Sjögren's UK

A Concise Guide **to Diagnosis and Management** for Health Professionals

Fourth edition

The Sjögren's UK is a registered charity and self-help organisation dedicated to providing mutual support and information to individuals affected by Sjogren's Disease. We aim to educate people about the condition, raise awareness surrounding its existence, and support research into its cause and treatment.

The Sjögren's UK offers the following services to its members:

- A subscription to Sjogren's Today, which provides an excellent source of up-to-date information
- Website with members only area including a forum
- Regional meetings, providing a network of support from fellow suffers and their families, as well as health care professionals
- Access to a members helpline - 01214781133
- A variety of further reading, including 'Advisory Guide for Patients and Doctors' and 'A Concise Guide to Diagnosis and Management'
- Membership to our 'Make a friend' scheme, which puts patients in contact with sufferers in your area.

Education and research

The Sjögren's UK strongly supports research into the cause and treatment of Sjogren's Disease. We award an annual research grant to applicants who have been reviewed by a medical panel which has an interest in the disease. We hope it will raise awareness of Sjogren's Disease and encourage young medics and dentists to take an interest in the condition.

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Background

Sjögren's Disease is a common disorder, which is under-diagnosed and may frequently go untreated. Its diverse symptomatology and a general lack of awareness of the condition are major barriers to diagnosis and treatment. There is also a perception that the condition is mild and that therapy is either not available or is not necessary.

The purpose of this document is to provide clear guidance for health professionals on the steps in diagnosis and management of suspected Sjögren's Disease. Effective therapies are available for many aspects of the disease and their introduction can improve patient care and quality of life.

These guidelines are based on the best data available at the time of preparation. However, the information should be considered as advisory only and the treatment and management of an individual patient should always be modified according to individual needs. Often a multidisciplinary approach is required.

Overview

Sjögren's Disease is a systemic autoimmune disorder of unknown aetiology characterized by inflammation of the exocrine glands (e.g. the lacrimal and salivary glands or the secretory glands of the vagina), and leading to clinical symptoms of dryness, particularly of the eyes and mouth 1. It can occur as a primary disorder

(primary Sjögren's Disease) or in patients with other rheumatic disorders, such as rheumatoid arthritis and systemic lupus erythematosus (secondary Sjögren's Disease). Sjögren's Disease affects women in their 40's and above, although up to 10% of cases occur in men and it is also seen in younger people. It affects one in 2000 women in the UK.

Sjögren's Disease is a debilitating condition giving rise to symptoms of disabling fatigue, low mood, irritability, headache, gastrointestinal symptoms, and impaired concentration and memory. A number of studies have shown that the health related quality of life of patients with primary Sjögren's Disease is significantly decreased and is comparable with that of patients with rheumatoid arthritis or systemic lupus erythematosus.[2,3,4]

Presentation

The clinical presentation of Sjögren's Disease is variable and can include exocrine (glandular) and/or non-exocrine (extraglandular) symptoms. Dry eyes and/ or dry mouth are the most common presenting clinical features1 but other forms of dryness (sicca) occur, including dry skin or dry cough. Patients with vaginal dryness may present to a gynaecologist complaining of painful intercourse.5 Occasional patients present acutely, with swelling of the major salivary glands. Usually, however, the onset is insidious and patients often have difficulty in deciding when the clinical features actually began. In patients with more severe dryness, dental decay, tooth loss and corneal damage can occur if the condition is left untreated.

Another common presentation is with non-specific complaints such as arthralgia and fatigue, which may lead to a primary diagnosis of fibromyalgia rather than of

Sjögren's Disease. There is some overlap between these conditions, since about 5% of patients with Sjögren's Disease will also have fibromyalgia. Some patients present with arthritis, typically of the small joints of the hands and wrists, which may initially be diagnosed as rheumatoid arthritis.

Because of the diverse nature of these symptoms, undiagnosed patients may present to a wide range of clinical specialties depending on their symptoms (including oral medicine/surgery, ophthalmology, rheumatology, gynaecology, ear nose and throat specialists, etc) and diagnoses may be delayed by up to 10 years, from the onset of the condition. Secondary Sjögren's Disease should always be considered in any patient known to have a rheumatic disorder who complains of dry or gritty eyes and/or dry mouth symptoms.

