World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-23, June 2023
ISSN: 2749-3644

THERAPEUTIC POTENTIAL AND PROSPECTS FOR THE USE OF SERMIONE (NICERGOLINE) INNEUROLOGICAL PRACTICE CAUSES

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Article history:

Received: April 11th 2023
Accepted: May 11th 2023
Published: June 20th 2023

Abstract:

Nicergoline (Sermion) is a hydrated semi-synthetic derivative of ergoline (contains an ergoline core and a bromo substituted nicotinic acid residue). The pharmacotherapeutic efficacy of this drug is determined by two main properties: α-adrenoblocking action leading to blood flow improvement and direct effect on cerebral neurotransmitter systems – noradrenergic, dopaminergic and acetylcholinergic

Keywords: nicergoline (Sermione), vascular dementia, Alzheimer's disease

INTRODUCTION. Nicergoline is used for the treatment of cerebrovascular insufficiency, cognitive disorders in elderly people, including different forms of dementia, and some other disorders, mostly of vascular nature [1- 4, 9, 16, 18]. The drug was developed in the late 1960s and its clinical use started in 1970s, first in Italy and then in other countries [16, 18]. Currently, nicergoline is registered in more than 50 countries (Europe, Asia, Latin America) [18].

From a clinical point of view, nicergoline was originally considered as a vascular drug acting antagonistically on α_1 - adrenergic receptors and its therapeutic effectiveness was associated with vasodilatation, reduction of vascular resistance and increase in arterial blood flow [1, 8, 16, 18]. Therefore, it was mainly used for the treatment of dementia due to cerebrovascular insufficiency. However, further studies have shown that nicergoline has a much broader spectrum of action

– at molecular and cellular levels, acting not only on vessels, but also on blood cells (thrombocytes) and neurons [18]. Currently, the drug is used in dementia of different genesis (Alzheimer's disease, vascular dementia), cerebrovascular disorders (including stroke, transient ischemic attacks, post- stroke disorders, migraine), peripheric vascular disorders (obliterating atherosclerosis of lower limb vessels), balance disorders of vestibular genesis, glaucoma, disease Parkinson's disease, as well as benign prostatic hyperplasia (18).

When administered orally, the drug has a linear pharmacokinetics that is almost independent of age; it is rapidly and almost completely absorbed in the gastrointestinal tract [1, 18]. Food intake has no significant effect on the absorption of nicergoline. In contrast to another ergot derivative, hydergine, nicergoline is mainly excreted in the urine (80%) as metabolites, and only about 20% is excreted in the feces [1, 18]. In healthy volunteers, it has been shown that after tablet administration, maximum serum concentrations are achieved within 3 hours, with a half-life of approximately 15 hours (18). Nicergoline is usually given as a twice-daily dose of 30 mg, with a treatment duration of 2 to 12 months or longer (16, 18). In Asian countries, nicergoline is usually used in lower doses (as are other drugs with similar effects) [18].

MECHANISM OF ACTION

Data from numerous experimental studies indicate a wide spectrum of action of nicergoline, which explains its effectiveness in various etiologies and pathogenesis of diseases. It improves cognitive function regardless of the etiology of the disease [6].

The increase of regional cerebral blood flow, improvement of glucose utilization, activation of protein synthesis is observed during nicergoline administration [1, 2, 4, 16, 18]. The nicotinic acid residue contained in the nicergoline molecule has a direct myotropic spasmolytic effect on the muscular membrane of vessels, especially in brain and limb vessels. It has been shown in experiments that nicergoline reduces vascular resistance in the carotid and vertebral-basilar systems and improves cerebral blood flow and metabolism [18]. There a positive effect of course intake of nicergoline on lipid metabolism was noted [3].

The resulting improvement in metabolic

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Available Online at: https://www.scholarexpress.net
Volume-23, June 2023
ISSN: 2749-3644

processes in the brain parenchyma has been confirmed by spectroscopic data [18]. At the same time, the literature emphasizes that this drug has a positive effect on basic, fundamental molecular processes underlying the onset and progression of dementia [16, 18].

