

# Examination of the conservative treatment possibility of conjunctivochalasis – A preliminary examination

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**Purpose:** Examination of the efficacy of a preservative-free, 0.015% sodium hyaluronate and isotonic glycerol containing artificial tears with especial regard to the effect on the conjunctivochalasis.

**Patients and methods:** A prospective, unmasked, one month long study with the involvement of 20 patients suffering from advanced dry eye representing a high degree of conjunctivochalasis. 16 female and 4 male patients aged  $64.0 \pm 17.8$  years participated in the study.

**Results:** After one month of use of the artificial tears, the grade of the conjunctivochalasis decreased from a mean LIPCOF score of  $2.9 \pm 0.4$  to  $1.8 \pm 0.9$  on the right, and to  $1.6 \pm 0.8$  on the left eye ( $p_{od, os} < 0.001$ ). The OSDI score indicating the subjective complaints of the patients also decreased from a mean value of  $36.2 \pm 25.3$  to  $22.6 \pm 21.9$  ( $p = 0.0008$ ).

**Conclusion:** In the course of the study, the applied artificial tears decreased the conjunctivochalasis after one month of regular use from the LIPCOF score 3 considered as indication of conjunctival surgery to 2 or less requiring a conservative therapy.

**Key words:** conjunctivochalasis, dry eye, artificial tears

## INTRODUCTION

The dry eye complaints occur in 5-30% of the population (21) and are ranked into the most frequent symptoms of the patients paying visit to the ophthalmologists' office (13, 15). The importance of this problem and its financial consequences are well indicated by the fact that 7-10 million of patients with dry eye complaints purchase artificial tears in a value of approximately 100 million US dollars in the United States annually (1).

The dry eye disease is resulted by the reduced production of the tear film and/or by the improper quality thereof. The evolution of the dry eye disease may lead through the chronic inflammation of the ocular surface to changes in the ocular surface formations. Beside the injuries of the conjunctiva and the epithelium of the cornea, the conjunctiva may sag and lipid parallel conjunctival folds (LIPCOF) may appear (20).

The severe conjunctivochalasis, the high LIPCOF degree is also considered as the reason for the dry eye disease and not only as the consequence thereof (9). The LIPCOF scores exhibit a good correlation with the subjective and objective complaints of the dry eye disease, with the severity of the disease (12), therefore in the course of our current study the main emphasis was laid on the observation of the changes in the LIPCOF

scores. The tests studying the objective symptoms and functions of the ocular surface even in the case of such an objective test method as the determination of the tear film osmolarity should be evaluated together (18), therefore in the course of our study, beside the changes in the LIPCOF degree, we determined other ocular surface parameters as well, the subjective complaints were recorded by using the OSDI (Ocular Surface Disease Index), which is considered as the method easiest to follow (16).

The therapy of the dry eye disease is mainly conservative, artificial tear eye drops are used decisively. The use of sodium hyaluronate containing artificial tears has been known for a long time, it is a safe and efficient method. The hyaluronic acid of natural origin binds the water on the ocular surface and it is a material ensuring a proper lubricant effect at the same time (14). Its effect prolonging the non-invasive tear film break up time (NIBUT) (10) and healing the epithelium injuries developed as a consequence of the dry eye disease (22) and decreasing the LIPCOF degree has been demonstrated in several studies (7).

The preservative content of the artificial tear preparations is of primary importance because of their chronic use. The effect of the benzalkonium chloride definitely damaging the vitality, barrier function of the epithelium of the

cornea is well known, however, the administration of preservative-free preparations is even more beneficial than the use of the products containing newer preservatives (23). From among the preservative-free preparations the systems operating on the nano-filtration principle are to be mentioned (19), however, because of the porous filter dripping from them may be difficult. The use of the artificial tears of daily dose packaging is simple, safe, and they do not become infected within 24 hours counted from opening (17).

In the case of severe conjunctivochalasis (LIPCOF degree 3), surgical therapy may be also necessary (25). The spectrum of the anti-conjunctivochalasis operations and their resolutions full of ideas, such as the treatment of the conjunctival folds with argon-laser (24) or with heat cauterization (11) are well known.

