

Hyaluronic acid gel implants for correction of pathological conditions of the orbit and eyelids

Y.O. GRUSHA^{1,2}, V.A. SHEPTULIN¹, J.U. PRAUSE³, S.S. DANILOV¹

¹Research Institute of Eye Diseases, 11A Rossolimo St., Moscow, Russian Federation, 119021; ²I.M. Sechenov First Moscow Medical University, 8-2 Trubetskaya St., Moscow, Russian Federation, 119991; ³Eye Pathology Institute, University of Copenhagen, 10 Nørregade, Copenhagen, Denmark, 1165

Purpose — to evaluate the effectiveness of injectable implants made of hyaluronic acid gel (HAG) in ophthalmoplastics. **Material and methods.** The study included 57 patients (37 patients with lagophthalmos related to acute or chronic facial nerve palsy, endocrine ophthalmopathy; 20 patients with enophthalmos, anophthalmic syndrome). Depending on filler particle size, the patients received either intrapalpebral or intraorbital HAG injection. The biometric measures of palpebral fissure, the position of the eye/implant, and the condition of the cornea were evaluated during the follow-up period (12 months for eyelid and 18 for orbital injection). **Results.** In the course of the follow-up, all patients showed reliable reduction of lagophthalmos; additionally, improvement of the condition of the cornea was observed in patients after intrapalpebral injection; patients after intraorbital injection exhibited reduction in enophthalmos, upper orbital palpebral fold retraction and upper eyelid excursion. No serious complications have occurred after the injection. **Conclusion.** As minimally invasive method of treating various pathologies of the orbit and eyelids, HAG fillers showed good clinical effectiveness and safety.

Keywords: fillers, injectable implant, hyaluronic acid gel, lagophthalmos, enophthalmos, anophthalmic syndrome.

Vestnik_Oftalmologii_2018-5(1)_061EN

At present, fillers (injectable implants) made of hyaluronic acid gel (HAG) are effectively used by not only cosmetologists but also cosmetic surgeons. They help with aesthetic defects caused by soft tissue deficit after traumas or surgeries.

There have been a number of studies in both Russian and foreign literature in the past decade concerning effectiveness and safety of HAG with small particles (particle diameter of 400 µm) in the treatment of various pathological conditions of the eyelids (retraction, positional abnormalities) accompanied by lagophthalmos [1–3], as well as with particles of large diameter (2000 µm) used for minimally invasive correction of enophthalmos and anophthalmic syndrome [4–7].

In these studies, however, the duration of injection effect varied, only isolated cases were reported, no patient randomization by pathology was done; potential complications and their prevention were not considered in sufficient detail. In view of the above, the present study is aimed to evaluate the effectiveness of the procedure and the duration of its effect, and to reveal the possible complications of the minimally invasive correction of various pathological conditions of the eyelids and/or the orbit with fillers made of HAG.

Material and methods

The study included 57 patients with various pathological conditions of the eyelids and/or the orbit who were examined and treated at Research Institute of Eye Diseases (Moscow). The patients were divided into two main groups. The first group consisted of 37 patients with lagophthalmos of varying etiology; the second group included

20 patients with enophthalmos or anophthalmic syndrome.

The present study used fillers made of stabilized hyaluronic acid gel Restylane® (Galderma Nordic AB, Sweden) in two different modifications: with 400 µm particles (100 000 particles in 1 mL) for eyelid injections, and 2000 µm particles (1000 particles in 1 mL) for intraorbital injections.

The study was approved by the local ethics committee of Research Institute of Eye Diseases (protocol №18 dd. 17.02.2014) and the interuniversity ethics committee of the association of medical and pharmaceutical universities (protocol №09-09 dd. 18.11.2009).

Injection technique. Patients of the first group received intrapalpebral injection by a new revision of the previously proposed technique [3]. The filler was injected on the reverse movement of 27G cannula or needle under palpebral or preseptal part of the orbicular muscle of the eye under local anesthesia (lidocaine + prilocaine) and local hypothermia (cooling pack) of the upper eyelid area. Immediately after the injection, circular motions were applied to spread the filler evenly in order to prevent it from contouring under the skin. The injection was performed with the patient in sitting position in order to be able to perform visual evaluation of the achieved effect during the process (**Fig. 1, a**).

In the second group, the filler was injected intraorbitally using authors' original technique. The patient is lying on his back under local infiltration anesthesia (0.2 mL

Contact information:

Sheptulin Vladimir Arkad'evich — Candidate of Medical Sciences, Researcher at the Department of Orbital and Ocular Reconstructive Surgery
e-mail: vsheptulin@gmail.com

Ultracaine solution); his tarsal orbital fascia is perforated in the lateral third of the lower eyelid in the projection of lower orbital edge at 90° angle by a knife or 18G needle of 1–2 mm diameter. Along the lower orbital wall a 21G cannula with its hole oriented upwards is injected up to half-length without touching the periosteum. The filler is injected extraconally, slowly, during the backward motion of the cannula rotating it counter-clockwise. The achieved effect of the injection was controlled by comparing it with the intact side (see Fig. 1, 6).

In addition to standard examination (visometry, tonometry, biomicroscopy), patients of the first group underwent dynamic photoregistration performed using digital cameras Canon EOS 5D and 10D, their palpebral fissure was measured – including the size of lagophthalmos, its position (margin-to-reflex distance test 1 (MRD1)) and excursion of the upper eyelid before and after the injection. In the second group, patients had enophthalmos and hypophthalmos/prosthesis retraction measured using Hertel exophthalmometer and Naugle orbitometer, the changes in excursion of the upper eyelid before and after the intraorbital injection compared; the condition and mobility of the stump and implant were evaluated in anophthalmic patients. The examination also included evaluation of reposition of the eyeball/prosthesis done by ocular compression test using forceps, as well as other instrumental methods – ultrasound B-scan of the orbit (GE Healthcare Volusion E8), computed tomography (CT), functional multispiral computed tomography (fMSCT) and/or magnetic resonance tomography of the orbit when necessary.

