Results of Corneal Defect Coverage with Amniotic Membrane

C. Ceban

Department of Ophthalmology
Nicolae Testemitanu State Medical and Pharmaceutical University, Chisinau, Republic of Moldova

Summary

The study included 53 patients with various pathologies of the cornea with prolonged absence of epithelialization of the surface or ulceration. Among our patients, the majority (52.8%) had deep ulcers, the second largest group had keratouveitis with ulcers (22.6%). Herpetic keratitis (7.5%) and corneal ulcer in systemic diseases (11.3%) had a relatively smaller incidence. The patients were divided into 2 groups depending on the applied surgical intervention: group I (20 patients – 20 eyes) – patients who underwent a single (simple) coverage of the cornea with lyophilised amniotic membrane; group II (33 patients – 33 eyes) – patients, following a double corneal coverage with lyophilised amniotic membrane. Results of treatment in group I: keratouveitis with ulceration (5 patients) – recovery in 2 cases and improvement in 3 cases, keratitis with ulceration (2 patients) – recovery in 1 case and improvement in 1 case, deep corneal ulcer (9 patients) – recovered in 4 cases and in 5 patients the ulcerative defect of the cornea almost epithelized, but maintained a residual infiltration of the stroma and a small swelling of the cornea. The visual acuity increased by 0.3 – 0.4 in comparison with the original data. After 6 -7 months after surgery, recurrence of herpetic keratitis in 1 case. Results of treatment in group II: keratouveitis with ulceration (7 patients.) – all cases recovered with complete epithelization of ulcers: in 5 cases with a transparent and in 2 cases with a "cloudy" opacity, among herpetic keratitis with ulceration (2 patients) were registered 1 recovery and 1 improvement, deep corneal ulcers (17 patients) recovered in 14 cases by full epithelialization of ulcers with the formation of a local opacity and improved in 3 cases. By the time of withdrawal of the biological coverage the visual acuity in this group increased by 0.5 – 0.7 from the original data. So, it was established that the double coverage of the cornea with amniotic membrane accelerated 2 times the corneal epithelization and the resorption of necrotic masses, caused a faster reduction of the inflammatory process, resulted in a transparent epithelization of ulcerous defect 4 times better and a period of hospitalization shortened by 2.5 times in comparison with the single coverage.

Key words: corneal pathology, amniotic membrane, keratoamnioplasty.

Результаты покрытия язвенного дефекта роговицы амниотической оболочкой

Под наблюдением находилось 53 пациента с различной патологией роговицы, сопровождающейся длительным отсутствием эпителизации поверхности или изъязвлением. В зависимости от проведенного оперативного вмешательства больные были распределены на 2 группы: I группа (20 больных – 20 глаз) – пациенты, которым было проведено кератопокрытие лиофилизированной амниотической оболочкой; II группа (33 больных – 33 глаза) – пациенты, после проведенного двойного кератоамнионопокрытия. Результаты лечения в I-й группе: кератоувеиты с изъязвлением (5 чел.) восстановились в 2 случаях, улучшения наблюдались в 3 случаях, кератиты с изъязвлением (2 чел.) – восстановление в 1 случае и улучшение в 1 случае, глубокие язвы роговицы (9 чел.) восстановились в 4 случаях, у 5 пациентов язвенный дефект роговицы почти эпителизировался, но сохранилась остаточная инфильтрация стромы и малое набухание роговицы. Динамика зрительных функций была на 0,3-0,4 выше, чем исходные данные. Через 6-7 месяцев после операции, рецидив герпетического кератита имел место в 1 случае. Результаты лечения во II-й группе: кератоиридоциклит с изъязвлением (7 чел.) и в 7 случаях была полная эпителизация язвы, в 5 случаях с прозрачной и только в 2 случаях с «облаковидным» помутнением, герпетический кератит с изъязвлением (2 чел.) – восстановление в 1 и улучшение в 1 случае, глубокие язвы роговицы (17 человек) эпителизировались полностью в 14 случаях с образованием местной прозрачности, улучшения отмечались в 3 случаях. Острота зрения в момент снятия биологического покрытия увеличилась на 0,5-0,7 от исходных данных. Таким образом, установлено, что двойное покрытие роговицы амниотической мембраной ускоряло в 2 раза эпителизацию роговицы и резорбцию некротических масс, обусловило быстрое снижение воспалительного процесса. Прозрачная эпителизация язвенного дефекта наблюдалась в 4 раза чаще, а период госпитализации сократился в 2,5 раза по сравнению с одиночным покрытием.

