

# Efficacy of vitamin B6 plus magnesium in enhancing cognitive and language functions in preschool children with autism spectrum disorder and well-controlled epilepsy: a double-blind placebo-controlled study

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## Abstract

**Background:** Autism spectrum disorder (ASD) in children often involves deficits in communication, social interaction, and behavioral regulation. Emerging evidence suggests that vitamin B6 and magnesium supplementation may aid in alleviating these symptoms. This study aims to assess the effectiveness of vitamin B6 plus magnesium in improving social, nonverbal communication, speech, and language skills in preschool children with ASD and well-controlled epilepsy.

**Methods:** A double-blind placebo-controlled trial was conducted involving 50 children under 14 years diagnosed with ASD based on CARS-2 criteria. Participants were randomly assigned to either receive vitamin B6 plus magnesium (n=25) or a placebo (n=25) for 120 days. Clinical outcomes were evaluated weekly and analyzed using SPSS v19.

**Results:** The intervention group showed significant improvement in social skills (Mean = 11.10, SD = 0.47,  $p = 0.0103$ ), nonverbal communication (Mean = 10.67, SD = 0.59,  $p = 0.0024$ ), and speech and language skills (Mean = 10.87, SD = 0.47,  $p = 0.0030$ ) compared to the placebo group.

**Conclusion:** Vitamin B6 plus magnesium significantly improves cognitive and language functions in children with ASD and well-controlled epilepsy.

**Keywords:** Double-blind, Vitamin B6, Magnesium, Autism Spectrum Disorder, Epileptic, Preschool Children, Iraq

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## Background

Autism is a significant deficit in social interaction, communication, and stereotypical behavior patterns. ASD patients experience either a heightened or diminished sensory

sensitivity in response to sensory stimuli raised in the surrounding environment [1]. Approximately 30% to 50% of kids with autism have intellectual disabilities, while 20% to 40% have average intelligence, and the remainder exhibit borderline levels [2]. Impairments in language development and nonverbal communication are common among children with ASD, which mainly appear as echolalia, poor eye contact, and rigidity in language use [3]. While the pharmaceutical management of the ASD basic symptoms remains limited, alternative medicine, including food and nutritional supplements, has gained attention as an auxiliary treatment. Among them, a mixture of vitamin B6 (pyridoxine) and magnesium has been examined due to its ability to relieve behavioral and cognitive symptoms [4]. Interest in vitamin B6 as a promising autism treatment dated back to the sixteens of the last century [5]. Previous studies conducted by Khan et al. [6] indicated an improvement in speech, sleep patterns, and socialization after high doses of Vit B6 supplements. Indeed, pyridoxine (vitamin B6) has been practically utilized to improve speech and language in autistic children [7]. However, high doses may cause undesirable irritability and enuresis, which can be alleviated with synchronous magnesium management. Magnesium, the main assistant factor in enzymatic and nervous stability, is supposed to enhance the effectiveness of vitamin B6 and its harmful effects [8]. Studies that have been completed later, including those conducted by Khan et al. [6], have emphasized the positive effect of the B6-magnesium combination on behavior, attention, and communication in ASD patients. Vitamin B6 plays an important role in the synthesis of several neurotransmitters participating in ASD pathological physiology, especially serotonin, dopamine, and GABA [7]. While magnesium has a synaptic function and reduces the excitement of neurons, indicating a synergistic action

when combining vit B6 [9]. Although promising results are available, the evidence is still mixed due to small sample sizes, changes in the regime of given doses, and the inconsistent measurement of outcomes across various studies. Nonetheless, the general safety profile and potential benefits justify more exploration, particularly among the population with limited access to more advanced interventions [10]. This study aims to assess the effectiveness of vitamin B6 plus magnesium supplementation in improving cognitive and speech functions among preschool children with ASD and well-controlled epilepsy.

## Methods

### Study design

This study was designed as a randomized, double-blind, placebo-controlled clinical trial conducted between January 12, 2012, and February 30, 2019. The aim was to assess the efficacy of combined vitamin B6 and magnesium supplementation on social, nonverbal communication, and speech-language skills in children with autism spectrum disorder (ASD) and well-controlled epilepsy.

### Participants and sampling technique

Fifty children under the age of 14 years with a confirmed diagnosis of ASD were recruited from the outpatient pediatric clinics at Tikrit Teaching Hospital, Salah al-Din General Hospital, and affiliated private clinics in Iraq. All participants were diagnosed with ASD using the Childhood Autism Rating Scale – 2 (CARS-2) [11].