Systemic Features

Other extraglandular manifestations include vascular/vasculitic manifestations (Raynaud's phenomenon, purpura, cutaneous vasculitis), pulmonary (interstitial lung disease), haematologic (idiopathic thrombocytopaenic purpura, autoimmune haemolytic anaemia, monoclonal gammopathy, cryoglobulinaemia, non-Hodgkin's lymphoma), renal/bladder (renal tubular acidosis, interstitial nephritis, interstitial cystitis) and nervous system involvement (peripheral or cranial neuropathy, focal neurological deficits, multiple sclerosis-like lesions, or loss of cognitive function). Occasional patients will present with one or more of these features. The diagnosis and management of such patients will not be addressed in these guidelines.

Compared to the general population, patients with Sjögren's Disease have a 44 times increase in the relative risk of developing non-Hodgkins lymphoma6 (although the absolute risk is still modest). Patients with autoantibodies, low complement levels, monoclonal gammopathies, cryoglobulins, major salivary gland swelling, histological evidence of premalignant lesions such as myoepithelial sialadenitis or who have other systemic involvement should be monitored carefully for the development of such a malignancy.

Anti-Ro/La antibodies are directed against auto-antigens found in the lacrimal and salivary glands, and other tissues. They can cross the placenta and are associated with an increased risk of fetal or neonatal heart block, rashes and other systemic features[7]. Rarely, intra-uterine death can occur[7]. Some women are first diagnosed during or after pregnancy, following the development of these features in their child. This is a specialist area and the management of such pregnancies is beyond the scope of these guidelines.

Principles of diagnosis

The diagnosis of primary Sjögren's Disease should be considered in any patient complaining of dry mouth, gritty eyes or unexplained lethargy. Table 1 lists the 6 EU screening questions used to identify dry eye or dry mouth symptoms.[8] Table 2 sets out the EU-USA consensus classification criteria for Sjögren's Disease.[8] The differential diagnosis includes a wide spectrum of infectious, inflammatory, metabolic and behavioural (i.e. anxiety, depression) conditions as well as the list of exclusion criteria in Table 2.

Table 1: EU screening questions for dry eye and mouth symptoms

Ocular symptoms:

- Have you had daily, persistent, troublesome dry eyes for more than 3 months?
- Do you have a recurrent sensation of sand or gravel in the eyes?
- Do you use a tear substitute more than 3 times a day?

Oral symptoms:

- Have you had a daily feeling of dry mouth for more than 3 months?
- Have you had recurrently or persistently swollen salivary glands as an adult?
- Do you frequently drink liquids to aid in swallowing dry foods?

Table 2: EU-USA classification criteria for Sjögren's Disease	
I	Symptomatic xerostomia for >3 months, persistently swollen salivary glands as an adult, or frequent use of liquids to aid in swallowing food
II	Symptomatic dry eyes for >3 months, recurrent 'grittiness', or use of tear substitutes >3 times a day
III	Positive Schirmer's I test or rose Bengal score (or other ocular dye score e.g. lissamine green)
IV	Abnormal lower lip biopsy (focus score 2-:1)
V	Positive result for unstimulated whole salivary flow (:S1 .5 ml in 15 minutes)
VI	Antibodies to Ro (SS-A) or La (SS-B), or both

Exclusions

Any patient with past head and neck radiation treatment, hepatitis C infection, Acquired Immunodeficiency Disease (AIDS), pre-existing lymphoma, sarcoidosis, graft versus host disease, use of anticholinergic drugs

Table 2 also lists the examinations (Schirmer's test of tear flow and unstimulated salivary flow rate) and investigations (anti-Ro/La antibodies and labial gland biopsy) necessary to confirm a diagnosis of Sjögren's Disease.