Ключевые слова: патология роговицы, амниотическая мембрана, кератоамнионопластика.

Introduction

The inflammatory diseases of the cornea occupy about 20% of the overall incidence of eye morbidity, of which the most severe are herpes, abscesses, and keratitis that occurs against a background of systemic diseases of the body [1, 4].

Treatment of patients with inflammatory diseases of the cornea, accompanied by violation of the integrity of the epithelium, is one of the most difficult problems in modern ophthalmology. Very often these inflammatory processes have a prolonged or recurrent nature. Various methods of antibacterial, enzymatic, catalytic regeneration therapy do not always have the necessary therapeutic effect [1, 2, 3]. Failure of medical therapy justifies the need to develop new methods of effective surgical treatment of ulcerative processes of the cornea. Of the existing methods of treatment of diseases of the cornea, we focused on the curative biological coverage with amniotic membrane, which is motivated by the amniotic membrane's unique antibacterial, antiviral, immunosuppressive, protective and antihypoxic properties [5, 6].

Aim of the study – to examine the effectiveness of biological corneal coverage with amniotic membrane in patients with long-lasting keratitis.

Material and methods

The study included 53 patients with various pathologies of the cornea with prolonged absence of epithelialization of the surface or ulceration. Patients' age ranged from 22 to 73 years, the average age was 65.5 ± 3.8 years.

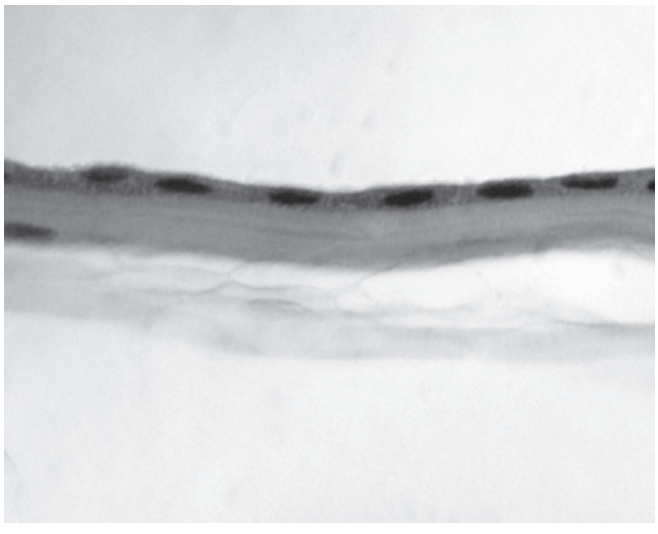

Fig. 1. Lyophilized amniotic membrane. Haemtoxillin-Eosin. x 120.

The bio-microscopic examination of the patients showed the presence of hyperemia and edema of the conjunctiva in 78.5%, pericorneal or mixed injection of the eyeball was observed in 100% of cases. Different shape, color, depth and localized corneal infiltrates were detected in 68.6% cases, edema of the stroma of the iris in 18.6% and hypopion in 18.4% cases. Corneal sensitivity was reduced in 18.6% of cases. The fluorescein probe revealed staining of random degree in 100% of cases. When examining the Schirmer test of tear production in these patients, its decrease was noted in 6 patients (15.7% of cases), in other cases it increased.

Due to the failure of medical therapy the patients underwent the surgical treatment of biologic corneal coverage with amniotic membrane (Fig. 1, 2).

Depending on the surgical intervention the patients were divided into 2 groups:

- Group I (20 patients – 20 eyes) underwent single corneal coverage with lyophilized amniotic membrane;
- Group II (33 patients – 33 eyes) followed double corneal coverage with lyophilized amniotic membrane.

