ESSENTIAL ROLE OF BRADIKININ IN THE COURSE OF BASIC LIFE PROCESSES

Victoria Vladimirovna Sarkisova
Umida Negmatovna Mavlyanova
Assistants of Samarkand State Medical Universitety
Regina Olegovna Xegay
Amina Aslamovna Numonova
Students of Samarkand State Medical Universitety

https://doi.org/10.5281/zenodo.7423783

Abstract. *Kinins are polypeptides formed from α 2-globulins in blood plasma under the influence of the enzyme kallikrein (kallikrein-kinin system). Most famous of them are bradykinin and kallidin. Bradykinin, as a member of the kinin group of proteins, is a physiologically and pharmacologically active peptide with vasodilatory properties. Due to its specific action, blood vessels expand and blood pressure drops. It is important to note that his actions are local in nature. This feature of the peptide is currently widely used in pharmacology for the treatment and prevention of heart failure and arterial hypertension. With discovering of an increasing number of processes under the influence of bradykinin and related diseases, as well as due to the extreme relevance of the topic due to the COVID-19 pandemic, at the moment the topic needs extensive research.*

Keywords: *bradykinin, bradykinin storm, kinins, vasodilator, COVID-19, hypotension, inflammation, humoral regulation.*

ESSENTIAL ROLE OF BRADIKININ IN THE COURSE OF BASIC LIFE PROCESSES

Аннотация. *Кинины — полипептиды, образующиеся из α2-глобулинов в плазме крови под влиянием фермента калликреина (калликреин-кининовая система). Наиболее известны из них брадикинин и каллидин. Брадикинин, входящий в группу кининовых белков, представляет собой физиологически и фармакологически активный пептид с сосудорасширяющими свойствами. Благодаря его специфическому действию расширяются сосуды и падает артериальное давление. Важно отметить, что его действия носят локальный характер. Эта особенность пептида в настоящее время широко используется в фармакологии для лечения и профилактики сердечной недостаточности и артериальной гипертензии. В связи с обнаружением все большего числа процессов под влиянием брадикинина и связанных с ним заболеваний, а также в связи с чрезвычайной актуальностью темы в связи с пандемией COVID-19, в настоящий момент тема нуждается в обширном исследовании.*

Ключевые слова: *брадикинин, брадикининовый шторм, кинины, сосудорасширяющие средства, COVID-19, гипотензия, воспаление, гуморальная регуляция.*

Relevance

In 2018 Russian researcher Natalya Lapina, with her colleagues from the University of Heidelberg, conducted an experiment on 42 male laboratory rats of the Spreg-Dawley line weighing 300-350 g, to study the effect of bradykinin. As result they discovered the role of the peptide in brain recovery after ischemia. It turned out that bradykinin relaxes the walls of the vessels of the brain and improves the blood supply to its damaged regions. The group of scientists concluded that it helps to restore the functioning of the cerebral vessels after focal

ischemia. Also in September 2020, a group of American scientists led by Joe Roche, relying on an analysis of the expression level of all genes of COVID-19 patients in comparison with gene expression in patients of the control group, discovered new aspects in the pathogenesis of COVID-19. The explanation for many of the symptoms of patients with COVID-19 was an elementary increase in the level of bradykinin, which is currently called the bradykinin storm.

Main part

The peptide was found in the brain of rabbits and studied by a group of Brazilian scientists under the leadership of M. Rocha e Silva in 1948. Moreover, its hypotensive properties were discovered practically in the same period.

The vasodilatory effect of bradykinin is almost 10 times greater than the effect of histamine and equally extends to the vessels of skeletal muscles and internal organs, including the coronary vessels. But this substance is unstable, bradykinin acts only for a few minutes. Its inactivation occurs with the participation of the enzyme carboxypeptidase, also called a converting enzyme. Interesting to note that this enzyme plays an extremely important role in the activation of angiotensin.

Bradykinin is produced in the kidney (a characteristic feature of the kidney is the secretion of a large amount of biologically active substances), in the lacrimal and sweat glands, where it locally expands the vessels of the skin. It is also secreted by basophils and mast cells.

As the reader knows, there are several regulatory mechanisms of vital activity in the human body. Bradykinin is one of the components of regulation by means of tissue hormones. The kinin group, to which bradykinin belongs, are tissue hormones. They occupy an intermediate position between hormones and metabolites as humoral regulation factors (paracrinia). These substances have a regulating effect on tissue cells by changing their biophysical properties (membrane permeability, their excitability), the intensity of metabolic processes, the sensitivity of cellular receptors, the formation of second intermediaries. As a result, the sensitivity of cells to nervous and humoral influences changes. Therefore, tissue hormones are called modulators of regulatory signals: they have a modulating effect. Tissue hormones are formed by non-specialized cells, but they act through specialized cellular receptors. Talking the regulatory mechanisms, we can also note the participation of bradykinin in the humoral regulation of gastrointestinal activity. It enhances the motility of the small intestine together with gastrin, serotonin, motilin, HCC, histamine, substance P, vasopressin and oxytocin, acting on myocytes and neurons of the enteral nervous system. Recent studies have shown possible causes of increased blood supply during gastrointestinal activity. Some glands of the gastrointestinal tract release two kinins into the wall of the digestive tract — collidin and bradykinin, at the same time they secrete their secret into the lumen of the digestive tube. These kinins seem to cause significant vasodilation of the mucous membrane that occurs during secretion.

