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EXTENDED REPORT

Sialendoscopy enhances salivary gland function in Sjögren's syndrome: a 6-month follow-up, randomised and controlled, single blind study

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ABSTRACT

Objectives To assess the effect of sialendoscopy of the major salivary glands on salivary flow and xerostomia in patients with Sjögren's syndrome (SS).

Methods Forty-nine patients with SS were randomly assigned to a control group (n=15) and two intervention groups: irrigation of the major glands with saline (n=16) or with saline followed by triamcinolone acetonide (TA) in saline (n=18). Unstimulated whole saliva flow (UWS), chewing-stimulated whole saliva flow (SWS), citric acid-stimulated parotid flow (SPF), Clinical Oral Dryness Score (CODS), Xerostomia Inventory (XI) score and the European League Against Rheumatism (EULAR) SS Patient-Reported Index (ESSPRI) were obtained 1 week (T0) before, and 1 (T1), 8 (T8), 16 (T16) and 24 (T24) weeks after sialendoscopy.

Results Median baseline UWS, SWS and SPF scores were 0.14, 0.46 and 0.22 mL/min, respectively. After intervention, significant increases in UWS and SWS were observed in the saline group (at T8 (P=0.013) and T24 (P=0.004)) and the saline/TA group (at T24 (P=0.03) and T=16 (P=0.035)). SPF was increased significantly in the saline/TA group at T24 (P=0.03). XI scores declined after sialendoscopy in both intervention groups. Compared with the control group, CODS, XI and ESSPRI improved in the intervention groups. UWS, SWS and SPF were higher in the intervention groups compared with the control group, but these differences were not significant except for SPF in the saline/TA group at T24 (P=0.005).

Conclusions Irrigation of the major salivary glands in patients with SS enhances salivary flow and reduces xerostomia up to 6 months after sialendoscopy.

INTRODUCTION

Sjögren's syndrome (SS) is an autoimmune disorder causing chronic inflammation and irreversible damage of the exocrine glands. SS is characterised by mononuclear infiltrates and IgG plasma cells in salivary and lacrimal glands which lead to irreversible destruction of glandular tissue.[1] SS affects 0.01%–4% of the population, with a female-to-male ratio of 9:1.[2–5] SS causes a gradual reduction in the quantity and quality of saliva.[6] Because of hyposalivation, patients with SS suffer from a sensation of oral dryness (xerostomia) and its related complaints (eating and swallowing problems, lack of taste, speech problems), and are prone to develop progressive dental decay and inflammation of the oral mucosa.[7]

No effective treatment is available for SS or its related hyposalivation. Systemic treatment is often ineffective and can result in major side effects.[8] However, some biologic disease-modifying antirheumatic drugs have shown promise for improved efficacy with mostly mild adverse events.[9] Biologicals will probably not be effective for all patients with SS, but only in subgroups of patients with SS.[10]

No effective therapy is currently available that reduces complications associated with SS.[11]

In a recent case series and in two pilot studies, sialendoscopy of the major salivary glands appeared to alleviate symptoms of SS and improve salivary function.[12–14] Sialendoscopy is used for diagnostic purposes as well as to treat chronic obstructive salivary disorders caused by strictures, mucus plugs and sialoliths (figure 1).[15–19] Irrigation of the ductal system, either with saline or a solution of saline and corticosteroids, was suggested to alleviate complaints in patients affected by salivary gland inflammatory diseases and xerostomia.[12–14 20]

The aim of this study was to assess the effect of sialendoscopy with saline or saline followed by saline/corticosteroids on salivary gland function, oral dryness and symptoms in patients with SS. Comparisons were made between these treatments, baseline levels and non-treatment controls.

METHODS

Study population

Patients with SS between 18 and 75 years of age with a baseline unstimulated whole saliva flow (UWS) >0.0 mL/min or evidence of glandular reserve function (stimulated baseline whole saliva flow (SWS) ≥0.02 mL/min) were included. All patients fulfilled the 2002 American–European Consensus Group classification criteria.[21]

Patients with acute sialadenitis, severe illness, physical conditions interfering with a treatment under general anaesthesia or a history of head and neck radiotherapy were excluded. Use of sialogogues was not allowed during the study. Written consent was obtained from each patient.