The assignation of the patients by pathology is shown in table 1.

Table 1

The assignation of the patients by pathology

Pathology	Number of patients (number of eyes)		
	Total (n = 53)	Group I (n = 20)	Group II (n = 33)
Kerato-uveitis with corneal ulcer	12	5	7
Herpetic keratitis with ulceration	4	2	2
Trophic keratitis	3	1	2
Deep corneal ulcers	28	9	19
Corneal ulcer in systemic diseases	6	3	3

Among our patients, the majority (52.8%) had deep ulcers, the second largest group had keratouveitis with ulcers (22.6%). Herpetic keratitis (7.5%) and corneal ulcer in systemic diseases (11.3%) had a relatively smaller incidence.

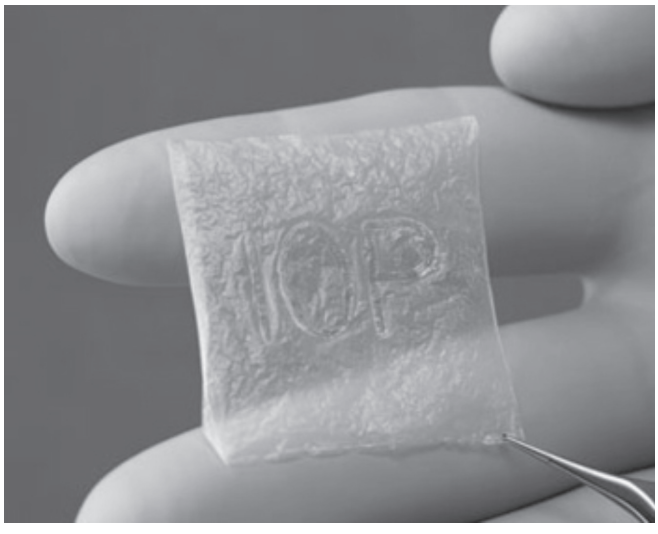

Fig. 2. Lyophilized amniotic membrane (natural size).

The study did not include the patients with severe purulent processes of the cornea, accompanied by perforation of the cornea of varying degree. In these cases it has been recommended the subtotal or total keratoplasty or it was pursued alternatively to autokonjunctivoplasty. Timely execution of penetrating corneal transplantation with the necessary amount of reconstruction of the anterior segment of the eyes in the acute stage of purulent process of the cornea, as at its end, makes it possible to save the eye as an organ and to obtain an intense therapeutic effect even in the terminal stage of the corneal disease.

The assignation of the patients by etiology of the corneal disease is shown in table 2.

Table 2

The assignation of the patients by etiology of the corneal disease

Etiological factor	Number of patients (number of eyes)
Trauma	28
Surgery	3
Herpes infection	4
Contact lenses	3
Diseases of the musculoskeletal apparatus	6
Dry-eye syndrome	4
Unknown etiology	5
Total	53

Accordingly, as set out in table 2, the most frequent of the etiological factors of the inflammatory diseases of the eye were traumatic (52.8%) and herpetic lesions (7.5%). The percentage of inflammatory diseases of the cornea with unknown etiology was large enough (9.4%), which can be explained by the difficulties of differential diagnosis in this group of diseases and polymorphism of clinical manifestations of the same infection.

Results and discussion

The most frequent complaints of the examined patients in both groups were: pain (96%), decreased visual acuity (100%),

photophobia, lacrimation (98.8%), redness of the eyes (100%) edema of the eyelids (87%). The frequency and severity of a complaint depended on the form and severity of the disease.

The diagnosis of keratouveitis (12 cases) was determined by the presence of corneal syndrome, injection of the eyeball, the presence of inflammatory infiltrates in the cornea, hyperemia and edema of the stroma of the iris with the deposition of fibrin on it, opalescence of anterior chamber's moisture, anterior and posterior synechiae.

In 4 cases herpetic keratitis had a recurrent evolution. It was noted the clouding of the deep layers of the cornea with ulcer symptoms and Descemet's membrane folds.

