Survey of artificial tear and saliva usage among patients with Sjögren’s syndrome

Sjögren’s syndrome (SS), a chronic immune mediated disease associated with xerostomia and keratoconjunctivitis sicca, may occur alone (primary SS) or with other autoimmune diseases (secondary SS). The benefits of substitution treatment for dry eyes and mouth seem very variable. This survey assessed patients’ experience of the wide variety of tear and saliva substitutes available.

Patients with SS, from Cannock Chase Hospital, City Hospital Birmingham, City Hospital Birmingham, or Birmingham Heartlands and Solihull Hospitals, completed a questionnaire, returned at their clinic visit or by prepaid post. SS was defined by the presence of four from six EC diagnostic criteria, with primary SS must have anti-Ro antibodies and saliva usage among patients who have had a lip biopsy (by enzyme linked immunosorbent assay (ELISA) or countercurrent immunoelectrophoresis) and/or have had a lip biopsy demonstrating features typical of SS. The questionnaire asked patients to identify, from a comprehensive list, all tear and saliva substitutes that they had ever heard of, had ever used, or were currently using, to identify useful source(s) of information about substitute treatment, and to rate the effectiveness of any treatments they had ever used, on 10 cm visual analogue scales (VAS). The duration of any substitute treatment was not recorded.

Demographic, clinical, and laboratory data for each patient were obtained by chart review. The Mann-Whitney U test was used to compare results between groups. Research ethics committee approval was obtained for this survey.

Fifty patients (two male), including 40 with primary SS, were included in the survey. Mean age (range) was 57 (33–82) years and disease duration 5 (0–14) years. Forty three patients had symptomatic dry eyes, 36 had dry mouth, and 31 patients used tear substitutes three or more times each day. All complained of a dry mouth, 42 had difficulty swallowing dry food, and 23 patients had recurrent or persistent salivary gland swelling. Thirty two patients had positive anti-Ro antibodies and 39 patients had undergone a diagnostic labial salivary gland biopsy. On a 10 cm VAS, the mean rating of disease severity was 6.2 cm (range 0.0–9.8).

Non-proprietary hyaluronan eye drops and Viscoatears were the most widely known and used tear substitute treatments (table 1). Four patients had never heard of any of the tear substitutes listed, despite two having symptomatic dry eyes; six had never used any and 11 were not currently using any. Oralbalance, Glansosane spray, Salivara Orana spray and lozenges, and Salivix pastilles were the most widely known and used saliva substitute treatments. Eight patients had never heard of any of the saliva substitutes listed, despite all having a symptomatic dry mouth; nine had never used any and 22 were not currently using any. Patients’ rated the effectiveness of any replacement product they had used (fig 1). The median (range) VAS score for all tear products was 5.35 (0.25–9.8), which was significantly higher than for saliva products where the median (range) was 3.15 (0.2–9.5) (p<0.002)). There was no significant difference between the effectiveness ratings of any of the tear or saliva products, except that Salivix pastilles were rated significantly higher than Glansosane spray (p<0.05). Seventeen patients viewed their general practitioner as a good source of information about substitute treatments, 34 highlighted the importance of doctors and patients having a symptomatic dry mouth; nine had never used any and 22 were not currently using any. Oralbalance and Salivary Orna spray were the most widely known and used saliva substitutes, though the internet may help to remedy this for doctors and patients (http://www.dry.org/ ss95gui.html). This study has also shown the gulf remaining between the many available tear and saliva replacement products and their use by patients.

We thank Dr L Rankin, Dr P Jobanputra, and Dr R Jubb for allowing us to survey their patients at Selly Oak Hospital, Birmingham.

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Y chromosome microchimerism in Sjögren’s syndrome

There are many similarities between graft versus host disease (GVHD) and some autoimmune diseases, such as systemic sclerosis (SSc), Sjögren’s syndrome (SS), and primary biliary cirrhosis. Bianchi et al reported that fetal cells could survive in the maternal circulation for up to 27 years after pregnancy.9 We have recently searched for male microchimerism in minor salivary glands tissue from six women with SS and at least one male pregnancy or miscarriage (table 1, patients 1–6). A diagnosis of SS was made according to EEC criteria.9 As control we used DNA from minor salivary biopsy samples of three women with SS and with only a female pregnancy (patients 7–9), and two healthy women, one with a male pregnancy and one with a female pregnancy (patients 11, 12). Table 1 gives details of the patients.

