Treatment of the dry eye in case of lipid phase deficiency

Brandl H.
Ophthalmologist, German Air Force - Institute of Aviation Medicine, Fürstenfeldbruck

Introduction

Dry eye is the most frequent eye disease worldwide. Due to this high frequency, dry eye is an urgent problem also in the field of aviation medicine.

According to the well-established definition in the international literature, dry eye is a disorder of the tear film due to tear deficiency or excessive tear evaporation which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort [1].

Tear film deficiencies always reduce the quality of vision.
There are high demands on the vision of servicemen of the military flying service of the German Air Force. Therefore dry eye and especially the choice of treatment are significant issues.

The tear film has traditionally been described as a trilaminar structure:

The inner mucin component is a thin mucous phase adhering on the ocular surface. Its main function is to merge the tear film and the hydrophobic ocular surface. The majority of mucins are produced by the conjunctival goblet cells.

The aqueous phase of the tear film is midway and in terms of size is the main part. The roles of the aqueous layer are lubrication, nutrition and protection of the cornea. It consists of water and contains the substances required for nutrition and defence, such as proteins, vitamins and electrolytes. The lacrimal glands produce the aqueous phase. It has been established that aqueous phase deficiency alone is only rarely associated with dry eye. In fact it has been observed in only 8 % of the patients [2].

The superficial lipid layer covers the surface of the tear film and is produced by the meibomian glands in the eyelids. The lipid secretions are delivered through orifices onto the lid margin. An intact lipid phase reduces aqueous evaporation on 90 - 95% [3]. Moreover, it provides tear film stability, prevents spillover of tears over the lid margins (“tearing eye”) and provides a smooth surface of the tear film which is important for its optical quality.
Lipid layer deficiencies were observed in just under 80 % of the patients [2] and are regarded as basic cause of dry eye [4].

The major problem of dry eye is the excessive aqueous evaporation predominantly caused by disturbances of the tear film lipid layer.

Wearing contact lens further increases evaporation [5], because the lipid layer is disrupted by the contact lens.
Therefore, it seems to be unsurprising that more than 50 % of contact lens wearers complain about symptoms of dry eye [6].

Also the poorer quality lipid layer may predispose to symptoms of dry eye after LASIK surgery [7].

In addition, various air pollutants affect the tear film lipid layer [8].

In the civilian as well as the military aviation the problem of excessive evaporation is aggravated by unfavourable environmental conditions, wherefore the typical symptoms occur frequently and with greater intensity:
A defined barometric pressure is generated in the aeroplane cabin by compression of air in the engine. Due to the technical compression of the outer air, relative humidity inside the cabin amounts to just 8 to 14 % [9]. This intensifies the excessive evaporation even further.
Higher humidity levels correspond to lower evaporative rates [10]. A study demonstrated significant changes of the lipid layer following alterations in the environmental humidity, although the mechanism whereby this process occurs remained unclear. However, it is presumed that an increase of the environmental humidity level allows improved spreading of the lipid on the tear film [11].

In this study, the efficiency of the treatment with phospholipid-liposomes was tested in patients suffering from dry eye focussed on lipid deficiency.

Methods

42 servicemen of the flying service of the German Air Force Institute of Aviation Medicine at Fürstenfeldbruck participated in the study.

The age of participants varied between 29 and 54 years. Only patients on whom a dysfunction of the lipid layer was ascertained to be causal or concurrently causative were included in the study.
Dysfunction of the lipid layer was diagnosed by a reduced tear film break-up time and by slit lamp examination of the eyelids, particularly with regard to inflammation of the anterior or posterior lid margins (chronic blepharitis) [12].

Patients were instructed to apply the liposomal eye spray tree times per day onto the closed eye. The study spanned a period of nine months. Check-ups were carried out at intervals of four weeks, three months, six months and nine months.
Amongst others the measurement of tear film break-up time (BUT), Schirmer`s I test and slit lamp examination of the eyelids were carried out in the check-ups. In addition, the patients were interviewed about their subjective sensations.

Results

As a result of the interviews it was observed that 35 patients (83.3 %) had suffered dry eye complaints for more than one year and that they had already applied various lubricants. These participants indicated that previous treatments had not resolved the condition.
Seven patients had not started any treatment before beginning of this study.

Subjective rating

The patients unanimously characterised the performance of TEARS AGAIN® eye spray as good or very good. The patients identified the key attributes of TEARS AGAIN as, firstly, the fast speed of action and, secondly, the long duration of relief obtained.

