MedCrave
Step into the World of Research

Journal of Neurology & Stroke

Case Report

Open Access

CrossMark

Parenteral megavitamin therapy with folinic acid and a complex homeopathic preparation in an older child with grade 2 autism spectrum disorder: a case report

Abstract

Background: There is still no approved pharmacological therapy for the core symptoms of autism spectrum disorder (ASD). While there is some clinical evidence supporting the use of megavitamin therapy in ASD, its efficacy in older children with established ASD has yet to be studied. The potential adjunctive role of folinic acid, a biologically active folate derivative increasingly implicated in ASD neurodevelopment, has not previously been examined in combination with megavitamin and homeopathic approaches.

Case Presentation: A 7-year-old male (34 kg) with grade 2 ASD diagnosed according to DSM-5 criteria presented after minimal functional progress with intensive specialized rehabilitation. His parents continued to be concerned with limited expressive speech, marked social withdrawal, and significant cognitive delay, with a baseline Childhood Autism Rating Scale, Second Edition (CARS-2 ST) score of 31. A 25-session parenteral protocol of B-vitamin megadoses, folinic acid, vitamin C, and the complex homeopathic preparation Coenzyme Compositum was administered over alternating weeks. Following protocol completion, the patient significantly improved across all assessed domains, with the CARS-2 ST score decreasing to 24.

Conclusion: These findings extend the evidence base for integrative megavitamin approaches to older children with ASD and suggest a possible adjunctive role for folinic acid. Larger controlled trials are warranted.

Keywords: Autism Spectrum Disorder (ASD), folinic acid, leucovorin, megavitamin therapy, homeopathy, integrative medicine, CARS-2, treatment-refractory

Volume 16 Issue 2 - 2026

Maja Roje Novak MD, MS
Private Neurology Clinic Neurologija – dr Maja Roje Novak doo, Pavla Hatza 27, 1000 Zagreb, Croatia

Correspondence: Maja Roje Novak, Private Neurology Clinic Neurologija – dr Maja Roje Novak doo, Pavla Hatza 27, 1000 Zagreb, Croatia

Received: March 15, 2026 | **Published:** March 31, 2026

Introduction

Autism spectrum disorder (ASD) describes a heterogeneous group of complex neurodevelopmental conditions defined by impairments in social communication and interaction as well as restricted and repetitive patterns of behavior.[1] ASD is relatively common, and its prevalence is increasing, affecting approximately 1 in 100 children worldwide.[2] ASD shows significant sociodemographic variability, with a male predominance (approximately 4:1), higher prevalence in high-income settings, and substantial prevalence heterogeneity across regions reflecting differences in awareness, diagnostic practices, and access to services.[2] Beyond the core behavioral features, ASD is associated with a significantly increased risk of mortality and impairments in adult quality of life, including occupational underachievement and social isolation.[3] These consequences mandate a search for new and effective interventions, particularly for children with persistent and disruptive symptoms who fail to improve using standard behavioral and pharmacological approaches.

Pharmacological treatments for ASD remain limited. Atypical antipsychotics, especially aripiprazole and risperidone, are licensed by the US Food and Drug Administration (FDA) for the management of irritability and challenging behaviors in ASD, but they do not address the core deficits of social communication or restricted and repetitive behaviors.[4,5] Behavioral interventions, including applied behavioral analysis and structured teaching, remain the cornerstone of management and show moderate efficacy when initiated early in development.[6] However, many individuals, particularly those with more severe presentations or who begin structured intervention later, show only limited responses to established approaches. This resistance to conventional treatment prompts many individuals with ASD to use complementary and alternative medicines (CAMs), with ~45% of adults with ASD using CAM therapies at some point.[7]

Individuals with ASD often try nutritional supplements as a CAM strategy. A meta-analysis of 27 randomized double-blind controlled trials demonstrated that dietary, omega-3, and vitamin supplementation were more effective than placebo in improving ASD symptoms and patient function, with vitamin supplementation showing particular efficacy across global severity, language, stereotypy, and behavioral domains.[8] Mechanistically, oxidative stress and defective cellular energy metabolism appear to be central to ASD pathobiology, providing a rationale for nutritional interventions targeting these pathways.[9–12] There is also evidence that folate metabolism contributes to ASD pathobiology, as disturbances in one-carbon metabolism, including abnormalities in folate and methylation pathways, have been identified in ASD populations.[13] Furthermore, a subset of children with ASD show evidence of cerebral folate deficiency, arising in some cases from the presence of folate receptor autoantibodies that block folate transport across the blood-brain barrier, and supplementation with folinic acid (leucovorin) has been associated with clinical improvements.[14,15]

