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RESEARCH ARTICLE

Evaluation of magnetic resonance sialography and ultrasonography findings in salivary glands of patients with xerostomia

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ABSTRACT

Objectives: The aim of the study was to assess MR sialography and Ultrasonography as objective tools to examine salivary glands in patients with xerostomia.
Materials and Methods: In this Cross-sectional descriptive study, MR sialography using salivary secretion stimulation was performed in 16 patients (with the chief complaint of xerostomia) and 11 healthy volunteers. Visibility of the main duct and ductal branches were evaluated before and after stimulation in axial and oblique sagittal plans, and were classified in to three grades (poor, fair & good). Patients and volunteers were also examined by ultrasonography; their parenchymal homogeneity of the salivary glands was graded from 0 to 5 and their echogenicity was divided to three levels: hypoecho, isoecho and hyperecho. Size of the salivary glands was also measured. Dependent T-test and independent T-test,Spearman and Chi-square analysis were performed to analyze the results.
Results: In this study the results showed no significant difference in the visibility of salivary glands ducts before and after salivary secretion stimulation in healthy volunteers. In the patients group, however, significant difference was seen in the visibility of salivary glands ducts after stimulation in sagittal planes of right and left parotid glands (P-Value=0.033) as well as left submandibular glands (P-Value=0.035). No significant difference in the visibility of salivary glands ducts was observed between healthy volunteers and patients,except in sagittal plan of left parotid glands (P-Value=0.004). In addition, there was no significant difference in parenchymal characteristics and size of salivary glands in ultrasonography results in the two groups. No Significant correlation could be established between MR Sialography and Ultrasonography findings.
Conclusions: Achieving no significant difference in imaging results between patients and volunteers suggests that MR sialographic images and US features may not serve as suitable diagnostic criteria in patients with xerostomia.

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INTRODUCTION

Xerostomy is a common complaint among patients referring to dentists, and causes several problems, including oral pain, dysphasia, and generally reduced quality of life. Detecting presence or absence of structural changes in salivary glands in patients with dry mouth will help to determine the cause and its treatment.[1]

A variety of methods are used to evaluate hypoactive salivary glands, for instance: use of standardized research questionnaires about xerostomia, and measurement of salivary flow.[2] Imaging techniques are also used to assess functionality of salivary glands, including conventional sialography, in which contrast medium is injected through the opening of salivary glands, thereby providing accurate structural information about salivary ductal system. However, since the technique requires cannulation of ducts, it is considered invasive, and is contraindicated in cases such as acute infection of salivary duct or allergy to contrast medium (iodine) (3). Combination of sialography and advanced imaging techniques (such as CT scan) are used for accurate examination of salivary glands, which causes the same problems for the patient as in sialography conducted alone, plus posing greater risk of ionizing radiation[3]. In salivary gland scintigraphy, measurement of absorption of technetium-pertechnetate (TC) and its secretion into the oral cavity can reveal functionality of acinar tissue of salivary glands. This technique is also associated with patient's exposure to radiation.[1,4]

MRI is an imaging technique that uses magnetic field instead of ionizing radiation. As in conventional sialography, MR sialography is a technique used to examine the structure of salivary gland ducts. MRI enables visualization of fluids so the saliva in salivary gland ducts can be visualized, and allows assessment of the anatomy of salivary ducts without the need for invasive procedures like cannulation of ducts, injection of contrast medium and radiation methods.[4,5]

Ultrasound is an effective non-invasive technique for identifying changes in gland's parenchyma as well as internal and external structures of salivary ducts, especially cysts.[1]

Since no study has been conducted on structural changes of salivary glands in patients with xerostomia (except cases of proven changes in salivary glands, such as Sjogren's and radiotherapy) through concurrent use of ultrasound and MR sialography, this study aims to investigate findings of MR sialography and ultrasound images in people with xerostomia, and compare them with conditions of salivary glands in healthy people.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted over one year on parotid and submandibular salivary glands involving 16 patients (11 females, and 5 males) of 27 to 64 years old (mean 43.9 years) presenting with dry mouth at the Department of Oral Medicine, School of Dentistry in Mashhad, and 11 healthy volunteers without dry mouth complaint (9 females and 2 males) of 26 to 54 years old (mean 37.5 years).

