Aminoglycoside antibiotics: from selective toxicity to homeopathic and isopathic therapy

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Aminoglycoside antibiotics are among the oldest antibacterial agents. The experience of clinical use of streptomycin has about 60 years, the same amount of time known for its most serious side effect - cochleo- and vestibulotoxicity with a frequent transition to irreversible sensorineural hearing loss or vestibulopathy. These effects, as is currently known, are caused by almost all aminoglycosides [1].

However, in our opinion, this effect carries a certain therapeutic potential for use in clinical medicine for indications based on the “principle of similarity”. In accordance with it, aminoglycosides can be used as drugs for the treatment of auditory and vestibular disorders that have developed as a result of side effects on the inner ear (this approach is called "isopathy"), and etiologically unrelated to aminoglycosides (which corresponds to the homeopathic approach).

At first glance, the idea of using potentiated aminoglycosides for the treatment of auditory and vestibular disorders according to the principles of isopathy and homeopathy is new and unexpected, although, from the point of view of homeopathy, it is quite logical, and the approach itself is routine.

The purpose of this article is to substantiate the principle of application potentiated (with dynamization, as is customary in homeopathy) aminoglycosides to eliminate auditory and vestibular disorders, both etiologically related and not related to their pharmacotherapeutic use.

In otorhinolaryngology, there is a generally accepted opinion about the irreversibility of the processes of degeneration of the neuroepithelium of the organ of Corti, which is based on the experience of using a huge number of drugs of various pharmacological groups and other methods of treatment. This is evidence that in clinical medicine there are no effective conservative methods for the treatment of sensorineural hearing loss caused by the use of aminoglycoside antibiotics. This is especially true in cases when there is sensorineural hearing loss with stabilization of hearing thresholds and the completion of the process of degeneration of cochlear receptors and neurons of a specific auditory pathway. In such cases, according to N.A. Preobrazhesky and B.M. Sagalovich, the leading methods are reeduction,

However, in recent decades, works have appeared in the literature that inspire optimism in solving this problem. It is associated with data on the ability of hair cells of the neuroepithelium of the organ of Corti, partially damaged

the introduction of aminoglycosides, to regeneration [3]. At the same time, other authors point to the possibility of restoring the population of hair cells due to phenotypic conversion of cells of the supporting epithelium [4].

In addition, a large amount of evidence has recently been obtained that refutes the toxic mechanism of side effects of aminoglycosides on the hair cells of the cochlear and vestibular systems, translating the problem into the sphere of “paradoxical” effects, denoted by the term “idiosyncrasy” [5].

Indeed, the "toxic potential" of aminoglycosides cannot be associated with their concentration in the media and tissues of the organ of Corti [6], with the chemical structure [5], in the experiment the effect is reproduced not in all experimental models, and the tropism to the structures of the inner ear differs in different drugs. although any antibiotic can cause any manifestation of ototoxicity. However, in the same patient, either auditory or vestibular disorders prevail [6].

Hearing disorders are more often associated with the use of amikacin, kanamycin, neomycin, netilmicin and paromycin [1, 6]. Neomycin is the most cochleotoxic aminoglycoside, while netilmicin is characterized by the least toxicity [7]. With the use of aminoglycosides, auditory disorders are presented by ringing, tinnitus and hearing loss of varying degrees, up to deafness. Decreased perception of high-frequency tones can only be detected by audiometric examination [6]. Vestibular disorders most often develop with streptomycin, gentamicin, or tobramycin and are represented by nausea, vomiting, dizziness, nystagmus, oscillopsia, and ataxia. These manifestations intensify in the dark [5].

The first symptoms of the side effect of aminoglycosides on the inner ear in the form of tinnitus may occur as early as 3-5 days of antibiotic use, but may also appear several days or weeks after stopping its use. The latter circumstance is a negative prognostic sign and indicates the development of chronic hearing loss [8].

Risk factors for the development of these symptoms are old age, initial hearing loss or vestibular apparatus, large doses of drugs, long courses of treatment, concomitant use of other ototoxic drugs [1].

These observations suggest that there is a certain psychophysical type of persons (by analogy with constitutional types in homeopathy), sensitive to aminoglycosides. If the psychological characteristics of such persons remain a mystery, then the somatic signs quite definitely indicate that there is a congenital "weakness" of the auditory and vestibular systems.