This mechanistic evidence provided the rationale for a parenteral integrative protocol that combines B-vitamin and vitamin C megadoses with the complex homeopathic preparation Coenzyme

Compositum to simultaneously target oxidative stress and defective energy metabolism in ASD. In a preliminary case series of three young children with ASD, this approach resulted in a significant increase in spoken vocabulary and a noticeable improvement in social interaction skills after three months.[16] The case report describes a novel adaptation of the previously described integrative megavitamin and complex homeopathic protocol[16–18] that incorporates folinic acid as an adjunct, applied to an older child with grade 2 ASD and a documented history of treatment failure.

Case presentation

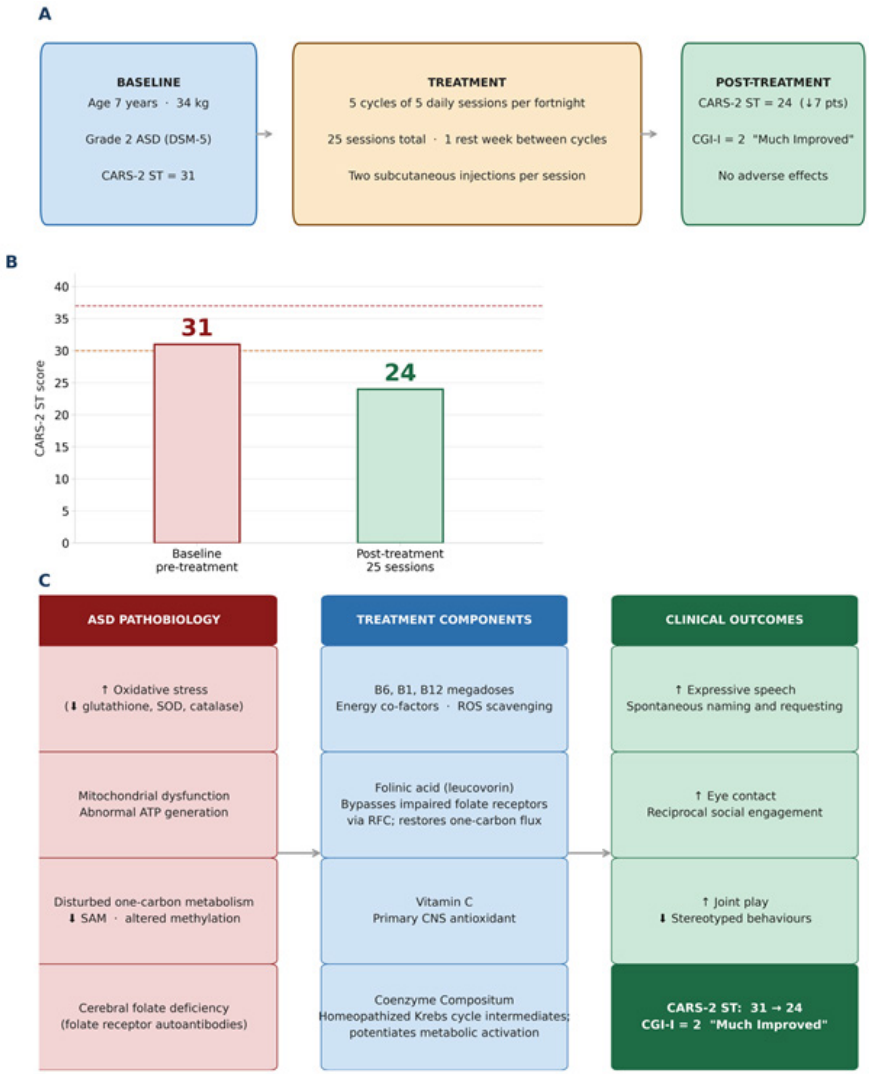
Clinical features

A seven-year-old male (weight 34 kg) presented to a private neurology clinic in Zagreb, Croatia. He had previously been diagnosed with ASD, grade 2 severity, established according to DSM-5 criteria, with significant deficits in social communication and the presence of restricted and repetitive behaviors that required substantial support. His developmental history was notable for delayed speech acquisition, minimal joint attention, and severely limited expressive communication. At presentation, his spoken language was largely non-functional, confined to occasional isolated words produced inconsistently and not reliably used for communicative intent. His social engagement was markedly impaired, characterized by limited eye contact, absence of reciprocal play, and pronounced social withdrawal. Cognitive evaluation was consistent with significant intellectual delay.