Although bradykinin has an adaptive-trophic effect on the tissues of the nervous system, it is noteworthy that it belongs to the group of chemical stimuli. Receptors or free nerve endings that are present in teeth, skin, muscles, vessels, internal organs are excited by the action of these stimuli. As is known, one of the non-gas exchange functions of the lung is the function of enzymatic cleavage: more than 80% of bradykinin injected into the pulmonary bloodstream is destroyed by a single passage of blood through the lung. The kinin system is a single system with the process of blood clotting and fibrinolysis, the complement system. Its initial component, the Hageman factor, is activated on a negatively charged surface and, through a series of

cascading enzymatic reactions, leads to the conversion of bradykinogen into bradykinin, which dramatically increases the permeability of capillaries and promotes the attraction of phagocytic cells to the focus of inflammation from the blood. At rest, only 25-30% of the capillaries of their total number function in many tissues, and when active, their number increases - for example, in skeletal muscles up to 50-60%. The permeability of the vascular wall increases under the influence of histamine, serotonin, bradykinin, apparently due to the transformation of small pores into large ones. Bradykinin causes both an increase in capillary permeability and a significant expansion of arterioles. For example, injection of I mcg of bradykinin into the human brachial artery causes an increase in blood flow in the upper limb by at least 6 times. An even smaller amount of bradykinin injected locally into the tissues causes local hyperemia and edema, since there is an increase in the permeability of the capillary wall. Prostaglandins and bradykinin contribute to an increase in GFR. Hormones and biologically active substances, prostaglandins (PGE2 and PGI2) and bradykinin, cause vasodilation and increased blood flow together with GFR. Although these vasodilators normally do not play an important role in the regulation of renal blood flow or GFR, they can be a kind of buffer that softens the vasoconstrictor effect of sympathetic nerves or angiotensin II, especially in the fetal arteriole. In recent years, the role of various oligopeptides in the formation of motivations has been shown. Angiotensin, bradykinin, vasopressin change behavioral reactions formed on the basis of fear motivation. In some sources, bradykinin is included in the group- Neuropeptide slow-acting mediators, or growth factors. Bradykinin also plays an important role in the regulation of osmotic pressure and fluid volume in the body along with natriuretic hormone, natriuretic factor, plasmakinins, parathyroid hormone. By the beginning of the new century, humanity was faced with a global problem.

Materials and methods

Analysis of statistical data based on the official websites of Tass Nauka, the Federal State Budgetary Institution NATIONAL Medical

RESEARCH CENTER OF CARDIOLOGY" of the Ministry of Health of the Russian Federation and the publishing house "Internauka"

Results and discussions

They were made a small hole ("window") in the skull above one of the points of the right hemisphere. A miniature Doppler device was inserted into it to assess the blood supply to brain tissues fed by the middle cerebral artery. Then the scientists tied one of the internal carotid arteries (located in the neck) to rats with a special thread to disrupt the blood flow in the middle cerebral artery of the right hemisphere. After two hours, the thread on the internal carotid artery was untied and for 22 hours, blood circulation was restored in the tissues of the right hemisphere, that is, reperfusion occurs. After a day of observation, the brain of rats was extracted and the right and left middle cerebral arteries were separated from it. They were placed in a solution with a salt composition close to blood. A substance blocking one of two types of bradykinin receptors was added to it: in half of the cases it was a B1-receptor antagonist, in half it was a B2-receptor antagonist. After half an hour, the toxin U46619 was injected into the solution, causing narrowing of blood vessels, and after some time, bradykinin itself was injected in concentrations from 10-12 to 10-5 mol / L.

Conclusion

Since the discovery of bradykinin and its specific properties, scientists have been discovering more and more processes that it affects. Of course, bradykinin has extensive

physiological and pharmacological effects. This feature is very beneficial to scientists, who today see it as a solution to a huge number of problems. Since 2018, a huge number of experiments have been conducted to clarify the role of bradykinin not only in normal physiological processes, but also in the pathogenesis of particularly dangerous diseases. Of course, scientists recommend not to abuse this knowledge, warning against suddenly relying only on new data on the bradykinin storm in the treatment of the disease. However, the main breakthrough in the study of the effect of bradykinin on the body has been made. Perhaps in the near future, based on this knowledge, a new model of perception of the body and new methods of treatment of both congenital and acquired diseases will be created.