The transition of the purulent infiltrates into corneal ulcers with deep defect was observed in 52.8% of cases. Ulcers of the cornea were characterized by the following clinical picture: pronounced corneal syndrome, mixed injection of the eyeball, corneal neovascularization edema of the endothelium. In patients with deep corneal ulcers most often the ulcerative defect, clinically, was 4 - 6 mm wide with a purulent infiltration on the bottom and edges of the ulcer with necrosis of the epithelium, of different layers of the corneal stroma and marked perifocal edema. Ulcers were located in the middle or paracentral in 94% of cases and paralimbal in 6% of cases.

Evolution of the clinical manifestations of the inflammatory process in corneal ulcer depending on the applied surgery method is presented in table 3.

Table 3

The evolution of clinical manifestations of the inflammatory process in corneal ulcer depending on the applied surgery method

Clinical symptome		Surgery method	
		Simple coverage (group I) (n = 20)	Double coverage (group II) (n = 33)
Epithelization of cornea, days:	beginning	5.6 ± 0.16	3.7 ± 0.15***
	finishing	11.0 ± 0.16	6.2 ± 0.17***
Infiltration resorption, days:	beginning	5.1 ± 0.17	2.9 ± 0.16***
	finishing	8.5 ± 0.16	5.2 ± 0.15***
Resorption of hypopyon, days:	beginning	3.8 ± 0.17	1.9 ± 0.17***
	finishing	5.5 ± 0.16	3.7 ± 0.17***
Disappearance of inflammation, days		14.5 ± 0.16	8.2 ± 0.17***

Note: *** - $p < 0.001$ - statistical differences between group I and group II.

In all patients, following a biological coverage of the cornea using amniotic membrane, the inflammatory process and the symptoms of corneal syndrome disappeared. In group I, there were 2 cases of recurrent inflammatory process in 7-8 months after treatment. Thus, all cases of recurrence were provoked by herpetic infection. The results of treatment in the group II were stable during the whole period of further observation (from 6 to 36 months) after surgery.

In surface processes, as a result of treatment after the double coverage of the cornea (group II) translucent, delicate corneal opacity was observed in 33.3% of cases (11 people).

Transparent healing corneal defects were noted in 15% of cases in patients of group I, while in the group II – transparent epithelization was observed in 51.5% of cases.

In both groups, in deeper ulcerative process the outcome of the process had varying degrees of intensity of turbidity, but in patients following the double coverage with amnion membrane the turbidity of the cornea was much less intense, these patients were 2, i.e. 22.2% of the patients in this group (they later held transcornean keratoplasty), in group I an intense turbidity appeared in 47.4% of cases.

The results of the outcome of treatment by application of the biological coverage with amniotic membrane (tab. 2) varied clearly in the studied groups after the surgery. Thus, in patients who received biological coverage with amniotic membrane improvement was observed in 50% of cases, and the remaining 50% held an obvious improvement with positive dynamics. After double cover with amnion membrane, complete recovery was obtained, in 93.9% of cases clear positive dynamics were observed in the remaining 6.1% of cases.

Double coverage of the corneal ulcer (group II) resulted in more rapid normalization of systemic markers of inflammation. Thus, at the end of the treatment in blood serum sialic acid level decreased from 264.2 ± 1.4 to 161.8 ± 2.0 uc ($p < 0.001$), the seromucoid - from 0.367 ± 0.5 to 0.214 ± 0.5 uc ($p < 0.001$), the fibrinogen - from 8.4 ± 0.10 to 6.3 ± 0.14 g/l ($p < 0.001$). By day 14 of treatment, C-reactive protein concentration decreased from 12.1 ± 0.3 to 8.5 ± 0.4 mcg/ml ($p < 0.001$), but remained 1.5 times higher than the standard indices (5.9 ± 0.6 mcg/ml).

In patients of group I, the sialic acid decreased from 262.3 ± 1.6 to 199.3 ± 1.7 c.u. ($p < 0.001$), the seromucoid – from 0.361 ± 0.9 to 0.231 ± 0.6 c.u. ($p > 0.1$), the fibrinogen – from 9.0 ± 0.20 to 8.8 ± 0.29 g/l ($p > 0.1$), C-reactive protein concentration decreased from 12.6 ± 0.4 to 11.8 ± 0.4 mcg/ml ($p > 0.1$).

