

TEAR OSMOLARITY IN PATIENTS WITH LAGOPHTHALMOS

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SUMMARY

Introduction: Lagophthalmos can be characterized as the dysfunction of the eye aperture and in some cases even by the disruption of tear production. Dry eye syndrome can consequently develop. Instability of the tear film, hyperosmolarity and inflammatory reaction are considered as the key mechanisms of dry eye syndrome. In our report we monitored the tear osmolarity of patients with postsurgical unilateral lagophthalmos. Results were compared with tear osmolarity of the non-lagophthalmic eyes.

Methods: We examined 10 patients (6 women, 4 men) with postsurgical facial nerve palsy and lagophthalmos complicating management of either cerebellopontine (8 patients) or salivary gland tumors (2 patients). Only patients without severe corneal defects enrolled the study. The tear osmolarity was measured in lower tear meniscus by TearLab Osmolarity System device. The lagophthalmic eye was always examined first. The results are presented as mean plus/minus the standard deviation. The paired t-test was used for statistical data processing. The p-value $\leq 0,05$ was considered as statistically significant.

Results: The mean tear osmolarity of the lagophthalmic eyes was $296 \pm 15,0$ mosmol/l (275–315 mosmol/l). In case of healthy eyes the mean osmolarity was 310 ± 12 mosmol/l (292–336 mosmol/l). The tear osmolarity in case of lagophthalmos was significantly lower than in the healthy eyes ($p = 0,05$).

Conclusion: In contrary to the studies demonstrating higher tear osmolarity under the scenario of dry eye syndrome, we found lower tear osmolarity in the lagophthalmic eyes than in the healthy eyes. The possible reason could be the changes in tear dynamics of the lagophthalmic eye due to disturbance of eye lid function. Our results also stress the need of evaluation of the actual tear osmolarity in the view of complex clinical eye findings. The place of tear collection should also be considered.

Key words: lagophthalmos, dry eye syndrom, tear osmolarity

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INTRODUCTION

Homeostasis of the ocular surface is secured by a complex system composed of the tear gland, the surface tissue of the eye (meibomian glands, conjunctiva, cornea), the eyelids, and the sensory and motor innervation of these components. The system is named the lachrymal function unit (14, 15). Dysfunction in any of its components may influence homeostasis of the entire system and impair its function, which has the consequence of leading to subjective symptoms of discomfort and development of dry eye syndrome (DES).

DES is a chronic pathology characterised by a marked variability of clinical symptoms. Instability of the lachrymal film, hyperosmolarity of tears and development of secondary inflammation are considered key mechanisms in the development of DES (3, 2, 8). In healthy individuals osmolarity of the lachrymal film is within the range of 289–304 mosmol/kg (7, 19). In patients with DES the values are higher, a value of 316 mosmol/kg is usually considered beyond the limit value of severe DES (13, 16, 20), but values as high as 440 mosmol/kg have been measured (6). At the same time, however, it is known that the real value of tear osmolarity may fluctuate substantially in different locations on the ocular surface (1, 9).

Lagophthalmos is a condition which results in the impairment of the ability or complete inability to close the ocular aperture. This leads to a malfunction of distribution of the lachrymal film. A part of the conjunctiva and cornea remains constantly exposed, in which the surface of the eye is unevenly moistened with tears, which evaporate more rapidly. The condition leads to drying of the cornea, the occurrence of epitheliopathy, exposure keratitis or corneal ulcer, with subsequent pronounced deterioration of the visual functions of the afflicted eye. In extreme cases the cornea may even perforate. Typical symptoms of lagophthalmos include a feeling of dry eye, a feeling of sand in the eye and lachrymation, or a feeling of blurred vision (18).

According to the classification of the DEWS (Dry Eye Workshop 2007), lagophthalmos can be ranked among pathologies of the ocular surface. Secondly it causes DES due to evaporative causes, i.e. DES caused by increased evaporation of tears due to the influence of pathology of the ocular aperture (3, 2). Dysfunction of the eyelids also leads to a breakdown of the normal function of the meibomian glands. In certain cases, when lagophthalmos occurs on a background of disorder of the nervus facialis (n.VII), innervation of the eye and the tear gland may be impaired by fibres of the parasympathetic nervous system, with im-

pairment of the reflexive curve maintaining homeostasis of tear formation (5, 17). The result is a malfunction of tear production (3, 2).