We assayed by PCR for a specific Y chromosome sequence, SRY, and for the homologous gene of amelogenin.1 We tested our primers by diluting male peripheral blood DNA with female blood DNA. The sensitivity of our methodology was 10 pg for SRY primers and 100 pg for amelogenin. Given the sensitivity of the method, a cautionary note has to be made about laboratory personnel. When a male operator performed the DNA extraction and PCR a random positive case was obtained.

We have not found any male DNA either in the tissue from women with SS and a male pregnancy or in the controls. As far as we know this is the first study of fetal microchimerism in minor salivary gland tissue from a patient with SS.

Although this preliminary study does not seem to support the hypothesis that microchimerism has a role in the pathogenesis of Sjögren’s syndrome, we cannot exclude the possibility that the time lag between the last pregnancy and sampling might have influenced the result. On the other hand, Evans and colleagues found male microchimerism in women with scleroderma even up to 38 years after pregnancy.2

In conclusion, a larger number of patients, with a more recent pregnancy, should be evaluated in order to confirm or refute the role of fetal microchimerism in women with primary SS.

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Figure 1 Patients’ ratings of the effectiveness of (A) tear and (B) saliva replacement treatments for ocular or oral dryness. Patients were asked to rate any product, which they had ever used, on a 10 cm visual analogue scale (VAS), for each product. Results are shown as mean (SD) VAS scores. The p value refers to a comparison of results for Glandosane spray and Salivix pastilles (Mann-Whitney U test).

Mean (SD) of VAS scores (0–10)

<table>
<thead>
<tr>
<th>Product</th>
<th>Mean (SD)</th>
<th>VAS Scores</th>
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<tbody>
<tr>
<td>Glandosane spray</td>
<td>5.0 (2.5)</td>
<td>5.0</td>
</tr>
<tr>
<td>Salivix pastilles</td>
<td>7.5 (5.0)</td>
<td>7.5</td>
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<tr>
<td>Hypromellose eye drops</td>
<td>2.5 (0.0)</td>
<td>2.5</td>
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<td>Lacto-Lube</td>
<td>5.0 (2.5)</td>
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<td>Sterile tears</td>
<td>7.5 (5.0)</td>
<td>7.5</td>
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<tr>
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<td>5.0 (2.5)</td>
<td>5.0</td>
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<tr>
<td>Tears Naturale</td>
<td>5.0 (2.5)</td>
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<tr>
<td>Rubik</td>
<td>7.5 (5.0)</td>
<td>7.5</td>
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<tr>
<td>Gel tears</td>
<td>5.0 (2.5)</td>
<td>5.0</td>
</tr>
<tr>
<td>Oralbalance</td>
<td>7.5 (5.0)</td>
<td>7.5</td>
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<tr>
<td>Viscotears</td>
<td>5.0 (2.5)</td>
<td>5.0</td>
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<tr>
<td>Lacri-Lube</td>
<td>7.5 (5.0)</td>
<td>7.5</td>
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<tr>
<td>Sno tears</td>
<td>5.0 (2.5)</td>
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| Artificial saliva products

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Pitting oedema in early diffuse systemic scleroderma

The term “puffy skin” is not infrequently noted at initial presentation of patients with systemic scleroderma. However, this is generally described as “non-pitting” oedema. The following case history challenges the latter widely held assumption, showing that its measurement is simple and may offer a more sensitive method of assessing response to treatment than the modified Rodnan skin score.1

CASE REPORT

A premenopausal computer analyst first presented in May 1999 with a two month history of finger stiffness. The next 10 months were spent investigating and treating the cause of her iron deficiency anaemia—gastric ectasia (watermelon stomach). The diagnosis of diffuse systemic scleroderma was made in March 1999. At this time she presented with persisting symptoms of skin stiffness, burning and pruritis, especially in the early morning, affecting the skin of her arms and legs, face, and upper chest. Clinical examination showed finger clawing, sclerodactyly, and scleroderma affecting its arms to the mid-upper arm, the face, neck, upper chest, thighs, and calves. Pitting oedema, noted in the forearms, upper arms, chest, and thighs, had the following characteristics: it occurred in areas of affected skin—typically it occurred in the advancing front of skin involvement, was slow to induce (of bees’ wax consistency), and it affected non-dependent areas. Her skin was also erythematous in parts. Livedoid patterning over the knees was also noted. The rest of the clinical examination, including musculoskeletal cardiac, and respiratory systems, was unremarkable. A skin biopsy specimen from the upper right forearm and dorsum of the left fifth proximal interphalangeal joint had the following characteristics: it occurred non-dependent areas.