Inflammatory process in corneal ulcers manifested by increased systemic concentrations of proinflammatory cytokines (IL-1β, TNFα, IL-8) in the blood serum. The dynamics of the concentrations of cytokines is presented in table 4.

Table 4

The dynamics of the concentrations of cytokines in blood (M ± m)

Indices	Groups of patients	
	Simple coverage (Group I) (n = 20)	Double coverage (Group II) (n = 33)
IL-1β, pg/ml		
initial	99.4 ± 6.3	95.4 ± 5.8
after 7 days	76.3 ± 4.1***	82.8 ± 6.1***
after 14 days	21.3 ± 5.8***	49.4 ± 4.9***
TNFα, pg/ml		
initial	87.1 ± 4.3	88.5 ± 5.6
after 7 days	62.9 ± 5.4***	71.2 ± 4.8***
after 14 days	18.4 ± 5.1***	31.3 ± 5.3***
IL-8, pg/ml		
initial	112.3 ± 5.3	110.4 ± 5.3
after 7 days	81.9 ± 4.9***	92.8 ± 4.7***
after 14 days	45.7 ± 6.0***	70.8 ± 6.0***

Note: *** - $p < 0.001$ - statistical differences between group I and group II.

Thus, it was established (tab. 4) that under the influence of double coverage, the concentration of interleukin-1β (IL-

1β) in serum decreased from 99.4 ± 6.3 to 76.3 ± 4.1 pg/ml (23.2%, $p < 0.001$) on the 7th day of treatment, and at the 14th day - 4.7 times, reaching the average level of 21.3 ± 5.8 pg/ml ($p < 0.001$) in the whole group. In spite of the veridical decrease of IL-1β, the concentration of this cytokine remained increased compared to the conditionally healthy individuals (8.6 ± 1.5 pg/ml). Simultaneously with this fact, it was determined that treatment with Bio-R caused the decrease of TNFα concentration from 87.1 ± 4.3 to 62.9 ± 5.4 pg/ml (with 27.8%, $p < 0.001$) on the 7th day and to 18.4 ± 5.1 pg/ml at day 14, being about 2.6 times higher compared to its indexes in healthy individuals conditioning (7.1 ± 1.1 pg/ml). At the end of the treatment with Bio-R the level of interleukin-8 (IL-8) decreased from 112.3 ± 5.3 to 45.7 ± 6.0 pg/ml or 2.5 times ($p < 0.001$) compared with the original data.

In patients of group I, who made the simple coverage of the cornea, the concentrations of all proinflammatory cytokines decreased as well, but were less obvious: IL-1β decreased from 95.4 ± 5.8 to 82.8 ± 6.1 pg/ml (13.2%, $p < 0.001$) at day 7 of treatment and to 49.4 ± 4.9 pg/ml ($p < 0.001$) on the 14th day, i.e. 1.9 times. Simultaneously, there was a decrease in the concentration of TNFα from 88.5 ± 5.6 to 71.2 ± 4.8 pg/ml (by 19.5%, $p < 0.001$) to the 7th day and to 31.3 ± 5.3 pg/ml at day 14 of treatment, while being increased 4.4 times compared with its level in healthy persons conditioning (7.1 ± 1.1 pg/ml). At the end of the study, patients in group II IL-8 decreased from 112.3 ± 5.3 to 45.7 ± 6.0 pg/ml or 2.5 times ($p < 0.001$) in comparison with the original data.

The results of treatment for each group separately for nosological form of the disease

The criteria for allocation of patients in the group "cured" and the group of "improved". As "cured" we considered the full subsided inflammation, reduction of pain syndrome, complete epithelization of the ulcer, the outcome of which was a clear cornea and a small superficial corneal opacity, and the outcome of deep ulcers - a local turbidity. The category of "improved" - we included the patients with an almost complete subsided inflammatory process, but with preservation of the residual infiltrate.

The results of treatment in group I

The contact of the amniotic membrane with the cornea lasted from 3 to 7 days.