In our study we observed tear osmolarity in the lower tear meniscus in patients with postoperatively occurring lagophthalmos and compared the values with the osmolarity value in the healthy eye.

Cohort of patients and method

Within the framework of the study we examined 10 patients (6 women, 4 men) following surgery on a tumour of the cerebellopontine angle (7 patients with vestibular schwannoma and 1 patient with epidermoid – cholesteatoma) and a tumour of the thyroid gland (2 patients with pleomorphic adenoma of the thyroid gland), in whom the n.VII was afflicted with subsequent unilateral lagophthalmos. The second intact eye served as a control. An examination was conducted on average 14 months after surgery (earliest 2 months and latest 87 months, i.e. 7 years after the operation).

The size of lagophthalmos was within the range of 3-9 mm. The degree of damage to the eye, evaluated with the help of vital staining fluorescein (Oxford schema, 3), reached an average of 4.1 ± 3.0 (within the range of 0-11) in the eyes with lagophthalmos, and 0.4 ± 0.8 in the healthy eyes (within the range of 0-2).

Best corrected visual acuity (BCVA) of the eyes with lagophthalmos was within the range of 0.3-1.0. BCVA of all healthy

eyes was 1.0-1.5. All the patients had a pacific appearance of the surrounding area of both eyes and the adnexas, without oculomotor malfunction, with isocoria and normal direct and indirect photoreaction of the pupils. Intraocular pressure was within the range of normal values (10-19 torrs, the average value in eyes with lagophthalmos was 14 torrs and in healthy eyes 16 torrs).

In six patients external partial tarsorrhaphy had been indicated previously. Locally the patients were using only preparations of the type of artificial tears in drops or grease according to individual requirement. Patients with a further ocular pathology of the anterior segment of the eye who additionally used another local therapy were excluded from the study.

For all patients tear osmolarity was examined in the lower tear meniscus using the instrument TearLab Osmolarity System (TearLab Corp, San Diego, California, USA). The examination was conducted in the morning hours, always at least 2 hours after the last application of preparations of the type of artificial tears, according to the instructions of the manufacturer. The lagophthalmic eye was always examined first. The findings in the eye with lagophthalmos were compared with the finding in the healthy eye. The results are presented as the average \pm standard deviation. A pair t-test was used for the statistical processing. The value of $p \leq 0.05$ was considered to be the statistically significant level.

Table 1 Characteristics of cohort and osmolarity values

Patient	Sex	Dg	Age of patient (years)	Time from surgery (months)	Staining FR	BCVA	IOP (torr)	Lago (mm)	Tars	Osmo (mosmol/l)
1	F	VS	71 years	14	2-2-2 0-0-0	0,5 0,67	11 17	9	-	283 314
2	F	E CPA	61 years	2,5	0-0-0 1-1-1	1,0 0,67	15 16	5	-	336 301
3	F	VS	57 years	2,5	0-1-1 0-0-0	0,5 1,0	14 16	5	+	293 318
4	F	Adenoma of PG	29 years	2	0-1-0 0-0-0	1,0 1,5	13 14	3	-	309 308
5	M	VS	54 years	3	2-3-2 0-0-0	0,67 1,0	19 18	3	+	283 310
6	M	Adenoma of PG	51 years	3	0-0-0 0-0-0	0,67 1,0	18 16	6	+	304 302
7	F	VS	67 years	18	1-3-1 0-0-0	1,0 1,0	12 17	6	-	315 307
8	M	VS	36 years	87	2-3-2 0-0-0	1,0 1,0	10 13	4	+	315 292
9	F	VS	65 years	3	3-5-3 1-0-1	0,3 1,0	15 16	6	+	275 303
10	M	VS	74 years	3	2-0-2 1-0-1	0,4 0,79	16 18	6	+	276 318