One of the mechanisms of action of nicergoline is a disaggregating effect due to decreased platelet aggregation and increased erythrocyte plasticity, which in combination with the effect on cerebral vessels leads to improved regional cerebral blood flow in the ischemic tissue [1, 18]. Given its positive effect on platelet and erythrocyte aggregation, nicergoline is considered to reduce the risk of cerebral thromboembolic complications [18].

The study of the microcirculation of the bulbar conjunctiva showed that blood flow acceleration and a decrease in the severity of sludge syndrome were observed under the influence of nicergoline treatment [3]. This effect was registered more frequently in arterioles and capillaries and less distinctly in venules. Dilation of conjugated arterioles up to 10% of initial diameter was seen in 1₃ patients, and 15-30% of patients (depending on age) had increasing number of functioning capillaries per unit area of bulbar conjunctiva [3]. In 1/₃ elderly patients, perivascular oedema was eliminated or reduced in this study.

Recently, its effects on neuroplasticity processes [8, 16, 18] and neuroprotection mechanisms have been shown [2, 7]. It is important to note that the neuroprotective properties of nicergoline are not related to its direct effect on noradrenergic α_1 -receptors and serotonergic 5-HT1A-receptors but are of global nature. This is due in no small part to the ability of nicergoline, acting through endogenous neurotrophic factors, to ensure the trophic functions of cholinergic neurons [16], which leads to their survival in pathological conditions, including aging [10]. Experimental data indicate the increased concentration of nerve growth factor in frontal parts of the brain in old animals (rats) that were given nicergoline [18]. These mechanisms explain the ability of sermione (nicergoline) to slow down the progression of cognitive disorders in cerebral vascular pathology and Alzheimer's disease [6]. Current evidence suggests the ability of nicergoline to "protect" neurons from the toxic effects of beta-amyloid, thus slowing the progression of Alzheimer's disease [7].

Experimental studies have shown the neuroprotective effect of nicergoline in hypoxia, even under conditions of hypercapnia, when cerebral vessels are in a state of dilatation, indicating its direct effect on the brain parenchyma [8]. Nicergoline injection into the ventricles of the brain has been found to affect both blood pressure and heart rate in dogs under anesthesia, as well as inhibits T- and L-type neuronal calcium channels [8]. The neuroprotective properties of this drug are manifested in the protection of neurons from death under oxidative stress [16, 18]. Administration of nicergoline reduces lipid peroxidation processes and decreases excessive free radical formation. There is evidence [16] that the antioxidant effect of nicergoline is comparable with that of the classic antioxidant tocopherol (vitamin E). Nicergoline also affects the process of apoptosis [2, 16].

Nicergoline increases acetylcholine synthesis by activating choline acetyltransferase, increases acetylcholine release from presynaptic terminals, reduces acetylcholine decay by acetylcholinesterase inhibition, and acts on postsynaptic M-cholinoreceptors in the central nervous system [18]. It increases acetylcholine levels in the cortex and striatum of old animals (rats), while no change is observed in young animals [15, 18]. In addition, nicergoline restores the age-related decrease in acetylcholine levels in the hippocampus [15, 16, 18]. Acetylcholinesterase inhibition with nicergoline is comparable to that of physostigmine, although inferior to that of tacri [16]. A decrease in acetylcholinesterase activity in the brain after intravenous and intraperitoneal administration of nicergoline was confirmed in an experiment [18]. The observed changes of the acetyl cholinergic system in the experimental animals were accompanied by better performance in the tests of mnestic functions [18]. An additional positive effect of nicergoline is due to its effect on other neurotransmitter systems (adrenergic, serotoninergic) [15, 16].

Animals treated with nicergoline show an improvement in the performance of tasks related to mnestic activities [15]. The degree of improvement increases with the duration of therapy [15].

The nootropic and anti-amnestic activity of nicerolin has been confirmed in models of experimental cerebral ischemia and in the use of toxic agents that selectively impair mnestic functions [18].