Keratouveitis with ulceration (5 patients) was recovered in 2 cases: we have full subsided the symptoms of iridocyclitis, epithelization of the ulcer with the formation of a gentle "cloudy" opacity.

There was improvement in 3 cases, but there remained moderate "roughness" of the epithelium of the cornea, swelling of iris and isolated posterior synechiae.

In the cases of keratitis with ulceration (2 patients), recovery was observed in 1 case - the corneal and inflammatory syndromes have been cropped, there was also a complete epithelialization of ulcers, with the formation of semitransparent opacity.

Improvement occurred in 1 case, characterized by almost complete epithelization of the ulcer, pronounced eyes injection, subtotal turbidity in the inflammation area.

Deep corneal ulcer (9 patients) recovered in 4 cases, i.e. cropping of the inflammatory process and complete epithelialization of the ulcer was observed.

In 5 patients an ulcerative defect of the cornea almost epithelized, but maintained a residual infiltration of the stroma and a small swelling of the cornea.

Visual acuity of patients in this group before and after biological coverage reflected in table 5.

Table 5

Dynamics of the visual acuity after biological coverage

Visual acuity	Before operation (number of eyes)	After operation (number of eyes)
1/∞ p.l.c – 0.01	12 (60%)	1 (5%)
0.02 – 0.04	3 (15%)	2 (10%)
0.05 – 0.07	2 (10%)	1 (5%)
0.08 – 0.1	2 (10%)	10 (50%)
0.2 – 0.4	1 (5%)	4 (20%)
0.5 – 0.7	0	2 (10%)
Total	20 (100%)	20 (100%)

Dynamics of the visual functions amounted to 0.3 – 0.4 higher than the original data. After 6 -7 months after surgery, recurrence of herpetic keratitis occurred in 1 case. Deep corneal ulcer epithelized with ingrowth of a large number of newly formed vessels. Inhibition of existing vascularization was not fixed in any case. In 7 cases (35%) on the background of the formed intensive corneal opacity it was recommended to execute keratoplasty in terms of 3 to 7 months after the coverage with amnion.

The results of treatment in group II

In group II, after the operation of double keratoplasty, the contact of amnion with the infected cornea had an average of 18 days.

Keratoiritis with ulceration (7 patients): recovery - in 7 cases, i.e. we observed a complete epithelization of ulcers in 5 cases with transparent and only in 2 cases with a "cloudy" opacity, complete relief of the inflammatory process, the disappearance of the corneal and pain syndromes, lack of infiltration of the stroma.

Among herpetic keratitis with ulceration (2 patients) 1 recovery was registered, which marked a complete epithelialization of the cornea with the formation of a tender "cloudy" opacity.

Improvement - 1 (deep herpetic corneal ulcer) - after removing the biological cornea coverage we noted incomplete subsided inflammation, almost complete epithelization of the affected area, and a moderate infiltration of the corneal stroma.

In deep corneal ulcers (17 patients) we noted recovery in 14 cases, which was characterized by full epithelialization of ulcers with the formation of a local opacity, subsiding inflammation, disappearance of winking spasm, lacrimation and pain.

Improvement was noticed in 3 cases, which, when pronounced positive dynamics, were characterized by the presence of residual petechial inflammatory infiltrate.

Visual acuity at the time of removal of the biological coverage increased by 0.5 – 0.7 ± 0.06 from the original data.

When viewed after 6 and 12 months, in some patients improvement was noted in visual acuity which was at 0.1 – 0.2.

The dynamics of visual functions of patients following a double coverage of the cornea with amnion membrane are reflected in the table 6.

Table 6

Dynamics of visual functions of patients following a double coverage of the cornea

Visual acuity	Before the surgery (number of eyes)	After the surgery (number of eyes)
1/∞ p 1.c – 0.01	14 (42.4%)	0
0.02 – 0.04	12 (36.3%)	3 (9.1%)
0.05 – 0.07	3 (9.1%)	2 (6.1%)
0.08 – 0.1	2 (6.1%)	16 (48.5%)
0.2 – 0.4	2 (6.1%)	5 (15.1%)
0.5 – 0.7	0	7 (21.2%)
Total	33 (100%)	33 (100%)

Low visual acuity was observed mainly in elderly patients and this was due to the residual corneal opacity, cataract development, changes in the retina and optic nerve, destructive changes in the vitreous body.