In the course of our study, we have observed the effects of a daily dose packaging, preservative-free, sodium hyaluronate and isotonic glycerol containing artificial tear, with special respect to its effect exerted on the conjunctivochalasis, raising the opportunity of whether the conjunctivochalasis of LIPCOF degree 3 considered as indication for surgery can be reduced with a conservative therapy to a LIPCOF score 2 or a lower one not requiring invasive therapy.

## PATIENTS AND METHODS

We have selected voluntary adult subjects applying at the general outpatient unit of the Department of Ophthalmology of the Semmelweis University into our prospective study approved by the Scientific and Research-Ethics Committee (Ref. No. 21455-1/2011-EKU).

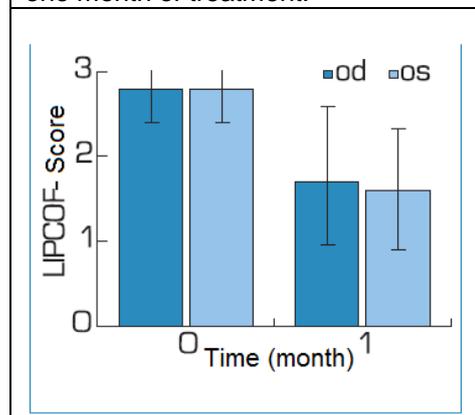
Inclusion criteria were the conjunctivochalasis of severe grade (at least LIPCOF degree 2) and the lissamine green staining of minimum grade 1 on the Oxford scale, indicating a more advanced dry eye disease. As exclusion criteria, pregnancy and lactation, pterygium, prolonged treatment with eye drops with the exception of artificial tears, active allergic keratoconjunctivitis, keratitis of infectious origin and conjunctivitis, respectively, and operation affecting the eye surface as well as injuries occurred within 3 months before starting the treatment were given. The previous prolonged treatment with artificial tears was not an exclusion criterion, all our patients have regularly used artificial tears already before starting the study. Our patients selected into stopped the use of their earlier artificial tears 3 days before the first visit.

In our study, 20 voluntary subjects gave their informed consent to the examination. Among the participants there were 16 female and 4 male patients with a mean age of  $64.0 \pm 17.8$  years (between 25 and 85 years of age).

At the inclusion visit, 0.015% sodium hyaluronate and isotonic glycerol containing, preservative-free artificial tears of daily dose packaging (Conheal®) provided by Pannonpharma Ltd. was given to our patients which they dropped into their both eyes four times a day for one month.

At the first visit, the best corrected visual acuity, the degree of conjunctivochalasis, the extent of the injuries of the conjunctiva and cornea with lissamine green staining and the tear film break-up time on both eyes were determined. Their subjective complaints, the impact of the dry eye complaints on their everyday life were recorded with the aid of the OSDI questionnaire (16). After expiration of the one-month study time, our patients were subjected to the same examinations.

Figure 1: Value of the conjunctivochalasis (mean and standard deviation) on the right and left eyes before treatment and after one month of treatment.



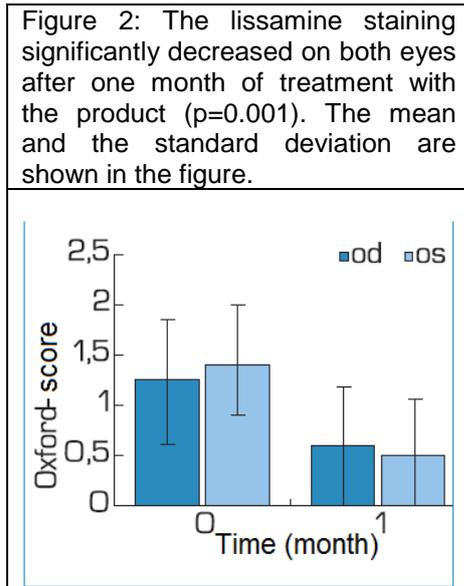
The severity of the conjunctivochalasis was determined in terms of LIPCOF degrees according to the Höh method (4). The lissamine green staining was evaluated according to the Oxford scale. The tear film break-up time was measured in a standard way with the aid of fluorescein. Our patients were asked to fill out the OSDI questionnaire translated into Hungarian with their own hands after receiving the general instructions.

