Summary

The cause of the dysfunction of the salivary glands in the course of AITD has not been elucidated. The presence of salivary gland dysfunction in euthyroid patients is noteworthy. Former research have shown disorders in the antioxidant barrier of saliva and the contribution of OS in the development and progression of salivary gland dysfunction in the course of other autoimmune diseases: psoriasis vulgaris, systemic sclerosis, rheumatoid arthritis, type 1 diabetes, multiple sclerosis, Sjögren's syndrome, and systemic lupus erythematosus. The genetic and immunopathological similarity between Sjögren's syndrome (SS) and AITD (98-100) suggests that disorders of the secretory function of the salivary glands, by analogy with SS, may be immunologically related and result from disturbances in the secretion of cytokines, chemokines and growth factors. A fortiori there is a reduction in the size and increases the inflammatory infiltration in the salivary glands of mice (without the gene encoding tyrosulprotein sulfotransferase) with hypothyroidism due to autoimmune inflammation (101).

The research was approved by the Bioethics Committee in Białystok (R-I-002/386/2016). Each of the patients and control group participants was informed about the objectives and methodology of the present experiment and gave their written consent to participate in the study.

The aim of publication 1 was to evaluate the parameters of antioxidant defense and the measurable effects of oxidative stress in unstimulated and stimulated saliva and plasma / erythrocytes of patients with euthyroid AITD, and to compare the obtained results with the results of the control group.

The study group consisted of 45 women diagnosed with AITD. The disease was confirmed when serum levels of anti-TG and / or anti-TPO were above the norm in the plasma and occurred with parenchymal heterogeneity on ultrasound of the thyroid gland. The study group included patients only with euthyroid AITD [free thyroxine (fT4) and normal thyroid stimulating hormone (TSH)], including 24 patients treated with Eutyrox (doses from 50 to 150 mg; the last tablet taken 24 hours before the hormone level test) ) and 21 untreated. Patients reported for follow-up appointments to the Department of Endocrinology, Diabetology and Internal Medicine, Medical University of Bialystok. We decided to create only one group due to the fact that the results of the individual redox balance tests did not differ between patients undergoing hormone therapy and those who did not require it.

The reference group consisted of 45 generally healthy women, matched to the study group in terms of age and BMI, selected from those who reported for follow-up visits to the Department of Conservative Dentistry of the Medical University of Bialystok. The participants of the control group had normal thyroid ultrasound examination results, as well as blood levels of TPO-Ab, TG-Ab, fT4 and TSH were normal for healthy people. The inclusion and exclusion criteria for research and the exact research methodology are presented in publication 1, which is the basis for this dissertation.

The secretion of unstimulated saliva (NWS) was significantly lower in patients with AITD compared to healthy controls, as was the activity of salivary amylase in NWS and stimulated saliva (SNS). The activity of CAT and Px was significantly higher in the NWS and SWS of patients with AITD, while the concentrations of GSH and UA were significantly lower

compared to healthy subjects. Total antioxidant potential was significantly lower, while the total oxidative status and levels of protein oxidation products (advanced glycation end products, advanced protein oxidation products) and lipids (MDA, lipid hydroperoxides) were significantly higher in NWS, SWS and plasma of AITD patients compared to to the control group. A detailed description of the results can be found in publication 1, which is the basis of the present dissertation.

Conclusions

1. The parotid and submandibular glands in patients with euthyroid AITD showed an impaired ability to maintain the redox balance at the level observed in the salivary glands of control women.

2. The saliva of patients with AITD in euthyroidism showed a reduced antioxidant potential. Moreover, a significant increase in the concentration of oxidatively modified biomolecules in NWS and SWS suggests the failure of the antioxidant barrier of the salivary glands in combating the excessive production of ROS.

3. OS in NWS and SWS in women with AITD appears to be closely related to autoimmunity-related inflammation rather than thyroid hormone or TSH levels.

4. The secretory function of the submandibular glands is reduced in patients with euthyroid AITD, which is manifested by a significant reduction in unstimulated saliva secretion.

The aim of publication 2 was to assess the degree of disturbances in the functioning of the salivary glands and the occurrence of subjective and objective symptoms of salivary gland dysfunction in patients with AITD in the state of spontaneous euthyrosis, never undergoing hormonal treatment. Salivary levels of selected cytokines, chemokines or growth factors in the course of AITD have not been determined so far, which seems necessary to explain the role of immunological mechanisms in the development of salivary gland dysfunction in the course of this disease. The results of the research included in publication 2 are also intended to assess whether the obtained concentrations of selected cytokines, chemokines and growth factors in saliva may be related to the rate of unstimulated saliva secretion and the symptoms of xerostomia.

The study group consisted of 25 female patients diagnosed with Hashimoto's disease. The diagnosis of the disease was based on a positive ultrasound examination and the presence of TPO-Ab and TG-Ab antibodies in the blood above the laboratory norm. The selected patients were women with euthyroid AITD, which, importantly, had never been treated with synthetic and natural thyroid hormones, and had not received any other therapies. The patients reported periodic check-ups at the Department of Endocrinology, Diabetology and Internal Medicine, Medical University of Bialystok. The control group consisted of 25 generally healthy women matched in terms of age and BMI, who reported for dental follow-up visits to the Department of Conservative Dentistry. The participants of the control group had normal thyroid ultrasound examination results, as well as blood levels of TPO-Ab, TG-Ab, fT4 and TSH were normal for healthy people. The inclusion and exclusion criteria for research and the exact research methodology are presented in publication 2, which is the basis for the present dissertation.

In more than half of the examined patients, I noted UWS secretion below 0.2 mL / min, indicating a weakened secretory function of the salivary glands. Additionally, I proved that the clinical symptoms of salivary gland insufficiency deepen with the duration of the disease, however, the inflammatory changes occurring in them are independent of the inflammatory changes accompanying AITD. The obtained results indicate the occurrence of disturbances in the profile of cytokines, chemokines and growth factors in UWS and plasma of patients with AITD in euthyrosis, and the concentrations of IL-6 and IL-1 as well as INF-□, TNF-α, IL-12 may be potential biomarkers of dysfunction. salivary glands in the course of AITD. A detailed description of the results can be found in publication 2, which is the basis of my dissertation.

Conclusions:

1. The reduction of NWS secretion by euthyroid AITD patients compared to control is an expression of impaired function of the salivary glands. Moreover, observed in 60% of the studied patients with AITD, UWS below 0.2 mL / min, is a clinical evidence of secretory dysfunction of the salivary glands.

2. The severity of the secretory dysfunction of the salivary glands is closely related to the concentration of antibodies.

3. Clinical symptoms of salivary gland insufficiency deepen with the duration of the disease.

4. The evaluation of the concentrations of the tested cytokines in the saliva and plasma of euthyroid HT patients does not indicate the dominance of any of the branches of the immune response.

5. IL-6 and IL-1 as well as INF-□, TNF-α, and also IL-12 may be potential biomarkers of salivary gland dysfunction in the course of AITD.

6. Inflammatory changes and the related dysfunction of the salivary glands is not related to systemic inflammation.

7. Salivary IL-12 (p40) may be helpful in assessing the progression of autoimmune thyroiditis.