Study design

Participants were randomly assigned to a non-intervention control group (n=15) or two sialendoscopy (intervention) groups: irrigation of the ductal system with saline (n=16) or with saline followed by triamcinolone acetonide 40 mg/mL (TA; Kenacort-A 40; Bristol-Myers Squibb, New

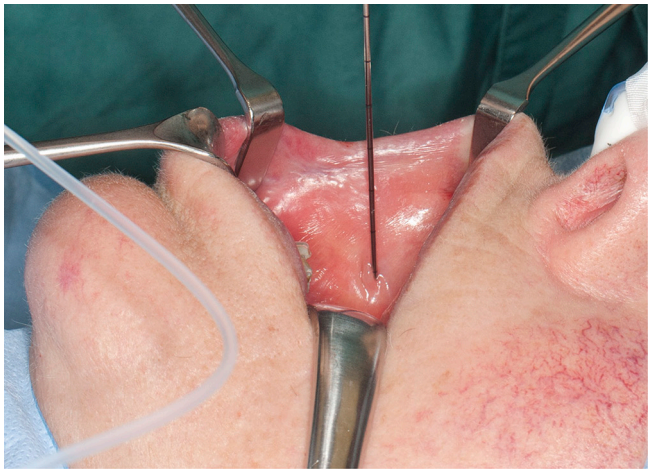

Figure 1 During the procedure, a sialendoscope is introduced into the orifice of the parotid duct after dilation of the papilla.

York, USA) in 5 mL saline at the end of the procedure (n=18). Controls were not blinded on their allocation to the non-intervention group. Such a design would have required sham sialendoscopy in controls, which was not permitted by the Research Ethics Board.

In all groups, UWS, SWS and stimulated parotid flow (SPF) were collected and measured at five research appointments: 1 week before intervention (T0), and 1 (T1), 8 (T8), 16 (T16) and 24 (T24) weeks after intervention. The Clinical Oral Dryness Scale (CODS),[22] Xerostomia Inventory (XI) score[23] and the European League Against Rheumatism (EULAR) SS Patient-Reported Index (ESSPRI)[24] were scored at every appointment. The study protocol is registered at the US National Institutes of Health (ClinicalTrials.gov; number: NCT02112019). The design and reporting of this study agrees with the Consolidated Standards of Reporting Trials statement.[25]

Randomisation

Participants were randomly assigned (blocked randomisation), using randomising software (www.randomizer.org), to either the non-intervention control group or an intervention group.

Outcome measures

Sialometry

Patients were instructed to refrain from eating/chewing, drinking, brushing teeth and smoking for 90 min prior to each visit. To minimise diurnal variation, all appointments were planned on the same time of the day and in the same room (temperature 21°C±2°C, humidity 50%–60%). To collect UWS, patients were instructed to start collecting saliva immediately after an initial swallow, and subsequently expectorate into a preweighed container every 30 s for a 5 min period. To collect SWS, patients were asked to chew a 5×5 cm sheet of paraffin (Parafilm M, Pechiney, Chicago, USA) and expectorate into a preweighed container every 30 s during a 5 min period. Reweighing each container after collection and subtracting the weight of the empty container determined UWS and SWS flow rates. Values are expressed as millilitres per minute.[26] Parotid-stimulated saliva was collected in plastic tubes from each parotid gland using modified Lashley cups. Stimulation was with citric acid (2% w/v) applied with a cotton wool swab to the lateral border of the tongue at 30 s intervals.[27] All assessments were performed by the same observer (FM), blinded for the therapeutic interventions (saline vs saline/TA) and condition of the patients.

Clinical Oral Dryness Score

The CODS is a validated clinical guide designed to assess oral dryness by clinical and visual inspection of the oral cavity based on several signs of oral dryness such as presence of frothy saliva and stickiness of the dental mirror to the tongue or buccal fold.[22 28] The scores for each of the 10 features were added together, resulting in score from 0 (no oral dryness) to 10 (extreme oral dryness).

Xerostomia Inventory

The summated XI is a validated questionnaire containing 11 questions about mouth feel and oral dryness, using a five-point Likert scale to indicate the frequency of symptoms. Scores from the 11 questions are added together, resulting in a total XI score varying from 11 (no dry mouth) to 55 (extremely dry mouth).[23]

EULAR SS Patient-Reported Index

ESSPRI is a patient-administered questionnaire to assess disease symptoms on a 10-point scale for pain, fatigue and dryness. ESSPRI is sensitive for measuring changes in disease symptoms after therapeutic intervention. Only the dryness domain was used in the analysis. A change of two or more points was considered clinically relevant.[24]