The results found before and after one month of treatment were compared by using the Statistica 8.0 software (StatSoft Inc., Tulsa, OK, USA) with a non-parametric probe (Wilcoxon pairwise t-test), while the differences

in the changes of the two eyes were compared with t-test.

## RESULTS

After one month of properly scheduled treatment with artificial tears containing 0.015% sodium hyaluronate and isotonic glycerol regularly instilled four times a day, both the subjective and objective symptoms of our patients improved.



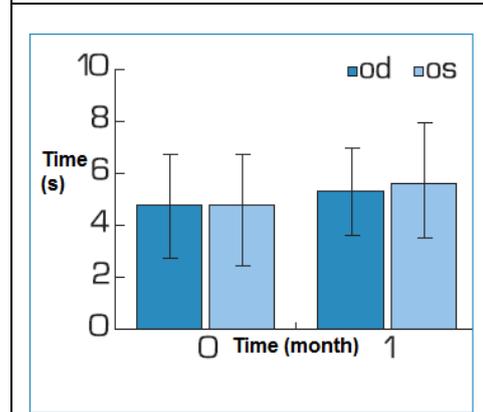
The degree of the conjunctivochalasis was  $2.9 \pm 0.4$  on the average on both eyes on enrolment, which was reduced to  $1.8 \pm 0.9$  on the right eye and to  $1.6 \pm 0.8$  on the left one. Between the results found on the inclusion and on the control after one month, a significant difference could be observed ( $p_{od}=0.0004$ ,  $p_{os}=0.0002$ ), while no significant difference could be found between the decrease in the LIPCOF scores on the two sides ( $p=0.3$ ) (Figure 1). In 19 cases of the 20 patients, a decrease in the LIPCOF scores could be recorded. In the case of one patient, there was no change in the LIPCOF-degree.

At the first visit, with lissamine green staining, a mean staining of  $1.3 \pm 0.6$  on the right eye and of  $1.4 \pm 0.6$  on the left eye according to the Oxford scale could be observed which was significantly ( $p=0.001$ ) decreased to a staining of  $0.6 \pm 0.6$  and  $0.5 \pm 0.6$ , respectively, by the end of the first month (Figure 2). There was no significant difference between the changes on the right and left eyes ( $p=0.4$ ).

The tear film break-up time of  $4.8 \pm 1.9$  seconds on both eyes at the beginning increased with an average of 16% to  $5.4 \pm 1.6$  seconds on the right eye and to  $5.7 \pm 2.1$  on the left one

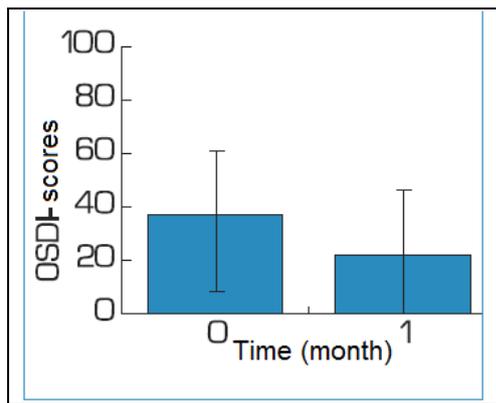
( $p_{od}=0.003$ ,  $p_{os}=0.007$ ) (Figure 3). No significant difference could be found between the changes on the two eyes ( $p=0.4$ ).

Figure 3: The tear film break-up time was prolonged with 16% on the average on both eyes after one month of regular use of the artificial tears ( $p_{od}=0.003$ ,  $p_{os}=0.007$ ). The error lines show the standard deviation.



On the enrolment, the subjective complaints measured with the OSDI questionnaire could be quantified as  $36.2 \pm 25.3$  on the average, which was reduced to a value of  $22.6 \pm 21.09$  by the control after one month ( $p=0.0001$ ) (Figure 4). The high standard deviation is resulted by the broad spectrum of the OSDI data, in 18 cases of the 20 patients a decrease could be experienced. With one patient the OSDI showed a growth of one point, while with one patient it remained unchanged. During the study period no complaint, no adverse reaction was reported.

