AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 6. No 02. February ,2026

ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN: AN ANALYSIS OF THE RESULTS OF THE MEGA STUDY ON THE USE OF MEXIDOL

Majidova Yo.N.
MD, PhD, Professor, Chief Neurologist of the Ministry of Health of the Republic of Uzbekistan, Head of the Department of Neurology, Pediatric Neurology, and Medical Genetics, Tashkent State Medical University

Abstract
The present paper provides a systematic review of the etiopathogenetic mechanisms underlying the development of attention deficit hyperactivity disorder (ADHD). Particular emphasis is placed on the role of neurometabolic imbalance, oxidative stress, and membranopathies in the pathogenesis of cognitive and behavioral dysfunction. The rationale for including neuroprotective agents in therapeutic protocols is substantiated. The results of the multicenter randomized double-blind placebo-controlled clinical study "MEGA" are presented, demonstrating the efficacy and safety profile of Mexidol (ethylmethylhydroxypyridine succinate) in the correction of the ADHD symptom complex in children aged six to twelve years.

Keywords: ADHD, neuroplasticity, oxidative stress, neurotransmitter metabolism, dopaminergic system, Mexidol, MEGA study, pharmacotherapy.

Introduction

Attention deficit hyperactivity disorder is one of the most prevalent neurodevelopmental disorders, affecting, according to current meta-analyses, between five percent and seven point two percent of the pediatric population worldwide [1, 2]. In the Republic of Uzbekistan, in line with global epidemiological trends, an increase in the detection rate of this pathology has been observed, which is attributable both to improvements in diagnostic algorithms and to an increase in perinatal risk factors of hypoxic-ischemic origin.

The clinical phenomenology of ADHD, manifested by the classical symptom triad of inattention, motor hyperactivity, and impulsivity, leads to significant adverse social consequences, including school maladaptation, conflicts within the microsocial environment, and, in the long term, an increased risk of deviant behavior and addictions [3]. In this regard, the search for pathogenetically substantiated and safe methods of pharmacological correction remains a priority task of modern pediatric neurology.

Modern Perspectives on Etiopathogenesis

The traditional "dopamine theory" of ADHD, which postulates a deficiency of catecholamines in the prefrontal cortex and basal ganglia, is currently regarded not as an isolated primary cause but as a consequence of deeper metabolic disturbances. Contemporary studies [4–6] emphasize the role of oxidative stress and impaired neuroplasticity.

Oxidative stress as a trigger of neuronal dysfunction.

The brain, as an organ with an extremely high level of aerobic metabolism and a significant

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 02. February ,2026

content of polyunsaturated fatty acids, is particularly sensitive to imbalances between pro-oxidant and antioxidant systems. In children with ADHD, signs of systemic oxidative stress have been identified, characterized by increased total oxidant status and oxidative stress index, along with reduced activity of key antioxidant enzymes [4, 5].

Oxidative imbalance in ADHD leads to a cascade of pathological changes at the molecular level:

- **Initiation of lipid peroxidation:** reactive oxygen species attack polyunsaturated fatty acids in neuronal membranes, triggering chain reactions of free radical oxidation. This results in the formation of toxic aldehydes, such as malondialdehyde and four-hydroxynonenal, which disrupt the integrity of cellular membranes [4, 5].
- **Alteration of membrane biophysical properties:** lipid peroxidation products modify the structure of the phospholipid bilayer, leading to loss of membrane elasticity, increased microviscosity, and impaired functioning of embedded membrane proteins [4, 5].
- **Dysregulation of neurotransmitter systems:** oxidative damage to membrane proteins and lipids alters receptor complex activity and disrupts the normal functioning of enzymes and neurotransmitters. In particular, elevated hydrogen peroxide levels suppress dopamine release in the striatum, which may represent one of the mechanisms of dopaminergic insufficiency in ADHD [6, 7]. Thus, even with adequate neurotransmitter synthesis, the efficiency of synaptic transmission remains reduced.

Impaired neuroplasticity.
Chronic hypoxia and oxidative stress suppress the expression of neurotrophic factors, particularly brain-derived neurotrophic factor, thereby inhibiting synaptogenesis and the maturation of regulatory structures of the frontostriatal system responsible for executive functions [8].

Diagnostic Criteria

The diagnosis of ADHD is based on strict criteria of international classifications and requires a multidisciplinary approach.