BCVA – best corrected visual acuity, E – epidermoid, Dg – diagnosis, FR – fluorescein, Lago – lagophthalmos, M – male, F – female, CPA – cerebellopontine angle, IOP – intraocular pressure, Osmo – osmolarity (mosmol/l), PG – parotid gland, VS – vestibular schwannoma, Tars – tarsorrhaphy, highlighted in bold – eye with lagophthalmos

RESULTS

The average tear osmolarity value in the entire cohort of eyes with lagophthalmos was 296 ± 15 mosmol/l (275-315 mosmol/l), and in the healthy eyes 310 ± 12 mosmol/l (292-336 mosmol/l). The value was statistically significantly lower in the case of lagophthalmos ($p=0.046$).

The tear osmolarity value did not differ clinically in 2 patients following surgery on a tumour of the thyroid gland (no. 4 and 6). The osmolarity value was higher in the lagophthalmic eye in 2 patients (no. 7 and 8), in whom the malfunction of the n.VII was however older than 18 months (see table no. 1, graph no. 1).

DISCUSSION

The lachrymal film forms a very thin, approximately 3 μ m thick layer on the ocular surface. However, it plays a fundamental role for the optical system of the eye, ensures nutrition and protection, and supports the differentiation of superficial epithelial cells (13).

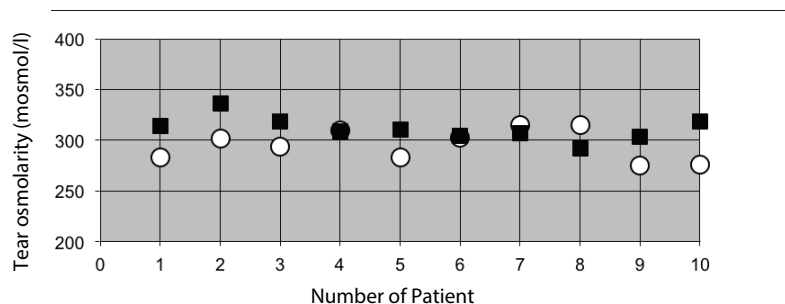
Instability of the lachrymal film, together with hyperosmolarity of tears, is considered a fundamental mechanism in the origin of DES (1, 2, 3). It is assumed that instability of the lachrymal film is caused as a consequence of increased evaporation, which also leads to an increase of tear osmolarity in the given location. Hyperosmolarity represents stress for the superficial cells. The result is the production of local agents and the incidence of secondary inflammation (10).

Tears are primarily secreted as an isotonic fluid in comparison with plasma (approx. 300 mosmol/l) (10). However, the final tonicity of tears is influenced by a range of factors: the quantity of produced tears, the movement of the tears around the ocular surface, the integrity of the lipid layer of tears, size of the ocular aperture, direction of gaze, temperature, moisture and flow of surrounding air and frequency of blinking. The measured value is also influenced by the location in which the sample of tears is taken (19). Mathematical models exist focusing on the movement of tears around the ocular surface, from which it is also possible to deduce changes of osmolarity in individual areas (1). In healthy persons the measured osmolarity value was lowest in the upper fornix (289 mosmol/l), and was somewhat higher

in the lower meniscus (304 mosmol/l) (10). In the exposed areas of the conjunctiva and cornea osmolarity may fluctuate markedly depending on the movement of the eyelids and distribution. In areas with an unstable and diminished lachrymal film, it may reach values of up to 3000 mosmol/l (1). Models work with the fact that in areas with a thin lachrymal film, proportionally more pronounced losses of water take place due to the influence of more pronounced evaporation, whilst at the same time there is an unchanged number of dissolved particles than in areas with reservoirs of tears, such as the lower tear meniscus. This "reservoir" is larger due to the influence of the reduced tension of the muscles of the eyelids in patients upon paresis of n.VII. This could explain why the osmolarity value in our patients was lower in the eye with lagophthalmos than in the healthy eye, and approached the value of primarily secreted tears.