Facilities or time constraints in the community may sometimes make it impossible to carry out a Schirmer's test or measure unstimulated salivary flow rate, but antiRo/La antibody tests can be performed routinely and are requested from hospital immunology departments. Further Investigations at this stage or in secondary care may include a full blood count, ESR, liver function tests, antinuclear antibodies, rheumatoid factor, lgG, lgA and lgM levels and thyroid function tests. Hypergammaglobulinaemia can lead to a raised ESR and finding a raised ESR in the presence of a normal or near-normal CRP is often an indicator of this. Specialist referral is usually dictated by the severity and nature of patient symptoms.

Labial gland biopsy

The characteristic histological features of Sjögren's Disease are of at least one or more clusters ('foci') of 50 or more lymphocytes surrounding salivary ducts per $4mm^2$ high-powered field. This is likely to be reported as being 'consistent with a diagnosis of Sjögren's Disease'. If this is not seen, but the normal diffuse scattering of plasma and other cells is observed, then this may be reported as showing features of 'non-specific sialadenitis'. An inadequate sample should be reported as such.

Primary Sjögren's Disease

In the absence of exclusion criteria, the classification criteria for a diagnosis of primary Sjögren's Disease are fulfilled if any 4 of the 6 items listed in Table 2 are positive, as long as this includes either item IV (Histopathology) and/or item VI (Serology). The criteria also allow for the occasional asymptomatic patient in that three positive results out of the four objective items (ocular signs, histopathology, salivary gland involvement or serology) are also considered to fulfil the criteria for a diagnosis of primary Sjögren's Disease.

Secondary Sjögren's Disease

In patients with another connective tissue disease such as rheumatoid arthritis, the presence of item I or item II plus any two from among items 111, IV and Vin Table 2 may be considered as indicative of secondary Sjögren's Disease. Anti-Ro/La antibody serology is not helpful In diagnosing secondary Sjögren's Disease.

'Sicca Syndrome'

The term 'sicca syndrome', meaning 'dryness' is sometimes given to patients who have some dryness of their eyes and/or mouth, for example as a result of agerelated reduction in glandular function, x-ray irradiation or illness, but do not meet criteria for the diagnosis of Sjögren's Disease. Symptomatic treatment similar to that of patients with Sjögren's Disease should be offered to these patients.

The role of secondary care

The accurate diagnosis of both primary and secondary Sjögren's Disease is relatively simple, based on the recognition of characteristic clinical findings and the results of simple diagnostic tests.

Ophthalmology and Oral Medicine/Surgery

Depending upon the initial assessment and diagnosis, most referrals of patients with dry eyes from primary care will be to ophthalmologists, while those with dry mouth will be referred to consultants in oral medicine or oral surgery. Our recommendation is that all such patients should undergo a full assessment for the presence of Sjögren's Disease. Anti-Ro/La antibody testing and objective tests will capture up to 70% of patients. For those patients who have a negative anti-Ro and/or anti-La antibody test a minor labial gland biopsy is the confirmatory test. This test should be performed by an experienced specialist, in which case the incidence of complications is low.

We recognize, however, that the volume of such referrals and the constraints of time and facilities may make this approach difficult to achieve in routine clinical practice. If this is the case, then an alternative strategy to identify 70% of patients is to request anti-Ro/La antibody testing in patients referred with dryness symptoms (eyes and/or mouth) who are found to have objective evidence of dryness of the eyes and/or mouth clinically (Figure 1). **Using this strategy, those patients with objective evidence of oral and/or ocular dryness and a positive anti-Ro/La antibody test should be referred to a rheumatologist or Sjögren's Disease specialist for further evaluation.** Patients whose anti-Ro/La antibody test is negative should be offered symptomatic therapy. Further follow-up depends on the clinical judgement of the specialist in charge. In oral medicine or surgery clinics where labial gland biopsy is available, this test should still be considered In patients with objective evidence of oral dryness, even if anti-Ro/La antibody testing was negative.

Rheumatologists

Sjögren's Disease should be considered in any patient presenting with non-specific symptoms, arthralgia, fatigue or arthritis. The diagnosis of primary Sjögren's Disease should follow the EU-USA Consensus Criteria described above with the assessment of dryness symptoms, objective tests and anti-Ro/La antibody tests. If anti-Ro/La antibodies are negative a labial gland biopsy is then required to confirm or refute the diagnosis. If labial gland biopsy is not available then a similar strategy to that described above should be followed.