Follow-up visits of the first group were appointed at 2 weeks after the injection, and then after 1, 2, 4, 6, 9 and 12 months during the period of 1 to 2 years. Mean follow-up time was 14.8 months (4 to 36 months). Check-ups of the second group patients were done immediately after the injection, after 1 months, and then every 3 months for the next 18 months. Mean follow-up period in this group spanned 19.2 months (18 to 40 months).

Statistical analysis of the results was completed using SPSS 20 and MedCalc software. Dynamic assessment of the obtained data versus baseline was done using Wilcoxon signed-rank test by comparing two dependent samples. Correlation of the changes of certain parameters to the volume of injected agent was evaluated using Spearman's rank correlation coefficient.

Results

Effectiveness of intrapalpebral injections. All 37 patients (40 eyes) of the first group had lagophthalmos (inability of the eyelids to fully close) of various degrees (from 1 to 8 mm), exposure keratopathy of various degrees in the lower third of the cornea, or peripheral superficial corneal opacification, which does not affect visual acuity. In 7 cases, corneal erosion was observed, and in one case – corneal ulcer. Additionally, all patients complained of pain, discomfort, burning and “sandpaper” in the eyes, hyperemia and lacrimation.

The patients were divided into 3 clinical subgroups according to lagophthalmos etiology.

Subgroup 1A included 10 patients (10 eyes) who had lagophthalmos associated with facial nerve palsy. Mean patient age was 59.4 years (31 to 72 years old), mean duration of palsy was 1.7 months (1 to 3 months), mean volume of the injected filled was 0.32 mL (0.1–0.5 mL).

Subgroup 1B included 20 patients (20 eyes) with chronic paralytic lagophthalmos. Among them, 14 had lagophthalmos appear after removal of acoustic neuroma, 3 – after traumatic injury, 2 – as the result of acute brain circulatory disorder, and in 1 – as a complication of diabetes. Mean patient age was 68.3 years (31 to 72 years old), mean duration of palsy was 36.7 months (4 to 78 months), mean volume of the injected filled was 0.36 mL (0.1–1.2 mL).

Subgroup 1C included 7 patients (10 eyes) with lagophthalmos associated with endocrine ophthalmopathy (EOP) that had been inactive for more than two years;

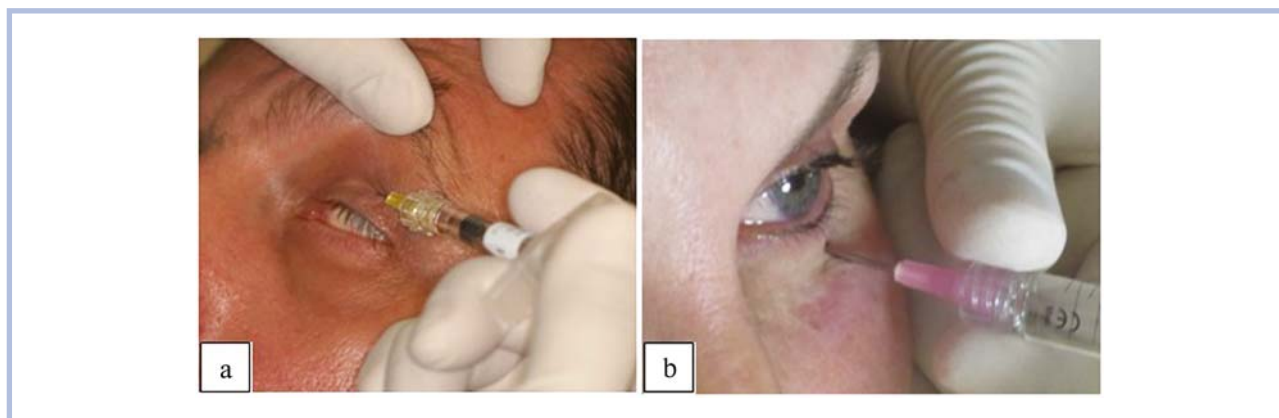


Fig. 1. Technique of HAG injection — intrapalpebral (a) and intraorbital (b).

among them, 3 patients (3 eyes) had undergone graded decompression of orbital fat and wall and surgical correction of eyelid retraction. Mean patient age was 56.5 years (42 to 78 years old), mean volume of the injected filler was 0.17 mL (0.1–0.4 mL).

All patients of subgroup 1A had statistically significant reduction of lagophthalmos and MRD1 immediately after the injection and during the follow-up, after which MRD1 failed to return to baseline – but without clinically significant ptosis. Evaluation of the mobility of upper eyelid in this subgroup showed statistically reliable increase immediately after the injection. After 2 months, reduction of eyelid retraction was observed; however, by 12th month the pre-injection values were not achieved (Fig. 2).

Contrarily to the achieved results, assessment of the long-term effect of filler injection for correction of lagophthalmos in acute facial nerve palsy is complicated due to gradual recovery of the function of orbicular muscle of the eye in all patients of the subgroup. However, the effectiveness of the injection in acute lagophthalmos is undeniable.

In subgroup 1B, patients also exhibited statistically significant reduction of lagophthalmos and MRD1 during the follow-up period. Excursion of the upper eyelid in this subgroup has reliably increased after injection.

(Fig. 3). Mean duration of the effect of one HAG injection was 9.05 months. Gradual reduction of the injection effect in all patients was observed starting with 6th month of the follow-up. Specifically, by the 6th month the indices had reached pre-injection values in 10 patients, by 9th month – in 13 patients, and by 12th month – in 14 patients. The residual effect of the injection in 6 patients (30%) remained for more than 12 months.

At 4 and 6 months after the filler injection, 2 patients (10%) with chronic lagophthalmos were excluded from the study due to surgical correction of lagophthalmos using a permanently weighting gold implant. In those cases, the biopsy sample of the eyelid tissue taken from HAG injection area during the surgery was sent for histological examination. According to morphological results, the filler resided in the cellular depot restricted by collagen septa of varying thickness, which correlated with the results of an experimental study published earlier (Fig. 4) [8].