Intervention

Sialendoscopy was performed by one experienced surgeon (KHK). Sialendoscopy consisted of irrigation of the ductal system of both parotid and submandibular glands with saline or with saline followed by 40 mg/mL TA in 5 mL saline at the end of the procedure. Saline/TA was injected intraductally under direct vision and maintained in the glands by temporarily occluding the ductal orifices with a microvascular clamp until the end of general anaesthesia (±10 min). Strictures were dilated using hydrostatic pressure. Sialoendoscopy was performed using 0.8 or 1.1 mm diameter Erlangen sialendoscopes (Karl Storz GmbH & Co, Tuttlingen, Germany). Sialendoscopy was performed under general anaesthesia in order to standardise treatment among patients and to avoid patient discomfort because of the operation time (45 min).

Sample size and statistical analysis

A sample size of 14 patients per group was calculated, based on a previously performed pilot study, using PS power software.[13 29] Differences between time points within the three groups were examined using Wilcoxon signed-rank tests (data without normal distribution) or analysis of variance for repeated measurements (normally distributed data). Assumption of sphericity was tested with Mauchly's test. Differences between groups were assessed using the Mann-Whitney U test (data without normal distribution) or independent t-test (normally distributed data). The assumption of homogeneity of variances was tested via Levene's F-test. If the assumption of homogeneity of variances was rejected, the Welch-Satterthwaite method was used to adjust the degrees of freedom. Data were analysed with SPSS V.22.0 (IBM, Armonk, USA). A P value of 0.05 or lower was considered statistically significant.

RESULTS

Between July 2014 and November 2016, 51 patients were included. The last patient ended the follow-up period in May

Table 1 Characteristics of the study population and baseline values for all parameters

	Mean±SD or n (%)	Median (IQR)
Patient variables		
Age (years)	59 (10.37)	59.7 (54–67.1)
Female gender, n (%)	43 (87.8%)	
Disease duration (years)*	10±8.9	7 (3–13)
Control group	10.4±8.7	7.5 (3–18.8)
Saline group	8.1±9.7	6.5 (3–7.5)
Saline/TA group	11.1±8.8	11 (2.5–16.5)
Primary SS, n (%)†	34 (68%)	
Control group	9 (60%)	
Saline group	13 (81.25%)	
Saline/TA group	12 (66.7%)	
Secondary SS, n (%)†	15 (30%)	
Control group	6 (40%)	
Saline group	3 (18.75%)	
Saline/TA group	6 (33.3%)	
Autoantibodies to anti-SSA or anti-SSB§	43 (87.8%)	
Positive salivary gland biopsy	39 (79.6%)	
Objective ocular involvement (Schirmer test)	47 (96%)	
Baseline UWS (mL/min)	0.14±0.15	0.1 (0.0–0.19)
Control group	0.13±0.11	0.09 (0.03–0.18)
Saline group	0.17±0.21	0.1 (0.04–0.19)
Saline/TA group	0.13±0.11	0.1 (0.06 – 0.17)
Baseline SWS (mL/min)	0.46±0.44	0.3 (0.13–0.7)
Control group	0.49±0.46	0.25 (0.15–0.73)
Saline group	0.43±0.21	0.25 (0.07–0.7)
Saline/TA group	0.46±0.40	0.37 (0.13–0.62)
Baseline SPF (mL/min)	0.22±0.26	0.17 (0.05–0.37)
Control group	0.20±0.21	0.17 (0.00–0.47)
Saline group	0.18±0.24	0.11 (0.00–0.21)
Saline/TA group	0.28±0.30	0.18 (0.03–0.47)
XI	44.6±6.3	46 (41–50)
ESSPRI (all domains)‡	6.7±1.64	
ESSPRI (dryness domain)	7.6±1.52	
Clinical Oral Dryness Score	2.74±1.15	2 (2–3.5)
Gland variables		
Total number of glands accessible and rinsed	100 (73.5%)	
Glands accessible and rinsed—saline group	48 (75%)	
Parotid glands	30 (93.8%)	
Submandibular glands	18 (56.3%)	
Glands accessible and rinsed—saline/TA group	52 (72.2%)	
Parotid glands	34 (94.4%)	
Submandibular glands	14 (38.9%)	

Both mean (±SD) and median (IQR) are presented for non-normally distributed data. The number of glands successfully rinsed during sialendoscopy is presented.
*Disease duration is defined as years since diagnosis.
†Classified according to the 2002 American–European Consensus Group Criteria. All patients classified as secondary SS suffered from rheumatoid arthritis.§anti-SSA, anti-SSB.
‡Defined as the total ESSPRI score divided by 3.
anti-SSA, anti Sjögren's Syndrome related antigen A; anti-SSB, anti Sjögren's Syndrome related antigen B; ESSPRI, EULAR Sjögren's Syndrome Patient-Reported Index; SPF, stimulated parotid flow; SS, Sjögren's syndrome; SWS, stimulated whole saliva flow; TA, triamcinolone acetonide; UWS, unstimulated whole saliva flow; XI, Xerostomia Inventory.