In rheumatology clinics existing patients with rheumatoid arthritis or other rheumatic diseases may also present with the secondary form of the syndrome. For these patients, confirmatory diagnosis is from positive symptomatology plus objective evidence of dry eye/dry mouth, and a positive labial gland biopsy if required.

Other specialties

A similar approach to that described above under ophthalmology/oral medicine/surgery can be followed for patients presenting to gynaecologists, dermatologists, ear nose and throat specialists etc with dryness of other systems. Patients presenting to oral medicine, oral surgery or ear nose and throat departments with salivary gland swelling will need to be carefully evaluated clinically, radiologically and if necessary by histological examination of biopsy/excision specimens to exclude infection, malignancy or other inflammatory disorders.

Principles of treatment

The goals of treatment are to manage the symptoms and to prevent or limit organ damage. This may involve symptomatic and/or systemic treatment depending on the clinical features.

Summary

- For dryness symptoms a stepped approach can be followed starting with general advice and simple topical preparations (artificial tears/saliva substitutes/lubricants/emollients). The severity of the condition and patient preference will often guide the choice of agents used.
- Use a secretagogue (e.g. pilocarpine) in patients with more severe dry eyes or dry mouth, who have some degree of residual exocrine gland function, where topical therapy is insufficient.
- Consider punctal plugs or punctal occlusive surgery for severe dry eye.
- Oral candida infection should be identified and treated promptly.
- Systemic treatment may be required as clinical features dictate.

General advice

We advise that patients should:

- be encouraged to attend their dentist regularly (at least every 6 months).
- receive advice on appropriate diet (avoidance of sweet food) and the maintenance of good dental hygiene (brushing, interdental cleaning and use of fluoride supplements).
- be advised to avoid strong soaps. Use aqueous creams and emollients (and barrier creams in the summer).
- be advised to avoid dry, external or internal environments.
- be advised to avoid tobacco smoking and excess alcohol consumption.
- receive information about self-help organisations (Sjögren's UK charity; Arthritis Research Campaign).
- Female patients of child-bearing age with anti-Ro/La antibodies should be advised of the potential fetal risks prior to planning a pregnancy.

Other tips that may be helpful include:

- **Eye irritation:** Wear dark or tinted spectacles in bright sunlight. Wear moisture-conserving spectacles out of doors. Use tear substitutes in smoky atmospheres. Avoid using contact lenses.
- **Dry mouth:** Sip water, suck ice cubes, use sugar-free chewing gum,sweets or pastilles.
- **Cracked lips:** Use petroleum jelly.
- **Mouth ulcers:** Use diluted chlorhexidine mouthwash (stains teeth so avoid continued use). Refer to oral specialist if they persist.
- **Dry itchy skin:** Shower rather than bath. After bathing blot the skin dry, allowing a slight amount of moisture to remain.
- **Vaginal dryness:** Use lubricants.
- **Dry cough:** Humidifiers and plants with large leaves in rooms may help. Avoid drugs that aggravate symptoms.

Tear substitutes and mucolytic agents

T he commonest treatment for dry eyes is artificial tears. T heir main limitation is their short duration of action. Most preparations contain polymers to increase the retention time on the eye.

Tear substitutes fall into five main groups according to the polymer that they contain:

- **Carboxy methyl cellulose** (e.g. Hypromellose BP, lsopto plain®, lsopto alkaline®, Tears Naturale®)
- **Polyvinyl alcohol** (e.g. Hypotears®, Sno Tears®, Liquifilm® tears)
- **Sodium Hyaluronate** (e.g. Hylo-Tears, Hyabak, Vismed)
- **Aqueous carbomer gels** (e.g. Viscotears®, Geltears®)
- **Paraffin ointments** (e.g. Lacri-Lube®, VitA-Pos)

Also available are:

- **Mucolytic drops** (e.g. llube®, acetylcysteine 10%)

Hypromellose eye drops are an inexpensive, over the counter (OTC) preparation,

widely used as first-line treatment. Other, more expensive OTC preparations are also available. As with other lubricants, they should be instilled into the eyes as frequently as necessary to alleviate symptoms.9 In patients who require more frequent use, aqueous carbomer gels have a longer duration of action and may be used as an alternative.