During the follow-up, patients of the 1C subgroup had statistically significant reduction of lagophthalmos and MRD1. Lagophthalmos size median returned to baseline values 12 months after the injection; however, in two (28%) patients (4 eyelids), the correction fully remained even 1 year after the injection. Patient anamnesis showed that 5 years prior to EOP development they had under-

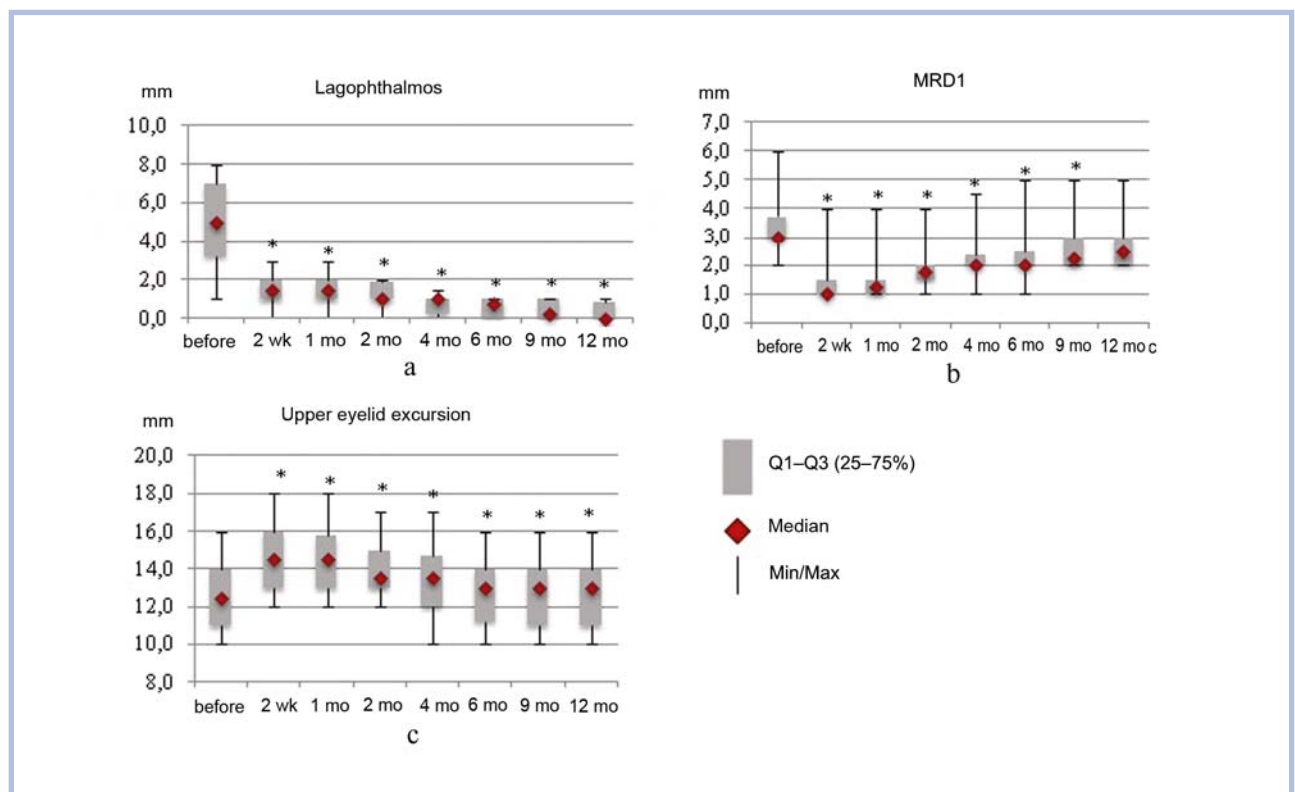


Fig. 2. Measurement dynamics of lagophthalmos (a), MRD1 (b) and upper lid excursion (c) before and after HAG injection in patients with acute facial nerve palsy.

* – $p < 0.05$; ** – $p < 0.001$.