At first, the subjects signed an informed consent form and completed a xerostomia questionnaire that was based on previous studies, with 10 questions on dry mouth sensation.[6] If any question received an affirmative response and xerostomia was diagnosed by clinical examination in the Oral Disease Department according to clinical symptoms,[7] then subjects were included in the xerostomia group. Patients with Sjogren's syndrome, those undergoing radiotherapy of head and neck (due to their destructive effect on salivary structure) and people with contraindication of MRI imaging were excluded from the study. Both groups underwent MR sialography at Parsian Imaging Center in Mashhad. As some patients refused to remain in the study, only 14 patients with xerostomia (10 females, 4 males) and 10 healthy volunteers (8 females, 2 males) underwent ultrasound examination performed by a medical radiologist at the radiology department of Ghaem Hospital in Mashhad.

MR sialography

Selected subjects underwent MR sialography of the parotid and submandibular salivary glands before and after stimulation employing a salivary flow stimulant (lemon juice). A few drops of lemon juice in a syringe were poured in the corner of mouth, and subjects were asked not to swallow for as long as possible. The 1.5 Tesla MRI system (Siemens Symphony) and special head coils together with flexible surface coils were used to achieve high resolution images. Images were prepared in T2-HASTE-fs (Fat saturation) protocol with TR/TE 5000/89 imaging specification in axial and sagittal planes, with thickness of 3.2 mm and MIP of 15 mm, with FoV phase:%100 and FoV read:208 mm, and NEX=2. Overall imaging duration was 10 minutes (5 minutes before, and 5 minutes after stimulation). To obtain images, both sides of parotid and submandibular glands in each plane were exposed. Visibility of primary and secondary salivary ducts before and after stimulation was evaluated based on Wada[7] study, and was classified in to three grades (good, fair, and poor)[7] (Figure 1).

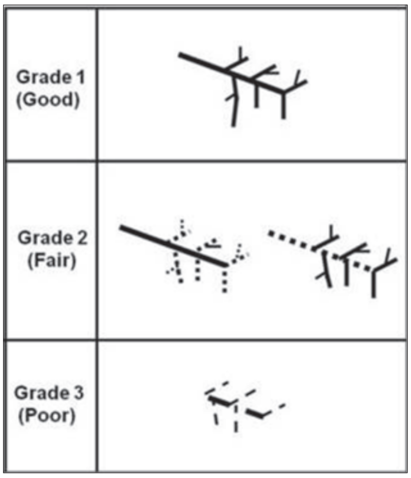

Figure 1. Grading of Salivary ducts visibility

Ultrasound

Salivary glands of participants were studied by an experienced medical radiologist at Ghaem Hospital in Mashhad using a 10-7.5 MHz General Steel ultrasound system with linear transducer. In terms of parenchymal homogeneity, salivary glands were divided into 5 groups (homogeneous parenchyma=0, mild non-homogeneous=1, moderate non-homogeneous=2, severe non-homogeneous=3, and glandular atrophy=4), and in terms of echogenicity in to three groups (hypo-echo, iso-echo, and hyper-echo), compared with surrounding muscles.[5,8] Longitudinal and transverse dimensions were examined for every parotid and submandibular gland. As for parotid gland, depth was also examined.

To avoid observer bias, each MR sialography image was coded with a numerical ID.

Age and sex of the subjects were thus unknown to the observer. All of the images were scored by one examiner (maxillofacial radiologist) and all subjects were re-examined after two weeks by the same examiner. Both readings were then analysed using paired t-test. The two readings were computed for percentage agreement, and the remainder was evaluated by figuring the over- and under-stage assessments.

RESULTS

Prior to stimulation of salivary flow, visibility of salivary duct system in MR sialography was rated as follows(Based on Wada's study) (7):

1st degree (good): Clear observation of main and secondary ducts.

2nd degree (moderate): Clear observation of main duct or secondary ducts.

3rd degree (poor): Failure to clearly observe main and secondary ducts (Figure 1).

After stimulation,improvement in visibility of salivary ducts was assessed as: 1st degree (good), 2nd degree (moderate), and the 3rd, no change in clarity of ducts (poor) (Figure 2).

