

observe good clinical practice in one when providing medical services throughout the patient's journey To and from the healing structure.

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MODERN METHOD FOR THE ASSESSMENT OF THE STRUCTURAL CHANGES IN THE MAJOR SALIVARY GLANDS

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СОВРЕМЕННЫЙ МЕТОД ОЦЕНКИ СТРУКТУРНЫХ ИЗМЕНЕНИЙ БОЛЬШИХ СЛЮННЫХ ЖЕЛЕЗ

Abstract. Changes in the parenchyma and ducts of the major salivary glands in case of the Sjogren's syndrome are detected by the contrast-enhanced sialography. However, its performance requires the intraductal administration of the iodine-containing radiopaque agent, which is contraindicative for patients with the iodine allergy and is not advisable in case of the thyroid gland pathology.

In this study, the parotid salivary glands of the patients with the Sjogren's syndrome were studied using the magnetic resonance sialography, which is based on the contrast enhancement of the ductal system with natural salivary secretions, it was performed the sialometry and biopsy of the minor salivary glands. The obtained data were analyzed against each other. Similar pathological changes in the form of the fibro-fatty replacement of the glandular tissue were revealed on MR-sialograms of the parotid salivary glands and histological specimens of the minor salivary glands of the patients with the Sjogren's syndrome.

Key words: magnetic resonance sialography, parotid salivary glands, minor salivary glands, Sjogren's syndrome.

Introduction

Sjogren's syndrome (SS) is a systemic autoimmune disease characterized by the lymphocytic infiltration of the salivary and lacrimal exocrine glands, leading to the development of xerostomia and xerophthalmia [1, 4].

According to the literature, among all non-tumor pathologies of the major salivary glands, the prevalence rate of SS is 0.1 to 3.3% with the disease incidence of 5–25% in patients with systemic diseases of the connective tissue, and 50–75% in patients with the autoimmune abnormalities in the liver and thyroid gland [1, 2].

The clinical dental signs of SS are divided into two groups, the main signs are associated with the changes that occur with the involvement of organs, they include the xerostomia, abnormal salivary glands, development of the parenchymatous parotitis. The additional signs include: the multiple cervical caries, dry vermilion transitional zone, angular cheilosis, stomatitis of different etiologies, enlarged regional lymph nodes [3].

According to the classification criteria for SS proposed by the American-European Consensus Group in 2002, the diagnosis is established based on the clinical manifestations, serological and radiological studies, as well as Schirmer test, sialometry and biopsy of the minor salivary glands (MSG) [4].

The main methods for the detection of changes in the glandular tissue in case of the Sjogren's syndrome are biopsy of MSG and sialography of the parotid salivary glands (PSG) [12].

The destructive diseases that develop in the ductal system and the parenchyma of PSG are usually revealed by the sialography and manifested in the indistinct injection of the ducts (symptom of the high permeability) and the presence of the multiple round-shaped cavities in the parenchyma filled with the radiopaque agent with a diameter of more than 1 mm [5, 6, 7, 8].

However, taking into consideration that its performance requires the intraductal administration of the iodine-containing contrast agent, this method is contraindicative for the patients with the iodine allergy and is not advisable in case of the thyroid gland pathology. The ducts obstructions can also stand in the way of the sialography [4, 9].

In such cases, the non-invasive method used is the ultrasound examination of the salivary glands. The main diagnostic criterion of the SS during the ultrasound examination is the heterogeneity of the parenchyma. It manifests itself as the hypoechogenic areas surrounded by the hypoechogenic line or spot that is similar to the meshed image [10]. At the same time,

this symptom-complex can correspond to both the cluster of the lymphoid cells and microfocal lymphomas, and can be misinterpreted [11].

The pathological changes of the PSG in the form of the presence and distribution of fibrous and adipose tissue can be revealed by the magnetic resonance imaging (MRI). This is a method without radiation exposure that can also be used during the aggravation of the sialadenitis. Most commonly, it is performed according to the traditional method using the devices with a capacity of 1.0 Tesla and 1.5 Tesla. Using the CT native images, the structure of the parenchyma is assessed, and the ductal system is not visible [2].

The foreign literature describes few examples of the use of the magnetic resonance sialography (MR sialography) for the diagnosis of the salivary glands diseases. It is based on the principle of the magnetic resonance hydrography and is applicable to the non-invasive techniques, which does not require the administration of the iodine-containing agent, since the contrast enhancement of the ducts is effected on account of the presence of their own salivary secretions [2, 9, 12, 0].

The necessary step of the SS diagnosis confirmation is the morphological examination of MSG. The pathognomonic evidence of the disease is the lymphocytic and plasma cell infiltration, which, according to the degree of the disease progression, has the destructive effect on the ducts and acinar tissue [3, 5, 6, 7, 8]. In his study, Iu.M. Gitikhmaev (2018) determined the morphological features of MSG and major salivary glands in case of different sialadenoses and somatic diseases and revealed the similar changes [13, 14].