All the 45 patients were satisfied with the achieved recovery.

The new application with a spray on the closed eyelid was considered to be very convenient, particularly since the handling is quick and easy.

Moreover, patients thought it was positive that vision was not even temporarily affected after application of the liposomal eye spray. This is a common complaint when applying the lubricants in gel-form as previously used by many of the participants.

Objective results

A clear increase in tear film break-up time (BUT) was observed within a few minutes of application of the phospholipid-liposomes.
Whereas in the beginning of the study nine patients (21.4 %) had a BUT below 5 seconds and 31 patients (73.8 %) had a BUT between 5 to 10 seconds, a significant extension and stabilisation of the BUT was observed in the check-ups.
After nine months, the BUT of none of the patients was still below 5 seconds, the BUT of only two patients (4.7 %) was found to be between 5 to 10 seconds.

The tear volume measured by the Schirmer`s I test also increased during the period of examination.
At the beginning of the study, the wetting of the test strip of 19 patients (45.2 %) showed a value below 5 mm within 5 minutes and 20 patients (47.6 %) had a value between 5 to 10 mm within 5 minutes.
In the end of the study only one patient (2.3 %) was found to have a value below 5 mm within 5 minutes.

Whereas, in the beginning of the study the value of only 3 patients (7.2 %) was above 10 mm within 5 minutes, 14 patients (33.3 %) achieved this value only after four weeks treatment and 19 patients (45.2 %) achieved this value in the end of the study.

Chronic blepharitis, which was ascertained in all patients, was clearly reduced after just four weeks of treatment, at which time 16 patients (38.1 %) still showed an inflammation of the lid margin.
By the end of the study, inflammation of the lid margin – a typical characteristic of this condition – was no longer detected in any patient under slit lamp examination.

Discussion

Evaporation rate does not explicitly correlate with lipid layer thickness [13, 14].
It is not the thickness but rather the stability of the lipid phase which is crucial for an effective reduction of evaporation.

Today, the lipid phase itself is differentiated between an outer, thick non-polar phase and a thin polar phase adjacent to the aqueous phase [15].
In simple terms, only the surfactant polar phase enables the non-polar lipids to spread over the tear film, since neutral fat (non-polar lipids) and water reject each other.
Evaporative dry eye is associated with a defect in polar lipids [16]. The polar lipids predominantly consist of phospholipids [17].
The instability of the lipid layer is not primarily caused by insufficient lipid secretions [18], but rather by a faulty composition of the lipid secretion and the consequent polar lipid deficiency, particularly in patients with chronic blepharitis.

Moreover, the spreading and stability of the lipid layer is enhanced by the tear protein lipocalin which forms complexes with polar lipids [20].
Since there is an age-related decrease in lipocalin [21], stabilisation of the polar phase seems to be of greater importance when treating the dry eye.

Interestingly the application of artificial tears actually increases evaporation [22].
Therefore, the application of such artificial tear preparations seems to be out of question in case of lipid deficiencies, because this would further aggravate the real problem of excessive evaporation.

In contrast, the new therapy concept with the liposomal eye spray (TEARS AGAIN®) has proved to be very efficient for treatment of lipid deficiencies, as seen in both subjective and objective measures presented in this study.

The phospholipids in form of liposomes are sprayed on the eyelids. There they will mix with the meibomian lipid secretions on the lid margins, whereby a polar lipid deficiency could be equalised, so that the required stability of the lipid layer will be provided.

It is noteworthy that the inflammations of the lid margins (chronic blepharitis), which are difficult to manage successfully, disappeared – as a secondary effect – thanks to the liposomal eye spray and without any additional treatment.

The results presented in this study correspond to the results of a double-blind study, which was performed with the preparation TEARS AGAIN® and which were published recently [23].

Conclusions

As already proposed by other authors, the liposomal eye spray TEARS AGAIN®, whose efficiency here was proved again, is to be considered the preparation of choice for treatment of the dry eye, since lipid layer deficiencies are the major cause of dry eye in almost 80 % of patients.

From the point of view of aviation medicine, the preparation can be recommended without reservation since dry eye occurs very frequently in aviation due to the environmental conditions described in the introduction.
In addition, the eye spray not only provides the important advantage of maintaining complete vision, but even improves vision slightly due to the stabilisation of the lipid layer and this is an advantage of crucial importance to the crews of the flying service.

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