According to the results of axial images of MR sialography, of the 50 parotid glands examined, visibility of ducts improved after stimulation in 8 (16%) glands of healthy individuals, and 11 (22%) glands of patients with xerostomia.In sagittal images, of the 32 glands examined, visibility improved after stimulation in 5 (15.5%) glands of healthy individuals, and 6 (18.7%) glands of people suffering xerostomia. (Figures 3, 4).

In MR sialography on axial images, of the 48 submandibular glands examined, visibility of ducts improved after stimulation in 1 (2%) gland from a healthy individual and 5 glands (10%) from people with xerostomia, while on sagittal images, of the 28 glands examined, visibility improved after stimulation in 8 (28.5%) glands, all from the xerostomia-suffering group. (Figures 5, 6).

The ultrasound results revealed a range of echostructure of parotid gland in healthy subjects including: 70% homogeneity, 20% mild heterogeneity, and 10% distinct heterogeneity, and in terms of echogenicity: 60% were hyperechoic, and 40% were isoechoic.

The scope of Echostructure concerning the parotid gland in people with xerostomia included: 57% homogeneity, 22% mild heterogeneity, and 14% distinct heterogeneity, and in terms of echogenicity: 78% were hyperechoic and 22% isoechoic. (Figures 7, 8).

Also, submandibular echostructure in healthy people yielded a breakdown as: 80% homogeneity, 10% mild heterogeneity, and

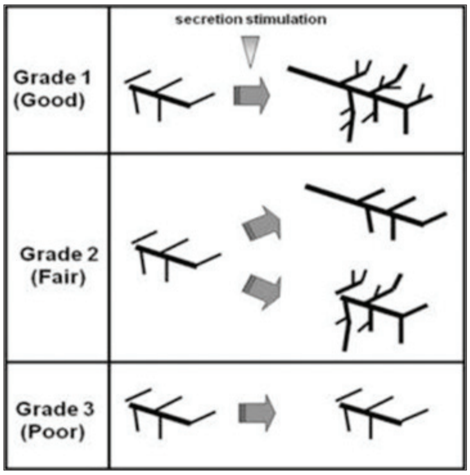

Figure 2. Improvement in Salivary ducts visibility after stimulation.

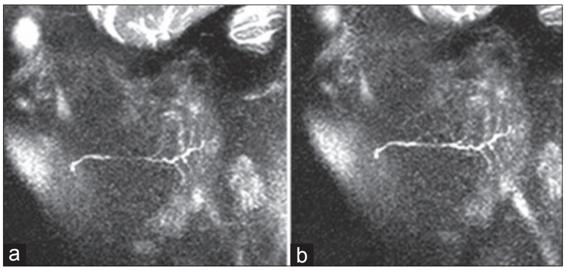

Figure 3. (a) Salivary ducts in parotid gland of xerostomia patient before stimulation (MR sialography, oblique sagittal plan) (b) same patient after stimulation

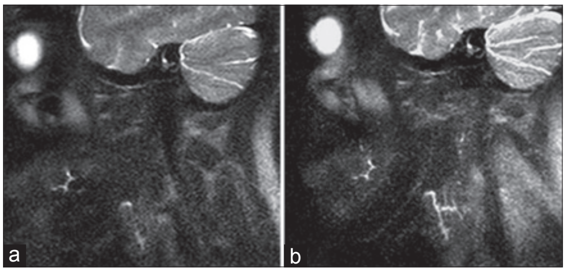

Figure 4. (a) Salivary ducts in submandibular gland of xerostomia patient before stimulation (MR sialography, oblique sagittal plan) (b) same patient after stimulation

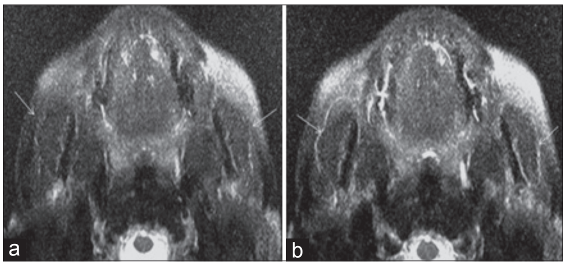

Figure 5. (a) Salivary ducts in parotid gland of xerostomia patient before stimulation (MR sialography, axial plan) (b) same patient after stimulation

