

Peculiarities of local immunity in dry eye disease on the background of hormonal dysfunction

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ABSTRACT

Aim: to determine the state of local immunity in DED on the background of hormonal dysfunction.

Materials and Methods: Of 32 women, 17 patients with diagnosed SM and 15 women of the control group were examined. The Ocular Surface Disease Index and the state of local immunity were defined by determining Ig As in lacrimal fluid (LF) by radial immunodiffusion in Mancini agar.

Results: During the OSDI questionnaire, a mild degree of DED was detected in 21 (65.6%) women, and an average degree was observed in 11 (34.4%) patients with SM. On average, OSDI was 34.54 ± 2.01 . As a result of studies of the state of local immunity in patients with SM, a tendency to increase Ig As was noted, compared with the control group. An increase in Ig As in the lacrimal fluid in patients with SM to 0.34 ± 0.09 g/l was found, compared with the control group (0.24 ± 0.03 g/l).

Conclusions: Using the OSDI questionnaire, the presence of DED was detected in women with SM, mainly mild and moderate degree. The obtained results of the state of local immunity indicate in favor of a nonspecific inflammatory process, accompanied by a decrease in local immune protection and leading to further changes in the ocular surface.

KEY WORDS: dry eye disease, tear film, surgical menopause syndrome, hormonal dysfunction, secretory Ig A

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INTRODUCTION

Dry eye disease (DED) is a multifactorial disorder in which insufficient quantity or quality of tears does not provide proper moistening of the surface of the eye, characterized by impaired tear film homeostasis (TF). Today, there is a tendency to increase patients with DED, and ranges from 5% to 70%. The correlation of patients diagnosed with DED increases towards women over the age of 45. According to WHO, by 2030 this number will increase to 1 billion 200 million people [1-4].

Dysfunction of the ocular structures that create and regulate components of TF, including the tear glands, meibomian glands, cornea and conjunctiva, causes qualitative and/or quantitative tear deficiency, leading to instability and hyperosmolarity of TF. Violations of the structure of TF are accompanied by an inflammatory reaction and secretion of inflammatory factors, which leads to the involvement of immune cells and clinical pathology. As a result, there is a "circulus vitiosus" of inflammation and damage of the surface of the eye, which impairs the quality of life, causing symptoms such as discomfort, eye pain and deterioration of visual acuity of patients suffering from DED [5-8].

There are several risk factors that contribute to the development of DED. One of them is changes in the balance of sex hormones (estrogens, progesterone and androgens) that occur in perimenopausal women and affect the functioning of the tear, meibomian glands, as well as goblet cells of the conjunctiva on the production of components of the tear film, which leads to the development of DED. It is known that the resulting deficiency of sex steroids causes systemic changes in the tissues of the eyelids and the development of atrophic processes in the conjunctiva due to a disorder of hormonal homeostasis [9,10].

A special place among the estrogen deficiency states of women, which can lead to changes in the eye surface, is occupied by the surgical menopause syndrome (SM), which differs from age menopause by the simultaneous cessation of the functions of the uterus and ovaries. This, in a certain way, affects the rapid development of menopausal disorders. SM occurs after total and subtotal hysterectomy for benign neoplasms, as well as as radiation treatment for malignant formation [11-13].

The sudden shutdown of ovarian function creates a deficiency of estrogen, testosterone and progesterone,

which increases the risk of the onset and subsequent progression of postovariectomy syndrome (POES).

According to the modern definition, POES is a complex of symptoms that manifests itself as vegetative-vascular, psycho-emotional, exchange-endocrine disorders and is observed in 60-80% of patients after complete removal of the ovaries. The resulting deficiency of sex steroids causes systemic changes in organs and tissues due to a disorder of hormonal homeostasis. Some researchers believe that symptoms of estrogen deficiency may appear in the first weeks after ovariectomy in 72.3-89.6% of women [14-16].

On the background of deficiency of sex hormones, there are vasomotor disorders, psycho-emotional disorders (40-60%), urogenital disorders and changes in the skin, nails and hair (30-50%), osteoporosis and diseases of the cardiovascular system (25-40%) [17,18].

The effect of hypoestrogenia on connective tissue can be manifested as an increase in pain in the joints, dryness and fragility of hair and nails and "dry" eyes. It should be emphasized that in this period patients often experience discomfort when using contact lenses [19,20].

