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Review Article

Modern approaches and perspectives on the prevention and treatment of high-intensity noise damage in military personnel

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The specifics of military labor, the effect of harmful, and sometimes dangerous factors in the form of impulse noise, shock waves, and constant high-level noise, leads to the risk of developing atraumatic damage to the hearing organ in military personnel. The urgency of the problem is caused by the lack of a unified theory of the pathogenesis of the disease, the low efficiency of currently existing treatment approaches and the insufficient implementation of a system of preventive measures aimed at hearing preservation and health improvement of people working in conditions of increased noise load. The effect of high-intensity noise causes a disorder of microcirculation in the inner ear resulting in the development of hypoxia. As a result of the above-mentioned processes, there are changes in the bioenergetics of cells, accumulation of reactive oxygen and nitrogen forms, leading to oxidative stress, and then to their programmed and/or necrotic death. In addition to hair cell damage, irreversible damage to spiral ganglion neurons also occurs. According to current studies, it has been established that the key role in the regulation of oxygen homeostasis under hypoxia is played by a molecule of the factor induced by it. This undoubtedly stimulates the search for drugs acting on it as a target molecule for the treatment of hearing loss of noise etiology. The paper presents data on the incidence of atraumatic damage to the hearing organ due to noise of high intensity in military personnel, as well as the current views on the pathogenesis of the disease. Particular attention is paid to the analysis of approaches to the treatment of acute sensorineural hearing loss and the prospects for preventive and therapeutic use of antihypoxants.

Keywords: acoustic trauma; antihypoxants; treatment; acute sensorineural hearing loss; prevention; high-intensity noise; hypoxia-inducible factor.

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Обзорная статья

Современные подходы и перспективные направления в профилактике и лечении повреждения органа слуха шумом высокой интенсивности у военнослужащих

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Специфика военного труда, действие вредных, а подчас и опасных факторов в виде импульсного шума, ударной волны, постоянного шума высоких уровней приводят к риску развития акутравматического повреждения органа слуха у военнослужащих. Актуальность проблемы обусловлена отсутствием единой теории патогенеза заболевания, низкой эффективностью существующих в настоящее время подходов к лечению и недостаточной реализацией системы профилактических мероприятий, направленных на сохранение слуха и укрепление здоровья лиц, работающих в условиях повышенной шумовой нагрузки. Действие шума высокой интенсивности вызывает нарушение микроциркуляции во внутреннем ухе и как следствие приводит к развитию гипоксии. В результате указанных выше процессов происходят изменение биоэнергетики клеток, накопление активных форм кислорода и азота, приводящих к окислительному стрессу, а затем к их программируемой и/или некротической гибели. Помимо повреждения волосковых клеток происходит и необратимое повреждение нейронов спирального ганглия. По данным современных исследований установлено, что ключевая роль в регуляции кислородного гомеостаза в условиях гипоксии отводится молекуле индуцированного ею фактора. Это, несомненно, стимулирует поиск препаратов, действующих на нее как на молекулу-мишень, с целью купирования тугоухости шумовой этиологии. В статье приводятся данные о частоте акутравматического повреждения органа слуха шумом высокой интенсивности у военнослужащих, а также современные представления о патогенезе заболевания. Особое внимание уделено анализу подходов к лечению острой сенсоневральной тугоухости и перспективам профилактического и лечебного применения антигипоксантов.

Ключевые слова: акустическая травма; антигипоксанты; лечение; острая сенсоневральная тугоухость; профилактика; шум высокой интенсивности; гипоксией индуцированный фактор.

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BACKGROUND

Acoustic damage to the ears remains a problem because of the lack of a unified theory of the pathogenesis of the disease, the low efficiency of current treatment approaches, and insufficient realization of preventive measures aimed at preserving hearing and improving the health of persons working in conditions with increased noise load [1].

According to the literature, noise >90 dB is classified as high intensity [2]. Acutraumatic damage of the ears by high-intensity noise is observed in workers of various industries; however, it is more characteristic of military labor [3–5]. The adoption of new weapons and military equipment and the low level of hygienic competence of personnel when using personal hearing protection equipment lead to decreased military professional potential and increased incidence of diseases of the ears of servicemen [6, 7]. According to Labarere et al., the prevalence of acute acoustic trauma in servicemen is 156 per 100,000 people [8]. In a cross-sectional analysis, 10487 acoustic injuries were recorded in French military personnel between 2007 and 2014. The duration of the injury did not exceed 25 years, and men had nearly almost twice the risk of injury than women. Injuries were most often established during military exercises [9]. The tearing threshold of military personnel after basic training in ballistic weapon firing is approximately 13% [10].

Unfortunately, this pathology was not diagnosed and treated promptly, which led to persistent hearing impairment and disability of the victims [11, 12].