CLINICAL TRIALS

Nicergoline has been successfully used for the treatment of dementias of various genesis [1, 9, 11, 16, 18]. Positive effects in the form of cognitive and behavioral decline have been reported in nearly 89% of patients (with placebo administration, improvements, usually of a transient nature, have been reported in 26-50% of cases) [18].

The first studies investigating the efficacy of

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Volume-23, June 2023
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nicergoline in dementia used the Sandoz clinical geriatric scale (SCAG) and the general clinical impression scale (CGI); subsequent studies used the brief mental status assessment scale (MMSE) and the Alzheimer's Disease Assessment Scale (ADAS) [18].

The differences in the clinical effect between the group of patients treated with nicergoline and those treated with placebo range from 5 to 30%, depending on the duration of the course of therapy and the characteristics of the patients included in the study (9).

Data from clinical studies [13, 14, 18] indicate that treatment with nicergoline improves the condition of patients with both Alzheimer's disease and vascular (multi-infarct) dementia during nicergoline therapy. In addition, the drug is also effective in dementia of mixed (Alzheimer's and vascular) type [11, 18]. In addition to a direct positive effect on cognitive function, a fairly rapid reduction in the severity of apathy was observed [11].

For example, significant improvement has been observed in younger patients and in patients with less severe cognitive impairment [18]. In addition, nicergoline therapy is considered to result in a marked improvement in vascular dementia than in Alzheimer's disease or other types of dementia [18]. However, it is possible that this is due to differences in the design of the studies conducted to date. Interestingly, the effects of therapy on the P300 cognitive evoked potential latency dynamics in vascular (multi-infarct) dementia and Alzheimer's disease are not different in nature [18].

In patients with dyscirculatory encephalopathy, after a course of therapy with nicergoline, improvement of subjective state in the form of reduction or cessation of headaches, dizziness, noise in the head, fatigue is observed [3]. According to neuropsychological testing, a significant decrease in time to complete tasks according to Schulte's tables was found [3]. It is important to note that the positive effects of the drug were maintained for a long period of time after the therapy was completed.

The effect of nicergoline is dose-dependent, which is confirmed by the results of electrophysiological studies [16]. Nicergoline therapy increases α- and β-activity in EEG in dementia patients – combined with a decrease in α- and Δ-waves, which, in turn, correlates with an improvement in attention and memory [1, 13, 14].

The improvement in cognition is paralleled by an increase in blood flow in the middle and peripheral cerebral arteries as well as in the right parietal area [18].

It should be noted that nicergoline is considered to be an effective drug for the treatment of various types of vascular dementia, including multi-infarct dementia [5, 12]. As the duration of treatment increases from 6 months to 12 months, the efficacy of therapy also increases [9]. In addition, the progression of cognitive impairment slows down during nicergoline treatment [16], and differences between the group of patients receiving nicergoline and those receiving placebo increase with the study period [11]. In this regard, the results of evaluating the effectiveness of nicergoline during long-term (24 months) therapy in patients with leukoareosis against the background of arterial hypertension, but without dementia, in the group of patients receiving the drug, there was a slowdown in the progression of cognitive disorders, and for some neuropsychological parameters (memory, attention) - their improvement [6].

The efficacy of the drug in moderate to severe Alzheimer's disease has been confirmed in a multicentre, double-blind, placebo-controlled randomised trial conducted in 33 European centers (Italy, Sweden, UK, Belgium and Germany) [17].

Another indication for prescribing this drug is post-stroke disorders [3, 18]. In addition to the improvement in the cognitive sphere, as confirmed by the P300 cognitive evoked potential wave data, a decrease in the severity of post-stroke motor defect was observed in patients [18]. The most significant result was seen in patients with lesser degrees of hemiparesis. Thus, nicergoline administration in stroke patients improves the rehabilitation period, accelerates recovery of both cognitive and motor functions, and ultimately has a positive effect on the patients' quality of life.

There are few studies on the efficacy of nicergoline in Parkinson's disease, but there has also been a reduction in cognitive, emotional, personality and behavioral disorders with this medication [18].