On the background of hormonal dysfunction, changes in the indicators of cellular, humoral and local immunity are revealed. When studying the immune status in women of fertile age, 30-33% of the examined were found to have initial premorbid abnormalities of some immunogram parameters [21,22].

The local representations of the immune system are located in various tissues, organs and systems of the body. These factors can be found in suitable biological material. The concentration of individual products, for example immunoglobulins, may depend on the level of local synthesis and/or on the increased permeability of histohematic barriers [23,24].

An important marker of tear gland function is the content of immunoglobulins that are synthesized by plasma cells: secretory IgA is the main immunoglobulin in TF, IgG and IgE are present in lower concentrations.

There is evidence that one of the possible reasons for the decrease in immunological protection is hypoestrogen, because estrogens are hormones that increase the activity of non-specific resistance factors [25,26].

Secretory IgA is the main secretory immunoglobulin contained in the secrets of the body, namely tears. Secretory IgA is distinguished by the presence of an additional secretory component (S), synthesized by epithelial cells of the mucous membranes and attached to the IgA molecule at the time of its passage through epithelial cells. The main functions of secretory IgA are the binding of microorganisms on the surface of the mucous membranes, the activation of an alternative

complement pathway and the activation of inflammatory reactions.

Ig As deficiency leads to repeated infections and autoimmune disorders. On the mucose surface the Ig As antibodies are usually concentrated directly in the mucus due to their interaction with the cystine contained in mucin. Thus, Ig As antibodies can participate in the process of immune defense [25,27].

An increase in the level of Ig As in LF relative to the norm, which may indicate a defect in local immunity and a tendency to nonspecific inflammatory processes on the mucous membranes. Compared with the norm of 0.165 ± 0.02 g/l, a decrease in the level of Ig As in LF is manifested by a tendency to allergic diseases and recurrent local viral infections with a prolonged course [23,28].

In case of defects of local immunity for verification of immunodeficiency, it is advisable to conduct an immunological study of those biological secrets that correspond to the localization of clinical lesions, and not to blood serum. With a defect of local immunity, because selective Ig As deficiency, changes in this immune factor in the lacrimal fluid are noted at normal or even increased Ig A content in serum [27,29].

AIM

To determine the state of local immunity in DED against the background of hormonal dysfunction.

MATERIALS AND METHODS

The study involved 32 women, from 36 to 59 years old - 17 patients with diagnosed SM from 2 months to 4.5 years old, and 15 women of the same age group who did not make complaints indicating DED and the pathological course of the perimenopausal period (control group).

An examination was performed that included the determination of the Ocular Surface Disease Index using the OSDI questionnaire and the state of local immunity, by determining Ig As in lacrimal fluid (LF).

A micropipette with a dispenser was used for LF sampling. LF was collected in sterile Eppendorf tubes using a plastic nozzle from the lower conjunctival sac of both eyes (approximately 1 ml) for 7-15 minutes. Previous epibulbar anesthesia of conjunctiva and eyeball was not performed. The biological material was delivered to the immunological laboratory no later than 2 hours after obtaining. The concentration of Ig As in LF was determined by radial immunodiffusion in Mancini agar. The method is based on the reaction of the formation of an insoluble complex of immunoglobulin with specific

antibodies to it in a thin layer of agar. The precipitate has the shape of a ring, the diameter of which is directly proportional to the logarithm of the concentration of the antibody (Ig As) determined.

RESULTS

The Ocular Surface Disease Index (OSDI) is a questionnaire used to assess the severity of patients' dry eye symptoms. It provides a quantitative assessment of the condition and can also be used to monitor the dynamics of symptoms over time and assess the effectiveness of treatment.

An OSDI questionnaire of 32 women with DED on the background of SM was conducted. The obtained data showed a mild degree of DED was detected in 21 (65.6%) women, and an average degree was observed in 11 (34.4%) patients with SM. Severe DED was not determined by the OSDI questionnaire. On average, OSDI was 34.54 ± 2.01 , suggesting the presence of moderate DED symptoms in patients with SM.

The results of the OSDI survey indicate that DED is a common problem in women with SM. Symptoms of DED can range from mild to severe, and can significantly affect the quality of life of patients.

But should be considered that OSDI is a subjective research method that depends on the patient's indications and sensations. This may lead to an underestimation or overestimation of the severity of DED. Therefore, it is more appropriate to use this study in combination with objective methods for diagnosing a violation of the ocular surface.

