RHEUMATOLOGY

Guidelines

doi:10.1093/rheumatology/kex163

The British Society for Rheumatology guideline for the management of adults with primary Sjögren's Syndrome

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Key words: Sjögren's, guideline, management, sicca

Executive summary

Background

Primary SS (pSS) is a classic, immune-mediated, condition [1] typically presenting in women in their fifth or sixth decade, although up to 10% of cases occur in men. The prevalence in women in the UK is 0.1–0.4% [2]. Patients characteristically present with dryness of the eyes and mouth but systemic features are common and B-cell lymphoma affects 5–10% [3, 4].

NICE has accredited the process used by the BSR to produce its guidance for the management of primary Sjögren's Syndrome in adults. Accreditation is valid for 5 years from 10 June 2013. More information on accreditation can be viewed at www.nice.org.uk/accreditation. For full details on our accreditation visit: www.nice.org.uk/accreditation.

Objective of guideline

This document aims to provide a pragmatic, practical guideline for the management of adults with pSS. The Full Guideline is available at *Rheumatology* Online.

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Submitted 7 September 2016; revised version accepted 20 March 2017.

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GUIDELINES

Target audience

The target audience includes rheumatologists, general physicians, general practitioners, specialist nurses and other specialists (e.g. ophthalmologists, dental practitioners and ENT specialists).

Areas not covered

This guideline does not cover the detailed management of patients with secondary Sjögren's or patients with lymphoma, who should be managed in conjunction with oncologists and haematologists. The management of children is not specifically covered although is similar to that for adults with special emphasis on good dental care and hygiene.

Rigor of development and limitations

A search was undertaken for all relevant evidence from 1990 to January 2016. The level of evidence (LOE) was graded from Ia through to IV and A through to D. See Appendix 1 for full details of search criteria and LOE definitions.

A strength of agreement (SOA) was calculated for each recommendation and the results expressed as an SOA score (0–10) with percentage of respondents scoring the recommendation $\geqslant 7$ in parentheses. Recommendations were only included where the mean SOA was $\geqslant 7$ and $\geqslant 75\%$ respondents scored $\geqslant 7$.

The guideline

Eyes

(i) Conservation of tears by humidification and avoidance of systemic medication that exacerbates dryness. LOE Ib/A; SOA 8.9 (97%).
(ii) Stimulate meibomian gland secretion daily using warm compresses, commercially available eye bags or other devices and perform lid hygiene if required. LOE III/C; SOA 8.9 (93.3%).
(iii) If persistent meibomian gland inflammation and blepharitis treatment with doxycycline 50 mg od for a minimum of 3 months may be effective. LOE IV/D; SOA8.83 (92.9%).
(iv) Early referral to an ophthalmologist for review and consideration of insertion of punctual plugs or cauterization. LOE II/B; SOA 9.27 (100%).
(v) Recommend liposomal sprays to reduce evaporative tear loss and replace the meibomian gland layer. LOE III/C; SOA 8.29 (92.8%).
(vi) Start with simple lubricating drops using the most cost-effective options (see Table 1 for preparations). LOE IV/D; SOA 9.3 (93.3%).
(vii) Avoid preservative-containing preparations. LOE I/A; SOA 9.21 (92.9%).
(viii) Refer patients with severe dry eye, not responding to conventional treatment, to specialist commissioned centres for consideration of serum eye drops. LOE IIb/B; SOA 9.5 (100%).
(ix) Low dose steroid-containing eye drops for short term use under ophthalmic supervision only. LOE Ib/A; SOA 9.64 (100%).
(x) Avoid long term use of topical steroids. LOE Ib/A; SOA 9.64 (100%).
(xi) Ciclosporin eye drops or ointments under ophthalmic supervision for chronic inflammation. LOE Ib/A; SOA 9.38 (100%).
(xii) Use topical NSAIDs with caution under ophthalmic supervision only. LOE IIb/B; SOA 9.86 (100%).
(xiii) A trial of pilocarpine 5 mg once daily increasing stepwise to 5 mg qds is recommended for patients with significant sicca symptoms. LOE IIb/B; SOA 9.08 (92.3%).
(xiv) Prescribe mucolytic eye drops to patients with mucous threads or ocular surface filaments. LOE III/C; SOA 9.38 (100%).
(xv) Refer patients with severe dry eye and associated blepharospasm to a specialist centre for consideration of botulinum toxin treatment. LOE III/C; SOA 9.17 (100%).
(xvi) Refer patients with severe dry eye and corneal ulceration, not responding to conventional treatment, to a specialist centre for consideration of bandage contact lenses or corneal grafting. LOE III/C; SOA 9.15 (92.9%).