Figure 4: In the figure, the mean and the standard deviation of the OSDI scores are shown displaying its impact on the subjective complaints and the complaints' impact on the everyday life. The OSDI scores showed a significant decrease by the end of the first month ( $p=0.0002$ ).



## DISCUSSION

In the course of our study carried out with the preservative-free, 0.015% sodium hyaluronate and isotonic glycerol containing artificial tears, our finding was that after already one month of use the Conheal® eye drops significantly decreased the number and severity of the conjunctival folds, the LIPCOF score decreased from the 3 considered as surgery indication to 2 or a lower a degree. Besides, attributable to the regular dripping, the corneal epithelial defects of the patients ceased, their subjective complaints have improved. The patients having earlier used other artificial tears, beside the improved objective symptoms, were satisfied subjectively as well. During the study, no complaint, no adverse reaction was reported by the patients.

From among the received results, the effect of the artificial tears exerted on the conjunctivochalasis, which was drawn up as the purpose of the study and is the main point of our paper, is accounted as a novelty in the literature. The LIPCOF score decrease has been earlier described in the evaporative dry eye diseases upon the effect of the treatment with lipid containing eye spray or eye drops, respectively (2, 5, 7, 6), however, we were the first who demonstrated the decrease of conjunctivochalasis with the patents suffering from keratoconjunctivitis sicca upon the effect of the treatment with eye drops not containing lipids. This result calls the attention to the fact that there is such a conservative therapy in the case of the severe conjunctivochalasis, which leads to the reduction of the LIPCOF score. Beside the artificial tears applied in the course of the study, the LIPCOF score 3 considered as indication for surgery becomes controllable with conservative therapies known until now as well, resulted in essentially less complaints.

Our further results are in agreement with the results of the clinical studies performed with artificial tear preparations of similar composition. Similarly to the earlier studies

carried out with sodium hyaluronate containing products, the tear film break-up times obtained by us showed an improvement (an increasing tendency) (10), the injuries developed because of the chronic harms to the corneal epithelium were reduced (22). Similarly to our results, prolongation of the tear film break-up time was recorded with isotonic glycerol containing artificial tears as well (6). The subjective complaints of the patients measured with the OSDI questionnaire (16) ensuring a good follow-up have decreased which correlates well with the degree of the conjunctivochalasis (12), as it was described by *Németh et al.* Our patients having used other artificial tears regularly earlier were also satisfied subjectively, beside their improved objective symptoms.

It is known from the literature that in conjunctivochalasis of severe degree and lissamine green staining the HLA-DR level is elevated (3). The possibility is arisen that the artificial tears investigated by us – attributable either to its hyaluronate or glycerol content - reaches the decrease in the severity of the conjunctivochalasis through lowering the HLA-DR level.

The special composition of the artificial tears enhances its long-term tolerability to a high extent. The use of the sodium hyaluronate in the artificial tear preparations is known for a long time and is safe (14). The preservative-free artificial tears are the less harmful to the corneal epithelium (23). The containers of the artificial tears of daily dose packaging do not become infected while using up within 24 hours as indicated in the instructions for use (17). It may be resulted by these favourable parameters that no complaint, no adverse reaction was reported by the patients during the study period.

The primary symptomatic treatment of the dry eye syndrome is represented by the administration of artificial tears. However, the severe conjunctivochalasis of LIPCOF score 3 already means the indication for operative treatment (25).

## CONSEQUENCES

The preservative-free Conheal® artificial tears administered four times a day in the course of our study resulted in a significant change on the ocular surface already after one month of regular use. The degree of the conjunctivochalasis associated with severe dry eye complaints has decreased from the LIPCOF score 3 representing an indication for surgery to LIPCOF score 2 or to a lower degree which means a status controllable with

conservative therapy. The clinical importance of this change is well demonstrated by the fact that the subjective complaints of the patients have significantly improved as well. The fact that in spite of the use of other artificial tears for a long time the patients participated in the study got to the LIPCOF score 3 degree, while by using the investigational eye drops, already after one month of use, they showed a

significant improvement, clearly proves the special effect of the investigational product.

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