This is confirmed by the data of genetic studies, according to which the development of hearing disorders as a result of the use of aminoglycosides is associated with genetic mutations in the 12S position of ribosomes designated as A1555G and DT9HCN. In carriers of these mutations, hearing disorders often develop without the use of aminoglycosides [9], which gives

reason to attribute this pathology of idiosyncrasy to aminoglycosides, where the latter cause only the phenotypic manifestation of the mutation. There is evidence, albeit few, that the described mutations suggest toxic damage to the cochlea without involvement of the vestibular system in the process [10].

Aminoglycosides, along with inner ear symptoms, cause a variety of other serious side effects such as nephrotoxicity, neuromuscular blockade with respiratory depression, and complete paralysis of the respiratory muscles. The risk of the latter increases sharply when aminoglycosides are used by patients with parkinsonism, myasthenia gravis, and they are dose-dependent. Unlike other aminoglycosides, hepatotoxicity (increased activity of "hepatic" transaminases and hyperbilirubinemia) has been described for sisomycin, at the same time hepatoprotective and antitoxic effects have been noted [11].

Thus, it can be assumed that there are two main types of sensitivity: neomycin, with a predominant lesion of the cochlear neuroepithelium, and streptomycin, with involvement of the vestibular system in the process, and potentiated aminoglycosides are constitutional drugs for persons with corresponding auditory and vestibular disorders. At the same time, the lack of results of trials (provings) of drugs on healthy subjects, as is customary in homeopathy, can be compensated for by clinical descriptions of the manifestations of the toxic effects of aminoglycosides, which may well be combined into drug pathogenesis, as is customary in homeopathy.

Within the framework of academic medicine, the use of aminoglycosides according to the principles of isopathy and homeopathy (in the case of idiosyncrasy to aminoglycosides, the line between isopathy and homeopathy is practically erased) can be scientifically substantiated from various positions.

First, from the standpoint of the phenomenon of pharmacological hormesis (inversion of the effect) [12]. In the literature, facts are described when chemical and physical factors, with a decrease in the intensity of their impact on a living organism, have unexpected, sometimes opposite in direction, effects. A large number of studies in ecotoxicology and pharmacology have been devoted to these effects, and, despite the polarity of opinions regarding the mechanisms and biological significance, the objectivity of such phenomena is beyond doubt.

Secondly, the literature describes cases when the symptoms of acute or chronic intoxication with any substance are eliminated by prescribing the same substance in a potentiated form [13]. This isopathic approach is illustrated by experiments in a double-blind controlled study, where mustard gas burns were treated with small doses of the same mustard gas. There is evidence that potentiated prednisolone has been successfully prescribed for such a complication of corticosteroid therapy as Itsenko-Cushing's syndrome [14].

Third, meta-analysis controlled clinical trials potentiated drugs (used according to the principles of isopathy and homeopathy), carried out on the basis of modern principles of evidence-based medicine, showed the advantage of these methods over placebo [15].

Fourthly, in modern clinical medicine one can find quite a lot of cases of drug use, when the indications are justified on the basis of pharmacological mechanisms of action, and upon close examination, such prescriptions are based on the same “principle of similarity”, which is routine for homeopathy. Thus, morphine (or other narcotic analgesics) for the purpose of relieving pulmonary edema in cardiac asthma is the drug of choice, which is justified by its sedative and peripheral venodilatory effects [16], while from toxicology it is known that pulmonary edema, along with respiratory depression, is the most a common cause of death from opiate drug overdose [17].

Antihypertensive drug clonidine (Gemiton, clonidine) at exceeding the dose causes the opposite effect - an increase in blood pressure, and the dose of 0.075 mg in 1 tablet is comparable to the 3-hundredth homeopathic potency [11]. The homeopathic pathogenesis of cardiac glycosides consists of a large number of cardiac symptoms, including symptoms of severe heart failure and rhythm disturbances [18], which are the main indications for their use in cardiology [11]. This list of examples can be continued.

According to the classic of homeopathy D.T. Kent, the author of the fundamental works on the philosophy of homeopathy and the homeopathic Materia Medica: “It follows from all this that if a person did not have susceptibility, if there was no such condition as idiosyncrasy, then there would be no homeopathy. If there was no susceptibility, there would be no disease, and homeopathy would not be needed ”[19].

Output

The approaches to solving the problems of drug disease outlined in the article open up new directions for the treatment of aminoglycoside sensorineural hearing loss.

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Abakarov, M.G. Aminoglycoside antibiotics: from selective toxicity to homeopathic and isopathic therapy / M.G. Abakarov, M.M. Magomedov // Traditional Medicine. - 2006. - No. 2 (7). - P.7-10.

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