The development of drugs for medication correction of hearing impairment of noise etiology is an urgent task [13]. The main therapeutic strategy is the development of drugs that have a pathogenetic effect at the molecular level [14].

RESEARCH

According to modern clinical recommendations, glucocorticosteroids, vasoactive drugs, antihypoxants and antioxidants, vitamins, and nootropics are used to treat acute hearing loss in adults [15].

The validity of glucocorticosteroid use in acute sensorineural hearing loss was first proved in a double-blind study by Wilson et al. [16]. This group is currently considered the “gold” standard in the treatment of this pathology.

Various ways of drug administration of this group are used: oral, intravenous, transtympanal, transtubar, or their combinations. However, currently, no consensus has been established on the dose, administration route, and treatment duration.

Chang et al. substantiated the necessity of early treatment initiation and the effectiveness of oral and intratympanic administration of steroids for the treatment of patients with acoustic trauma following training firing [17]. Choi et al. recommend oral administration of prednisolone at a dose of 60 mg per day for 10 days with subsequent reduction of the drug dose for the treatment of atraumatic damage of the ears by high-intensity noise [18]. However, some authors questioned the efficacy of systemic glucocorticosteroid use because of the lack of statistically significant difference between the group receiving them and the group receiving placebo when compared with groups receiving other medications [19].

In the presence of excessive noise load, pathologic changes in the cortical organ are associated with microcirculatory disorders caused by spasms of the labyrinthine artery [20]. Thus, vasoactive drugs are shown to improve the blood supply to the cochlea and normalize the rheological parameters of blood.

Some authors suggest that the first stage should be a course (within 10 days) of parenteral administration of glucocorticosteroids with peripheral vasodilators, followed by oral administration of the latter from 1 to 3 months. Thus, in the treatment of 64 servicemen with acoustic trauma by applying this scheme, Mardassi et al. observed the restoration of hearing thresholds in 52 (81%) cases [21]. A good therapeutic effect was observed when using a combination of vasoactive therapy (xanthinol nicotinate and pentoxifylline) in combination with B vitamins. In patients with I and II degrees of hearing loss (62%), hearing recovery was complete [22].

Microcirculation disturbances in the inner ear during atraumatic exposure lead to vascular band edema, hypoxia, and oxidative stress [23]. Active oxygen and nitrogen trigger cell death pathways (necrosis and apoptosis) of hair cells, which is clinically manifested by sensory neural hearing loss [24]. Thus, the preventive (otoprotective) and therapeutic use of antioxidants and antihypoxants in firearms noise exposure has been substantiated [25, 26].

The first antihypoxants (gutimin and amtisol) were synthesized and examined under the guidance of Professors Vinogradov and Pastushenkov at the Department of Pharmacology of the Kirov Military Medical Academy [27]. Despite their high efficacy, they had unstable dosage forms and are currently not produced.

The study of hypoxia-inducible factor (HIF), for the discovery of which Greg Semenza, Peter Radcliffe, and Bill Kaelin were awarded the Nobel Prize in Physiology or Medicine in 2019 [28], is currently receiving much attention worldwide. Under hypoxic conditions, two subunits (HIF1α and HIF1β) penetrate the cell nucleus and regulate the expression of hundreds of target genes involved in angiogenesis, erythropoiesis, carbohydrate metabolism, cell proliferation, etc. [29]. Pak found that under conditions of preconditioning with cobalt dichloride,

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the expression of HIF1α and the protective effect on the organ of Corti during noise exposure is increased [30]. In the experimental studies of antihypoxant (triazino-indole derivative) on the acoustic trauma model, we found a dose-dependent increase in HIF expression in hair cells and spiral ganglion both during its prophylactic and therapeutic application. Moreover, the normalization of electrophysiological parameters of hearing in experimental animals (mice) was observed [31].

CONCLUSION

Therefore, based on the analysis of literature data, several main groups of drugs are used for the treatment and prevention of hearing organ damage during noise exposure, and the effect is directed at different pathogenetic links of the disease. Although well-studied and quite safe, some of them (vasoactive drugs, antioxidants, and vitamins) are not effective enough. Others (glucocorticosteroids) have several contraindications and side effects.

Antihypoxants are a promising group of drugs that require further study and introduction into clinical practice to prevent functional degenerative changes in the peripheral auditory analyzer during acute traumatic exposure.

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Conflict of interest. The authors declare that there are no obvious and potential conflicts of interest related to the publication of this article.

Ethical Review. The conduct of this study was approved by the local ethical committee of S. M. Kirov Military Medical Academy.

Authors' contribution. All authors substantially contributed to this study and article and have read and approved the final version of this article before publication.

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