Study objective: to provide evidence for the effectiveness of the magnetic resonance sialography in the diagnosis of the Sjogren's syndrome.

Materials and methods

30 patients with the diagnosed Sjogren's syndrome, aged 50 to 75 years, were under examination and medical treatment at the FSBSI "Research Institute of Rheumatology named after V.A. Nasonova". To confirm the diagnosis (perform the private and special methods of investigation), the patients were referred to the Dentistry Department of the Federal State Budgetary Institution "Central State Medical Academy" of the Administrative Department of the President of the Russian Federation.

The inclusion criteria were the patients with the diagnosed Sjogren's syndrome.

The exclusion criteria were the patients with the cardiac pacemakers, metal implants, sialodenoconuses and claustrophobia.

30 patients with the Sjogren's syndrome, depending on the stage of the disease, were divided into several groups:

I group – 17 patients with the clinically apparent disease;

II group - 13 patients with the advanced disease.

The control group included 12 patients without the salivary glands pathology.

For all subjects it was used the general, private and special methods of investigation for the diagnosis of the Sjogren's syndrome.

The sialometry was performed using the Lashley-Iushchenko-Krasnogorskii cup, which was installed on the mouth of the duct of the parotid salivary gland, then, after the first drop of saliva appeared, the salivary discharge was stimulated for 5 minutes using 2% ascorbic acid solution, and the obtained secretions was collected into the graduated test tube.

The magnetic resonance sialography was performed at the Department of the Roentgen Diagnostics and Tomography of the Federal State Budgetary Institution “Central State Medical Academy” of the Administrative Department of the President of the Russian Federation using the 3.0T GE Signa MRI scanner.

Two hours before the start of the study, the patients were asked not to take food. First, the mouth of the excretory duct of the PSG was examined with a bougie with the subsequent obturation using the disposable plastic probe. After that, the salivary discharge was stimulated for 15 minutes with a 2% ascorbic acid solution. Then, the head and neck regions were scanned in three projections (axial (Ax), coronal (Cor) and sagittal (Sag)) on a series of T1-, T2-weighted tomograms and T2- with fat suppression and in FIESTA mode. The slice thickness was 1-5 mm.

The degree of duct imaging on the MR-sialograms depended on the amount of the saliva produced in them. For the calculation of the fluid volume in the ductal system it was used the formula for the calculation of the volume in the cylindrical vessel (Vm^3). Since the ducts on MR-sialograms were visible due to the presence of the natural secretions in them, the volume of the vessel (duct) and the fluid in them were the same.

To determine the volume of a vessel, it is necessary to measure its length and radius, which value should be constant. Taking into consideration that the ductal system of the parotid salivary glands at the different sections had the different diameters, the volume of the duct section with the same radius was determined as an initial matter. For this purpose, it was measured the length of the duct fragment (ΔXi) in the sagittal projection and its radius (r^2) over this length in the coronal projection.

The volume of the duct section (ΔVi) was calculated using the following formula:

$$\Delta Vi = \pi r^2 \times \Delta Xi, \text{ where}$$

ΔVi - is the volume of the duct section with the same radius;

r^2 - is the radius of the duct;

ΔXi - is the length of the duct section.

Then the volume of the duct sections (ΔVi) was added together and the total volume of the vessel V_i (m^3) was obtained:

$$V_i = \Delta Vi_1 + \Delta Vi_2 + \Delta Vi_3$$

The obtained data were converted into milliliters (V_{ml}) that corresponded to the volume of fluid in the duct.

During the biopsy of the minor salivary gland from the lower lip, under the infiltration anesthesia, it was performed the longitudinal section in the mucous membrane of the lower lip, the minor salivary gland was isolated and removed using the hemostatic “mosquito” forceps, and the wound was sutured with the interrupted stitches. The biopsic material, according to the standard practice, was fixed in the 10% neutral buffered formaline; and then for the preparation of the histological specimens it was sent to the FSBSI “Research Institute of Rheumatology named after V.A. Nasonova”. The specimens were stained using the hematoxylin-eosin technique.

When interpreting the results of the histologic examination of the minor salivary glands, the presence of lymphoid infiltration, fibrous and fatty replacement of glandular tissue was assessed.

Study findings

During examination of the patients of the control group, the PSG were not palpated, the oral mucosa was pale pink, moderately moist. From the mouths of the excretory ducts of the PSG during kneading, a clean, clear secret was excreted. The sialometry results were within the normal range of 3.88 ± 0.93 ml.

On the MR-sialograms, the glandular part of the PSG was distinctly visible and was without pathological changes with a homogeneous structure and even clear contours. The ductal system along its entire length was filled with naturally produced secretions, therefore, the main duct and ducts of the first and second orders had clear, even contours. The secretions volume in them on the MR-sialogram was 2.18 ± 0.3 ml.