It should be noted that the very next day after surgery, we recorded cupping of the cornea syndrome as well as ciliary pain and discomfort, which were continuously present before the treatment.

The inflammatory process was stopped after 5-7 days, which was characterized by the disappearance of eye injection; after the biological coverage a significant decrease was noticed in the diameter of the deep ulcers and complete epithelialization in superficial processes.

There was a positive subjective assessment of the treatment by the patients.

The patients were examined 3, 6, 12, 18, 24 and 36 months after the treatment to confirm the stabilization of the positive dynamics in the absence of the phenomena of inflammation.

After eliminating the double biological coverage in all cases, the inhibition of vascularization of varying degrees was observed. After 1-1.5 months in some patients a continuation of the, "clearage" of the newly formed vessels in the cornea was registered.

In no case of keratoplasty was there a toxic or allergic reaction of the eye to the amnion membrane was registered.

The average period of stay in the hospital of patients with inflammatory diseases of the cornea in group 1 was 16.5 ± 2.4 days, in the II-nd – 7.0 ± 1.5.

On the basis of these studies indications for the double coverage of the cornea with amnion membrane were elaborated.

Indications for the double coverage of the cornea are:

- absence of a positive effect on the ongoing conservative therapy within 3 days of treatment starting in hospital;
- the progression of the pathological process in the cornea, leading to thinning of the cornea;
- long-term non-healing ulcers, which may represent an input "gate" for a secondary infection, which may be the immediate cause of death of the eyes;
- serious somatic diseases (diabetes, asthma, coronary heart disease, hypertension, etc.) are a contraindication for conducting more extensive surgeries;
- lack of donor material for the needed surgery.

Conclusions

The following incidence of etiological factors of the corneal ulcer were registered: 52.8% - ocular trauma, 7.5% - herpes infection, 9.4% - unidentified etiology.

Double coverage of the cornea with amniotic membrane doubled the speed of the corneal epithelization and the resorption of necrotic masses, and it caused a faster reduction of the inflammatory process in comparison with the single coverage.

Transparent epithelization of ulcerous defect occurred in 50% of cases in patients who had double coverage and in 12% cases of patients who made a simple coverage.

The period of hospitalization in patients who have made a double coverage was on average 2.5 times shorter than in patients with simple coverage of the cornea.

Bibliography

1. Аветисов СЭ, Петров СЮ, Бубнова ИА, и др. Современные методы диагностики и лечения заболеваний роговицы и склеры. М, 2007;240-242.
2. Тарасова ЛН, Кудряшева ЮИ. Новые технологии в лечении язвы роговицы: науч.-практич. конф. Москва, 2005;673-678.
3. Груша ЯО, Каспаров АА, Ксиелева ТН, и др. Комбинированное хирургическое лечение язвы роговицы. *Вестник офтальмологии.* 2008;124(6):57-59.
4. Лазук ВА, Малшконян ВР, Варнаков СИ, и др. Анализ структуры офтальмологических больных, получавших высокотехнологичные (дорогостоящие) виды медицинской помощи в лечении глазных болезней. РАМН. 2005;61-63.
5. Иванова ОВ, Степанов ВК, Малов ИВ, и др. Результаты применения биопокрытия с помощью амниотической оболочки: сообщение 1. *Вестник офтальмологии.* 2008;124(6):13-15.
6. Степанов ВК, Масауд Ю, Иванова ОВ. Результаты применения биопокрытия с помощью амниотической оболочки: сообщение 2. *Вестник офтальмологии.* 2008;124(6):15-17.

Corresponding author
Cornelia Ceban, *Doctoral Student*
Department of Ophthalmology
Nicolae Testemitanu State Medical and Pharmaceutical University
29, N. Testemitanu Street, Chisinau
Republic of Moldova
Telephone: +37322 403557

Manuscript received April 02, 2010; revised manuscript May 11, 2010