The patient had previously undertaken several years of intensive specialized rehabilitation, including speech and language therapy and structured behavioral intervention, with very little functional progress reported by his parents or treating therapists. His parents, seeking a meaningful change in therapeutic approach, provided written informed consent for the initiation of an integrative medicine protocol. Baseline severity was formally assessed using the Childhood Autism Rating Scale, Second Edition – Standard Version (CARS-2 ST),[19] giving a score of 31, consistent with mild to moderate ASD.

Treatment protocol

The treatment protocol consisted of 25 sessions of combined parenteral megavitamin and homeopathic therapy, delivered as five consecutive daily sessions per fortnight (Monday to Friday on alternating weeks), for a total period of ten weeks (Figure 1A). The parenteral route was selected to circumvent gastrointestinal absorption variability and to ensure maximal bioavailability of the administered compounds, which is of particular importance in children with ASD, in whom gastrointestinal dysfunction is common.[20]



Citation: Novak MR. Parenteral megavitamin therapy with folinic acid and a complex homeopathic preparation in an older child with grade 2 autism spectrum disorder: a case report. *J Neurol Stroke.* 2026;16(2):72–76. DOI: 10.15406/jnsk.2026.16.00655

Figure 1 Integrative megavitamin protocol and clinical outcomes in a 7-year-old child with grade 2 autism spectrum disorder. (A) Treatment protocol. The patient received 25 parenteral sessions over 10 weeks, structured as five cycles of five consecutive daily sessions per fortnight, with one rest week between each cycle. Each session included two subcutaneous injections administered under medical supervision following topical anesthesia with 0.5% EMLA cream. (B) CARS-2 ST score before and after completion of the 25-session protocol. A 7-point reduction was observed, corresponding to a CGI-I rating of 2 ("much improved") and a shift below the mild–moderate severity threshold. Dashed lines indicate published CARS-2 ST severity boundaries: amber, mild–moderate threshold (≥30); red, moderate–severe threshold (≥37).[19] (C) Proposed mechanism. Key pathobiological abnormalities implicated in ASD (left column) correspond to the individual treatment components designed to target them (center column) and to the clinical outcomes observed following the protocol (right column). Abbreviations: ASD, autism spectrum disorder; CARS-2 ST, Childhood Autism Rating Scale Second Edition – Standard Version; CGI-I, Clinical Global Impressions – Improvement; CNS, central nervous system; GSH, glutathione; RFC, reduced folate carrier; ROS, reactive oxygen species; SAM, S-adenosylmethionine; SOD, superoxide dismutase.

Each treatment session included two subcutaneous injections. Before injection, the gluteal skin was anaesthetized with 0.5% EMLA cream (lidocaine/prilocaine). The first injection, administered at 10:00 am using a 5 ml syringe with insulin needles, consisted of B-vitamin megadoses combined with folinic acid (leucovorin), diluted in one 2.2 ml vial of Coenzyme Compositum (Heel, Germany; patent reference: PCT HR 2010/000015): vitamin B6, 25 mg; vitamin B1 (thiamine), 15 mg; vitamin B12 (cyanocobalamin), 100 µg; and folinic acid (leucovorin), 3 mg. The second injection, given immediately after, contained vitamin C (20 mg) diluted in a second 2.2 ml vial of Coenzyme Compositum. The doses of B6 (RDA 1.3–1.7 mg), B1 (RDA 1.1–1.2 mg), and B12 (RDA 2.4 µg) were supraphysiological by design, consistent with the megavitamin approach, while the folinic acid dose was within the therapeutic range used in documented clinical trials for ASD.[14] Coenzyme Compositum is an over-the-counter preparation containing homeopathized Krebs cycle intermediates and herbal homeopathic remedies.[16–18,21] All injections were administered under direct medical supervision to ensure correct technique, consistency of administration, and immediate management of any adverse events.