The immune system controls the stability of the cellular and humoral composition of the body. Changes in Ig As lead to a decrease in immunological protection. It is known that with age, the reactions of cellular immunity decrease, the amount of Ig A in the secretions decreases, which increases the sensitivity of the mucous membranes to infections. The absolute number of lymphocytes decreases, the ability to antibody formation and the proliferative activity of T cells decreases, suppressor activity begins to prevail.

Local immunity of the cornea and conjunctiva plays an important role in protecting the eyes and is represented by various cells of the immune system that produce cytokines and immunoglobulins. IgA is a type of immunoglobulin that is secreted by the mucous membranes, including the conjunctiva. A number of studies have shown that patients with DED have a change in the state of local immunity, namely a decrease in IgA production in the lacrimal fluid and an increase in the concentration of pro-inflammatory cytokines.

The study compared the level of IgA in the tear fluid in patients with SM and in the control group. As a result

of studies of the state of local immunity in patients with SM, a tendency to increase Ig As was noted, compared with the control group. An increase in Ig As in the lacrimal fluid in patients with SM to 0.34 ± 0.09 g/l was established, compared with the control group (0.24 ± 0.03 g/l). This fact may be related to the activation of local immunity. An increase in IgA levels in the lacrimal fluid in patients with SM may be associated with an increase in IgA production by conjunctival plasma cells and an increase in the permeability of conjunctival vessels, which leads to the release of IgA from the blood into the lacrimal fluid.

DISCUSSION

Previous DED studies have shown that at the present time, the incidence of the disease ranges from 5% to 70% and there is a tendency to increase such patients [1-4]. Violations of the TF structure are accompanied by a specific reaction and secretion of inflammatory factors, which leads to the involvement of immune cells and clinical pathology that impairs the quality of life, causing symptoms such as discomfort, eye pain and deterioration of visual acuity of patients suffering from DED [5-7]. As you know, one of the risk factors that contribute to the development of DED are changes in the balance of sex hormones (estrogens, progesterone and androgens), which occur in women in perimenopause and affect the functioning of the tear, meibomian glands, as well as goblet-shaped cells of the conjunctiva on the production of components of the tear film. On the background of hormonal dysfunction, changes in the indicators of cellular, humoral and local immunity are revealed. An important marker of tear gland function is the content of immunoglobulins that are synthesized by plasma cells: secretory IgA is the main immunoglobulin in TF, IgG and IgE are present in lower concentrations. Hypoestrogenia causes changes in the amount of Ig As, which leads to a decrease in immunological protection, because estrogens are hormones that increase the activity of non-specific resistance factors [23,28]. There are single works that indicate that with a defect of local immunity, because of selective Ig As deficiency, changes in this immune factor in the lacrimal fluid are noted at normal or even increased Ig A content in serum [27,29].

The results of the study of determining the ocular surface disease index (OSDI) and the state of local immunity, by determining Ig As in the lacrimal fluid (LF) by radial immunodiffusion in the Mancini agar, indicate the presence of dry eye syndrome (DED) in women with surgical menopause (SM), mainly mild and moderate degree. In these patients, there are pronounced disor-

ders in the state of local immunological protection of the eyes, which are manifested in a decrease in S-Ig A in the tear, which indicates a non-specific inflammatory process and leads to further changes in the surface of the eye, which is expedient for the diagnosis and correction of changes in the eye surface.

CONCLUSIONS

DED is a significant problem for women with hormonal disorders. Researches show that it can significantly affect the quality of life and needs attention and correction. Total ovariectomy performed in women of reproductive age is accompanied by a complex of complicated reactions of the neuroendocrine system, characterizing the process of adaptation of the female body to new conditions.

The OSDI test is a useful instrument for assessing ocular surface conditions in patients with DED. The data

obtained using the OSDI questionnaire are informative and indicate the presence of DED in women with SM, mainly mild and moderate.

The immune system is a complex network of organs, tissues and cells that work together to keep the body healthy and protect it from external factors. Hypoestrogen can lead to changes in the amount of immunoglobulins, in particular secretory IgA, which is important for protecting the surface of the eye.

The obtained results of the state of local immunity evidence in favor of a nonspecific inflammatory process, accompanied by a decrease in local immune protection and leading to further changes in the ocular surface.

Determination of ophthalmic and immunological changes in patients with DED against the background of SM is expedient, because it helps to predict the further development of the disease, the possibility of influencing individual links of pathogenesis and, thereby, improving the quality of life of this category of patients.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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