Positive effects of nicergoline have also been observed in migraine. It reduces the severity of headaches and stops attacks [3].

Nicergoline is also indicated for balance disorders due to vestibular dysfunction. Experimental data suggest that this drug is able to improve the compensation of vestibular disorders due to its dopaminergic effect [10, 18]. In patients with balance disorders and vertigo as a leading symptom, a positive dynamic in the condition, accompanied by an improvement in quality of life, has been reported in 44-78% of cases [18]. The results of the clinical evaluation were confirmed by posturography. In patients with dyscirculatory encephalopathy, after a course of therapy with

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nicergoline, a decrease in dizziness and reduction or disappearance of staggering during the Romberg test were noted [3].

SAFETY AND TOLERABILITY

The drug is well tolerated [6, 10, 11, 16, 17]. In particular, the nature, frequency and severity of adverse reactions in patients treated with nicergoline are quite comparable with placebo [6, 16, 18]. However, even if adverse events do occur, they tend to decrease as therapy continues [1]. Adverse reactions that are fairly typical of the entire class of ergot derivatives include complaints of dry mouth, cramps and diarrhea. When administered orally, systolic and diastolic blood pressure are not significantly altered, and are only occasionally slightly decreased (no statistically significant difference with placebo patients) (18). A single intravenous injection of nicergoline showed a decrease in arterial blood pressure already in the 5th minute, which returned to the baseline level by the end of the first hour [3]. In this regard, a certain caution is emphasized when intravenously administering nicergoline to patients of older age groups [3]. Patients with baseline high blood pressure may experience a tension headache after administration [3].

As was found by B. Winblad et al. [17], in the group of patients receiving nicergoline, side effects that required discontinuation of treatment were observed in 8.5% of cases, in the group receiving placebo - in 8.3% of cases. There are no statistically significant changes in vital functions and laboratory parameters during nicergoline therapy, except for a slight increase in serum uric acid levels in some cases, which is not accompanied by any clinical symptomatology [16, 17]. However, this has to be considered in patients with a history of gout.

Thus, nicergoline has been used in clinical practice for almost 40 years. During this time, there has been considerable experience in the use of this drug for a variety of conditions.

The drug is used to treat pathogenesis-dependent conditions. Initially, nicergoline was considered to be an exclusively "vascular" drug, leading to improvement of cerebral blood flow due to its antagonistic effect on α_1 -adrenoreceptors, but later it was demonstrated to have a much wider spectrum of action.

CONCLUSIONS: Nicergoline positively affects cholinergic and catecholaminergic neurotransmitter systems, inhibits platelet aggregation, improves cerebral metabolism, increases the utilization of oxygen and glucose and has anti-apoptotic, antioxidant and neurotrophic activity. All this allows nicergoline to be considered not only as a symptomatic agent, but also as an agent with neuroprotective effect. The combination of efficacy and good tolerability makes Sermione (Nicergoline) highly demanded, especially in neurogeriatric practice.

