RISK FACTORS FOR OCULAR SURFACE DISORDERS IN PATIENTS WITH TYPE 2 DIABETES

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ABSTRACT

The tear film consists of a set of heterogeneous substances (lipids, proteins, mucin and water) combined in order to form a highly organic tropism structure specialized in the defense of the ocular surface.

We studied 45 patients affected by type 2 diabetes (27 F-18 M mean age 68 + / - 5 years) with signs of distress and/or dry eyes (burning, foreign body sensation, dryness and itching). Patients were treated with lipoic acid for 28 days. Subjective symptoms and objective signs were seen in the first visit and 5 days after the end of therapy. We considered the results of different tests, such as Schirmer I, Schirmer II, breakage of the film tears (BUT) and conjunctiva swab for the detection of aerobic and anaerobic bacteria.

For each tests we evaluated mean and standard deviation and we confronted the data obtained before and after treatment with a tear substitute next-generation alpha-lipoic acid, obtaining significantly statistical results in each confront.

The total number of bacteria isolations occurred before and after treatment showed a reduction of aerobic (from 25 to 19) and anaerobic strains (from 15 to 10).

These results show that alpha-lipoic acid has a good regulatory activity and its clinical efficacy is confirmed by an activity aimed to normalize clinical parameters of tears.

***Key words**: Dry eye, tear, ecosystem eye, alpha-lipoic acid.*

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Introduction

The tear film is a vital structure whose main roles are to protect the ocular surface from desiccating caused by the tear film evaporation and bacterial infections among others[1].

The quality of the tear film was shown to be affecting the visual acuity, while artificial tears were reported to improve vision of dry eye patients[2-4].

The tear film is transparent and has an aqueous/mucin phase, decreasing in mucin concentration towards as distinct superficial lipid layer.

The lipid layer of this film contains many different lipid species, including non- polar lipids (cholesterol and wax esters) and polar lipids (O-acyl-w hydroxyl fatty acids and phospholipids) which interact with the aqueous layer.

The alteration of this structure can cause a several disorders eyepieces. The dry eye syndrome is certainly the most important disorder. It is characterized by hypo secretion of a fragmented tear film that leads to altered metabolism of the corneal epithelium and dehydration of the corneal epithelium and conjunctiva.

This condition is aggravated in diabetic patients. The alpha-lipoic acid or thioctic acid is a powerful antioxidant active in a hydrophilic and lyophilized environment[5-12]. Recent studies have confirmed an excellent neuroprotective action of alpha-lipoic acid which seems to prevent non-enzymatic glycosylation of proteins implicated in the pathogenesis of diabetic complications[13-17]. It is composed by 8 carbon atoms and 2 sulfur and it is present in tissues rich in mitochondria; because of its chelating properties it is an excellent antioxi-

dant. The antioxidant therapy with alpha-lipoic acid improves and interferes positively in the prevention of diabetic neuropathy and simultaneously, increases insulin efficiency normalizing the level of glucose in the blood. The oxidative stress is a key point in the pathogenesis of diabetes and its complications[18-20].

In previous studies, in patients with type 1 diabetes, it was observed alteration of the tear film and ocular symptoms of discomfort. Furthermore it has been demonstrated that in these patients, the increase in some components of the tear film leads to a reduction of its stability[21-23]. It was also confirmed by impression cytology for the presence of conjunctiva squamous metaplasia and its possible correlation with diabetic retinopathy[24].

Presumably, quantitative alterations of tear film lead to a modification of the microbiota resulting in significant reduction of ocular immune system, thus facilitating the establishment of a possible infectious process[25-28]. In this study we evaluate the possible therapeutic role played by the acid alpha-lipoic acid in the ocular surface of patients with type 2 diabetes.

Materials and methods

Sixty patients with type 2 diabetes treated with oral hypoglycemic agents and / or insulin were recruited, but only 45 patients were admitted to the study (27 females and 18 males, mean age 68.55 ± 11. 1, tab. 1) with mean disease duration of 10.2 ± 2.5 years and in poor metabolic control (mean HbA1c 7.8 ± 0.4 %) presenting signs of discomfort and/or dry eyes (burning, foreign body sensation, dryness and itching).

Patients n°	N°. eyes	Sex		Age	Range
		M.	F.	(mean)	
45	90	18	27	68.55± 11.1	65-78

Table 1: Demographic characteristics of patients who completed the study.

None of the patients had infections of the ocular surface and appendages or allergic diseases of the ocular surface in the last 30 days.

We excluded patients with previous eye surgery, lachrymal disorders, and medical therapy with systemic or topical medications that alter the tearing and / or topical steroids during the 4 weeks preceding the start of the study.

In all patients was taken into account the subjective symptoms and objective signs at the time of enrollment visit and after 28 days of treatment. Five days after discontinuation of treatment (washout) clinical parameters were re-evaluated.

At the time of enrolment and at the end of the treatment, five days after washout, all patients received Schirmer I test, Schirmer II test, B.U.T. test and bacteriological research.

Schirmer I test

It was applied a strip of absorbent graduated paper long 35 mm to the outer third of the lower eyelid and it was asked to the patient to glance up. After 5 minutes, the strips were removed and it was estimated the length of wet paper (normal values between 10 and 15 mm).

Schirmer II test

We administered one drop of anesthetic (novesina) every three minutes for three times and we proceed as Schirmer I test. After 3 minutes the strips were removed, and it was estimated the portion of paper soaked (normal >10 mm).

Test B.U.T.

Small quantity of fluores¬cein was introduced into the conjunctiva sac and, by the use of a blue filter on a slit lamp bio-micros¬cope, was evaluated the time necessary for the appearance of the first break or dry spot on precorneal tear film (normal values range 10-15 sec.)