Preservative-free drops (e.g. Minims Tearse, Liquifilm Pf=tl, Hylo-Tears, Viscotearse single dose units and Celluvisce - a more viscous preparation) are available for patients who are obliged to use drops more than 4 times daily. They avoid the very real risk of preservative toxicity with frequent use and are recommended for patients who need to use drops more than 4-5 times a day. Single dose preservative free units should be discarded after each use and multi-dose bottles after one week, unless otherwise instructed by an ophthalmologist.

If mucous threads are a problem, or if the patient complains of sticky eyes on waking, then mucolytic agents such as acetylcysteine may be useful. Paraffin ointments, used before going to sleep may be helpful in providing prolonged overnight comfort and avoids the blurring which can occur with their daytime use. Warming the ointments before use will make it easier to put them in.

Patients with severe dry eyes, unresponsive to topical therapy, may benefit from moisture-conserving spectacles, humidifiers, moist chambers or swimming goggles. Blocking the drainage of residual or artificial tears from the eyes, using punctal plugs, can be beneficial. If plugs are successful then the canaliculi can be permanently closed surgically.

Saliva substitutes

Artificial saliva can provide useful relief of dry mouth. However, most saliva substitutes are water-based and remain in the mouth only a short time, and therefore, do not provide the protective roles of saliva.

Saliva substitutes can be grouped as follows:

- Carboxymethylcellulose sprays (e.g. Glandosane®, Luborant®, Salivace®, Saliveze®)
- Saliva Orthanae (spray or lozenge)
- Moisturising gels (e.g. Oralbalance®, Oralieve, BioXtra®)
- Alcohol-free mouth rinses and toothpaste (e.g. BioXtra®, Biotene®)

Saliva Orthana does not contain fluoride, Luborant does contain fluoride. Glandosane® has a relatively low pH, which could potentially encourage demineralization of teeth and may therefore be more appropriate in patients who no longer have their own teeth. Saliva Orthana® is similar to carboxymethylcellulose sprays, but uses animal derived gastric mucin, which may be unacceptable to some patients. Saliva replacement gels have been favoured by patients in terms of providing symptomatic relief.[9]

Mouth rinses and topical agents may soothe oral discomfort and potentially reduce the risk of gum disease and caries.

Salivary stimulants

- Local sialogogues (e.g. Biotene® dry mouth gum, BioXtra41J chewing gum, Salivix® pastilles)

Sugarless sweets, pastilles and chewing gum may stimulate salivary flow in patients with residual functioning salivary gland tissue. 10

Systemic sialogogues

Patients whose dryness symptoms are inadequately controlled with topical therapy can now be treated with a secretagogue (i.e. pilocarpine). Salagen® (pilocarpine) is the only systemic treatment licensed in the UK for the treatment of dry eyes and dry mouth associated with Sjögren's Disease. A large clinical trial in the USA has shown it to be well tolerated and effective in reducing symptoms of dry mouth, dry eyes and other dryness in patients with Sjögren's Disease[11]. It may also

reduce the frequency of long-term complications of Sjögren's Disease caused by untreated dryness.[12]