Follow-up and outcomes

The patient completed all 25 sessions of the protocol without interruption. Tolerance was excellent throughout the treatment course, with only transient discomfort at the injection site, which resolved within minutes of each administration. Characteristic changes in urinary color and odor consistent with elevated B-vitamin excretion were observed and anticipated. No systemic adverse effects, neurological events, or significant behavioral deterioration were recorded at any point during the protocol.

Clinical assessment following completion of the 25-session protocol revealed improvements in all four primary domains of cognition, speech and language, social interaction, and behavior. The CARS-2 ST score decreased from a baseline of 31 to a post-treatment score of 24, representing a clinically significant reduction of 7 points and a change from the mild–moderate to the sub-threshold severity band on the CARS-2 ST (Figure 1B).[19] Qualitatively, the child's parents and treating clinicians observed an increase in the functional use of spoken words, including spontaneous naming and simple requests; a notable improvement in eye-to-eye contact and responsiveness to name; an increased willingness to engage in joint play activities; and a reduction in stereotyped and repetitive behaviors. On the Clinical Global Impressions Improvement (CGI-I) scale,[22] the patient was rated as 2 (much improved).

Discussion

This report describes a clinically meaningful response to an integrative parenteral megavitamin and homeopathic protocol in an older child with grade 2 ASD who had failed to benefit from years of conventional rehabilitative therapies. The report extends preliminary observations reported in a case series of younger, lower-severity ASD children treated with a related but distinct protocol[16] and describes the first inclusion of folinic acid as an adjunct to this integrative approach.

This case has several unique features. First, the patient was older than those in the previous case series (7 years versus approximately 3 years of age) and had a more severe ASD phenotype (grade 2 versus unspecified lower-severity cases).[16] The neuroplasticity of the developing brain is known to decrease with age,[23] and the window of maximal responsiveness to language-based interventions is generally considered to be the preschool years. The significant functional improvement observed in this school-aged child with a long history of treatment failure is particularly notable and suggests that the therapeutic window for metabolic and nutritional intervention may extend beyond early childhood.

The mechanistic rationale for the therapy is presented in Figure 1C. There is now a good scientific rationale for megavitamin therapy in ASD. B vitamins are essential mediators of catabolic energy metabolism within the brain[23] and exert antioxidant functions through direct and indirect scavenging of reactive oxygen species (ROS) and modulation of cytokine-mediated oxidative stress.[24] Oxidative stress and mitochondrial dysfunction are among the most consistently replicated biological abnormalities in ASD, with impaired glutathione peroxidase, catalase, and superoxide dismutase activity documented in several studies,[10] and abnormal ATP levels detected in blood and brain tissue from ASD patients.[9,11,12] High-dose vitamin B12 in combination with glutathione precursors has been shown to improve speech, concentration, and social behavior in children with ASD.[25] Vitamin C is a critical central nervous system antioxidant whose deficiency is implicated in neurodevelopmental deficits,[26] and it was included based on a double-blind, placebo-controlled study demonstrating reduced autism severity with high-dose ascorbic acid supplementation.[27] Parenteral administration was used to circumvent the gastrointestinal dysfunction and reduced oral medication compliance commonly encountered in ASD populations.[20]

The inclusion of folinic acid in the current, adapted protocol represents a theoretically grounded and potentially clinically significant modification. Folate plays a central role in one-carbon metabolism, supporting nucleotide synthesis, DNA methylation, and production of S-adenosylmethionine (SAM), the principal methyl donor for neurotransmitter and myelin synthesis.[13] Disturbances in this pathway are well-documented in ASD: prenatal vitamin supplementation, including folate, is associated with a reduced risk of ASD in offspring,[28,29] and abnormalities in folate receptor function have been identified in a subset of children with ASD. Folinic acid (leucovorin), the biologically reduced and active form of folate, can enter the central nervous system via reduced folate carrier-mediated pathways, thus bypassing impaired folate receptor function.[15] Clinical trials of folinic acid supplementation in ASD have reported improvements in receptive and expressive language, attention, and stereotypy.[14] The selection of folinic acid rather than folic acid in the protocol was therefore deliberate, recognizing the possibility of impaired folate receptor function in the patient and the superior central nervous system bioavailability of the leucovorin formulation. At the administered dose of 3 mg per session, the preparation was within established safety parameters.