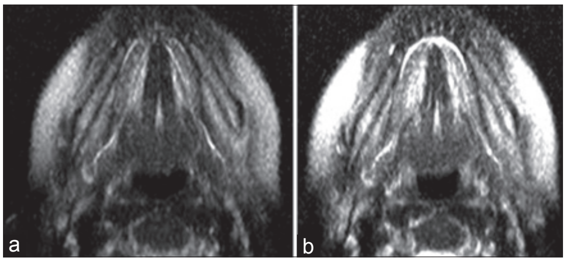

Figure 6. (a) Salivary ducts in submandibular gland of normal woman before stimulation (MR sialography ,axial plan) (b) same patient after stimulation. Detectable change in ductal system visibility wasn't seen

10% distinct heterogeneity, and in terms of echogenicity, 70% were hyperechoic and 30% isoechoic.

Submandibular echostructure in people with xerostomia followed this pattern:78% homogeneity, 14% mild heterogeneity, and 7% distinct heterogeneity, and in terms of echogenicity, 64% were hyperechoic and 36% isoechoic. Only one normal person showed distinct dishomogeneous image in the submandibular gland.

According to the results obtained from dependent t-test, there were no significant difference between visibility of salivary gland ducts in MR sialography before and after stimulation of salivary flow in axial and sagittal sections in healthy people (P>0.05).

Dependent t-test results showed a significant difference between visibility

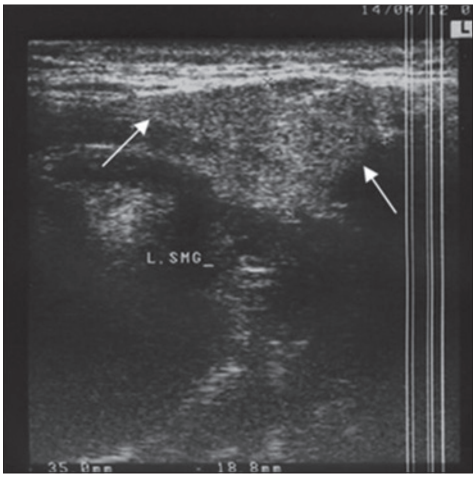

Figure 7. Ultrasonographic view of submandibular gland of a 33 years old patient. Mild non homogeneity and hyperecho parenchyma is visible

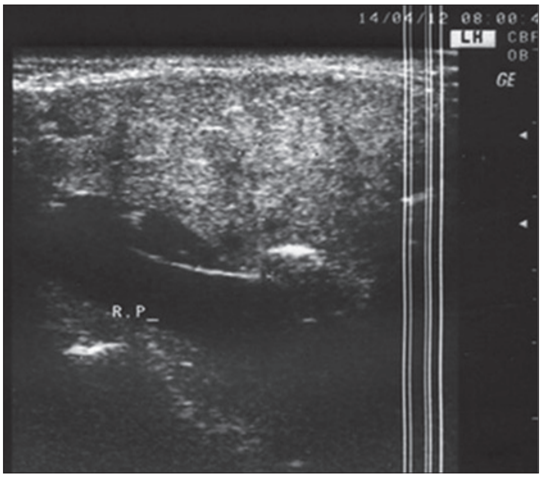

Figure 8. Ultrasonographic view of Parotid gland of a 56 years old patient. Heterogeneity and hyperechogenicity in parenchyma is visible

of salivary gland ducts in MR sialography before and after stimulation of salivary flow in people with xerostomia only in the left and right sagittal views of parotid gland (P=0.033), but no significant difference could be measured in other cases (P>0.05).

Dependent t-test results revealed a significant difference between visibility of salivary gland ducts in MR sialography before and after stimulation of salivary flow in people with xerostomia only in the left sagittal view of submandibular gland(P=0.035), but there was no significant difference in other cases (P>0.05).

Independent t-test findings revealed a significant difference between visibility of parotid and submandibular gland ducts in MR sialography before stimulation of salivary flow in healthy volunteers and people with xerostomia in the sagittal view of left parotid gland (P=0.004), but no significant difference could be observed in other cases (P>0.05).

