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НОВЫЙ ПОДХОД К ФАРМАКОТЕРАПИИ ГЕМОФТАЛЬМА

Мусаева Д.М.[1]

[1] к.м.н., доцент кафедры Фармакологии и клинической фармакологии Бухарского государственного медицинского института имени Абу Али ибн Сино МЗ РУз, г.Бухара ул. Наваи 1, 200100. e-mail: dilyafarma@mail.ru, https://orcid.org/0000-0002-7207-1479

Аннотация. Изучив сравнительную эффективность различных способов введения «Гемазы» при лечении пациентов с гемофтальмом, в клинических исследованиях нами были проанализированы результаты лечения пациентов, которые были разделены на 2 группы; в I (n = 25) — в субконъюнктивально «Гемаза»; во II (n = 25) — интравитреально «Гемаза». Интравитреальное введение вызывает ускоренное рассасывание гемофтальма и восстановление остроты зрения.

Ключевые слова: гемофтальм, фибринолитики, стекловидное тело, рассасывание крови, ферменты, «Гемаза».

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A NEW APPROACH TO THE PHARMACOTHERAPY OF HEMOPHTHALMIA

Musaeva D.M.[1]

[1] Candidate of Medical Sciences, Associate Professor of the Department of Pharmacology and Clinical Pharmacology of the Bukhara State Medical Institute named after Abu Ali ibn Sino, Ministry of Health of the Republic of Uzbekistan, Bukhara st. Navai 1, 200100. dilyafarma@mail.ru, https://orcid.org/0000-0002-7207-1479

Abstract. Having studied the comparative effectiveness of various methods of administration of "Gemase" in the treatment of patients with hemophthalmia, in clinical studies we analyzed the results of treatment of patients who were divided into 2 groups; in I (n = 25) - in subconjunctival "Gemase"; in II (n = 25) - intravitreal "Gemase". Intravitreal administration causes accelerated resorption of hemophthalmia and restoration of visual acuity.

Keywords: hemophthalmus, fibrinolytics, vitreous body, blood resorption, enzymes, «Gemase».

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RELEVANCE

Difficulties faced by ophthalmologists in the treatment of hemorrhagic complications in patients are associated with the anatomical and physiological features of the vitreous body. The vitreous body has practically no fibrinolytic activity, and blood resorption, in the case of hemophthalmos, proceeds slowly [7, 11], therefore, the use of enzymes in the treatment of vitreous hemorrhages is pathogenetically justified [1, 6]. Even with the use of modern enzyme preparations, resorption of hemorrhages occurs extremely slowly [3, 8, 12], which is due to the insufficient effectiveness of existing methods of drug administration and the impossibility of creating a sufficiently high concentration of the drug with extraocular methods of administration due to the high selective ability of the hematoophthalmic barrier [5, 10].

"Gemase" is a lyophilized enzyme preparation containing recombinant prourokinase (RPU) placed on an inert carrier, which includes dextran and sodium chloride. RPU catalyzes the conversion of plasminogen into plasmin, a serine protease capable of lysing fibrin clots, and has a high specificity of action, as it activates plasminogen mainly in the clot area, which reduces the risk of possible bleeding and hemorrhages [2, 4].In accordance with the manufacturing technology of the Gemase preparation, a sterile solution of rheopolyglucin is used to create an inert matrix, into which a purified enzyme, recombinant prourokinase, is introduced before the stage of sterilization and lyophilization of the preparation. Created on the basis of RPU drug "Gemase" is intended for use as a fibrinolytic agent in ophthalmology. The specific activity of "Gemase" is at least 85,000 IU per 1 mg of protein [2, 9]. The drug "Gemase" is highly soluble in water and isotonic sodium chloride solution, sterile and apyrogenic. Release form: 5000 IU lyophilized powder is packaged in 1 ml ampoules. "Gemase" is stored at a temperature not exceeding +25 °C in a dry place protected from light for 1 year. The dosage form of "Gemase" is approved for use by the Pharmacological Committee of the Republic of Uzbekistan. Department of State Control of Quality, Efficiency, Safety of Medicines and Medical Equipment of the Ministry of Health of the Republic of Uzbekistan.

THE AIM OF THE STUDY

was to study the effectiveness of various methods of administration of "Gemase" in the treatment of hemophthalmia.

MATERIALS AND METHODS OF RESEARCH

We observed 50 patients with the proliferative stage of diabetic retinopathy complicated by hemophthalmos, who were divided into 2 groups: Group I (n = 25) — in the hospital, 5000 IU of Gemase was injected into the sub-Tenon's space 1 time per day in dose of 5000 IU from 2 to 7 days (average 4 days). Group II (n = 25) — "Gemase" was injected intravitreally on the day of admission at a dose of 500-1000 IU once, then continued subconjunctivally daily at a dose of 5000 IU from 2 to 5 days (average 3.5 days). All patients were under the

supervision of an endocrinologist for type I diabetes mellitus for about 20 years.