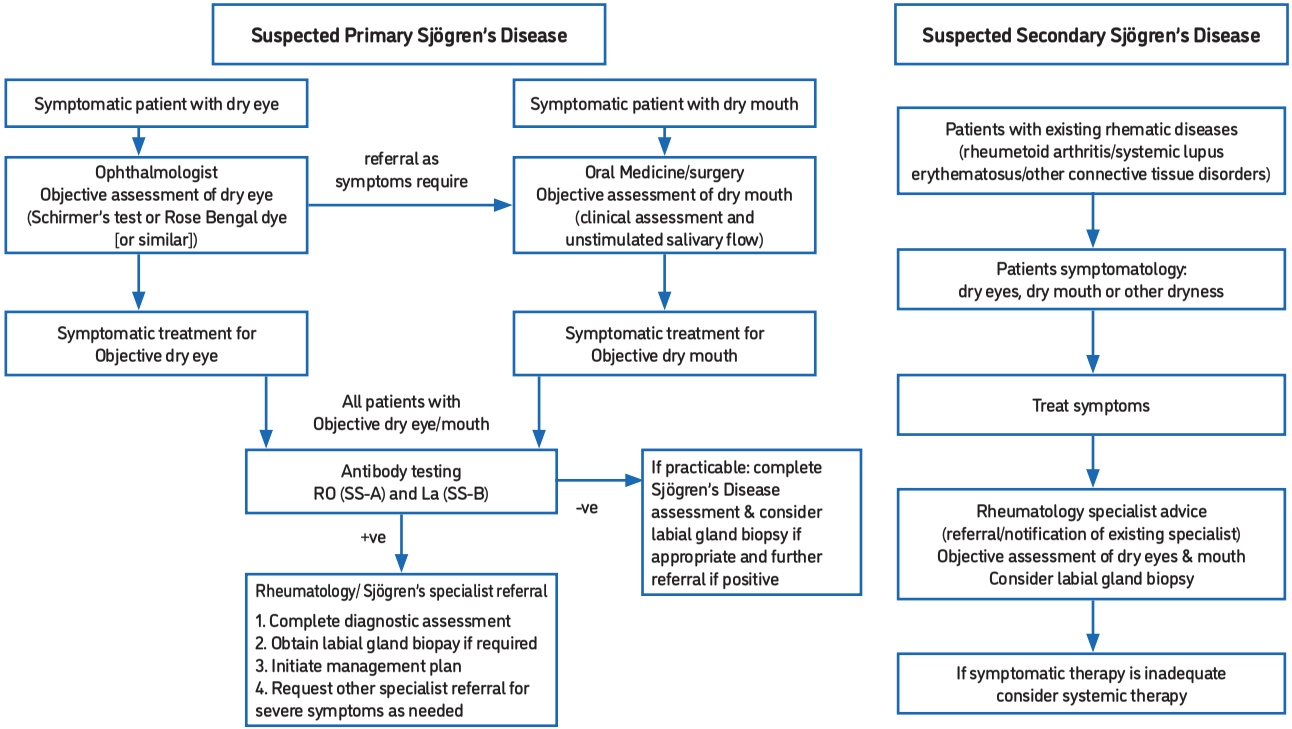
Pilocarpine cannot exert its secretagogue effects in patients who have no remaining exocrine function (e.g. patients whose Schirmer's test or stimulated salivary flow rate are persistently zero). For this reason it is more logical to use it earlier rather than later in the disease course. Although objective effects (e.g. improvement in salivary flow) are generally dose-dependent and detectable within 30 minutes of administration, symptomatic improvement takes a number of weeks to develop. In order to aid compliance, patients should therefore be advised at the outset that they will need to stay on treatment for a minimum of 6 weeks before they can expect symptomatic improvement.

The main side-effects experienced by some patients are diarrhoea and other adverse gastrointestinal side-effects, urinary frequency and flushing. However, these tend to decrease over time. It can be helpful to start pilocarpine at a low dose (e.g. 5mg once daily) and to advise patients to wait until any such symptoms have subsided (e.g. 6 weeks) before increasing the dose to twice daily and to then follow a similar strategy for further dose increases until the maintenance dose of 5mg four times a day is reached. Other specialists recommend increasing the dose more quickly than this (e.g. at weekly intervals).

Emollients and lubricants

A large number of soap substitutes, emollients and barrier creams are available over the counter or on prescription for patients with dry skin. Symptoms of vaginal dryness can be alleviated using lubricants (e.g. KY jelly, Replens® vaginal moisturising gel, Astroglyde® cream). Oestrogen creams can also help some patients.

Figure 1. Simplified algorithm for the diagnosis and treatment of Sjögren's Disease



Immunosuppressant and other therapies

Topical ciclosporin is now available in the UK for the treatment of chronic corneal inflammation in patients with Sjögren's Disease under ophthalmic supervision. Autologous serum has also been used in some centres as a tear substitute for patients with severe dry eyes. Occasionally, short-term use of topical corticosteroid eye-drops can be effective in relieving inflammatory eye symptoms. Because of their potential side-effects it is recommended that specialist ophthalmological advice is sought before their use.