Independent t-test results showed a significant difference between visibility of parotid and submandibular gland ducts in MR sialography after stimulation of salivary flow in healthy subjects and those with xerostomia only in the sagittal view of left parotid gland (P=0.042), but there was no significant difference in other cases (P>0.05) Tables 1 and 2.

According to Pearson Chi-squared test, there was an insignificant difference between echostructure of parotid gland in ultrasound of healthy people and those with xerostomia (P>0.05) (Table 3).

Pearson Chi-Square test also indicated an insignificant difference between echostructure of submandibular gland in ultrasound of healthy people and xerostomia-suffering cases (P>0.05) (Table 4).

Fisher's exact test showed insignificant differences between echogenicity of parotid glands in the two groups (P>0.05)(Table 5).

Fisher's exact test yielded insignificant differences between echogenicity of submandibular glands in the two groups (P=0.193) (Table 6).

Independent t-test results showed insignificant differences between size

Table 1. Comparative test of visibility of parotid ducts in MR sialography after stimulation of salivary flow in healthy people and people with xerostomia

Parotid Glands' ducts observation rate	f	Covariance p value	t	Degree of freedom	p-value
Left axial	0.458	0.506	−0.107	21	0.916
Right axial	1.873	0.186	0.304	21	0.764
Left sagittal	0.882	0.368	−2.301	11	0.042
Right sagittal	0.282	0.606	−0.325	11	0.751

Table 2. Comparative test of visibility of submandibular ducts in MR sialography after stimulation of salivary flow in healthy people and people with xerostomia

Submandibular Glands' ducts observation rate	f	Covariance p value	t	Degree of freedom	p-value
Left axial	1.695	0.206	−01.436	22	0.165
Right axial	1.316	0.264	−01.17	22	0.254
Left sagittal	2.014	0.179	0.322	13	0.752
Right sagittal	0.65	0.435	−01.249	13	0.234

Table 3. Pearson Chi-Squared test results of echostructure of parotid glands in healthy people and people with xerostomia in ultrasound exam

Parotid gland echostructure	Group	Homogeneous (0) (%)	Mild hetrogeneity (1) (%)	Distinct hetrogeneity (2) (%)	p-value
Left parotid	Healthy	30.4	8.7	4.3	1
	Xerostomia	34.8	13	8.7	
Right parotid	Healthy	30.4	8.7	4.3	1
	Xerostomia	34.8	13	8.7	

Table 4. Pearson Chi-squared test results of echostructure of submandibular glands in healthy people and people with xerostomia in ultrasound

Submandibular gland echostructure	Group	Homogeneous (0) (%)	Mild hetrogeneity (1) (%)	Distinct hetrogeneity (2) (%)	p-value
Left submandibular	Healthy	34.8	4.3	4.3	0.758
	Xerostomia	47.8	8.7	0.0	
Right submandibular	Healthy	34.8	4.3	4.3	0.706
	Xerostomia	52.2	4.3	0.0	

Table 5. Comparative test of echogenecity of parotid glands in ultrasound of healthy people and people with xerostomia

Parotid gland echogenecity	Group	Isoechoic (%)	Hyperechoic (%)	p-value
Left parotid	Healthy	60	35.3	0.316
	Xerostomia	40	64.7	
Right parotid	Healthy	50	38.9	0.550
	Xerostomia	50	61.1	

of parotid and submandibular glands in ultrasound of healthy people and those with xerostomia ($P>0.05$).

DISCUSSION

Xerostomia is defined as dry mouth feeling, which distinguishes this sensation from

Table 6. Comparative test of echogenecity of submandibular glands in ultrasound of healthy people and people with xerostomia

Submandibular gland echogenicity	Group	Isoechoic (%)	Hyperechoic (%)	p-value
Left	Healthy	54.5	27.3	0.193
	Xerostomia	45.5	72.7	
Right	Healthy	54.5	27.3	0.193
	Xerostomia	45.5	72.7	

salivary gland hypofunction, as the latter is induced by measurable changes in quantity or quality of saliva. Usually, when salivary flow is reduced to half of its normal level, a person is said to have xerostomia, which can occur even when salivary glands are functioning normally, for instance, in special psychological states such as anxiety, dehydration, short term use of drugs like antihistamine etc.[2] A dentist with knowledge of xerostomia symptoms and factors creating it, one who is also able to help the patient control oral complications of dry mouth such as dental caries, can play an important role in enhancing a patient's quality of life.[2,8]

