

## **Degenerative Changes of the Anterior Segment Tissues Depending on the Phenotype of Acetylation in the Experiment**

**TIAME Postgraduate Department of Ophthalmology (Tashkent, Uzbekistan)**

This research is a fragment of a scientific work «Reparation processes at burns of an organ of vision depending on an acetylation phenotype (kliniko-experimental researches)», ОНМИ ГНМБ МЗРУз: №002109 registration number.

**Introduction.** An ocular burn is a serious damage of the tissues of eye and on average its incidence rate is from 6.1 to 38,4% [4,6,11]. The incidence rate of chemical burns is from 25 to 80%. These burns facilitate the development of recurrent erosions, ulcerations, perforations, iridocyclitis, exsudation into anterior chamber, formation of corneal scars, which cause visually caused handicap and loss of ability to work in 40% of cases [1,2,10].

As we all know, major role in the development of the burn complications is attributed to the accumulation of the toxic products, which contribute to the progression of the anterior segment changes, slows and changes the regenerative process and leads to severe complications and visual loss. Tissue antigens (TA) in serum cause autointoxication and autosensibilization of the organism [11].

The process of xenobiotic detoxication occurs at the level of monooxygenase system in liver. It is well known, that there is acetylation system that functions similar to monooxygenase system in organism. N-acetylation is one of the major routes of biotransformation of xenobiotics and endogenous aminocompounds [3, 5, 7, 9].

According to the acetylation speed organisms are divided into two groups: fast (FA) and slow acetylators (SA). The magnitude of research suggests that acetylation phenotype is genetically determined [3,8].

Taking into account that the consequences of ocular burn and the efficiency of treatment to a large extent is dependent on the nature of reparative processes, determination of speed and activity of inflammation and regeneration of the ocular tissues may be critical. Hence, the study of the reparation processes in the eye in FA and SA will enhance the knowledge of pathogenesis of ocular burn and optimization of management. However, the study of N-acetylation in ocular burn have not been undertaken. The data on features of damage and reparation of ocular tissues in chemical burns in patients with various acetylation phenotype is absent.

The **aim of the research** is to study the features and the extent of the damage of tissues of anterior segment

in chemical burn in relation to acetylation phenotype (AP) in experiment.

**Material and methods.** The experiment has been performed on 100 white outbred male rats weighing 180-200 grams (Experiments were performed in the laboratory of "Chronic Infectious Process" Scientific Research Institute of Microbiology, Infectious Diseases Epidemiology, prof. N. G. Gulyamov).

All the animals have been divided into two groups depending on the acetylation phenotype: fast acetylators (FA) and slow acetylators (SA). Acetylation phenotype was determined by the study of the urine of the animals with norsulfazol.

For urine collection a special cell for animals with urine collecting mechanism was constructed.

To determine Acetylation phenotype norsulfazol was used (10 mg/kg orally). Acetylation capacity of organism was considered slow if the clearance of norsulfazol reached 50% in 24 hours, and it was considered fast if the clearance reached 50% or more in the same period.

A model of chemical burn was created by application of 10% solution of NaOH for 10 seconds.

As a control anterior segment of animals (fast and slow acetylators) bred in similar general conditions was used. The experiment was performed in 4 stages – on 2, 5, 12 and 30 day after the burn.

The animals in each experimental and control group was decapitated at the stages of natural regeneration of ocular tissues on 2, 5, 12 and 30 day after the burn.

The blood was collected to determine the antigen-binding lymphocytes to tissue antigen of conjunctiva, sclera, cornea and the lens in chemical burn. This test was performed to determine the degree of degeneration of these tissues during 30 day period in groups being compared.

The results in fast and slow acetylators were compared after statistical analysis using Student criteria for paired and unpaired units.

**Results.** The research showed the prevalence of slow acetylators – 64.0% over fast acetylators – 36.0% ( $p < 0.05$ ).

The following stage of the research was to study features of degenerative and reparative processes in the anterior segment tissues in relation to Acetylation phenotype.

The research showed severe degeneration in the studied tissues in fast and slow acetylators on 2, 5, 12 and 30 day (see **table**).

**Table**  
**Antigen-binding lymphocytes (ABL) to tissue antigens (TA) of the anterior segment in experimental animals in the dynamics of ocular chemical burn (n = 100)**

