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APPLICATION OF AEROSOL FORM OF NITROGLYCERIN IN EMERGENCY CARDIOLOGY (LITERATURE REVIEW)

Nitroglycerin is one of the most widely used treatments for coronary syndrome. The article provides an overview of nitrates and the primary efficacy of spray nitroglycerin as an ambulance.
Keywords: nitromint, aerosol, coronary syndrome

Nitroglycerin is one of the most widely used treatments for coronary syndrome. The chemical basis of the drug - glycerin trinitrate (1,2,3-propanetriol trinitrate) - was synthesized by the Italian chemist Ascanio Sobrero in 1846 during his research and search for new explosives. By the end of the 19th century, the list of diseases for which nitroglycerin was used was very wide: it included both angina pectoris and asthma, migraine and even epilepsy [1, 2].

Major research on the hemodynamic effects of nitroglycerin began in the last century, beginning in the 1930s. Since then, a large number of nitroglycerin preparations have been created in the world. Scientists have invented new forms of the drug, such as aerosol, sublingual tablets, oral tablets, buccal and intravenous [1, 2, 3]. However, the question of the most effective dosage form for relieving angina attacks continues to be debated.

Despite the fact that nitroglycerin preparations have been used for over 100 years, interest in this group of drugs is still quite high. This is due to the fact that new, previously unknown, mainly positive effects of drugs from this group are being discovered, which are widely used in the cardiological practice of emergency medicine.

Another colossal breakthrough in the development of medical science is associated with nitroglycerin. On the example of this substance, the withdrawal syndrome (rebound) was first described. He was noticed by doctors observing the workers of the first dynamite factories. At that time, as you know, no one thought about air purification at industrial enterprises. Therefore, the proletariat, daily inhaling the vapor of nitroglycerin, noticeably got used to it. During holidays and weekends without "their dose", young people in their prime began to feel a severe headache and even ... suddenly died from myocardial infarction. Moreover, atherosclerotic changes in the coronary vessels were often not detected. Savvy workers independently "invented" a method of combating withdrawal syndrome and a transdermal route of nitroglycerin administration. Going for the weekend, they simply "borrowed" a bottle of the coveted liquid and rubbed it into their whiskey.

Simultaneously with the withdrawal syndrome, nitroglycerin "pursues" another problem - the development of tolerance to the drug. That is, over time, in order to achieve a therapeutic effect, patients had to repeatedly increase the dose. So there were patients with angina pectoris between two fires. On the one hand, they must constantly take nitrates so that they do not develop withdrawal syndrome, on the other hand, their constant intake is associated with gradual addiction. The only way to deal with the latter until recently was an intermittent assignment scheme. This means that within 4-5 hours during the day, the concentration of nitrates in the blood should be minimal. Therefore, it is so important that patients taking nitrates adhere to the temporary treatment regimen prescribed by the doctor.

However, the fight against the deficiencies of nitroglycerin and nitrates (rebound syndrome and tolerance) had a very positive effect on the development of pharmacology. After all, she forced to seek more and more new dosage forms: sublingual capsules, aerosols, tablets, plasters, solutions for parenteral administration, retard forms ... Perhaps, it is difficult to find a substance that would be presented on the pharmaceutical market with such a variety of dosage forms. And what is important, they all have every right to exist and find their buyer. So, sublingual capsules, used since 1925, are designed for emergency relief of an attack of angina pectoris and are still considered the gold standard for solving this problem, despite their more than venerable age. And modern retard forms of tablets, taken by patients once a day, were invented to prevent the development of these very attacks, episodes of "silent" myocardial ischemia and to avoid the development of tolerance. That is, they maximally lengthen the period of action of the drug and create a safe, nitrate-free time period.

Since 1967, the production of aerosolized nitroglycerin began, the use of which in emergency cardiology has shown a number of advantages over other forms of nitroglycerin [3, 4].

The last significant nitroglycerin-related event occurred in 1998. Three scientists - F. Murad (University of Texas at Houston), R. Furchgott (State University of New York) and L. Ignarro (University of California at Los Angeles) - received the Nobel Prize for a detailed description of the physiological effects of nitroglycerin. Indeed, until then the mechanism of action of the drug was unclear and when it was prescribed, doctors relied only on empirical data. Nitroglycerin is converted to nitric oxide in smooth muscle cells in blood vessels, which in turn activates an enzyme that can relax smooth muscle cells and dilate the vessel. The result is a decrease in myocardial oxygen demand and an increase in oxygen saturation [5, 6, 7, 8].

Nitrates have a pronounced vasodilating effect, the most potent on the veins. As a result, venous flow to the heart is reduced, and left ventricular volume and tension (“preload”) are reduced. This leads to a decrease in myocardial oxygen demand. A decrease in myocardial oxygen demand, in turn, leads to a redistribution of coronary blood flow in favor of ischemic areas of the myocardium [8, 9, 10].

Among NG preparations, Nitromint (EGIS) deserves special attention - a nitroglycerin preparation stabilized with ethyl alcohol and propylene glycol in the form of a sublingual aerosol dosed at 0.4 mg / dose. The main indications for its use are:

- relief of acute attacks of angina pectoris
- prevention of angina attacks when used before physical or mental stress, which previously caused an angina attack
- adjunctive therapy in emergency cases with acute left ventricular failure (cardiac asthma).