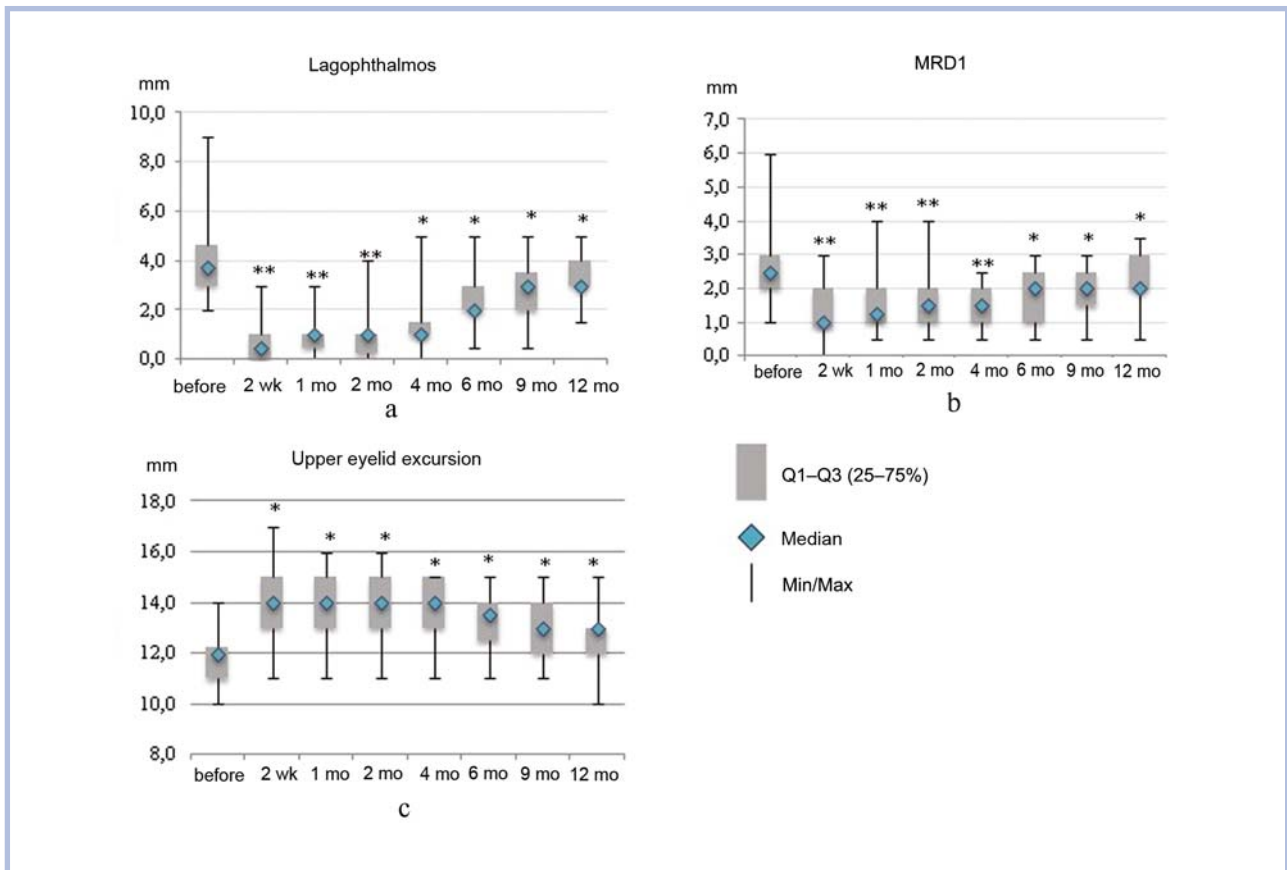


Fig. 3. Measurement dynamics of lagophthalmos (a), MRD1 (b) and upper lid excursion (c) before and after HAG injection in patients with chronic facial nerve palsy.

* — $p < 0.05$; ** — $p < 0.001$.

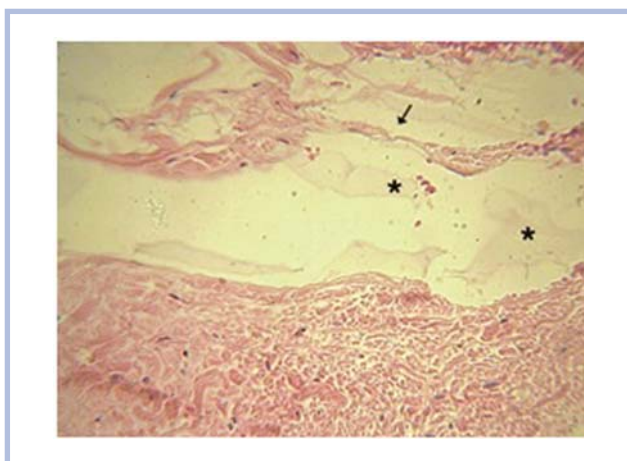


Fig. 4. Histologic picture of upper eyelid biopsy sample. HAG depot 6 months after injection.

Marked with asterisks are HAG particles in the depot surrounded by connective tissue septum (marked with arrow).

gone upper and lower blepharoplasty for cosmetic reasons (**Fig. 6**). Statistically significant improvement of the upper eyelid mobility after the injection was also observed in all patients, but it was less marked than in patients of the chronic paralytic lagophthalmos subgroup (**Fig. 5**). In the EOP subgroup, mean effect duration of one injection was 10.67 months.

Analysis revealed statistically significant correlation between the volume of injected filler and the amount of lagophthalmos in subgroups 1A and 1C after 2 weeks ($R=0.712$; $p=0.021$ and $R=0.524$; $p=0.018$, respectively), after one month ($R=0.780$; $p=0.008$ and $R=0.555$; $p=0.011$, respectively), and after 2 months ($R=0.666^*$; $p=0.036$ and $R=0.479$; $p=0.038$, respectively) following the injection. The correlation between the amount of lagophthalmos and the volume of injected filler in the EOP subgroup was statistically insignificant for the whole length of the follow-up.

For two weeks following the injection, all patients exhibited edema and hyperemia of the upper eyelid, as well as singular subcutaneous hemorrhages of varying severity. These adverse effects did not affect the long-term outcome of the injection and did not require additional treatment.