Citation: Novak MR. Parenteral megavitamin therapy with folinic acid and a complex homeopathic preparation in an older child with grade 2 autism spectrum disorder: a case report. *J Neurol Stroke.* 2026;16(2):72–76. DOI: 10.15406/jnsk.2026.16.00655

Coenzyme Compositum, the complex homeopathic preparation used in the current and previous protocols,[16,18] contains homeopathized Krebs cycle intermediates that are thought to act as non-specific metabolism activators according to the Reckeweg model of homotoxicology and isopathy.[16,18,21] The mechanism of action of homeopathic preparations is contested and is not fully explainable within the conventional biochemical receptor paradigm,[30,31] and competing mechanistic hypotheses continue to evolve in the field. The preparation may induce modest perturbations in cellular energy production that synergize with the administered vitamins to amplify their therapeutic effects, though this hypothesis requires formal testing. Nevertheless, a recent controlled study in patients with post-COVID asthenia syndrome provides independent clinical support for the therapeutic efficacy of parenterally administered Coenzyme Compositum.[32] In this study, a 15-injection course of Coenzyme Compositum combined with other bioregulatory medicines significantly reduced fatigue severity and improved quality of life compared with a reference group receiving conventional B-vitamin supplementation, further supporting a central, neuroregulatory effect.

This report has limitations. As a single uncontrolled case report, it is not possible to causally attribute the observed improvements to the applied protocol. Indeed, the decrease in CARS-2 ST scores might reflect the natural developmental trajectory or non-specific effects including placebo response. The protocol involved multiple active components administered simultaneously, so the relative contribution of individual elements is uncertain. The absence of biomarker data, such as plasma glutathione, vitamin levels, or folate receptor antibody status, limits mechanistic interpretation. The treatment period of ten weeks is relatively short, and further follow-up is needed to assess durability or the approach.

Nevertheless, the clinical improvement documented here, in a patient with a long history of treatment failure and grade 2 ASD, justifies further investigation. The encouraging safety profile and the clinically meaningful reduction in standardized autism severity scores suggest that this integrative parenteral approach should be further evaluated in adequately powered, randomized, placebo-controlled trial with longer follow-up and integration of metabolic biomarker monitoring.

Video.

Acknowledgments

None.

Conflicts of interest

The author declares that there is no conflicts of interest.