Among the advantages of nitromint are: more rapid onset of the effect (compared to tablet forms) [11, 12]; dosage accuracy - when you press the valve, a well-defined dose of nitroglycerin can be released; it is more convenient to use, the shelf life of aerosol nitroglycerin (4 years) is much higher than that of the tablet form. Nitromint can be effectively used in case of difficult contact with the patient, as well as in unconscious patients. Its antianginal activity is not inferior to parenteral forms with fewer side effects, which is especially important in an emergency medical service. Nitromint can be used for prophylaxis before physical activity, which is known to provoke angina pectoris. Nitromint has a slower onset of action than nitroglycerin due to its conversion to mononitrate in the liver.

The effectiveness of the introduction of nitroglycerin in the form of a spray has been studied in various studies [13, 14, 15, 16]. The results show that the use of Nitromint in the form of an aerosol in an emergency medical service in patients with coronary heart disease not only improves the quality of life due to the rapid cessation of angina attacks, but is also economically expedient, since it reduces the number of hospitalizations and treatment costs (P.A. Vorobiev, AV Vlasova, 2004) [14].

A multicenter open clinical study "NOKS" (nitrates and acute coronary syndrome) (Vertkin AL et al., 2005) was carried out at 13 ambulance stations in Russia and Kazakhstan. The study has proven that the use of nitroglycerin in the form of an aerosol is associated with fewer side effects than infusion of nitroglycerin. The study of nitroglycerin in the form of an aerosol in patients with ACS without ST elevation in terms of the intensity of the analgesic effect showed that it is not inferior to the parenteral forms [6]. Side effects in the form of hypotension and tachycardia after intravenous administration of nitroglycerin occurred in more cases than after sublingual administration, and facial hyperemia and headache after intravenous administration were diagnosed as often as with sublingual administration (Vertkin A.L., 2005).

A review of the latest 2019 ESC (European Society of Cardiology) Guidelines for the Diagnosis and Treatment of Chronic Coronary Syndromes [17] indicates that immediate relief of anginal symptoms or prevention of symptoms in circumstances that may cause angina pectoris is usually achieved with fast acting nitroglycerin preparations, sublingual and short-acting nitroglycerin spray preparations provide immediate relief of angina attacks. Aerosol of nitroglycerin acts faster than sublingual nitroglycerin [16, 17]. According to these guidelines, long-acting nitrate preparations (eg, nitroglycerin, isosorbide dinitrate, and isosorbide mononitrate) should be considered second-line therapy for angina relief when initial therapy with a beta-blocker or non-dihydropyridine is contraindicated, poorly tolerated, or insufficient to control symptoms. With prolonged use, long-acting nitrates cause tolerance with a loss of effectiveness, which requires the appointment of a period of rest from nitrates or a long interval between doses. Withdrawal syndrome is almost always accompanied by another danger - the development of tolerance to the drug.

The most common side effects of nitroglycerin are hypotension, headache, and flushing. Contraindications include severe hypotensive conditions and the simultaneous administration of phosphodiesterase inhibitors (eg, sildenafil, tadalafil or vardenafil) or riociguat [18, 19].

Correct use of modern forms of nitrates for the relief and prevention of angina pectoris in adequate doses and individually selected for the patient's regimen as monotherapy or as part of a combination of antianginal treatment can effectively solve the problems faced by cardiologists [20, 21].

Conclusion

After analyzing the literature data, among the advantages of the aerosol form of nitroglycerin Nitromint in comparison with the tablet forms, one can single out: faster onset of the effect; dosage accuracy; longer shelf life; the possibility of using in case of difficult contact with the patient, which is especially important in an ambulance.

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С.Ж. Асфендияров атындағы Қазақ Ұлттық медицина университеті жедел және шұғыл медициналық көмек кафедрасы

НИТРОГЛИЦЕРИНДІҢ АЭРОЗОЛЬДІ ФОРМАСЫН ШҰҒЫЛ КАРДИОЛОГИЯДА ҚОЛДАНУ (ӘДЕБИЕТТЕРГЕ ШОЛУ)

Түйін: Нитроглицерин коронарлық синдромды емдеудің ең кең таралған әдістерінің бірі болып табылады. Мақалада нитраттарға шолу және жедел жәрдем ретінде спрей түрінде нитроглицериннің алғашқы тиімділігі туралы ақпарат берілген.
Түйінді сөздер: нитроминт, аэрозоль, коронарлық синдром

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ПРИМЕНЕНИЕ АЭРОЗОЛЬНОЙ ФОРМЫ НИТРОГЛИЦЕРИНА В НЕОТЛОЖНОЙ КАРДИОЛОГИИ (ОБЗОР ЛИТЕРАТУРЫ)

Резюме: Нитроглицерин является одним из наиболее широко используемых средств лечения коронарного синдрома. В статье приводится обзорная информация о нитратах и преимущественной эффективности нитроглицерина в форме спрея в качестве средства скорой помощи.
Ключевые слова: нитроминт, аэрозоль, коронарный синдром