Several methods are used to assess structure and function of salivary glands. High resolution ultrasound is a non-invasive, available, inexpensive, and repeatable technique for assessment of salivary glands. Echogenicity and echostructure of salivary glands can be examined with Gray-Scale ultrasound, and the morphological data produced can be used as a guide to detect causes of xerostomia.[9,10]

MR sialography is a new technique applied as conventional sialography to examine salivary gland ducts but without the need for cannulation of ducts or use of ionizing radiation.[7,11]

In this study, ultrasound and MR sialography results from patients with dry mouth were compared with findings from salivary glands of normal people.

Niemela et al. compared ultrasound, MRI, and MR sialography results of patients with primary Sjogren's syndrome with those of normal people,[12] and found abnormal findings demonstrating dishomogeneity of parenchymal as well as accumulation of fat in salivary glands of 78% of patients and 4% of normal subjects. Furthermore, findings of parotid and submandibular glands showed an obvious relationship, except for accumulation of fat, which was observed more in parotid glands. In Niemela's study, parenchymal heterogeneity was presented as the most common ultrasound finding in patients with Sjogren's syndrome.[12] In the present study, heterogeneity in salivary glands was observed in one of the normal cases, which was traced to childhood mumps. Severe dishomogeneity or heterogeneity was not observed in other patients.

In the present study, ultrasound revealed hyperechoic parenchyma in parotid glands of 11 patients compared to submandibular glands (8 out of 13 patients), which showed higher accumulation of fat in parotid glands,which is believed to lead to increased echogenicity.

Homogeneity of parotid gland proved to be higher in healthy people (70%) than in those with xerostomia (57%). Also, parotid glands in patients showed higher echogenicity compared to healthy people (78% hyperechoic compared to 60% in healthy people), and no case of hypoechoic pattern could be observed.

In the present study, the difference in salivary glands' size between healthy people and those with xerostomia was insignificant, and the same applied to salivary gland parenchymal characteristics in these groups (P>0.05), which may have been due to the absence of change-induced parenchymal disorders affecting salivary glands in the patient group. In patients with radiotherapy-induced xerostomia, reduced length, width, and depth of salivary glands along with reduced parenchymal homogeneity have been reported in past studies.[10,13] Ultrasound is limited in detecting mild parenchymal changes, and can only detect obvious changes in advanced stages of Sjogren's syndrome.[12]

In a study by Morimoto et al., assessment of salivary gland function was performed with MR sialography, and time-dependent changes in visibility of salivary gland duct were analyzed and plotted, before and after stimulation of salivary flow (using citric acid). In their study, main ducts and secondary branches were clearly visible during the first 30 seconds of stimulation of salivary flow in all volunteers, but shortly after, main ducts began to fade. Moreover, a patient with excessive salivary flow and a patient with poor salivary flow were studied separately, and maximum and minimum variations in ductal area were evaluated. Also, the time required for visible ductal area to return to 50% of maximum level after stimulation was measured, which revealed that this time was shorter than the norm in the patient with excessive flow (150 s), and that it took longer for the person with poor salivary flow (210 s) to drain saliva from ducts.[14]

Results of this study can justify the lack of a significant difference between observed level of salivary glands ducts in MR sialography before and after stimulation of saliva in healthy people; since in our protocol, imaging time was 5 minutes, while in Morimoto study, in this length of time, visibility of ducts in people with normal saliva would have probably returned to the initial level. However, in people with xerostomia, there was a significant difference in ductal visibility, before and after stimulation of saliva flow,because the saliva inside the ducts, which accounts for clarity of their image, drains at lower rate.