2017. Characteristics of the study population are given in table 1 and allocation to the various groups is shown in figure 2.

The overall rate of complications was limited, and the complications were minor. A complicating factor was that it was not possible to identify or dilate the papilla to introduce the sialendoscope in all salivary glands. Analysis of the data for normality revealed that ESSPRI was normally distributed, and UWS, SWS, SPF, CODS and XI were not (Shapiro-Wilk; $P<0.001$). During sialendoscopy, strictures were present and removed for all treated salivary glands. Baseline comparison of the groups revealed no significant difference in outcome measures. Median UWS, SWS, SPF, CODS, XI and mean ESSPRI (dryness domain) scores are presented in tables 2 and 3 and figure 3. The percentage of patients in whom any improvement in salivation was observed after 24 weeks was 87.5% for UWS and 75% for SWS in the saline group and 72.2% for UWS and 61.1% for SWS in the saline/TA group. The percentage of patients who regained an adequate salivary flow (defined as UWS >0.1 mL/min and SWS >0.5 mL/min) after 24 weeks was 68.8% for UWS and 37.5% for SWS in the saline group and 66.7% for UWS and 55.6% for SWS in the saline/TA group. In the control group, measures did not change significantly in comparison to baseline.

Within group analysis: saline group

In the saline group, UWS increased after intervention and significant differences were found at T8 (median (Mdn)=0.14 mL/min; $Z=-2.49$, $P=0.013$, $r=-0.62$) and T16 (Mdn=0.13 mL/min; $Z=-2.35$, $P=0.019$, $r=-0.59$) compared with T0 (Mdn=0.1 mL/min).

SWS increased after intervention and significant differences were found at T24 (Mdn=0.30 mL/min; $Z=-2.90$, $P=0.004$, $r=-0.73$) compared with T0 (Mdn = 0.25 mL/min). A comparable effect was found for CODS. CODS decreased after intervention and a statistically significant difference was found at T1 (Mdn=1.5; $Z=-2.40$, $P=0.016$, $r=-0.6$) compared with T0 (Mdn=3).

XI scores in the saline group were lower after intervention at all time points compared with baseline. XI was significantly lower at T16 (Mdn=42; $Z=-2.22$, $P=0.027$, $r=-0.56$) and T24 (Mdn=38; $Z=-2.36$, $P=0.018$, $r=-0.59$) compared with T0 (Mdn=45), suggesting that sialendoscopy resulted in a reduced dry mouth feeling 16 and 24 weeks after intervention. Although numerically lower after intervention, no significant change in ESSPRI score was found in the saline group.

Within groups analysis: saline/TA group

In the saline/TA group, UWS increased after intervention and a significant difference was found at T24 (Mdn=0.12 mL/min; $Z=-2.18$, $P=0.03$, $r=-0.51$) compared with T0 (Mdn=0.1 mL/min). Furthermore, significant differences for UWS were found between T24 and T1 ($P=0.03$) and T8 ($P=0.007$).

SWS increased after intervention and a significant difference was found at T=16 (Mdn=0.64 mL/min; $Z=-2.11$, $P=0.035$, $r=-0.50$) compared with T0 (Mdn=0.37 mL/min). In this group, SPF increased over time and a significant difference was found between T0 (Mdn=0.18 mL/min) and T24 (Mdn=0.34 mL/min; $Z=-2.16$, $P=0.03$, $r=-0.51$).

A comparable effect was found for the CODS. CODS decreased after intervention and a statistically significant difference was found between T0 (Mdn=2) and T1 (Mdn=1.5; $Z=-3.09$, $P=0.002$, $r=-0.73$). All subsequent time points were significantly different compared with T0 indicating a more moist oral mucosa.