- **Clinical and psychological assessment:** validated rating scales, such as SNAP-IV (Swanson, Nolan and Pelham Rating Scale) and the ADHD Rating Scale-IV, represent the standard tools for assessing symptom severity and objectively monitoring therapeutic response [9].
- **Instrumental methods:** neuroimaging and neurophysiological techniques, including magnetic resonance imaging and electroencephalography, are used for differential diagnosis to exclude organic substrates, such as epileptiform activity or space-occupying lesions, that may mimic cognitive deficits.

Therapeutic Approaches and the Role of Antioxidant Therapy

International clinical guidelines consider psychostimulants, such as methylphenidate, and selective norepinephrine reuptake inhibitors, such as atomoxetine, as first-line pharmacological treatments for ADHD [10]. However, the use of psychostimulants alone, which influence

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 02. February ,2026

neurotransmitter release without correcting membrane defects, does not address all pathogenetic links.

In the context of the described molecular disturbances, the inclusion of agents with antioxidant and membrane-protective activity in therapeutic protocols appears pathogenetically justified. One such agent is Mexidol (ethylmethylhydroxypyridine succinate), which is widely used in pediatric neurology.

According to pharmacological studies [6, 7], Mexidol exerts a multimodal effect:

- **Inhibition of lipid peroxidation:** the drug blocks chain reactions of free radical oxidation, providing neuroprotection.
- **Modulation of membrane fluidity:** by restoring the structure of the lipid bilayer, Mexidol returns physiological elasticity to the membrane, which is necessary for the proper functioning of ion channels and receptors.
- **Sensitization of the receptor apparatus:** the drug increases receptor affinity for endogenous neurotransmitters without depleting their stores or causing dependence [6, 7].

Results of the MEGA Study

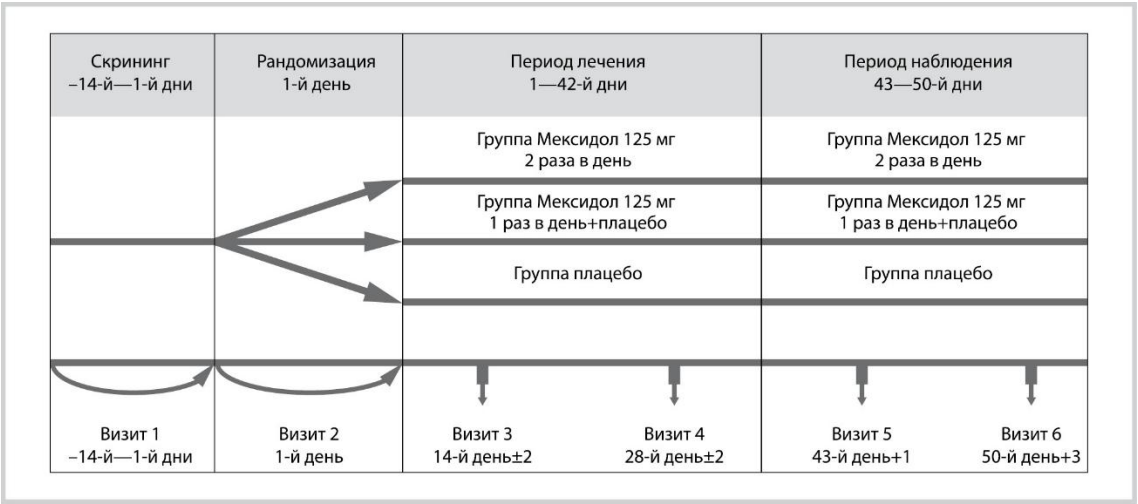
A key milestone in evaluating the efficacy of antioxidant therapy in ADHD was the multicenter randomized double-blind placebo-controlled clinical study “MEGA” [11].

Study design:
The study included three hundred thirty-three children aged six to twelve years with a confirmed diagnosis of ADHD according to ICD-ten and DSM-five criteria. The trial was conducted in fourteen clinical centers of the Russian Federation. Patients were randomized into three groups in a one-to-one-to-one ratio:

- **Group one:** Mexidol one hundred twenty-five milligrams twice daily
- **Group two:** Mexidol one hundred twenty-five milligrams once daily plus placebo
- **Group three:** placebo