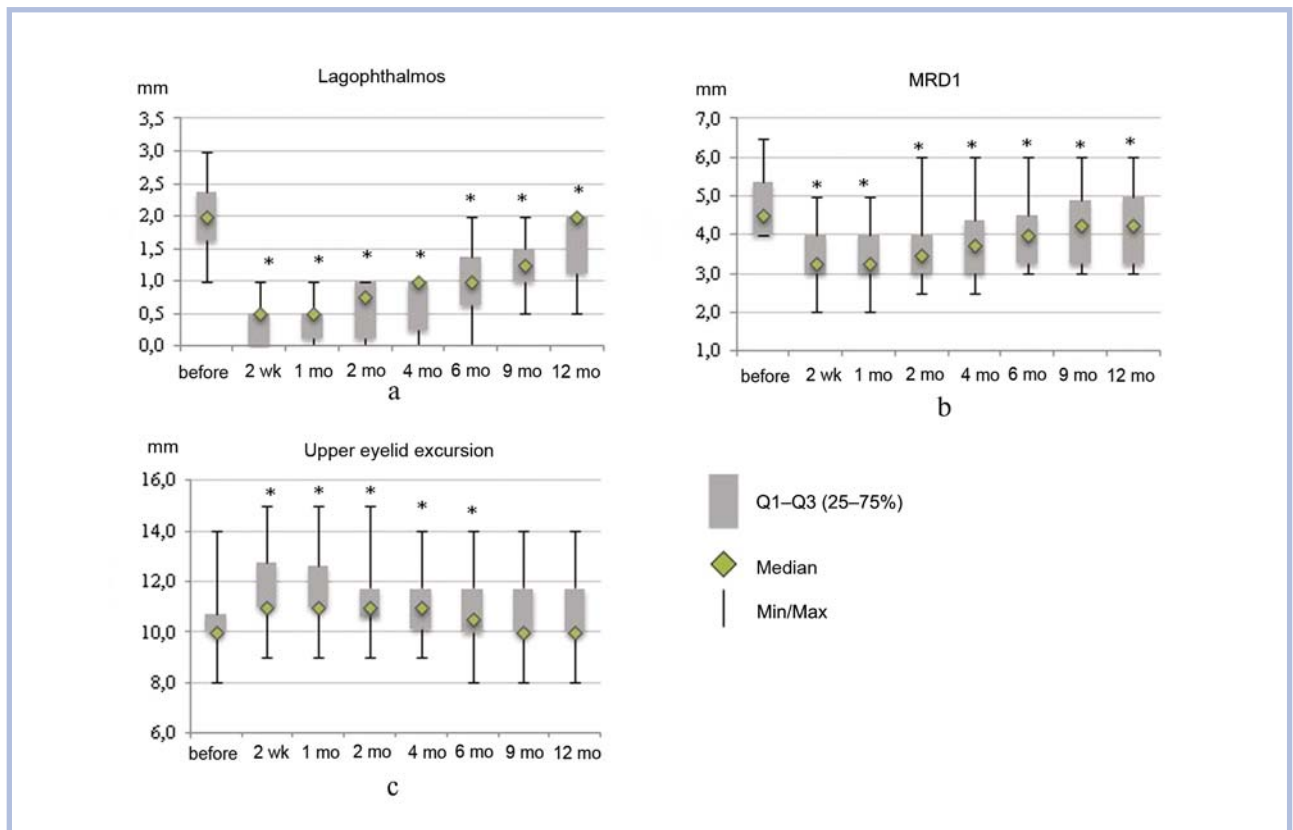


Fig. 5. Measurement dynamics of lagophthalmos (a), MRD1 (b) and upper lid excursion (c) before and after HAG injection in patients with endocrine ophthalmopathy.

* — $p=0.05$.



Fig. 6. Image of Patient L. (48 yr.) with EOP, lagophthalmos and bilateral upper eyelid retraction before (a) and 6 months after (b) HAG injection.

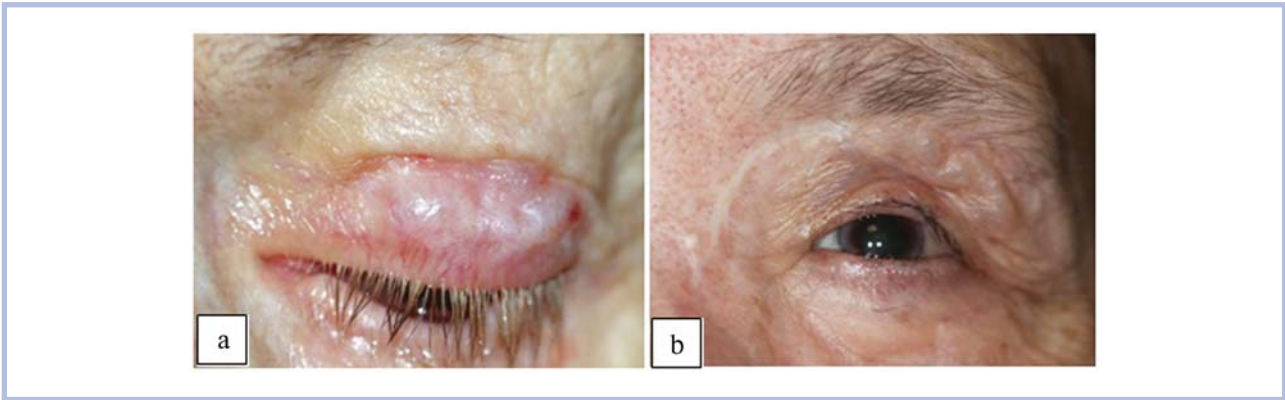


Fig. 7. Adverse events after intrapalpebral injection.

a — edema, hyperemia and subcutaneous hemorrhage; б — contoured drug reservoir.



Fig. 8. Image of Patient K. (76 yr.) with posttraumatic enophthalmos on the left eye before and 6 months after the injection.

Top — with head thrown back; middle — looking straight ahead; bottom — looking downwards.

In the context of this study, edema, hyperemia and subcutaneous hemorrhages can be considered natural local reaction to filler injection associated with skin damage caused by the needle/cannula (**Fig. 7, a**).

Seven patients had depot contouring when the volume of the injected filler surpassed 0.3 mL (**see Fig. 7, б**). None of them, however, complained about its presence, although the injected agent could be visualized under the skin in moderate blue for several months, which is known as Tyndall effect caused by refraction of light.

Effectiveness of intraorbital injections. To assess the effectiveness of HAG injections into the orbit in patients with enophthalmos of varying etiology, the study included 20 patients aged 45.5 years in average (24 to 76 years old) with mean volume of the injected filler 1.8 mL (1 to 3 mL).

The reasons for deficient orbit volume were: previously operated heavy traumatic deformation with implant injection (alloplant or demineralized bone autograft (DBAG)) and residual enophthalmos (8 orbits), silent sinus syndrome (1 orbit), hemifacial atrophy syndrome (1 orbit) — those patients comprised subgroup 2A. All patients with previously operated traumatic deformation of the orbit underwent computed tomography of both orbits to exclude unconsolidated defects of the bone wall, which could cause filler dislocation. All patients complained about the cosmetic defect caused by eyeball retraction, and two patients had exposure keratopathy due to inability to close the eyelids caused by limited mobility of the upper eyelid on the affected side accompanied by hyperemia and lacrimation.