Additionally, as the transparency of the optical media was restored, each patient recorded the day when the fundus was visualized.

To assess the general status, indicators of general clinical and biochemical blood tests were analyzed, as well as indicators characterizing the state of the coagulation system: prothrombin index, fibrinogen, active recalcification time, clotting time and bleeding time. These data were analyzed before treatment and again after 7 days.

Attention was drawn to the tolerance and development of local and systemic manifestations of allergic reactions when using drugs, as well as the frequency of repeated hemorrhages.

RESULTS AND ITS DISCUSSION

When studying the pharmacokinetics of "Gemase" [1, 5, 7, 12], it was proved that 90% of the administered dose enters the vitreous body during intravitreal administration. With extraocular methods of introducing "Gemase": subconjunctival, parabulbar, into the sub-Tenon space with a needle or using sub-Tenon implantation of a collagen infusion system (SICIS) in the vitreous body, its content is much less - from 0.05 to 5% of the administered dose.

When analyzing the dynamics of average indicators of visual acuity and "hemophthalmos index" in the groups, it was noted that after a day the highest visual acuity and the largest decrease in the "hemophthalmos index" occur in group II, where "Gemase" was administered intravitreally. The half-life of the drug from the vitreous body is about 8 hours [1, 5, 7], which allows you to start the fibrinolysis reaction in the vitreous body immediately after the administration of the drug. In group I, the accumulation of the drug in an amount sufficient for effective fibrinolysis occurs at a later date, so the lysis of the clot begins later, so the average visual acuity in these groups has a statistically significant difference from the initial one on the 3rd day of observation.

Since visual acuity may depend on the state of the retina, for an integral assessment of the restoration of the transparency of optical media, we analyzed the percentage of visualization of the fundus during ophthalmoscopy, depending on the timing of observation. The results show that in group II, the restoration of the transparency of optical media occurs much faster, and by the 7th day, in 90% of patients, the fundus is visualized, in group I, a little more than 50%.

Thus, "Gemase" should be used [1, 4, 10, 11] to increase the effectiveness of the treatment of hemophthalmia of various origins, the drug is most effective in resolving partial hemophthalmos. With recurrent hemophthalmia (including proliferative diabetic retinopathy), the effectiveness of the course of treatment is maximum with the first hemorrhage and decreases with subsequent relapses. There is a decrease in the effectiveness of the drug with the development of processes of mooring in the vitreous body. In severe proliferative changes in the retina with recurrent hemorrhagic complications, the use of Gemase may be associated with an increased risk of recurrent hemorrhage.

When evaluating the indicators of general clinical and biochemical blood tests, general urinalysis, no statistically significant differences were found in the groups, which confirms the absence of any systemic effect on the body with local administration of fibrinolytic drugs.

Separately, the coagulogram parameters were compared between the groups; no statistically significant differences were found in the average active recalcification time, prothrombin index, fibrinogen level, platelet count, bleeding time, clotting start and end times. This confirms the absence of a systemic effect on hemostasis with the local administration of Gemase.

CONCLUSIONS

Thus, the intravitreal administration of "Gemase" prevails over other methods and opens up opportunities for earlier laser surgery in diabetic retinopathy.

At the same time, no allergic complications from the use of Gemase were noted, and the frequency of repeated hemorrhages does not depend on the method of administration.

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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AVAILABILITY OF DATA AND MATERIALS

All data generated or analysed during this study are included in this published article.

AUTHORS' CONTRIBUTIONS

All authors contributed to the design and interpretation of the study and to further drafts. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

CONSENT FOR PUBLICATION

Not applicable.

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КОНФЛИКТ ИНТЕРЕСОВ

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов.

ИСТОЧНИКИ ФИНАНСИРОВАНИЯ

Авторы заявляют об отсутствии финансирования при проведении исследования.

ДОСТУПНОСТЬ ДАННЫХ И МАТЕРИАЛОВ

Все данные, полученные или проанализированные в ходе этого исследования, включены в настоящую опубликованную статью.

ВКЛАД ОТДЕЛЬНЫХ АВТОРОВ

Все авторы внесли свой вклад в подготовку исследования и толкование его результатов, а также в подготовку последующих редакций. Все авторы прочитали и одобрили итоговый вариант рукописи.

ЭТИЧЕСКОЕ ОДОБРЕНИЕ И СОГЛАСИЕ НА УЧАСТИЕ

Были соблюдены все применимые международные, национальные и/или институциональные руководящие принципы по уходу за животными и их использованию.

СОГЛАСИЕ НА ПУБЛИКАЦИЮ

Не применимо.

ПРИМЕЧАНИЕ ИЗДАТЕЛЯ

Журнал **"Интегративная стоматология и челюстно-лицевая хирургия"** сохраняет нейтралитет в отношении юрисдикционных претензий по опубликованным картам и указаниям институциональной принадлежности.

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