References

1. Lai MC, Lombardo MV, Baron-Cohen S. Autism. *Lancet.* 2014;383(9920):896–910.
2. Zeidan J, Fombonne E, Scorah J, et al. Global prevalence of autism: A systematic review update. *Autism Res*. 2022;15(5):778–790.
3. Howlin P, Moss P, Savage S, et al. Social outcomes in mid- to later adulthood among individuals diagnosed with autism and average nonverbal IQ as children. *J Am Acad Child Adolesc Psychiatry*. 2013;52(6):572–581.
4. Goel R, Hong JS, Findling RL, et al. An update on pharmacotherapy of autism spectrum disorder in children and adolescents. *Int Rev Psychiatry.* 2018;30(1):78–95.
5. McPheeters ML, Warren Z, Sathe N, et al. A systematic review of medical treatments for children with autism spectrum disorders. *Pediatrics.* 2011;127(5):e1312–1321.
6. Tachibana Y, Miyazaki C, Ota E, et al. A systematic review and meta-analysis of comprehensive interventions for pre-school children with autism spectrum disorder (ASD). *PLoS One*. 2017;12(12):e0186502.
7. Hofer J, Hoffmann F, Kamp-Becker I, et al. Complementary and alternative medicine use in adults with autism spectrum disorder in Germany: results from a multi-center survey. *BMC Psychiatry*. 2019;19(1):53.
8. Fraguas D, Diaz-Caneja CM, Pina-Camacho L, et al. Dietary interventions for autism spectrum disorder: A meta-analysis. *Pediatrics*. 2019;144(5):e20183218.
9. Al-Mosalem OA, El-Ansary A, Attas O, et al. Metabolic biomarkers related to energy metabolism in Saudi autistic children. *Clin Biochem*. 2009;42(10-11):949–957.
10. Ghanizadeh A, Akhondzadeh S, Hormozi M, et al. Glutathione-related factors and oxidative stress in autism, a review. *Curr Med Chem*. 2012;19(23):4000–4005.
11. Siddiqui MF, Elwell C, Johnson MH. Mitochondrial dysfunction in autism spectrum disorders. *Autism Open Access*. 2016;6(5):1000190
12. Theoharides TC. Extracellular mitochondrial ATP, suramin, and autism? *Clin Ther.* 2013;35(9):1454–1456.
13. James SJ, Melnyk S, Jernigan S, et al. Metabolic endophenotype and related genotypes are associated with oxidative stress in children with autism. *Am J Med Genet B Neuropsychiatr Genet*. 2006;141B(8):947–956.
14. Frye RE, Sequeira JM, Quadros EV, et al. Cerebral folate receptor autoantibodies in autism spectrum disorder. *Mol Psychiatry*. 2013;18(3):369–381.
15. Ramaekers VT, Blau N, Sequeira JM, et al. Folate receptor autoimmunity and cerebral folate deficiency in low-functioning autism with neurological deficits. *Neuropediatrics*. 2007;38(6):276–281.
16. Novak MR. A combined megavitamin and complex homeopathy regimen in children with autism spectrum disorder promotes speech development: a case series. *International Journal of Current Research.* 2020;12(1):9169–9172.
17. Novak MR. The SULPYCO Method: An observational study on the efficacy of low-dose sulpiride combined with a complex homeopathic preparation for the treatment of depressive syndrome. *Integrative Medicine.* 2013;12(6):19.
18. Novak MR. Combined Sulpiride, Olanzapine, and A Complex Homeopathic Preparation for Delusional Disorder. *Neurology Research and Surgery.* 2019;2(1):1–2.
19. Schopler E, Van Bourgondien ME, Wellman GJ. Childhood Autism Rating Scale, Second Edition (CARS2). Los Angeles, CA: Western Psychological Services; 2010.
20. Adams JB, Audhya T, McDonough-Means S, et al. Effect of a vitamin/mineral supplement on children and adults with autism. *BMC Pediatr*. 2011;11:111.
21. Witt CM, Bluth M, Albrecht H, et al. The in vitro evidence for an effect of high homeopathic potencies--a systematic review of the literature. *Complement Ther Med.* 2007;15(2):128–138.
22. Busner J, Targum SD. The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry (Edgmont).* 2007;4(7):28–37.
23. Kennedy DO. B Vitamins and the brain: mechanisms, dose and efficacy--a review. *Nutrients*. 2016;8(2):68.
24. van de Lagemaat EE, de Groot L, van den Heuvel E. Vitamin B(12) in Relation to Oxidative Stress: A Systematic Review. *Nutrients.* 2019;11(2):482.
25. Patel K, Curtis LT. A comprehensive approach to treating autism and attention-deficit hyperactivity disorder: a prepilot study. *J Altern Comple-*

ment Med. 2007;13(10):1091–1097.

26. Hansen SN, Tveden-Nyborg P, Lykkesfeldt J. Does vitamin C deficiency affect cognitive development and function? *Nutrients.* 2014;6(9):3818–3846.
27. Dolske MC, Spollen J, McKay S, et al. A preliminary trial of ascorbic acid as supplemental therapy for autism. *Prog Neuropsychopharmacol Biol Psychiatry.* 1993;17(5):765–774.
28. DeVilbiss EA, Magnusson C, Gardner RM, et al. Antenatal nutritional supplementation and autism spectrum disorders in the Stockholm youth cohort: population based cohort study. *BMJ.* 2017;359:J4273.
29. Schmidt RJ, Hansen RL, Hartiala J, et al. Prenatal vitamins, one-carbon metabolism gene variants, and risk for autism. *Epidemiology*. 2011;22(4):476–485.
30. Bell IR, Lewis DA, 2nd, Brooks AJ, et al. Improved clinical status in fibromyalgia patients treated with individualized homeopathic remedies versus placebo. *Rheumatology (Oxford).* 2004;43(5):577–582.
31. Taylor MA, Reilly D, Llewellyn-Jones RH, et al. Randomised controlled trial of homoeopathy versus placebo in perennial allergic rhinitis with overview of four trial series. *BMJ.* 2000;321(7259):471–476.
32. Khaibullina DK, Maksimov Y. Post-covid asthenia syndrome. Neuroscience and behavioral physiology. 2023;53(8):1347–1354.

Citation: Novak MR. Parenteral megavitamin therapy with folinic acid and a complex homeopathic preparation in an older child with grade 2 autism spectrum disorder: a case report. *J Neurol Stroke.* 2026;16(2):72–76. DOI: 10.15406/jnsk.2026.16.00655