A further factor may be the altered regulation of tear formation. The nervous regulation responsible for the secretion of the tear gland is an integral component of the functional unit of the tear gland, which is composed of sensory afferent nerves of the cornea and conjunctiva, efferent fibres of the parasympathetic and sympathetic nervous system, innervating the tear gland and the accessory tear glands, the tissue of the conjunctiva, cornea and tear drainage pathways (4). Of the effector systems, intact parasympathetic innervation has a fundamental role in the maintenance of a normal composition and quantity of the formed tears (13). In rabbits in whom preganglionic interruption of parasympathetic innervation was applied in an experiment, on the first day there was a decrease in the amount of formed tears to 30% of the values before the procedure, and this decrease persisted for a minimum of one week during the period of the experiment (17). Upon postganglionic denervation of the tear gland there was a decrease of the overall concentration of proteins in the tears, and a change of their composition (12).

However, the precise mechanism controlling the secretion of tears is not yet known (11, 17). In all cases, the cause of lagophthalmos in our patients was perioperative interruption of n. VII. In eight patients there was a breach of the nerve as a consequence of surgery in the cerebellopontine angle, and it is therefore possible to presume a preganglionic lesion of the parasympathetic fibres. It is worth noting the fact that in two patients (no. 4 and no. 6), in



Graph 1 Tear osmolarity values in lagophthalmic and healthy eye

whom the reason for the operation was parotid salivary glands, the tear osmolarity values measured in the healthy eye and in the eye with lagophthalmos were practically identical. In these patients there was a breach of the nerve beyond the interval of the branch innervating the tear gland. Even though the parasympathetic nervous system has a majority influence on the secretion of the tear gland, the sympathetic nervous system, hormones and a range of other factors, often locally produced and not entirely mapped agents, such as the group of epidermal growth factors (EGF) also share in the regulation of secretion and composition of tears (4, 10). Impairment of the balance of stimuli may also influence the regulation of secretion and composition of tears, and may be the reason for changes of their osmolarity. Furthermore, little is known about the secretion of electrolytes and water by the accessory tear glands, corneal and conjunctival epithelial cells and the regulation thereof (13). It is possible that over a longer time frame, interruption of parasympathetic innervation may lead to a partial development of compensatory mechanisms, primarily in the production of water components, although a malfunction of the regulation of tear composition persists, which influences the osmolarity value. A higher osmolarity value in the lagophthalmic eye in our cohort appeared in two patients, in whom lagophthalmos had persisted for 18 months or longer.

Long-term persisting malfunction of the eyelids and locally acting incipient hyperosmolarity of tears in certain areas due to the influence of impaired tear distribution may progressively lead to the development of damage to the ocular surface, the development of chronic inflammation, an exhaustion of compensatory mechanisms and the onset of a vicious cycle with classic symptoms of DES, including hyperosmolarity of secreted tears.

A limitation of our study is the fact that patients used

artificial tears. This concerns the first results of a prospective observation study and the frequency of use of preparations of the type of artificial tears was not regulated in any way. Under normal circumstances, locally applied substances persist in the lachrymal film only for a short period of time (10). In accordance with the instructions of the manufacturer and further studies evaluating tear osmolarity in patients with DES, patients were measured minimally 1.5-2 hours after the application of artificial tears. However, in patients with lagophthalmos the lachrymal pump, which normally contributes to the removal and renewal of tears, is also impaired due to the influence of the interrupted innervation of the eyelid muscles. It is therefore not possible to exclude the possibility that artificial tears persist especially in the lower tear meniscus for a longer time, and may thus influence the values of measured osmolarity. However, despite the probable individual differences in the frequency of application of artificial tears, the results are surprisingly uniform. Further research is required on a larger cohort of patients with lagophthalmos in order to provide a more detailed clarification of the potential influence of the fundamental diagnosis and use of artificial tears on values of measured tear osmolarity in these patients.

The results of our study also indicate the fact that despite substantial progress in understanding the significance of tear hyperosmolarity in the origin of pathologies of the ocular surface, it is always necessary to evaluate the current value of tear osmolarity in connection with the complete ocular finding, and to take into account also the place from which the sample of tears is taken.

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