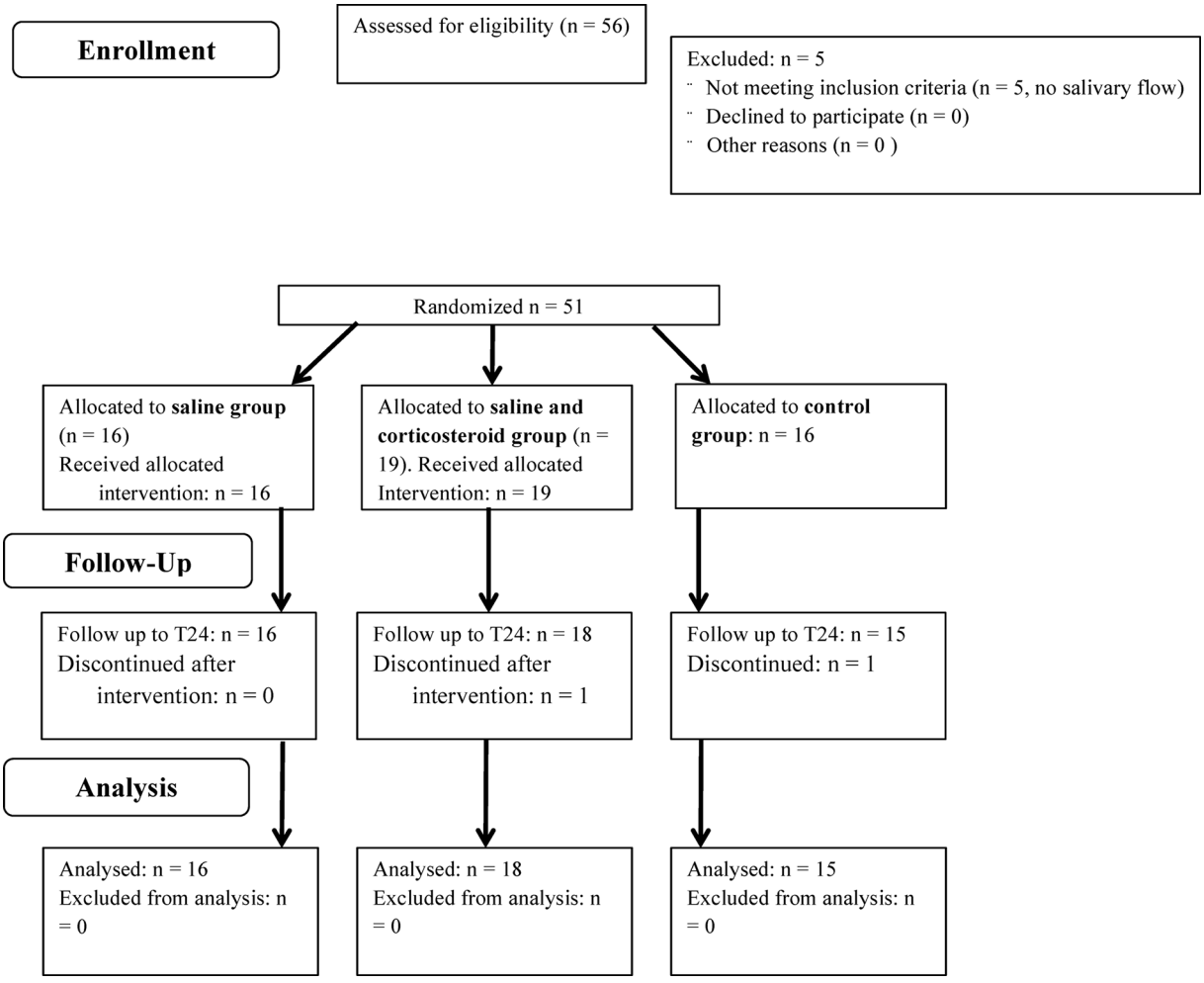

Figure 2 Flow diagram showing the allocation of participants to the various treatment groups. T24, 24 weeks after intervention.

XI scores in the saline/TA group were lower after intervention at all time points compared with baseline. XI was significantly lower at T8 (Mdn=44; Z=−2.17, P=0.03, r=−0.51) and T16 (Mdn=42.5; Z=−2.31, P=0.021, r=−0.54) compared with T0 (Mdn=45.5), suggesting that sialendoscopy resulted in a reduced dry mouth feeling 8 and 16 weeks after intervention. ESSPRI was significantly lower between T0 and T8 (P<0.001; 95% CI 0.87 to 2.51), T16 (P=0.006; 95% CI 0.51 to 2.55) and T24 (P=0.017; 95% CI 0.28 to 2.55). There was no violation of the assumption of sphericity: $\chi^2(9)=10.66$, P=0.30.