Tissue and decapitation day	ABL to TA in intact rats, %	ABL to TA in FA, %	ABL to TA in SA, %	P
<b>Conjunctiva</b> Day 3	1,1±0,015	4,3±0,36*	4,7±0,42*	>0,05
Day 5	0,8±0,01	3,3±0,33*	3,7±0,37*	>0,05
Day 12	0,9±0,02	5,7±0,31*	3,7±0,51*	<0,01
Day 30	1,6±0,007	9,0±0,54*	5,7±0,34*	<0,01
<b>Cornea</b> Day 3	0,7±0,02	6,0±0,52*	5,0±0,38*	>0,05
Day 5	0,7±0,008	3,7±0,33*	3,7±0,32*	>0,05
Day 12	1,2±0,03	5,3±0,41*	4,3±0,48*	>0,05
Day 30	1,1±0,03	6,3±0,44*	6,7±0,21*	>0,05
<b>Sclera</b> Day 3	0,7±0,01	5,7±0,38*	6,7±0,32*	>0,05
Day 5	0,9±0,03	7,0±0,55*	7,0±0,44*	>0,05
Day 12	0,8±0,02	5,7±0,42*	7,0±0,43*	>0,05
Day 30	1,0±0,02	4,3±0,22*	6,7±0,31*	<0,001
<b>Lens</b> Day 3	0,9±0,01	5,3±0,48*	7,0±0,16*	<0,01
Day 5	1,1±0,004	4,7±0,51*	4,6±0,22*	>0,05
Day 12	0,8±0,01	3,7±0,43*	5,3±0,33*	<0,05
Day 30	1,4±0,01	3,3±0,52*	8,0±0,36*	<0,001

**Note:** \* – reliability of difference of the appropriate units with similar values in intact animals, P – reliability of difference data in the groups being compared (FA and SA).

Comparative analysis of the ABL to TA of anterior segment showed that for FA and SA there are a number of similar features. Analysis of characteristics of

degenerative processes and ABL to TA showed that in FA on day 30 of the burn the severity of tissue damage reduces twofold, whereas in SA even on day 30 the extent of the vitreous syneresis is similar to the initial level of day 3-5 of the burn.

Similar results were obtained from the study of ABL to TA of choroid. Hence, in FA gradual restoration of choroid occurs and on day 30 it is only 1,5 times higher than normal level of ABL to TA of this tissue in 2%.

Comparative analysis of ABL to TA of cornea lens demonstrated that in FA damage of these tissues increased and on day 30 of the burn even prevailed the damage in SA.

As was indicated earlier, in SA it was noted that reparation of the tissues of anterior segment was slow and increased towards the end of the month. However, the ABL to TA of cornea and lens the process in SA was noted to be milder than in FA.

**Summary.**

- In FA animals restoration of vascular and scleral tissues of the eyes demonstrates positive dynamics, whereas in SA destruction of these tissues does not slow, but also it increases to day 30;

- In cornea and lens degenerative processes increase both in FA and in SA towards the day 30 of the experiment and ABL to TA of cornea and lens become more severe as compared to day 3. These changes are more pronounced in FA;

- In SA degeneration of anterior segment tissues follows slow and prolonged pattern and requires extensive treatment than in FA, especially in relation to damage of sclera and choroid.

**Prospects of further researches.** Based on the results of the study, optimization of ocular burn management depending on Acetylation phenotype is recommended.

**Bibliography**

1. Egorov V. V. Features of primary open angle glaucoma with normal IOP in patients with various constitutional types of metabolic status / V. V. Egorov, E. L. Sorokin, G. P. Smolyakovo // Rus. med. jour. – 2003. – Vol 4, №1. – P. 15-17.
2. Husainova V. H. Diagnosis, treatment and prophylaxis of synechial process in the minor pelvis in women with tuboperitoneal infertility / V. H. Husainova, T. A. Fedorova, N. I. Volkov // Gynecology. – 2003. – Vol. 5, №2. – P. 23-25.
3. Kovalov I. E. Immunochemical functional system of homeostasis in infectious and non-infectious pathology / [I. E. Kovalov, E. I. Musabaev, M. D. Ahmedova]. – Tashkent: Navruz, 1994. – 196 p.
4. Maksumov A. A. Evaluation of effectivity of new medication benketazon in the management of ocular chemical burn. Autoref. PhD / A. A. Maksumov/ – Tashkent, 2007. – P. 3.
5. Nabieva Sh. A. Effectivity of transcutaneous laser therapy in acute viral hepatitis B in children in relation to Acetylation phenotype. PhD dissertation / Sh. A. Nabieva/ – Tashkent, 2009. – p. 118.
6. Odilova G. P. Improvement of ocular burn management. Autoref. PhD / G. P. Odilova. – Tashkent, 2010. – P. 3.
7. Piruzyan L. A. Human metabolic passport – foundation of the new strategy in pharmacology / L. A. Piruzyan // Vestnik RAN. – 2004. – №7. – P. 610-618.
8. Piryzian L. A. The metabolite passport of human / L. A. Piryzian // Science magazine. – 2005. – V. 309. – P. 81.
9. Puzirev V. P. Pharmacogenetic / V. P. Puzirev // Medical gynecology. – 2003. – Jul. – P. 21-46.
10. Soblirova J. H. Fast Acetylation type – a possible marker of predisposition to urinary tract diseases / J. H. Soblirova, E. A. Harina // Nephrology and dialysis journal. – M., 1999. – T. 1, № 1-2. – P. 30-36.
11. Umarova L. F. Comparative morphological characteristic of various methods of treatment of corneal alkaline burn (experimental research) Autoref. PhD / L. F. Umarova. – Tashkent, 2005. – P. 3.