There is some evidence to support the use of hydroxychloroquine sulphate in patients with primary Sjögren's Disease. Anecdotally it seems to have a beneficial effect on overall wellbeing and improvement in symptoms of fatigue and arthralgia although there is no evidence of a direct effect on salivary or lacrimal flow.[13] Studies confirm a reduction in the ESR and immunoglobulin levels.[14] Studies of other disease modifying drugs such as methotrexate have been disappointing.[15]

There is conflicting data on the benefits of corticosteroids. In general, the use of corticosteroids or immunosuppressants is reserved for the more serious systemic complications of Sjögren's Disease which is beyond the scope of these guidelines.

References

1. Jonsson R, Haga H-J, Gordon T: Sjögren's Disease. In: Arthritis and Allied Conditions -A Textbook of Rheumatology, Koopman WJ, ed. 14th Edition. Lippincott Williams & Wilkins, Philadelphia, 2001, pp1736-1759.

2. Bowman SJ, Ibrahim GH, Holmes G, Hamburger J, Ainsworth JR. Estimating the prevalence among Caucasian women of primary Sjögren's Disease in two general practices in Birmingham, UK. Scandinavian journal of rheumatology. 2004;33(1):39-43

3. Sutcliffe N, Stoll T, Pyke S, Isenberg DA. Functional disability and end organ damage in patients with systemic lupus erythematosus (SLE), SLE and Sjögren's Disease (SS), and primary SS. J Rheumatol 1998. 25:63-8.

4. Strombeck B, Ekdahl C, Manthorpe R, Wikstrom I, Jacobsson L. Health-related quality of life in primary Sjögren's Disease, rheumatoid arthritis and fibromyalgia compared to normal population data using SF-36. Scand J Rheumatol 2000. 29:20-8.

5. Mulherin DM, Sheeran TP, Kumararatne DS, Speculand D, Luesley D, Situnayake RD. Sjögren's Disease in women presenting with chronic dyspareunia. Br J Obstet Gynaecol. 1997 Sep;104(9):1019- 23

6. Kassan SS et al. Increased risk of lymphoma in sicca syndrome. Ann Intern Med. 1978. 89:888-92.

7. Tseng CE, Buyon JP. Neonatal lupus syndromes. Rheum Dis Clin North Am 1997. 23:31-54.

8. Vitali C et al. Classification criteria for Sjögren's Disease: a revised version of the European criteria proposed by the American-European consensus group. Ann Rheum Dis 2002. 61 :554-558.

References

9. Mulherin D, Ainsworth JR, Hamburger J, Situnayake D, Speculand B, Bowman SJ. Survey of artificial tear and saliva usage among patients with Sjögren's Disease. Ann Rheum Dis 2001. 60:1077.

10. Foster HE, Gilroy JJ, Kelly CA, Howe J, Griffiths ID. The treatment of sicca features in primary Sjögren's Disease: a clinical review. Br J Rheum 1994. 33:278-282.

11. Vivino FB et al. Pilocarpine tablets for the treatment of dry mouth and dry eye symptoms in patients with Sjögren's Disease. Arch Int Med 1999. 159:174-181.

12. Vivino FB. The treatment of Sjögren's Disease with Pilocarpine tablets. Scand J Rheumatol 2001. Suppl. 115: 1-13.

13. Fox RI, Dixon R, Guarrasi V et al. Treatment of primary Sjögren's Disease with hydroxychloroquine; a retrospective, open-label study. Lupus 1996; 5 (Supp 1): 31-6.

14. Kruize AA, Hene RJ, Kallenberg CG et al. Hydroxychloroquine treatment for primary Sjögren's Disease; a two year, double blind cross over trial. Ann Rheum Dis 1993; 52, (ISS5): 360-4.

15. Skopouli FN, Jagiello P, Tsi Fetaki N et al. Methotrexate in primary Sjögren's Disease. Clin Exp Rheum 1996; 14, 555-8.

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