation, thereby reducing oral and ocular dryness[28]. Local therapies like sugar free gums, sour lemon lozenges, candies stimulate salivary flow. Xylitol, is a naturally acceptable artificial sweetener decrease dental caries. Carboxymethyl cellulose, mucin and glycerin will lubricate the oral mucosa. So these substances are used as lozenges, rinses, spray and swabs forms[29,30]. The major saliva substitutes are mucin preparations, linseed polysaccharides, polyacrylic acid and xanthan gum.

In post-menopausal women, Tibolone a synthetic steroid with androgenic properties at a dose of 2.5mg /day orally improves oral, ocular and vaginal lubrication[31]. Carboxymethyl cellulose, Yohimbin, Neostigmine and Pyridostigmine also stimulates the salivary glands but the use is limited.

Non visceral manifestations like arthralgia, myalgia are commonly treated with NSAIDs, Salicylates and Hydroxychloroquine. The Corticosteroids and Antimalarials drugs are commonly used in Sjogren syndrome. High dose of corticosteroids reduce

inflammation and may reduce joint damage[32]. Low doses of Prednisolone clears serological abnormalities, with significant decrease in serum IgG, anti Ro/SSA, anti La/SSB antibodies and Rheumatoid factor levels[33].

Hydroxychloroquine, a dose of 200mg/day improves arthritis and myalgias[34]. Administration of drug which decrease immunoglobulin in serum concentration, polyclonal hyperglobulinaemia and improvement in ocular symptoms[35,36,37]. The main side effect is retinopathy and it can be used safely upto 6-7mg/Kg/day[38,39].

**Cyclosporine:** Low dose of cyclosporine acts by inhibiting interleukin 2 and suppressing of T cell proliferation, thereby xerostomia symptoms should be improved[40].

**Rituximab:** Rituximab, anti CD20 monoclonal antibody which destroys B lymphocytes and used for severe inflammatory response in Sjogren syndrome[41].

**Zidovudine:** Zidovudine an antiretroviral agent, potentially benefits and it shows low risk in the treatment for Sjogren syndrome. It shows improvement in ocular, oral symptoms and extra glandular manifestation like fatigue, tenderpoints and arthralgia[42].

**Methotrexate:** Symptoms of xerophthalmia and xerostomia, dry cough, purpura and musculoskeletal symptoms should be improved with use of Methotrexate dose of 0.2mg/kg[43].

## CONCLUSION

Sjogren syndrome is a chronic autoimmune disease, but it is not life threatening. Regular dental and eye checkup are needed to monitor their conditions. Only symptomatic treatment given for Sjogren syndrome. Pilocarpine and Cevimeline are the main two drugs for the treatment of xerophthalmia and xerostomia. Careful attention should be taken by physicians while prescribing medicines to Sjogren syndrome patients as some of the medicines like antihistamines and antidepressants can cause mucosal damage.

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