Between group analysis: saline group versus control group

When comparing the saline group with the control group, no significant difference was found for UWS, SWS and SPF at any time point. A significant difference was found for CODS at T1 between the control group (Mdn=2) and the saline intervention group (Mdn=1.5; U=69, P=0.038, r=−0.49). XI scores in the saline group were significantly lower at T1 (Mdn=42; U=62, P=0.02, r=−0.54), T16 (Mdn=42; U=57, P=0.013, r=−0.59) and T24 (Mdn=38; U=45.5, P=0.003, r=−0.70) compared with the corresponding time points in the control group (table 2) indicating a reduction in xerostomia up to 6 months, after sialendoscopy with saline. Reduction of xerostomia was also found in the dryness domain of ESSPRI. ESSPRI scores were significantly (P<0.05) lower in the saline group compared with the control group at all time points after intervention. Levene's F-test showed that there was a significant difference in the variances between the groups at T24. Therefore, the Welch-Satterthwaite method was used to adjust the degrees of freedom. This had no effect on the results for T24.

Between group analysis: saline/TA group versus control group

When comparing the saline/TA group with the control group at the different time points, no significant difference was found for salivary flow at any time point except for SPF at T24, which was significantly higher in the saline/TA group (U=58, P=0.005, r=−0.40). CODS was significantly (P<0.05) lower in the saline/TA intervention group compared with the control group at all time points (table 1) indicating a more moist oral cavity.

XI scores in the saline/TA group were lower at all time points after intervention compared with the control group (table 1). But these differences were not significant.

For the ESSPRI, significant score differences were found between the saline/TA and control group at T8 (t(31)=3.49, P=0.01; 95% CI 0.83 to 3.13), T16 (t(31)=3.77, P=0.01; 95% CI 0.99 to 3.30) and T24 (t(31)=2.16, P=0.03; 95% CI 0.87 to 3.05). Levene's F-test showed that there was a significant difference in the variances between the groups at T24. Therefore, the Welch-Satterthwaite method was used to adjust the degrees of freedom. This had no effect on the results for T24.

Table 2 Median and IQR for UWS, SWS, SPF, CODS and XI scores for all groups and time points

	Control group		Saline group		Saline/TA group	
	Median	IQR	Median	IQR	Median	IQR
UWS (mL/min)						
T0	0.09	0.03–0.18	0.10 (*, †)	0.04–0.19	0.10 (‡)	0.06–0.17
T1	0.08	0.04–0.21	0.10	0.03–0.50	0.11 (§)	0.05–0.22
T8	0.07	0.04–0.27	0.14 (*)	0.07–0.48	0.09 (¶)	0.06–0.22
T16	0.10	0.02–0.28	0.13 (†)	0.04–0.45	0.11	0.05–0.27
T24	0.12	0.03–0.22	0.16	0.07–0.38	0.12 (‡, §, ¶)	0.08–0.27
SWS (mL/min)						
T0	0.25	0.15–0.73	0.25 (*)	0.07–0.70	0.37 (‡)	0.13–0.62
T1	0.18	0.11–0.74	0.35	0.08–0.72	0.36 (§, ¶, †)	0.20–0.60
T8	0.22	0.16–0.71	0.33	0.08–0.67	0.45 (§, **, ††)	0.18–0.77
T16	0.24	0.10–0.56	0.33	0.09–0.68	0.64 (‡, ¶, **)	0.17–0.90
T24	0.25	0.11–0.67	0.30 (*)	0.09–0.81	0.61 (†, ††)	0.19–0.80
SPF (mL/min)						
T0	0.17	0.00–0.47	0.11	0.00–0.22	0.18 (*)	0.03–0.47
T1	0.05	0.00–0.65	0.03	0.00–0.21	0.11 (†)	0.03–0.35
T8	0.13	0.00–0.41	0.08	0.01–0.30	0.16	0.06–0.41
T16	0.06	0.00–0.66	0.09	0.00–0.33	0.22	0.05–0.42
T24	0.06 (¶)	0.00–0.26	0.02 (§)	0.00–0.50	0.34 (*, †, ¶, §)	0.19–0.73
CODS (1–10)						
T0	3	2–4	3 (*)	2–4	2 (‡, ††, §§, §)	2–3
T1	3 (¶)	2–3	1.5 (*, ¶)	0–3	1.5 (‡)	1–2
T8	2	2–4	1.5	1–3.75	2 (††, ‡‡)	0.75–3
T16	2	1–4	2	1–3	1 (§§)	0–2
T24	2	2–3	1.5	1–3	1 (§, ‡‡)	0–2
XI (11–55)						
T0	48	41–51	45 (*, †)	41.25–48.75	45.5 (‡, §)	38.5–50
T1	48	41–51	42	34.50–46	44.5	39–50.25
T8	47	40–50	41	34–46	44 (‡)	37.50–47.25
T16	46	42–52	42 (*)	32.25–45.75	42.5 (§)	31.50–48.50
T24	47	42–51	38 (†)	33–44	43.5	36.25–49.25