REFERENCES

1. ABOUT THE CAUSES OF ENDOMETRIAL HYPERPLASIA AND FORMS OF ENDOMETRIAL HYPERPLASIA SV Vladimirovna - ResearchJet Journal of Analysis and Inventions, 2022
2. АНТИБИОТИКОРЕЗИСТЕНТНОСТЬ ИЛИ БОРЬБА С ГЛОБАЛЬНОЙ УГРОЗОЙ XXI ВЕКА V Sarkisova, A Numonova, R Xegay - Science and innovation, 2022
3. АСПЕКТЫ СОСТОЯНИЯ ВЕГЕТАТИВНОЙ НЕРВНОЙ СИСТЕМЫ ПРИ ГИПОКСИИ V Sarkisova, A Numonova, R Xegay - Science and innovation, 2022
4. CAUSES, DIAGNOSIS, CONSERVATIVE AND OPERATIVE TREATMENT OF UTERINE MYOMAV Sarkisova, R Xegay - Science and innovation, 2022
5. ВЗАИМООТНОШЕНИЕ РЕАКТИВНОСТИ ВЕГЕТАТИВНОЙ НЕРВНОЙ СИСТЕМЫ И МОРФОФУНКЦИОНАЛЬНОЙ АКТИВНОСТИ БАЗОФИЛЬНЫХ КЛЕТОК АДЕНОГИПОФИЗА В ПОСТРЕАНИМАЦИОННОМ ПЕРИОДЕ АГ Карабаев - Наука и мир, 2020
6. ВЗАИМООТНОШЕНИЕ РЕАКТИВНОСТИ ВЕГЕТАТИВНОЙ НЕРВНОЙ СИСТЕМЫ И МОРФОФУНКЦИОНАЛЬНОЙ АКТИВНОСТИ БАЗОФИЛЬНЫХ КЛЕТОК АДЕНОГИПОФИЗА В ПОСТРЕАНИМАЦИОННОМ ПЕРИОДЕ АГ Карабаев - Наука и мир, 2020
7. Патогенетические основы нарушения морфофункциональной активности аркуатного ядра гипоталамуса в постреанимационном периоде* АГ Карабаев - Журнал Новый день в медицине, 2021
8. Морфофункциональные изменения в гипоталамо-гипофизарно нейросекреторной системе в процессе умирания и оживления организма (экспериментальное исследование) КОРЗИНА ПОИСК НАВИГАТОР ЖУРНАЛЫ КНИГИ ПАТЕНТЫ ПОИСК АВТОРЫ ОРГАНИЗАЦИИ КЛЮЧЕВЫЕ СЛОВА РУБРИКАТОР Начальная страница СЕССИЯ КОНТАКТЫ ИНФОРМАЦИЯ О ПУБЛИКАЦИИ eLIBRARY ID: 30200573 МОРФОФУНКЦИОНАЛЬНЫЕ ИЗМЕНЕНИЯ В ГИПОТАЛАМО-ГИПОФИЗАРНО НЕЙРОСЕКРЕТОРНОЙ СИСТЕМЕ В ПРОЦЕССЕ УМИРАНИЯ И ОЖИВЛЕНИЯ ОРГАНИЗМА (ЭКСПЕРИМЕНТАЛЬНОЕ ИССЛЕДОВАНИЕ) КАРАБАЕВ АМИНЖОН ГАДОЕВИЧ Тип: автореферат диссертации Год: 1998 Язык: русский Город: Ташкент Число страниц: 20 Специальность: 14.00.16 Ученая степень: кандидат медицинских наук КЛЮЧЕВЫЕ СЛОВА: ПАТОЛОГИЧЕСКАЯ ФИЗИОЛОГИЯ …