In Murakami study, MR sialography was carried out employing HASTE (Half-Fourier Acquisition Single-shot Turbo spin Echo) sequence, which is similar to the protocol used in the present study.[15] In that study, main ducts and large branches of parotid and submandibular glands salivary ducts were visible on axial and sagittal images in 8 out of 12 patients. Limited observation of some intra-glandular ducts was attributed to artifacts from dental amalgams or insufficient suppression of fat in imaging. These reasons can also explain the failure to observe salivary ducts in some of our samples;in the case of three people from the normal group with poor visibility of ducts, for example, before stimulation of salivary flow. Murakami argues that visibility of fine ducts is poor in MR sialography, which was also evident in the present study.[15]

Minami et al. used Umeboshi (a kind of Japanese pickle) to stimulate salivary flow for MR sialography, and performed imaging for 5 minutes before stimulation and 10 minutes after stimulation, with a 1 minute interval, involving 3 volunteers, and concluded that persistent stimulation of saliva flow is possible, due to the semi-solid nature of this stimulant. The process achieved improved visibility of salivary ducts,and maximum improvement was measured 2 minutes after stimulation, but10 minutes after stimulation, was perceived rather late, particularly for examination of submandibular gland ducts.[16] In the present study, lime juice was used as stimulant, which was removed with swallow of saliva, and therefore failed to maintain persistent stimulation. In patients that had not swallowed their saliva during imaging, ducts were more clearly observed than in those who repeatedly swallowed their saliva (as mentioned by the patients), which resulted in impaired quality of the image due to elimination of stimulant and creation of motion artifact.

In Weber's study, MR sialography was performed using two types of conventional head and neck coil systems, and surface coil separately. It was concluded that both coils provided symmetric salivary duct observation of both sides, and observation of ducts improved through stimulation of salivary flow.[17] In their study, surface coil showed a poorer performance in displaying submandibular glandular ducts and intra-glandular ducts, and so it seems it can not be a suitable alternative to head and neck coil.

Pretorious argued that standard head coil would suffice for MR sialography, although, if required, a surface coil can also be simultaneously used adjacent to parotid gland to increase signal-to-noise ratio and improve image quality.[18] In the present study, head and neck coil, together with a flexible coil adjacent to salivary glands were used.

In a study by Sumi et al., ultrasound and MR sialography results from lacrimal and salivary glands of 3 patients with Mickulic's disease, were examined in relation to IgG_4. The ultrasound exhibiting parenchyma of these glands showed punched-out, soap bubble, and reticular patterns in hyperechoic parenchyma.[19] In the present study, only two persons showed punched-out pattern in salivary glands parenchyma in their ultrasound, and there was one patient with Sjogren's syndrome, who were all excluded from the study. The same was also observed in a healthy person with no clinical signs or history of salivary gland diseases, which could have been due to their childhood mumps or a normal variation.

Wada et al. investigated radiation-induced xerostomia,using MR sialography, and evaluated variations in observations of the main duct and secondary salivary ducts of parotid and submandibular glands before and after stimulation,deploying tartaric acid, and concluded that after stimulation of salivary flow, submandibular gland response was highly associated with clinical severity of xerostomia.[7] This result can be justified with the fact that submandibular glands are responsible for a large proportion of rest saliva. In the present study, the clinical examination placed the majority of the patients in the mild xerostomia group, and none showed severe xerostomia. An insignificant relationship was found between imaging results and severity of xerostomia, which could be attributed to the small sample size and the majority of patients being in the mild xerostomia group.

In the present study, parenchymal properties of salivary glands (echo-structure and echogenicity) in healthy people and patients with xerostomia presented insignificant differences in ultrasound. Also, the difference in size of salivary glands between the two groups was perceived as insignificant.

CONCLUSION

Ultrasound is a simple and reliable method for examining salivary gland variations and it is a valuable first step in assessment of impairments in these glands. However, it is rather limited in exploring mild parenchymal variations, and can only detect obvious variations, like variations in advanced Sjogren's syndrome.

In the present study, there were insignificant differences in size, echogenicity, and echostructure of salivary glands in ultrasound between people with xerostomia and healthy volunteers. With regards to MR sialography, significant differences were observed in visibility of salivary ducts before and after stimulation of salivary flow on sagittal images in patients with xerostomia.

Ultrasound and MR sialography results of healthy people and those with xerostomia revealed insignificant differences.We can conclude that in some patients,dry mouth is a subjective sensation with no evidence of altered salivary volume or structural changes in salivary glands, so radiographic features may not serve as appropriate diagnostic criteria in patients with xerostomia.

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