Bacteriological analysis

It was carried out testing of conjunctiva swab Hess, to search for aerobic and anaerobic bacteria. Samples from patients were seeded in the appropriate culture medium and incubated in aerobic and anaerobic atmosphere for the isolation and identification of bacteria, with separate counts for aerobic and anaerobic bacteria.

All subjects were treated with a tear substitute next-generation alpha-lipoic acid (Tioretin - Bioos Italy) 1 drop 3 times / day for 28 days.

Statistical Analysis

The data of clinical parameters (Fig. 1) Schirmer I test, Schirmer II test and BUT obtained before and after discontinuation of treatment with alpha-lipoic acid in the two study groups are expressed as mean and standard deviation (SD). The

statistical significance of differences between the group "A" before and the group "B" after treatment was calculated by applying the statistical test "t" student.

Results

The data obtained before and after the treatment were respectively the following: Schirmer I 8.1 ± 0.2 vs. 13.5 ± 0.4 (p <0,001); Schirmer II 3.7 ± 0.1 vs. 4.5 ± 0.2 (p < 0,001); BUT 4.2 ± 0.3 vs 6.5 ± 0.2 (p <0.001). (Fig. 1).

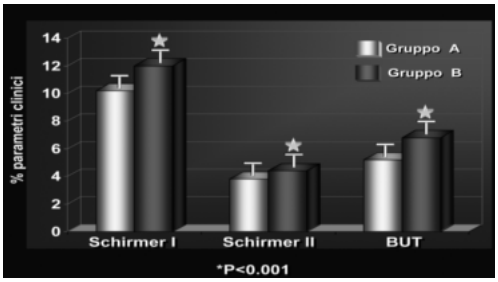

Figure 1: Statistical analysis of clinical parameters in diabetic subjects expressed the first "A" and after "B" treatment with a. alpha-lipoic acid (the fifth day after discontinuation of treatment).

Culture test showed initial bacterial growth in 37 out of 45 samples tested, corresponding to 41.1%. After treatment was found positive culture with growth of bacteria in 28 tests equal to 31.1% (table 2). The total numbers of isolations of aerobic and anaerobic bacteria found before and after treatment are shown in Table 3. A reduction of 25 to 19 strains of aerobic and anaerobic bacterial isolates from 15 to 10 has been found.

N°. Patients (45)	N°. Eyes (90)	Before		After	
		N°.	%	N°.	%
Culture test	90	37	41.1	28	31.1

Table 2: Overall incidence of culture positivity of bacteriological tests before and after treatment.

Microrganisms	Before	After
Aerobes	25	19
Anaerobes	15	10
Total strains	40	29

Table 3: Total number of aerobic and anaerobic isolates of cultures before and after treatment with alpha-lipoic acid.

Table 4 shows the species of aerobic and anaerobic bacteria found in diabetic patients before and after treatment on the fifth day after discontinuation of therapy: S. epidermidis from 30.0% to 41.4%, for the S. aureus by 17.5% to 17.2%, while for the rest of isolates showed a reduction of almost homogeneous aerobic Gram-negative before and after treatment. In the same table lists the species of anaerobic bacteria isolated before and after treatment: for Peptococcus spp. from 20.0 to 24.3%, the 6.9% to 12.5 ssp.dal Peptostreptococcus and Propionibacterium from 5 to 3.4%.

Microrganisms	Before		After	
	N°.	%	N°.	%
Aerobes				
S. epidermidis	12	30.0	12	41.4
S. aureus	7	17.5	5	17.2
S.pneumoniae	3	7.5	1	3.4
S.pyogens	2	5.0	1	3.4
H. influenzae	1	2.5	-	-
Anaerobes				
Peptococcus spp.	8	20.0	7	24.3
Peptostreptococcus spp.	5	12.5	2	6.9
Propionibacterium spp.	2	5.0	1	3.4
Total strains	40	100	29	100

Table 4: Overall incidence of culture positivity of bacteriological tests before and after treatment.

Discussion and conclusions

Type II diabetes is a disease characterized by chronic hyperglycemia that despite proper medical treatment can lead progressively to the development of chronic complications[29,30].

The link between insulin resistance and endothelial damage appear to play a pathogenic role in determining an alteration of the capillary network that prevents vascular tissue and cell tropism[31].

The tear film may be affected by these alterations too. Numerous studies have shown that in pati-

ents with type 2 diabetes there is an alteration of the tear film demonstrated by Schirmer and BUT tests[17,21,32,33].

Other authors have also demonstrated micro-angiopathic complications in patients without symptoms of dry eye and normal Schirmer test with degrees of squamous metaplasia[24].

In our study it was observed that treatment with alpha-lipoic acid induces physiological activity recovery of production the tear film.

The indirect activity of this molecule in the restoration of the normal microbiota of the eye, characterized by the increase in the percentage of bacteria normal present on ocular surface, seems to restore a good physiological ecology of the ocular surface[34,35].

The data of our study confirm a good activity of alpha-lipoic acid in enhancing the defense system of the ocular surface damage and chronic hyperglycemia probably responsible of alteration of the physiological components of the tear film[8-10].

In diabetic subjects in poor metabolic control and at risk of developing chronic complications of the disease, endothelial dysfunction could represent an important element in determining the changes in the tear film (hyposecretion, dry eye syndrome) with a high risk of eye infection[36].

Alpha-lipoic acid exerts both a direct activity that leads to normalization of clinical parameters of tear film and an indirect activity in restoring the ocular surface microbial ecology.

Further studies are needed to further clarify the role of alpha lipoic acid-the improvement of dry eye syndrome.

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