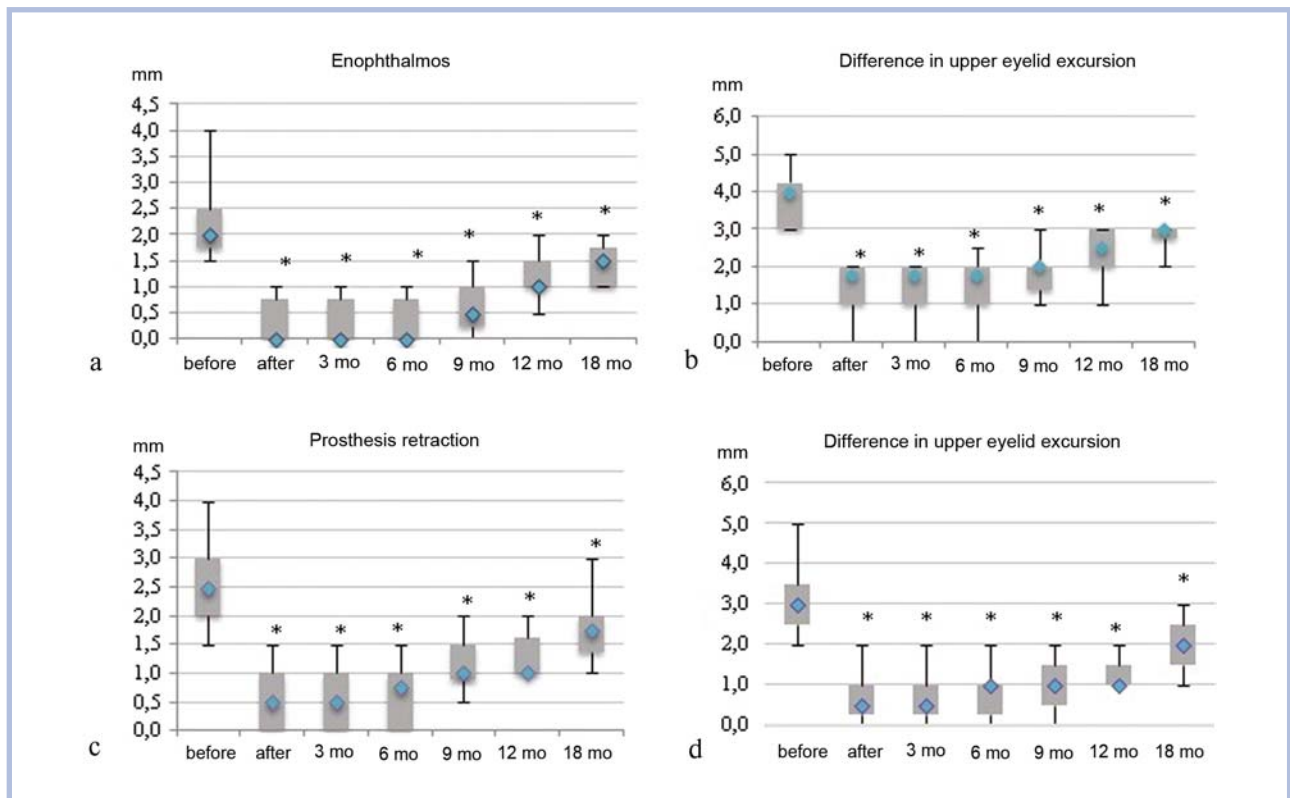


Fig. 9. Dynamics of enophthalmos (a), prosthetic retraction (b) and difference in excursion of the upper eyelid (c, d) compared with healthy eyes before and after HAG injection in patients with enophthalmos (a) and anophthalmic syndrome (b).

* — $p=0,05$.

Subgroup 2B included 10 patients with anophthalmic syndrome who has had a surgery involving formation of a locomotive stump, but the cosmetic effect was unsatisfying.

All patients of the 2nd group had insignificant enophthalmos/prosthesis retraction (1 to 4 mm), deepening of the orbital-palpebral fissure, hypophthalmos (1 to 2 mm), lagophthalmos (1 to 2 mm), limited mobility of the upper eyelid compared to the healthy eye (difference (D) in upper eyelid mobility), which improved after ocular compression test due to eyeball repositioning.

Injecting the filler into the orbit using the suggested technique proved to be beneficial for all patients of subgroup 2A in terms of eyeball repositioning and reduction of upper orbital-palpebral fissure retraction (Fig. 8). Six patients (60%) got enophthalmos fully corrected; in other cases, the remaining enophthalmos did not exceed 1 mm. Full correction was achieved in all 3 hypophthalmic patients (100%).

Statistically significant decrease of the filler's effectiveness was observed 9 months after the injection, but enophthalmos median did not return to baseline values. Pa-

tients of the subgroup also had statistically significant improvement of mobility (decreased D) during the whole long-term follow-up. Starting with 9th month after HAG injection, this parameter was gradually decreasing, but did not return to baseline values (Fig. 9, a). Only 3 patients (33%) retained the effect of the injection for more than 18 months.

In subgroup 2B, the patients were noted to have significant reduction of prosthesis retraction and statistically relevant improvement of upper eyelid excursion for 9 month after HAG injection. After that, the effect gradually decreased by 18th months of the follow-up (see Fig. 9, b). However, prosthesis retraction and upper eyelid mobility did not return to baseline values. The effect remained after 18 months of the follow-up in 4 patients (20%) of the subgroup.

According to correlation analysis, in patients of subgroup 2A there was a statistically significant connection between degrees of enophthalmos and hypophthalmos, and the volume of injected filler immediately after the injection ($R=0.757$; $p=0.049$ and $R=0.806$; $p=0.029$, respectively). A statistically significant correlation was also found

between the volume of injected filler and changes in mobility of the upper eyelid – immediately after HAG injection ($R=0.835$; $p=0.019$), also 3 months ($R=0.816$; $p=0.025$), 6 months ($R=0.899$; $p=0.006$), and 9 months ($R=0.874$; $p=0.01$) after the injection. No statistically significant correlation between those values was found at other follow-up points.

In subgroup 2B, statistically significant connection was found between the extent of prosthesis retraction and the volume of injected filler immediately after the injection ($R=0.722$; $p=0.043$) and at all the other follow-up points – after 3 and 6 months ($R=0.722$; $p=0.043$), 9 months ($R=0.932$; $p=0.001$), 12 months ($R=0.866$; $p=0.005$), and 18 months ($R=0.709$; $p=0.049$), but it had no correlation with changes in upper eyelid excursion.

None of the patients had clinically significant complications during and after the procedure. They felt moderate discomfort and pressure during the injection. There were no cases of implant dislocation either subcutaneously or into periorbital structures. Patients of subgroup 2A complained about slight diplopia in the far peripheral vision, in which cases the injection was stopped. Diplopia then regressed during 24 hours after the injection.

The described adverse events that occurred after intrapalpebral or intraorbital injections did not affect the effectiveness of the filler. Such severe adverse effects as hypersensitivity reaction, necrosis of the HAG injection area or decrease of visual acuity were absent. All patients were highly satisfied with the effect of the injection, and did not require hyaluronidase injection for enzymatic degradation of the injected filler.

Discussion

In recent years, injection fillers made of HAG are becoming increasingly popular in Russia as well as other countries. In ophthalmology, they are actively used not only on cosmetic, but also functional indications. This minimally invasive method is seeing wider use as an alternative to surgical treatment not only in lagophthalmos [9–11], but also enophthalmos [12], including previously adopted injection techniques [13, 14].