Mouth

(i) Advise excellent oral hygiene, limit sugar intake and avoid food and drinks other than plain water between meals and from 1 h before bedtime and through the night. LOE IV/D; SOA 9.8 (100%).
(ii) Advise assessment by an oral medicine specialist and/or regular visits to a general dental practitioner. LOE IV/D; SOA 9.8 (100%).
(iii) Avoid acidic and sugar-containing products in dentate patients. LOE IV/D SOA 9.87 (100%).
(iv) Humidify the environment. LOE III/C; SOA 9.13 (100%).
(v) Brush teeth at least twice daily (but not immediately after eating) including before bed using a pea sized amount of high fluoride toothpaste and use fluoride-containing oral gel on teeth twice daily. LOE I/A; SOA 9.8 (100%).
(vi) Alcohol-free chlorhexidene mouth wash twice daily for maximum of 2 weeks every 3 months can help prevent gum disease. LOE IV/D; SOA 9.0 (100%).
(vii) Use fluoride-containing mouth wash, gel or spray as required for symptomatic relief. LOE III/C; SOA 9.43 (92.8%).
(viii) Chew xylitol-containing sugar-free gum. LOE IIb/B; SOA 9.67 (100%).
(ix) A trial of pilocarpine 5 mg once daily increasing stepwise to 5 mg qds if significant sicca symptoms. LOE IIb/B; SOA 9.77 (100%).

Treatment of oral candida

(i) Simple candida infection (visible white plaques)—oral nystatin liquid 1 ml five times daily for 7 days. Repeat for 1 week in 8 if frequent recurrence. LOE IV/D; SOA 9.86 (100%).

Table 1 Dry eye topical therapies

Viscosity	Compound	Preserved	Non-preserved
Low	Hypromellose	Hypromellose MD[a] Xailin Hydrate MD Tears Naturale MD[a]	Artelac SDU Hydromoor SDU Tears Naturale SDU Tear-Lac MD
	Polyvinyl alcohol	Liquifilm Tears MD[a] Tubilux MD	Liquifilm Tears SDU Refresh SDU
Thin-medium	Carbomers	Viscotears Gel Tears[a] Clinitas Carbomer Gel Artelac Nighttime Gel	Viscotears SDU Visidic[b]
	Carmellose	Optive 0.5% MD Carmize 0.5% MD Lumecare Advance 0.5% MD	Celluvisc 0.5 or 1% SDU Xailin Fresh 0.5% SDU Evolve Carmellose 0.5% MD Carmize 1% MD
	Guar Gums	Systane MD Systane Ultra Systane Gel Systane Balance	Systane SDU, Systane Ultra SDU
Thick-medium	Sodium hyaluronates	Xailin HA 0.2% Blink Intensive Tears 0.2% MD Optive Fusion 0.1% MD Oxyal 0.15% MD Artelac Rebalance 0.15% MD	Vismed 0.18% SDU or MD Vismed gel 0.3% Clinitas 0.4% SDU Clinitas Multi 0.4% MD Hycosan[b] Hylo-Forte 0.2%, Hylo-Care 0.1%, Hylo-Tear 0.1% (MD) Artelac Splash 0.2% SDU Blink Intensive 0.2% SDU Evolve Hyaluronate 0.4% MD Lubristil 0.15%/1% xanthan gum
High	Paraffin/white petroleum	—	Lacri-lube VitA-Pos Xailin Night HydraMed Night
Others	Liposomes[b]	—	Actimist[b] Vizulize Dry Eyes Eye Mist[b] Eye Logic Liposomal Eye Drops and Spray (formerly Clarymist)[b]
	Soy bean/mineral oil	—	Emulstil SDU
	Mucolytics[c]	Aceylcesteine (Ilube)[c]	Acetylcysteine 10% MD (unlicensed)[c]
	Anti-inflammatory or immune regulators[c]	—	Ciclosporin 0.2% (unlicensed, Optimmune®) veterinary preparation[c] Restasis® (not licensed EU)[c] Ciclosporin 0.1% (licensed, Ikervis® SDU)[c]
	Disaccharides[b]	—	Thealoz MD[b] Thealoz Duo MD[b] Thealoz Duo SDU[b] Thealoz Duo Gel SDU[b] HydraMed [sodium hyaluronate (0.2% w/v), polysaccharide (0.2% w/v)]

A selection of ocular lubricants available in preserved and non-preserved forms. Most are available both over the counter and on prescription, some are prescription only and others are over the counter only. [a]Contain benzalkonium chloride (should be avoided). [b]Over the counter only. [c]Prescription only. MD: multi-dose bottle; SDU: single dose units.

(ii) Erythematous infection (red, raw tongue or oral cavity)—fluconazole 50 mg od for 10 days. LOE IV/D; SOA 9.86 (100%).
(iii) Treat angular cheilitis with miconazole topically for 2 weeks. LOE IV/D; SOA 9.86 (100%).

Management of salivary gland enlargement

(i) Consider baseline US to assess for active inflammation, infection and stones. LOE IV/D; SOA 9.7 (100%).
(ii) If acute inflammation, in the absence of infection and stones, consider short course of oral prednisolone or intra-muscular depomedrone. LOE IV/D; SOA 9.01 (100%).
(iii) Massaging the glands reduces inflammation in chronically inflamed glands. LOE IV/D; SOA 9.31 (92.8%).