UDC 17.72:616\_003.93-097:612.42:575.1

### **Degenerative Changes Of The Anterior Segment Tissues Depending On The Phenotype Of Acetylation In The Experiment**

**Maksudova L. M.**

**Summary.** The study was performed on 100 white rats weighing 180-200 g. Acetylation phenotype in rats was evaluated: fast acetylators (FA) and slow acetylators (SA). Research showed that SA are as twice common as FA (64% vs. 36%). In chemical burn degenerative changes of anterior segments of experimental animals lasting more than 30 days were noted independent of Acetylation phenotype. In FA animals restoration of vascular and scleral tissues of the eyes demonstrates positive dynamics, whereas in SA destruction of these tissues does not slow, but also it increases to day 30. In cornea and lens degenerative processes increase both in FA and in SA towards the day 30 of the experiment and ABL to TA of cornea and lens become more severe as compared to day 3. These changes are more pronounced in FA. In SA degeneration of anterior segment tissues follows slow and prolonged pattern and requires extensive treatment than in FA, especially in relation to damage of sclera and choroid. Based on the results of the study, optimization of ocular burn management depending on Acetylation phenotype is recommended.

**Key words:** ophthalmology, Acetylation phenotype, reparation, regeneration, tissue antigens (TA), antigen binding lymphocytes (ABL).

УДК 617.72:616\_003.93-097:612.42:575.1

### **ДЕГЕНЕРАТИВНЫЕ ИЗМЕНЕНИЯ В ТКАНЯХ ПЕРЕДНЕГО ОТРЕЗКА ГЛАЗА В ЗАВИСИМОСТИ ОТ ФЕНОТИПА АЦЕТИЛИРОВАНИЯ В ЭКСПЕРИМЕНТЕ**

**Максудова Л. М.**

**Резюме.** Исследование проведено на 100 белых крысах весом 180-200 г. Изучали фенотип ацетилирования у крыс: быстрые ацетиляторы (БА) и медленные ацетиляторы (МА). Установлено, что среди экспериментальных животных МА встречаются почти в 2 раза чаще, чем БА (64,0% и 36,0%). При химическом ожоге у экспериментальных животных отмечаются дегенеративные изменения всех отделов переднего отрезка глаз независимо от ФА, которые сохраняются более 30 дней. У животных с БА восстановление тканей сосудов глаз и склеры протекает с выраженной положительной динамикой, в то время как у МА процесс деструкции этих тканей не только не купируется, но и к 30 дню еще более нарастает. Со стороны роговицы и хрусталика дегенеративные процессы как у БА, так и у МА нарастают к 30 дню эксперимента и значительно превышают показатели АСЛ к ТА роговицы и хрусталика в первые 3 дня эксперимента и более выражены эти изменения у БА. У МА процессы дегенерации тканей переднего отрезка глаз носят более затяжной характер и требуют более продолжительной терапии, чем БА, особенно по показателям поражения склеры и сосудистой ткани глаз. Полученные результаты дают основание рекомендовать оптимизировать терапию ожогов глаз с учетом фенотипа ацетилирования.

**Ключевые слова:** офтальмология, фенотип ацетилирования, репарация, регенерация, тканевые антигены (ТА), антиген связывающие лимфоциты (АСЛ).

УДК 17.72:616\_003.93-097:612.42:575.1

### **ДЕГЕНЕРАТИВНІ ЗМІНИ В ТКАНИНАХ ПЕРЕДНЬОГО СЕГМЕНТА ОКА В ЗАЛЕЖНОСТІ ВІД ФЕНОТИПУ АЦЕТИЛЮВАННЯ В ЕКСПЕРИМЕНТІ**

**Максудова Л. М.**

**Резюме.** Дослідження проведено на 100 білих щурах вагою 180-200 р. Вивчали фенотип ацетилювання у щурів: швидкі ацетилятори (ША) і повільні ацетилятори (ПА). Встановлено, що серед експериментальних тварин ПА зустрічаються майже в 2 рази частіше, ніж БА (64,0% і 36,0%). При хімічному опіку у експериментальних тварин відмічаються дегенеративні зміни всіх відділів переднього сегменту ока незалежно від ФА, які зберігаються більше 30 днів. У тварин з ША відновлення тканин судин очей і склери протікає з вираженою позитивною динамікою, тоді як в ПА процес деструкції цих тканин не лише не купіюється, але і до 30 дня ще більш наростає. З боку рогівки і кришталіка дегенеративні процеси як в ША, так і в ПА наростають до 30 дня експерименту і значно перевищують показники АСЛ до ТА рогівки і кришталіка в перші 3 дні експерименту, і більш виражені ці зміни в ША. В ПА процеси дегенерації тканин переднього сегменту ока носять більш затяжний характер і вимагають тривалішої терапії, ніж ША, особливо за показниками поразки склери і судинної тканини очей. Отримані результати дають підставу рекомендувати оптимізувати терапію опіків очей з врахуванням фенотипу ацетилювання.

**Ключові слова:** офтальмологія, фенотип ацетилювання, репарація, регенерація, тканинні антигени (ТА), антиген зв'язуючі лімфоцити (ABL).

Стаття надійшла 8.11.2012 р.

Рецензент – проф. Воскресенська Л. К.