LITERATURE

1. Akramova D. et al. Stroke incidence and association with risk factors in women in Uzbekistan //Cerebrovascular Diseases. – Allschwilerstrasse 10, Ch-4009 Basel, Switzerland : Karger, 2017. – Т. 43.
2. Bobomuratov T.A., Sharipova O.A., Akramova N.T. Assessing the impact of secondary prevention among boys with bronchiectasis and delayed pubertal development // Science and Innovations in the Globalized world. San Diego, 2016. Vol. 1. P. 114-119.
3. Khamdamov B.Z. Indicators of immunocitocine status in purulent-necrotic lesions of the lover extremities in patients with diabetes mellitus.//American Journal of Medicine and Medical Sciences, 2020 10(7) 473-478.
4. M. I. Kamalova, N.K.Khaidarov, Sh.E.Islamov,Pathomorphological Features of hemorrhagic brain strokes, Journal of Biomedicine and Practice 2020, Special issue, pp. 101-105
5. Kamalova Malika Ilkhomovna, Islamov Shavkat Eriyigitovich, Khaidarov Nodir Kadyrovich. Morphological Features Of Microvascular Tissue Of The Brain At Hemorrhagic Stroke. The American Journal of Medical Sciences and Pharmaceutical Research, 2020. 2(10), 53-59
6. Khodjieva D. T., Khaydarova D. K., Khaydarov N. K. Complex evaluation of clinical and instrumental data for justification of optive treatment activites in patients with resistant forms of epilepsy. American Journal of Research. USA. № 11-12, 2018. C.186-193.
7. Khodjieva D. T., Khaydarova D. K. Clinical and neuroph clinical and neurophysiological ch ogical characteristics of teristics of post-insular cognitive disorders and issues of therapy optimization. Central Asian Journal of Pediatrics. Dec.2019. P 82-86
8. Kasimov, Arslanbek; Abdullaeva, Nargiza; Djurabekova, Aziza; Shomurodova, Dilnoza//Features of diagnosis and clinic of post-traumatic epilepsy against the background of concomitant somatic diseases. International Journal of Pharmaceutical Research (09752366) . Jul-Sep2020, Vol. 12 Issue 3, p1788-1792. 5p.

World Bulletin of Public Health (WBPH)
Available Online at: https://www.scholarexpress.net
Volume-23, June 2023
ISSN: 2749-3644

9. Kasimov Arslanbek Atabaevich, Bozorova Sabohat Normo'min qizi, & Gulkhayo Eshmatovna Zhumanova. (2022). Results of a study of clinical and neurophysiological changes in patients with post-traumatic epilepsy with concomitant somatic diseases on the basis of complex drug therapy. World bulletin of public health 10, 186-190
10. Kasimov Arslanbek Atabaevich. (2022). Dynamics of clinical and neurophysiological changes against the background of complex medical therapy in patients with posttraumatic epilepsy with concomitant somatic diseases. Frontline Medical Sciences and Pharmaceutical Journal, 2(03), 78–87.
11. Khudaynazarova Muattar Tokhirjonovna, Ruziyev Jononbek Elmurodovich, & Kasimov Arslanbek Atabayevich. (2022). Peculiarities of diagnosis and clinical picture of posttraumatic epilepsy against the background of concomitant somatic diseases. *World bulletin of public health*, *10*, 121-126.
12. Uralov, F. S. ., Khurramov, M. B. ., Kasimov, A. A. ., & Mamurova, M. M. . (2022). Modern Methods of Epilepsy Treatment and Prevention of Tactical and Therapeutic Errors in Epilepsy Treatment. *International Journal Of Health Systems And Medical Sciences*, *1*(4), 374–377.
13. Шомуродова Д. С., Джурабекова А. Т., Мамурова М. М. Особенности и прогноз поражения нервной системы у беременных женщин с преэклампсией характеризуемые методами функциональной диагностики //журнал неврологии и нейрохирургических исследований. – 2020. – Т. 1. – №. 2.
14. Мамурова, М., Рузиева, Ш., Олланова, Ш., Хакимова, С., & Джурабекова, А. (2015). Клинико-неврологические особенности Хронических цереброваскулярных заболеваний, обусловленных Артериальной гипертензией, у пациентов молодого возраста. Журнал вестник врача, 1(4), 39–42.
15. Мамурова М. М., Джурабекова А. Т., Игамова С. С. Оценка когнитивных вызванных потенциалов головного мозга (р-300) у лиц молодого возраста с артериальной гипотензией //журнал неврологии и нейрохирургических исследований. – 2021. – Т. 2. – №. 1.
16. Rakhmonova H.N., Rakhmonov Z.M. Innervation Relationships of the Gallbladder Nerve Apparatus with Spinal and Rheumatic Nerve Ganglia (Literature Review). Eurasian Medical Research Periodical, 18, 105-108.
17. 18 Рузиева, Ш., Мамурова, М., Хакимова, С., & Джурабекова, А. (2016). Клиническая характеристика больных с транзиторными ишемическими атаками. Журнал проблемы биологии и медицины, (2 (87), 79–82.