9. Relationship between the reactivity of the autonomic nervous system and the morphofunctional activity of basophilic cells of the adenohypophysis in the post-resuscitation period* AG Karabaev - SCIENCE AND WORLD, 2013
10. Карабаева Маржона Аминжоновна, Худоярова Дилдора Рахимовна. Вегетативной реактивности беременных при тяжелой формы железодефицитной анемии АГ Карабаев - Журнал. Новый день в медицине, 2021
11. ТЕМИР ТАНҚИСЛИГИ АНЕМИЯСИ БИЛАН КАСАЛЛАНГАН УРТАЧА СИМПАТИК НЕРВ ТИЗИМИ ТОНУСИГА ЭГА ТУГАДИГАН АЁЛЛАРДА ОНА-ЙУЛДОШ–ХОМИЛА ТИЗИМИДАГИ УЗГАРИШЛАР МА Карабаева, ДР Худоярова, АГ Карабаев - Gospodarka i Innowacje., 2022
12. REACTIVITY OF THE AUTONOMIC NERVOUS SYSTEM IN PREGNANT WOMEN WITH IRON DEFICIENCY ANEMIA OF MODERATE SEVERITY MA Karabaeva - Next Scientists Conferences, 2022
13. LEVELS OF PREGNANCY INFLAMMATION IN PHOSPHOROGANIC PESTICIDE POISONING KD Safoevna, MU Nematovna, LZ Xidirovna - Archive of Conferences, 2021
14. MNEMOTECHNIQUE AS ONE OF THE MODERN METHODS OF TRAINING OF FUTURE DOCTORS. DS KHAYDAROVA, UN MAVLYANOVA - … & APPLIED SCIENCE Учредители: Теоретическая и …, 2021
15. Application Of Mnemotechnique On Education In Medical Higher Schools KD Safoevna, MU Nematovna - The American Journal of Medical Sciences and …, 2020
16. 1.Tohirova J., Shernazarov F. ATHEROSCLEROSIS: CAUSES, SYMPTOMS, DIAGNOSIS, TREATMENT AND PREVENTION //Science and innovation. – 2022. – T. 1. – №. D5. – C. 7-12.
17. Farhod o'g'li S. F. GASTRIT—SABABLARI, ALOMATLARI, TASHXISLASH, DAVOLASH, DORILAR, ASORATLARI, OLDINI OLISH //Лучший инноватор в области науки. – 2022. – Т. 1. – №. 1. – С. 103-107.
18. Tohirova J., Shernazarov F. ATHEROSCLEROSIS: CAUSES, SYMPTOMS, DIAGNOSIS, TREATMENT AND PREVENTION //Science and innovation. – 2022. – T. 1. – №. D5. – C. 7-12.
19. F. Shernazarov ATHEROSCLEROSIS: CAUSES, SYMPTOMS, DIAGNOSIS, TREATMENT AND PREVENTION // SAI. 2022. №D5. URL: https://cyberleninka.ru/article/n/atherosclerosis-causes-symptoms-diagnosis-treatment-and-prevention (дата обращения: 20.10.2022).
20. F. Shernazarov, J. Tohirova, D. Jalalova TYPES OF HEMORRHAGIC DISEASES, CHANGES IN NEWBOENS, THEIR EARLY DIAGNOSIS // SAI. 2022. №D5. URL: https://cyberleninka.ru/article/n/types-of-hemorrhagic-diseases-changes-in-newboens-their-early-diagnosis (дата обращения: 20.10.2022).
21. Qizi T. J. I., Farrukh S. TREATMENT OF MYOCARDIAL INFARCTION AND FIRST AID //Science and innovation. – 2022. – T. 1. – №. D3. – C. 317-320.
22. Shernazarov F., Azimov A. INCREASED BRAIN PRESSURE-CAUSES, SYMPTOMS, COMPLICATIONS, TREATMENT //Современная медицина: новые подходы и актуальные исследования. – 2021. – С. 73-77.
23. qizi Tohirova J. I., og'li Ibragimov B. I., og'li Shernazarov F. F. CONGENITAL HEART DISEASE-CAUSES, CLASSIFICATION, DIAGNOSIS, TREATMENT,

COMPLICATIONS, CONSEQUENCES //Eurasian Journal of Medical and Natural Sciences. – 2022. – Т. 2. – №. 3. – С. 84-89.

24. Mratbaevna W. N., Farrux S. The Structure of the Heart and its Physiology in Regular Athletes //Eurasian Scientific Herald. – 2022. – Т. 8. – С. 102-105.
25. Farhod o'g'li S. F. GASTRIT—SABABLARI, ALOMATLARI, TASHXISLASH, DAVOLASH, DORILAR, ASORATLARI, OLDINI OLISH //Лучший инноватор в области науки. – 2022. – Т. 1. – №. 1. – С. 103-107.
26. Фаррух Ш. и др. ПУТИ УСТРАНЕНИЯ САХАРНОГО ДИАБЕТА //Science and innovation. – 2022. – Т. 1. – №. D3. – С. 313-316.
27. ПУТИ УСТРАНЕНИЯ САХАРНОГО ДИАБЕТА. Тоҳирова Жайрона Иззатилло Қизи, Шерназаров Фаррух «Science and innovation» 2022 yil 3-sonida 313-316 bet https://doi.org/10.5281/zenodo.6803520
28. Shernazarov Farrukh. (2022). TREATMENT OF MYOCARDIAL INFARCTION AND FIRST AID. "science and Innovation" International Scientific Journal. ISSN: 2181-3337, 1(3), 317–320. https://doi.org/10.5281/zenodo.6803550 Shernazarov Farrux. Eurasian Scientific Herald