Data sharing the same symbols (*, †, ‡, §, ¶, **, ††, ‡‡, §§) differ significantly.
CODS, Clinical Oral Dryness Score; SPF, stimulated parotid flow; SWS, stimulated whole saliva flow; TA, triamcinolone acetonide; T0, 1 week before intervention; T1, 1 week after intervention; T8, 8 weeks after intervention; T16, 16 weeks after intervention; T24, 24 weeks after intervention; UWS, unstimulated whole saliva flow; XI, Xerostomia Inventory.

Between group analysis: saline group versus saline/TA group

No significant difference was found between these groups except for SPF at T24 (Mdn=0.34 mL/min, U=78, P=0.02, r=−0.40), which was significantly higher in the saline/TA group compared with SPF at T24 (Mdn=0.02 mL/min) in the saline group.

DISCUSSION

The results of our study indicate that sialendoscopy reduces oral dryness objectively and subjectively. Previous studies found that stricture formation is the major cause of obstruction of the salivary ducts and recurrent sialadenitis in patients with SS and other autoimmune diseases.[12 17] It has been suggested that removal of these strictures could improve salivary flow.[12 30] In this study, strictures were present and removed in all treated salivary glands.

We presume that improvement of salivary flow is only possible if saliva-producing acinar cells are present and functioning in the glandular tissue or when the parenchyma recovers. Therefore,

Table 3 Mean ESSPRI score (dryness domain) for all groups and time points

	Control group		95% CI		Saline group		95% CI		Saline/TA group		95% CI	
	Mean	SD	Lower limit	Upper limit	Mean	SD	Lower limit	Upper limit	Mean	SD	Lower limit	Upper limit
T0	8.00 (*)	1.13	7.37	8.63	6.88 (*)	1.66	5.99	7.76	7.92 (§§,¶¶,***)	1.52	7.16	8.67
T1	7.87 (†)	1.60	7.01	8.73	6.34 (†)	1.90	5.33	7.40	7.50 (†††,‡ ‡‡)	2.12	6.45	8.55
T8	8.20 (‡, §)	1.15	7.57	8.84	5.75 (‡)	1.98	4.69	6.81	6.22 (§§,†††,§)	1.92	5.26	7.18
T16	8.53 (¶,**)	1.19	7.88	9.19	6.22 (¶)	2.10	5.11	7.33	6.40 (¶¶,‡‡‡,**)	1.91	5.44	7.34
T24	8.01 (††,‡‡)	1.49	7.24	9.00	6.28 (††)	1.83	5.31	7.25	6.50 (***,‡‡)	2.26	5.28	7.72

Data sharing the same symbols (*, †, ‡, §, ¶, **, ††, ‡‡, §§, ¶¶, ***, †††, ‡‡‡) differ significantly (P<0.05).
ESSPRI, EULAR Sjögren's Syndrome Patient-Reported Index; TA, triamcinolone acetonide; T0, 1 week before intervention; T1, 1 week after intervention; T8, 8 weeks after intervention; T16, 16 weeks after intervention; T24, 24 weeks after intervention.