Systemic dryness

(i) A trial of pilocarpine 5 mg once daily increasing stepwise to 5 mg qds if systemic dryness. LOE IV/D; SOA 9.08 (92.3%).
(ii) A non-hormonal vaginal moisturizer ± topical oestrogen if vaginal dryness. LOE I/A; SOA 9.8 (100%).

Treatment of systemic disease

Non-pharmacological interventions for systemic disease

(i) Advise a graded exercise programme for fatigue. LOE IIb/B; SOA 9.33 (93.3%).
(ii) Provide written information and details of appropriate support groups and online resources. LOE IV/D; SOA 9.8 (100%).

Pharmacological treatment for systemic disease

(i) HCQ (6 mg/kg) for those with skin, joint disease or fatigue. LOE IIa/B; SOA 9.64 (100%).
(ii) Ciclosporin A may be helpful in patients with significant joint involvement. LOE III/C; SOA 8.58 (85.7%).
(iii) AZA may be considered in patients with systemic complications. LOE III/C; SOA 9.09 (100%).
(iv) MTX is useful for patients with an associated inflammatory arthritis. LOE IV/D SOA 9.54 (100%).
(v) Mycophenolate may be considered in patients with systemic complications. LOE III/C; SOA 9.1 (100%).

Corticosteroids

(i) Intermittent short courses of oral or intramuscular steroid for systemic flares and significant organ manifestations with or without additional immunosuppressive treatment. LOE III/C; SOA 9.2 (100%).
(ii) Low dose oral prednisolone for persistent constitutional symptoms in patients with inadequate response to other immunosuppresants. LOE IIb/B; SOA 8.92 (100%).

CYC

(i) CYC (usually in combination with steroids) for patients with organ threatening systemic complications. LOE III/C; SOA 9.09 (100%).

Rituximab

(i) Rituximab for specialist use in patients with significant systemic manifestations refractory to other immunosuppresives and those with lymphoma, immune thrombocytopenia, vasculitic neuropathy or cryoglobulinaemia. LOE IIb/B; SOA 9.43 (100%).

IVIG

(i) Immunoglobulin treatment for Sjögren's associated myositis and neuropathies if the patient has failed to respond to treatment with conventional immunosuppression. LOE III/C; SOA 9.43 (100%).

Colchicine

(i) Colchicine as adjunctive treatment if cutaneous manifestations or pericarditis not responding to other treatments. LOE III/C; SOA 8.45 (85.7%).

Dapsone

(i) Dapsone as adjunctive treatment if cutaneous manifestations not responding to HCQ. LOE III/C; SOA 8.8 (100%).

Topical tacrolimus

(i) Topical tacrolimus as adjunctive treatment if cutaneous manifestations not responding to HCQ. LOE III/C; SOA 8.75 (100%).

Treatments NOT recommended

(i) LEF and penicillamine are not routinely recommended for pSS. LOE III/C; SOA 9.8 (100%).
(ii) Belimumab and abatacept are not currently recommended although they merit further study. LOE IIb/B & III/C; SOA 9.46 (92.8%).
(iii) Anti-TNF, IFNα and anakinra therapies are not recommended for treatment of pSS. LOE Ib/A; SOA 9.38 (85.7%).
(iv) Tociluzimab and efalizuab are not recommended for the treatment of pSS. LOE III/C; SOA 9.82 (100%).
(v) Dehydroepiandrosterone substitution treatment is not recommended in pSS. LOE Ib/A; SOA 9.45 (100%).

Management of pregnancy

(i) Consider low dose aspirin to improve placental implantation. LOE IIb/B; SOA 8.27 (92.8%).
(ii) Monitor with serial US if anti-Ro and/or anti-La positive and consider referral to specialist centre. LOE IIb/B; SOA 9.71 (100%).

(iii) Review all medication in pregnancy. HCQ may be continued throughout pregnancy and breastfeeding. LOE I/A; SOA 7.91 (85.7%).

Assessment and management of lymphoma

(i) Review high risk patients regularly and warn patients to report firm, painless glandular swelling that does not settle. LOA IV/D; SOA 9.86 (100%).
(ii) Investigate suspicious lesions with local US, biopsy and CT chest, abdomen and pelvis for staging. LOA III/C; SOA9.77 (100%).

Conclusion

pSS is a chronic, debilitating condition that warrants effective management. All patients should be counselled and offered topical management for sicca symptoms. Systemic treatment should be considered early in those with constitutional symptoms.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Disclosure statement: B.A.F. has received honoraria from Novartis and Medimmune. W.-F.N. has provided scientific consultancy for Takeda, MedImmune, UCB, Sanofi, Eli-Lily, AbbVie and have received research support from Resolve Therapeutics. S.B. has consulted for a number of Pharmaceutical Companies in the field of clinical trial design Sjogren's Syndrome (AstraZeneca/Medimmune, BMS, Celgene, Eli Lilly, Glenmark, GSK, MTPharma, Novartis, Ono, Pfizer, Takeda, UCB, xtlbio). F.B. works in a unit that has received funding from GSK and USB. All other authors have declared no conflicts of interest.

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