This study included 37 patients (40 eyes) with lagophthalmos. Patients of all subgroups formed according to disease's etiology experienced statistically significant lagophthalmos and MRD1 reduction, as well as improvements in upper eyelid mobility throughout the follow-up. Mean duration of the positive effect was 10 months. Starting from 2–4 months, the effect of the injection gradually decreased in all subgroups. An important difference should be noted about Graves' ophthalmopathy subgroup, in which the effect of the injection decreased faster than in other groups, and the improvement of upper eyelid mobility was less prominent. It may explain the remaining moderate inflammatory process in the orbit and periorbital tissues even in patients with inactive EOP. However, the disease did not reactivate in any of the patients of that

subgroup, which would cause increased exophthalmos and eyelid retraction. The described intrapalpebral HAG injection technique proved to be successful in correcting the upper eyelid position in all subgroups despite the mechanism of lagophthalmos development being different. Outcomes of this study correlate with the results seen in the studies by R. Goldberg et al [1] and M. Taban et al [2].

In 21% of study cases, the parameters under evaluation did not reach baseline values by 12th month. In his original study, J. Fezza (2008) described persistence of the filler injection effect similarly, with 70% of patients retaining it up to 12th month [15]. Another case found in foreign literature describes HAG filler persisting by up to 5 years after periocular injection [16]. The phenomenon can be explained by the specifics of filler distribution in the eyelid tissues providing the prolonged effect. In 2 patients with paralytic lagophthalmos, histological examination of the injection depot showed outcomes correlating with previously described specifics of HAG biological integration in experimental animals [8]. It should be noted that previous surgeries in the injection area may be able to affect the preservation of collagen structure of the injection depot, but additional studies are required to prove this.

In the enophthalmos group, average effect duration was 12 months due to various pathological conditions and anophthalmic syndrome. Consistent reduction of enophthalmos/prosthesis retraction and improvement of upper eyelid mobility was observed in all patients. Gradual reduction of the effect was seen starting with month 9 after the injection, but it is important to note that 30% of patients did not achieve baseline values by 18th month – similarly to the intrapalpebral injection group. An explanation of the longer lasting effect was provided by O. Crochelet et al, who noticed better stability of the filler in less mobile environments (such as in anophthalmic syndrome), but in their study they used an injection implant with longer effect duration as specified by the manufacturer. In the present study, the effect persisted even in patients without anophthalmic syndrome [17, 18].

Correlation between the volume of injected filler and the achieved correction is still being debated in literature [7, 17, 20]. Our study revealed statistically reliable positive correlation between the filler volume and the degree of enophthalmos correction, also with improved mobility of the upper eyelid, but not with the degree of correction of prosthesis retraction. Two patients had to undergo second injection after the initial follow-up period has ended in order to maintain the functional outcome.

The injection effect retaining in some of the patients could be attributed to incomplete biodegradation of the filler after an eyelid/orbit injection. Those patients may require less filler volume in further injections to preserve the cosmetic and functional outcomes. However, there is no data available today on repeated injections and possible risks and complications they pose.

The present study should be noted to have revealed minimal complications after injections, which is in accor-

dance with other studies [1, 6, 19]. Such severe complications as blindness (full or partial), necrosis of periocular tissues, eyeball damage or orbital hematoma did not occur in our study, but it is important not to overlook the risks. In order to eliminate or minimize those, specialists should remember to consider anatomical features of patients' faces, follow the injection algorithm in higher-risk areas and maintain visual control of the outcome using modern methods of radio and ultrasound diagnostics. More detailed recommendations can be found in a separate publication [21].

In conclusion, application of fillers made of HAG in pathologies of appendages of the eye is advantageous to surgical treatment methods in terms of faster outcomes,

lower frequency of complications, minimal invasiveness, and higher patient satisfaction. However, the method is a temporary, "off label" solution, and therefore requires disciplined approach when choosing the treatment tactics.

Author contributions:

Study conception and design: Y.G., V.Sh., J.P.

Acquisition and processing of data: V.Sh.

Statistical analysis: V.Sh.

Drafting of manuscript: Y.G., V.Sh.

Critical revision: Y.G.

The authors declare that there are no conflicts of interest.