Figure 1 outlines her treatment with pulse methylprednisolone and cyclophosphamide.

was added because of continuing disease activity. Before her first course of intravenous cyclophosphamide bilateral basal crepitations were noted. By 30 June 1999 skin hyperpigmentation and the development of mild dysphagia was noted. Concurrently, she also noted increased hair regrowth on the dorsum of her hands and lateral aspect of the calves. After her final course of cyclophosphamide her hands were no longer clawed into fixed flexion, the skin on the dorsum of the hands was again so supple that the dorsal hand veins were both visible, palpable and protruding from the skin surface; the fore arm skin biopsy site was no longer keloid, though that on her finger was still slightly raised and palpable; her skin was much less irritable or pruritic.

The most marked areas of skin improvement were those which were still oedematous at the start of treatment and where the skin was affected for the least time—upper arms, forearms, hand, thighs, and anterior chest. The area of skin least responsive to treatment was over the distal phalanges, which remained tethered and immobile.

DISCUSSION

This case is presented to demonstrate a diagnostic confusion in a patient known to have Behçet’s disease.

CASE REPORT

A 34 year old white woman presented with a small joint polyarthritis, low back discomfort, severe heel pain, and patchy sensory disturbance, after a febrile illness with a rash. She had had Behçet’s disease since the age of 3 years, manifest by arthralgia, mouth, nasal and genit al ulcers, conjunctivitis, facial swelling, and livedo reticularis. Before her presentation, her Behçet’s disease had been relatively well controlled by 100 mg of azathioprine a day, the only residual symptoms being pain and morning stiffness of 45 minutes affecting her fingers, wrists, elbows, and shoulders, and livedo reticularis.

On presentation she was afebrile, with cervical lymphadenopathy. The liver and spleen were palpable. She had mild metacarpophalangeal and wrist synovitis, bilateral knee effusions, and was exquisitely tender over the plantar fascia. Her sacroiliac joints were tender. There was subjective symmetrical sensory loss to pin prick and light touch on the dorsum of the feet and the lateral aspect of the hands. Neurological examination was otherwise unremarkable. An x ray examination of the hands, calcaneum, and sacroiliac joints was normal, as was the full blood count, and C reactive protein. Rheumatoid factor, antinuclear antibodies, antineutrophil cytoplasmic antibodies, and anticyclic citrulline antibodies were not detected.

She was treated initially with ibuprofen and acetylsalicylate (12.5 mg hydrocortisone acetate) brought about rapid improvement. The diagnosis in our case was complicated by parvovirus B19 infection [letter].

Parvovirus B19 is common, with 50–75% of UK adults having evidence of previous infection. Complications, such as arthritis, occur in a small minority. We report a case of parvovirus associated arthritis causing diagnostic confusion in a patient known to have Behçet’s disease.

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Parvovirus arthropathy masquerading as the arthritism of Behçet’s disease

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DISCUSSION

Sacroilitis is an unusual feature of Behçet’s disease, and plantar fasciitis has not been previously described in this disorder. Parvovirus arthritis is an uncommon sequela of a common viral exanthem. The usual presentation is that of an acute onset polyarthritis, resembling rheumatoid disease, which may follow a flu-like illness and rash. Transient neurological disease may occur. Parvovirus associated relapse of spondylitis after a symptom-free period of 15 years has been described.

The diagnosis in our case was complicated by superficial similarities to the arthritis of Behçet’s disease. The possibility of neurological involvement was a new, and worrying, feature. However, there were no active features of active Behçet’s disease, such as mouth or genital ulcers, which had been associated with previous exacerbations. The unusual features of seronegative arthritis and prior febrile illness raised the possibility of a coincidental reactive arthritis. Despite the presence of some atypical features, we consider parvovirus B19 to be the most likely cause of this patient’s illness, on both clinical and serological grounds.

This case illustrates the importance of considering the diagnosis of coincidental parvovirus in patients with pre-existing rheumatic diseases where there are unusual features. Because parvovirus associated arthritis is usually self limiting, this diagnosis may allow a more conservative approach to treatment.

We thank Professor AJ Pinching for allowing us to report on his patient.

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