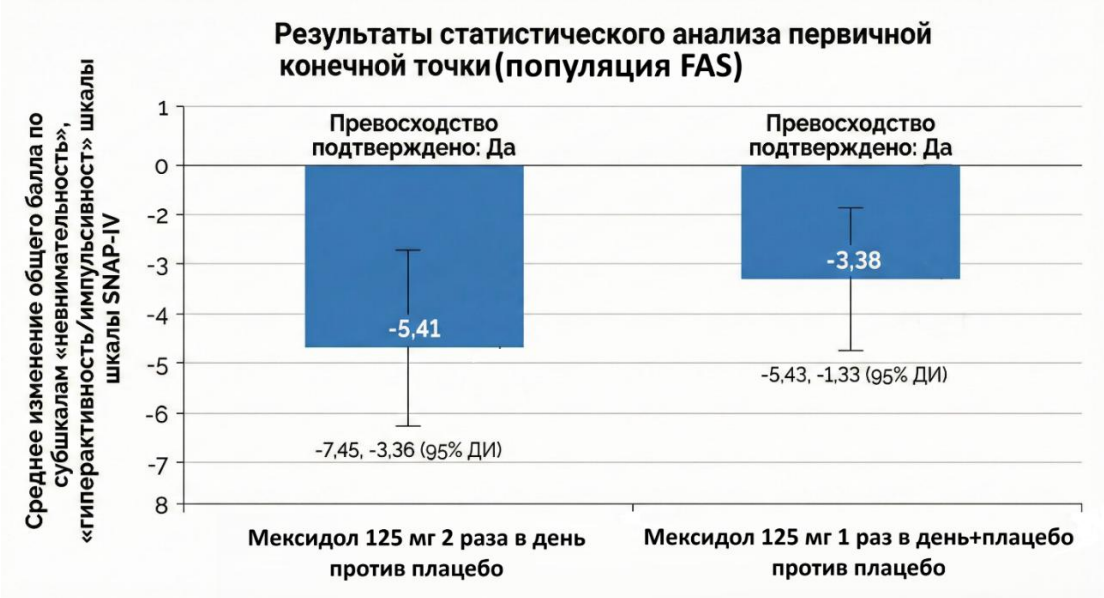
The duration of therapy was forty-two days. Three hundred thirty-two children completed the study.

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 02. February ,2026



Key results:

- **Symptom reduction:** in the group receiving Mexidol one hundred twenty-five milligrams twice daily, a statistically significant decrease in the total SNAP-IV score, including the inattention and hyperactivity/impulsivity subscales, was observed by the sixth week of therapy compared with the placebo group ($p < 0.001$ for both the per-protocol and full analysis set populations) [11].



- **Improvement in cognitive functioning:** a positive trend was observed in attention-related measures, reflected by a reduction in scores on the inattention subscale, along with a decrease in hyperactivity and impulsivity [11].

AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES
ISSN NUMBER: 2692 - 5206 Volume 6. No 02. February ,2026

- **Clinical significance:** positive changes were recorded on the CGI-ADHD-S and CGI-I scales, indicating clinically meaningful improvement in patients' overall condition [11].

Изменение значений по шкале CGI-ADHD-S через 6 нел терапии по сравнению с исходным уровнем (популяция FAS)

	Группа Мексидол 125 мг 1 раз в день+ плацебо (n= 111)				Группа Мексидол 125 мг 2 раза в день (n=111)				Группа плацебо (n=111)			
Показатель	исходно		6 нед		исходно		6 нед		исходно		6 нед	
	абс.	%	абс.	%	абс.	%	абс.	%	абс.	%	абс.	%
Уровень 2	0	0,0	8	7,2	0	0,0	8	7,2	0	0,0	2	1,8
Уровень 3	0	0,0	26	23,4	0	0,0	58	52,3	0	0,0	23	20,7
Уровень 4	111	100,0	77	69,4	111	100,0	44	39,6	111	100,0	86	77,5
Уровень 5	0	0,0	0	0,0	0	0,0	1	0,9	0	0,0	0	0,0

Изменение значений оценки по шкале CGI-I через 6 нед терапии по сравнению с исходным *уровнем (популяция FAS)*

Показатель	Группа Мексидол 125 мг 1 раз в день+ плацебо (n=111)		Группа Мексидол 125 мг 2 раза в день (n=111)		Группа плацебо (n=111)	
	абс.	%	абс.	%	абс.	%
Значительное улучшение	20	18,0	45	40,5	10	9,0
Незначительное улучшение	61	54,95	37	33,3	38	34,2
Без изменений	27	24,3	14	12,6	58	52,3
Весьма значительное улучшение	3	2,7	13	11,7	2	1,8
Незначительное ухудшение	0	0,0	1	0,9	3	2,7
Значительное ухудшение	0	0,0	1	0,9	0	0,0

- **Safety profile:** the incidence of adverse events in the Mexidol group was comparable to that in the placebo group, indicating a favorable safety profile of the drug in pediatric practice [11].

