INFLUENCE OF CURRENT METHODS TREATMENT ON THE CLINICAL AND HISTOPATHOLOGICAL ASPECTS OF THE OCULAR SURFACE IN PATIENTS WITH DRY EYE AND MAJOR COLLAGEN DISEASES

SUMMARY OF PHD THESIS

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I. THE GENERAL PART

The first chapter "Introduction" contains: general information, epidemiological aspects and the relationship between major collagenosis and dry eye. Chapter 2 “Anatomy and histology of the eye” presents the eye, the histological structure of the sclero-corneal layer of the eye and ocular adnexa. In Chapter 3 "Anatomy and physiology of the lachrymal system" are described: tear secretion system, tear film structure and functions, lachrymal excretory system and lachrymal types. Chapter 4 "Ethiopathogeny and classification of dry eye": etiological, histopathological and clinical grades of dry eye. Chapter 5 "Methods to determine tear film changes and ocular surface integrity" includes methods of quantitative and qualitative determination of tear film, and methods for assessing ocular surface integrity. Chapter 6 "Differential diagnosis of dry eye" presents the differential diagnosis of dry eye. Chapter 7 "Dry eye treatment" includes: hygiene and protection measures, medical and surgical treatment of dry eye.

II. THE PERSONAL PART

1. PURPOSE OF THE STUDY

We aimed to evaluate the treatment efficacy of dry eye in major collagenosis by quantifying the qualitative and quantitative tests of the tear film and by histopathological examination of the conjunctiva. The primary endpoint was to study the clinical and histopathological changes depending on the stage and treatment of dry eye, and secondary objectives were as follows: correlations between objective and subjective manifestations and to study the correlations between qualitative and quantitative assessment of tear film and ocular surface damages.

2. MATERIAL AND METHODS

We conducted a prospective three years study in Ophthalmology Clinic, Department of Rheumatology and Department of Histology, University of Medicine and Pharmacy Tg-Mures. The inclusion and exclusion criteria are presented. To assess the severity of dry eye symptoms, we used OSDI questionnaire (Ocular Surface Disease Index). For the evaluation of ocular surface integrity we performed: examination of the eye in natural light, anterior segment slit lamp examination directly and after vital dyes staining. We examined the quantitative and qualitative changes of tear film by performing: modified Schirmer test, test to assess basal tear secretion and meniscus evaluation, tear film break time and tear crystallization test. We evaluated the correlations between of quantitative and qualitative tear film tests and ocular surface changes. History and ophthalmologic examination allowed detection of other eye disorders. Highlighting histological changes consisted of conjunctival biopsy study in 22 patients. Conjunctival biopsies quantified: changes in stratified squamous epithelium, shape and size changes of the cells, vacuolation of cytoplasm, keratinization tendency, nuclear changes, goblet cells aspects and inflammatory reaction. We conducted three experimental studies: study of medical therapy efficacy, study for evaluating the efficacy of inferior lachrymal pathway occlusion and a study of conjunctival changes before and after 3 months treatment. We performed an observational study witch included 14 patients who underwent cataract surgery by phacoemulsification method. Statistical analysis was performed with SPSS 17.0 statistical software and GraphPad Prism. We used frequency tables, the $\chi^2$ test, Student's t test, and Mann-Whitney test. Differences were considered statistically significant at value of the p parameter less than 0.05.
3. RESULTS

We present the most conclusive results: our study included 336 patients. 65.2% suffered from rheumatoid arthritis, followed by those with mixed connective tissue disease (16.3%) and systemic lupus erythematosus (11.3%). We found a statistically significant association (p=0.001) between ocular damages and OSDI. There is no statistically association (p=0.164) between rheumatoid arthritis stage and eye damage. 75% had conjunctivitis sicca, 17.9% had superficial punctuated keratitis, 5.4% had filamentous keratitis and 1.8% had corneal ulcer. We found positive correlations between quantitative and qualitative tests of tear film and ocular damage severity (p<0.05). Cataract was the most frequently encountered in our study (46%). Patients with filamentous keratitis or superficial punctuated keratitis had less than 5 goblet cells/mm² epithelial tissue. We observed nonspecific inflammatory infiltrates with focal, diffuse or perivascular disposition. Results of the study to assess the effectiveness of medical treatment: OSDI had lower values in patients in the treated group than patients in the control group, statistically significant differences between the two groups, regarding modified Schirmer test values (p=0.0001) and tear film break up time values (p=0.0056). Results of the study to assess the effectiveness of inferior lachrymal occlusion: statistically significant differences between the two groups of modified Schirmer test values (p=0.0125) and no statistically significant differences (p=0.1088) in the tear film break time. Goblet cells number increased and inflammation decreased after 3 months of therapy. At 1 month after phacoemulsification we observed an increase of dry eye symptoms and signs in 8 patients and superficial punctuated keratitis in 6 patients. Postoperatively, a statistically significant decrease was revealed in basal secretion (p=0.0054) and tear film break up time (p=0.0112) than preoperative values.

4. DISCUSSION

The results are discussed on the basis of an extensive bibliography, carefully selected from literature, highlighting new and original aspects observed during investigations.

5. CONCLUSIONS

1. Dry eye was more frequently in patients diagnosed with rheumatoid arthritis, followed by patients with mixed connective tissue disease, systemic lupus erythematosus, polymyositis and progressive systemic sclerosis. 2. There are positive correlations between qualitative and quantitative tests of tear film and ocular damages. 3. Corneo-conjunctival damages do not correlate with the stage of rheumatoid arthritis. 4. Tear film instability due to alteration of the mucous layer causes severe ocular surface changes. 5. Dry eye is accompanied by pathological changes in the conjunctival surface epithelial cells, detectable through the conjunctival biopsy study. 6. Inflammation decreases and the goblet cells number. 7. Histological study of conjunctiva has an important contribution to the evaluation of ocular abnormalities, the assessment of therapy efficacy and hence the prognosis. 8. Ophthalmologic and systemic treatment of patients with secondary Sjögren's syndrome lead to lower subjective complaints and to an improvement of objective changes of the eye. 9. In patients with secondary Sjögren's syndrome preoperative preparation, intraoperative maneuvers and postoperative topical treatment causes a more severe ocular surface disease after surgery than preoperative status. 10. Visual prognosis of patients with secondary Sjögren's syndrome depends on early diagnosis, optimal therapy and appropriate monitoring of dry eye.