REFERENCES

1. Taban M, Mancini R, Nakra T, Velez FG, Ela-Dalman N, Tsirbas A, Douglas RS, Goldberg RA. Nonsurgical management of congenital eyelid malpositions using hyaluronic acid gel. *Ophthalmol Plast Reconstr Surg.* 2009;25(4):259-263. <https://doi.org/10.1097/IOP.0b013e3181ac984b>
2. Mancini R, Taban M, Lowinger A, et al. Use of hyaluronic acid gel in the management of paralytic lagophthalmos: the hyaluronic acid gel «gold weight». *Ophthalmol Plast Reconstr Surg.* 2009;25:23-26. <https://doi.org/10.1097/IOP.0b013e318192568d>
3. Груша Я.О., Агафонова Е.И., Исмаилова Д.С., Иванченко Ю.Ф. Первый опыт применения препарата стабилизированной гиалуроновой кислоты для коррекции лагофтальма. *Вестник офтальмологии.* 2010;1:39-42. [Grusha YaO, Agafonova EI, Ismailova DS, Ivanchenko YuF. The first experience in using the stabilized hyaluronic acid preparation to correct lagophthalmos. *Vestnik Oftal'mologii.* 2010;1:39-42. (In Russ.)].
4. Катаев М.Г. Применение имплантов внутридермальных Реплери на основе гиалуроновой кислоты для заполнения объема и коррекции дефектов мягких тканей орбитальной и периорбитальной области при анофтальме и наличии глаза. *Практическая медицина.* 2012;4(12):194-198. [Kataev MG. Use of Repleri hyaluronic acid injectable implant as a filler and corrector of and periorbital region soft tissues defects in case of anophthalmos and eye. *Prakticheskaya Meditsina.* 2012;4(12):194-198. (In Russ.)].
5. Груша Я.О., Стоюхина А.С., Киселева Т.Н. Синдром немого синуса (клинический случай). Новая возможность устранения энофтальма. *Вестник офтальмологии.* 2013;3:63-67. [Grusha YO, Stoiukhina AS, Kiseleva TN. Silent sinus syndrome (clinical case). New potential for enophthalmos correction. *Vestnik Oftal'mologii.* 2013;3:63-67. (In Russ.)].
6. Malhotra R. Deep orbital sub-Q Restylane (Nonanimal stabilized hyaluronic acid) for orbital volume enhancement in sighted and anophthalmic orbits. *Arch Ophthalmol.* 2007;125:1623-1629.
7. Zamani M, Thyagarajan S, Olver JM. Adjunctive use of hyaluronic acid gel (Restylane Sub-Q) in anophthalmic volume deficient sockets and phthisical eyes. *Ophthalmol Plast Reconstr Surg.* 2010;26(4):250-253. <https://doi.org/10.1097/IOP.0b013e3181ba76f5>
8. Груша Я.О., Федоров А.А., Праусе Ю.У., Шептулин В.А. Экспериментально-морфологическое исследование тканей век после введения геля гиалуроновой кислоты. *Вестник офтальмологии.* 2015;131(1):69-74. [Grusha YO, Fedorov AA, Prause JU, Sheptulin VA. Histopathological study of experimental intrapalpebral injection of hyaluronic acid gel. *Vestnik Oftal'mologii.* 2015;131(1):69-74. (In Russ.)]. <https://doi.org/10.17116/oftalma2015131169-74>
9. Tan ST, Staiano JJ, Itinteang T, McIntyre BC, MacKinnon CA, Glasson DW. Gold weight implantation and lateral tarsorrhaphy for upper eyelid paralysis. *J Craniomaxillofac Surg.* 2013;41(3):49-53. <https://doi.org/10.1016/j.jcms.2012.07.015>
10. Demirci H, Frueh BR. Palpebral spring in the management of lagophthalmos and exposure keratopathy secondary to facial nerve palsy. *Ophthalmol Plast Reconstr Surg.* 2009;25(4):270-275. <https://doi.org/10.1097/IOP.0b013e3181ab6f08>
11. Груша Я.О., Федоров А.А., Искусных Н.С., Богачева Н.В., Кобзова М.В., Новиков И.А., Фетцер Е.И., Шеголева Т.А. Коррекция лагофтальма при хроническом лицевого параличе золотым имплантатом (отдаленные результаты). *Вестник офтальмологии.* 2016;132(2):26-32. [Grusha YaO, Fedorov AA, Iskusnykh NS, Bogacheva NV, Kobzova MV, Novikov IA, Fettscher EI, Shchegoleva TA. Gold weight implants for lagophthalmos correction in chronic facial nerve paralysis (late results). *Vestnik Oftal'mologii.* 2016;132(2):26-32. (In Russ.)]. <https://doi.org/10.17116/oftalma2016132226-32>
12. Филатова И.А. *Анофтальм. Патология и лечение.* М.: ИП Степанов Борис Эдуардович. 2007. [Filatova IA. *Anoftal'm. Patologiya I Lechenie.* М.: IP Stepanov Boris Jeduardovich. 2007. (In Russ.)].
13. Давыдов Д.В., Валуев Л.И., Сытов Г.А., Перова Н.В., Кузина Л.Д., Усенко Я.Р., Валуев И.Л. *Гидрогели в реконструкции анофтальмической орбиты.* В кн.: Материалы II международной конференции «Современные подходы к разработке эффективных перевязочных средств, шовных материалов и полимерных имплантатов». М. 1998;310-311. [Davydov DV, Valuev LI, Sytov GA, Perova NV, Kuzina LD, Usenko YaR, Valuev IL. *Gidrogeli v rekonstruktsii anoftal'micheskoy orbity.* In book.: *Materialy II mezhdunarodnoj konferencii «Sovremennye podhody k razrabotke jeffektivnyh perevjazochnyh sredstv, shovnyh materialov i polimernyh implantatov».* М. 1998;310-311. (In Russ.)].
14. Каспаров А.А., Грязнова И.И., Важди А.С. Способ формирования мягкой опорно-двигательной культи после энуклеации. *Вестник офтальмологии.* 1984;3:36-39. [Kasparov AA, Griaznova II, Vakhedi AS. Spособ form of forming a soft supportive stump after enucleation. *Vestnik Oftal'mologii.* 1984;3:36-39. (In Russ.)].
15. Fezza JP. Nonsurgical treatment of cicatricial ectropion with hyaluronic acid filler. *Plast Reconstr Surg.* 2008;121:1009-1014. <https://doi.org/10.1097/01.prs.0000299382.31856.d>
16. Dayan SH, Arkins JP, Somenek M. Restylane persisting in lower eyelids for 5 years. *J Cosmet Dermatol.* 2012;11(3):237-238. <https://doi.org/10.1111/j.1473-2165.2012.00622.x>
17. Crochelet O, Maalouf T, Duron S, Froussart F, Rigal-Sastourné J-C, George J-C. Efficacy and tolerability of highly crosslinked hyaluronic acid injections in the management of the enophthalmous orbit. *Journal Français D'ophtalmologie.* 2012;35:441-447. <https://doi.org/10.1016/j.jfo.2012.04.005>
18. Carruthers J, Carruthers A. Facial sculpting and tissue augmentation. *Dermatol Surg.* 2005;31:1604-1612.
19. Goldberg RA, Lee S, Jayasundera T, et al. Treatment of lower eyelid retraction by expansion of the lower eyelid with hyaluronic acid gel. *Ophthalmol Plast Reconstr Surg.* 2007;23:343-348.
20. Tay E, Olver J. Intraorbital hyaluronic acid for enophthalmos. *Ophthalmology.* 2008;115:110-112. <https://doi.org/10.1016/j.ophtha.2008.02.015>
21. Груша Я.О., Федоров А.А., Шептулин В.А. *Инъекционные имплантаты на основе геля гиалуроновой кислоты при патологии придаточного аппарата глаза.* М.: ГЭОТАР-Медиа; 2017. [Grusha YaO, Fedorov AA, Sheptulin VA. *In'ektsionnye implantaty na osnove gelya gyaluronovoy kisloty pri patologii pridatochnogo apparata glaza.* М.: Geotar-Media; 2017. (In Russ.)].

Поступила 08.03.18