Clinical Recommendations

Based on the results of the MEGA study, the following algorithm for the use of Mexidol may be recommended for the correction of cognitive and behavioral impairments in ADHD:

- **Dosing regimen:** one hundred twenty-five milligrams (one tablet) twice daily.
- **Course duration:** six weeks, which is the period required for stabilization of membrane processes.
- **Monitoring:** assessment using the SNAP-IV scale before initiation of therapy and after completion of the course.

Conclusion

The multimodal nature of ADHD pathogenesis necessitates a comprehensive therapeutic approach. The inclusion of a drug with proven antioxidant and membrane-protective activity, such as Mexidol, in therapeutic protocols represents a pathogenetically justified strategy that complements standard treatment. The results of the MEGA study confirm that the drug promotes regression of ADHD symptoms by restoring functional brain activity through normalization of membrane processes, while demonstrating a favorable safety profile. Further research should

AMERICAN ACADEMIC PUBLISHER

INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

ISSN NUMBER: 2692 - 5206 Volume 6. No 02. February ,2026

focus on evaluating long-term efficacy and the potential for combination therapy with first-line agents.

References

1. *Polanczyk G., de Lima M.S., Horta B.L., et al.* The worldwide prevalence of ADHD: a systematic review and metaregression analysis // American Journal of Psychiatry. - 2007. - Vol. 164, № 6. - P. 942-948.
2. *Thomas R., Sanders S., Doust J., et al.* Prevalence of attention-deficit/hyperactivity disorder: a systematic review and meta-analysis // Pediatrics. - 2015. - Vol. 135, № 4. - P. 994-1001.
3. *Faraone S.V., Banaschewski T., Coghill D., et al.* The World Federation of ADHD International Consensus Statement: 208 Evidence-based conclusions about the disorder // Neuroscience & Biobehavioral Reviews. - 2021. - Vol. 128. - P. 789-818.
4. *Hatice Sezen, Hasan Kandemir, Emin Savik, Sultan Basmacı Kandemir,Fethiye Kilicaslan, Hasan Bilinc & Nurten Aksoy (2016) Increased oxidative stress inchildren with attention deficit hyperactivity disorder, Redox Report, 21:6, 248-253, DOI:10.1080/13510002.2015.1116729.*
5. *Verlaet AAJ, Breynaert A, Ceulemans B, et al. Oxidative stress and immune aberrancies in attention-deficit/hyperactivity disorder (ADHD): a case–control comparison // European Child & Adolescent Psychiatry. - 2019. - Vol. 28, № 5. - P. 719-729. https://doi.org/10.1007/s00787-018-1239-4.*
6. *Воронина Т.А.* Мексидол: спектр фармакологических эффектов // Журнал неврологии и психиатрии им. С.С. Корсакова. - 2012. - № 12. - С. 86-90.
7. *Хамитова Г.Р.* Применение препарата Мексидол® в детской неврологической практике // Неврология. - 2012. - С. 100-101.
8. *Cortese S., Adamo N., Del Giovane C., et al.* Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: a systematic review and network meta-analysis // The Lancet Psychiatry. - 2018. - Vol. 5, № 9. - P. 727-738.
9. *Swanson J.M., Kraemer H.C., Hinshaw S.P., et al.* Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment // Journal of the American Academy of Child & Adolescent Psychiatry. - 2001. - Vol. 40, № 2. - P. 168-179.
10. *National Institute for Health and Care Excellence.* Attention deficit hyperactivity disorder: diagnosis and management. NICE guideline [NG87]. - 2018.
11. *Заваденко Н.Н., Суворинова Н.Ю., Батышева Т.Т., и др.* Результаты многоцентрового двойного слепого рандомизированного плацебо-контролируемого клинического исследования по оценке эффективности и безопасности препарата Мексидол в лечении синдрома дефицита внимания с гиперактивностью у детей (МЕГА) // Журнал неврологии и психиатрии им. С.С. Корсакова. - 2022. - Т. 122, № 4. - С. 75-86. https://doi.org/10.17116/jnevro202212204175
12. *Заваденко Н.Н., Суворинова Н.Ю., Заваденко А.Н.* Возможности применения Мексидола в нейропедиатрии // Журнал неврологии и психиатрии им. С.С. Корсакова. Спецвыпуски. - 2023. - Т. 123, № 9-2. - С. 43-50. https://doi.org/10.17116/jnevro202312309243