The histological specimen of the undamaged MSG was represented by acini with the excretory ducts, which form lobules, separated by thin interlayers of the connective tissue - stroma.

The patients with the SS complained of the dry mouth, the inability to chew food without prewetting it with water, a periodic bilateral enlargement of the parotid salivary glands, dry eyes, painful joints. According to the anamnesis, 70% of the patients had the underlying rheumatoid arthritis, 26.7% of them had the autoimmune thyroiditis, and 3.3% of the patients had the systemic scleroderma.

During the clinical examination, the PSG were enlarged, painless in palpation, it was noted the dryness and hyperemia of the oral mucosa, small amount of the free saliva, and multiple non-carious cervical lesions of the hard tooth tissues were determined.

In the I group patients with the clinically apparent stage of the SS the secretion, the secretory function of the major salivary glands was reduced 2.9 times compared with the control group, the results of the

sialometry corresponded to the II degree of xerostomia and were 1.3 ± 0.34 ml ($p < 0.01$).

On MRI-sialograms of the PSG, the interstitial-fibrotic changes with the fatty involution were noted. Due to this, the structure of the parenchyma was heterogeneous. The main duct was visible prior to bifurcation and was uniformly filled with the parotid saliva along its entire length. The ducts of the I, II and III orders were not viewed due to the suppression of the secretory activity. The measurement of the PSG saliva volume (V ml) on the MR-sialogram showed its 3.6-fold decrease in comparison with the control group with the volume of up to 0.6 ± 0.15 ml ($p < 0.01$).

On the histological specimens of the MSG it was noted the significant diffuse lymphoid infiltration of the parenchyma and stroma, cluster of more than 50 lymphoid cells in 4 mm^2 of the salivary gland surface, as well as the periductal lymphoid infiltration. There was a moderate interlobular fibrosis and fatty replacement of the parenchyma. The specimens were stained using the hematoxylin-eosin technique, a - x150, b - x250.

In the II group of patients of with the advanced stage of the SS, the results of the sialometry showed a rapid suppression of the secretory activity of PSG by 7.8 times compared with the control group and amounted to 0.5 ± 0.17 ml ($p < 0.01$) that corresponds to the III degree of xerostomy.

When analyzing the data of MR-sialograms of the patients with the advanced stage of the SS, the parenchyma was not homogeneous, with a diffuse cellular structure, it was noted the significant fibro-fatty replacement of the parenchyma. Due to the rapid decrease in the secretory function, the ductal system was viewed only fragmentarily. The measurement of the secretion volume (V ml) of the PSG on the MR-sialograms also showed the significant function decrease by 7.3 times in comparison with the control group, the secretion was 0.3 ± 0.13 ml ($p < 0.01$).

On histological specimens of the MSG, similarly to the data of the obtained MR-sialograms, there was the significant fibrous degeneration of the glandular tissue of the MSG, it was noted the lobular dysmorphology of the organ, the number of acini was sharply reduced, the excretory ducts were enlarged. It was observed the moderate lymphoid infiltration in the stroma and parenchyma, cluster of more than 50 lymphoid cells in 4 mm^2 of the salivary gland surface. The specimens were stained using the hematoxylin-eosin technique, a - x150, b - x250.

Conclusion

The imaging of the ductal system of the PSG on the MR-sialograms was achieved by the contrast enhancement by the own saliva, it allowed us to evaluate the architectonics of the ducts, and at the same time to assess the functional activity. When analyzing the tomograms and sialometry data, it was established an evidential connection between the level of the PSG salivary discharge and the degree of imaging of the ductal system structure. By comparison of the average values, the calculation of Student's t-test showed that

the differences are statistically significant in all study groups, $p < 0.01$.

The similar pathological changes in the form of fibrous-fatty replacement of the glandular tissue, which were more significant by the degree of the disease severity, were revealed on the MR-sialograms of the PSG and histological specimens of the MSG of the patients with SS.

As can be seen from the above, the represented data prove that MR-sialography is the effective method of the SS diagnostic with the ability to evaluate the secretory function of the PSG.

Findings

1. MR-sialography can detect typical changes in the parotid salivary glands that are specifically attributed to the Sjogren's syndrome in the form of fibro-fatty replacement of the organ, and at the same time evaluate the secretory function by the contrast enhancement of the ducts by their own secretions, thereby replacing the multiple-stage diagnosis.

2. The changes that occur in case of the Sjogren's syndrome in the parotid salivary glands on the MR-sialograms and in the small salivary glands on the histological specimens are similar. On the MR-sialograms it was revealed the fibrocystic-fatty replacement of the organ, on the histological specimens - fibrosis and fatty degeneration of the gland with the lobular dysmorphology, lymphoid infiltration of the stroma and parenchyma.

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