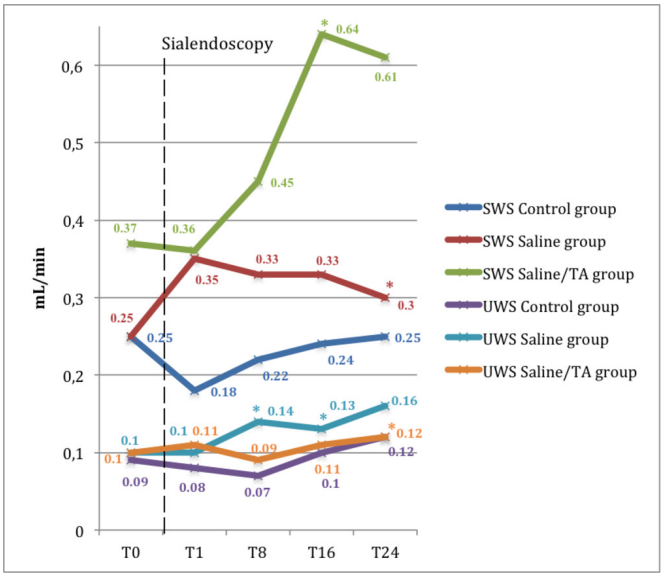

Figure 3 Change in median UWS and SWS before and after sialendoscopic rinsing. *P<0.05 compared with baseline (T0). SWS, stimulated whole saliva flow; TA, triamcinolone acetonide; T0, 1 week before intervention; T1, 1 week after intervention; T8, 8 weeks after intervention; T16, 16 weeks after intervention; T24, 24 weeks after intervention; UWS, unstimulated whole saliva flow.

the stage of the disease, the baseline level of stimulated salivary flow and the response of the glands to a stimulus are expected to have significant impact on the success of this treatment. It is possible that patients with recent onset of SS and more residual salivary gland capacity would benefit more from a sialendoscopic procedure than patients with long-standing disease. Ultrasound of the glands was not performed preoperatively, but might be useful to determine the stage of the disease in glands, thereby helping to identify which glands warrant sialendoscopy. In this study, the disease duration in the saline group was shorter than in the saline/TA group (8.1 and 11.1, respectively, table 1). As this difference was not significant, it could not fully explain differences between these groups in salivary flow after sialendoscopy.

Irrigation of the ductal system of the major salivary glands with saline/TA was not significantly more effective on SWS levels than irrigation with saline alone. It was expected that irrigation with saline/TA would have a larger effect than irrigating with only saline. Corticosteroids have anti-inflammatory effects, and inhibit T-cell activation. Salivary glands affected by SS are characterised by a focal periductal infiltrate consisting mainly of T lymphocytes and B lymphocytes.[31] Since the salivary gland duct directly connects to the gland, it could represent an effective route to deliver medications to the gland. However, it is questionable whether there is a large TA uptake by the tissues surrounding the duct during the relative short irrigating process. Another explanation for the larger effect of irrigating with saline/TA could be that in the saline/TA group the median baseline SWS level was higher compared with that in the saline group. Although this difference was not significant, it could be an explanation for the larger increase in SWS flow levels after sialendoscopy in the saline/TA group compared with the saline group suggesting a larger effect of sialendoscopy in patients with higher baseline salivary flow levels.

A complicating factor in this study was that it was not possible to identify or dilate the papilla to introduce the sialendoscope in all salivary glands. Along with the stage of the disease and baseline flow levels, this inconsistency could be a source of variation. It is possible that patients with more accessible glands benefited more from sialendoscopy than patients with blocked gland access. This study shows that mainly SPF improved after irrigation of the ductal system with saline/TA. This could also be explained by the accessibility of these glands. Sialendoscopy is more complicated to perform in submandibular glands affected by SS than in parotid glands. These anatomic conditions may impede the irrigating and the delivery of medication to the gland parenchyma.[18 32] Careful preoperative selection of patients and salivary glands could contribute to a higher percentage of successfully irrigated glands and more predictable results. Sialendoscopy of multiple salivary glands in the same session is safe and performing this procedure under local anaesthesia seems warranted.[33] In the saline/TA group, fewer submandibular glands (38.9%) could be irrigated compared with the saline group (56.3%). This could explain the smaller increase of UWS after sialendoscopy in the saline/TA group compared with the saline group. The follow-up period was too short to assess a long-term effect of sialendoscopy in patients with SS. Trials with a longer follow-up period are needed to prove the long-term sustainability of the observed effect of this treatment on salivary flow.

In our study, sialendoscopic intervention had a significant effect on the dryness domain of the ESSPRI and this result is partly supported by XI scores. This effect could be related to an increased flow, and to a change in salivary protein composition after sialendoscopy.[13] Improvement of the perceived oral dryness could also be related to a placebo effect, as it was not possible to perform the study as a double-blind randomised trial.

CONCLUSION

This randomised controlled trial assessed the effect of sialendoscopy of the major salivary glands on salivation and xerostomia in patients with SS. The results indicate that oral dryness improves up to 6 months after sialendoscopy, both subjectively and objectively, compared with baseline.

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Patient consent Obtained.

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