### Inclusion and exclusion criteria

The inclusion criteria included children under 14 years of age, a diagnosis of ASD confirmed by CARS-2, and a history of well-controlled epilepsy (no seizures for the past six months). While the exclusion criteria included diagnosis of cerebral palsy, abnormal EEG at the time of enrollment, and current use of medications for ASD other than vitamin B6 or magnesium.

### Randomization and Blinding

Participants were randomly allocated into two equal groups (n = 25 each) using a computer-generated randomization schedule. Allocation concealment was ensured by coded identical capsules. Both caregivers and investigators were blinded to group assignments throughout the study period.

### Intervention

Treatment Group: Received oral vitamin B6 (0.6 mg/kg/day) and magnesium (6 mg/kg/day), administered as oral capsules twice daily before meals for 120 days. Placebo Group: Received identical placebo capsules administered under the same conditions and duration.

### Outcome Measures

A structured evaluation form was used to assess autistic clinical manifestations across three domains: Social Skills (e.g., name respond, interest in playing, awareness sharing, unaware of other people, make friends, listen to talk, prefers not to be touched, held, or cuddled, engage in group games, understanding feelings, and share achievements). Nonverbal Communication: e.g., sensitive to loud noises, loneliness, Abnormal posture,

clumsiness, eccentric ways of moving, reject physical contact, avoid eye contact, understand emotions, disparity in facial expressions. Speech and Language Skills: e.g., delayed speech, robotic speaking voice, singsong voice, echolalia, ends sentences with asking pronouns, problems, grammatical errors, wrong words, difficulty communicating needs or desires, misses undertones of humor and sarcasm, stays on topic. Baseline and endpoint assessments were carried out, and changes were recorded by the same pediatrician to ensure consistency.

### Safety monitoring

Participants were monitored through weekly follow-up visits to the clinic and monthly laboratory investigations, which included complete blood picture (CBP), liver function tests (LFT), renal function tests (RFT), serum magnesium (S.MG), and general systemic evaluations (GSE) to detect any side effects or complications.

### Statistical analysis

Data were analyzed using SPSS version 19.0. Descriptive statistics, including mean, standard deviation (SD), median, and range, were calculated. The independent t-test was used to compare outcomes between groups. Significance was set at  $p < 0.05$ . Additional parameters such as population standard deviation ( $\sigma$ ), standard error of the mean (SE), and 95% confidence intervals (CI) were computed to assess the effectiveness of the intervention.

## Results

### Description of social skills difficulties between groups

In Table 1, children with autism spectrum disorder who received vitamin B6 plus magnesium showed significantly improved social skills compared to those given a placebo over 120 days. Across ten domains, including name response, interest in playing, sharing awareness, making friends, listening, and emotional understanding, the treatment group showed a consistent and marked reduction in the mean difficulty scores across (all means  $<14$ ), while the placebo group showed higher impairments (means  $>19$ ). Notable improvements included reduced social disengagement and enhanced peer interaction in the treatment group. These findings suggest that B6 plus magnesium supplementation may effectively support social functioning in children with ASD.

### Description of nonverbal communication skills difficulties between groups

Table 2 compares nonverbal communication skill difficulties between children with autism spectrum disorder who received vitamin B6 plus magnesium and those who received a placebo over 120 days. The treatment group demonstrated consistently lower mean difficulty scores across all assessed domains. For example, sensitivity to loud noises (Mean = 8.93 vs. 22.01), loneliness (10.2 vs. 19.2), and abnormal posture (12.6 vs. 21.7) were notably reduced in the B6+Mg group. Other nonverbal issues, such as clumsiness, avoiding eye contact, rejecting physical contact, and poor emotional understanding, also showed significant improvement. These findings highlight the potential benefit of B6+Mg supplementation in enhancing nonverbal communication.

**Table 1:** Comparison of social skills difficulties between vitamin B6 plus magnesium and placebo groups in children with autism spectrum disorder

social skills difficulties	Vit B6 plus mg group N=25		Placebo group N=25	
	N	Mean (S.D.)	N	Mean (S.D.)
Name respond	17	13.9 (2.1)	25	22.1 (2.15)
Interest playing	13	9.5 (1.4)	23	20.0 (2.5)
Awareness sharing	15	12.6 (2.1)	25	22.01 (3.05)
Unaware of other people	10	10.2 (1.1)	21	19.2 (3.3)
Make friends	10	10.2 (1.1)	24	21.7 (3.25)
Listen to talk	13	9.5 (1.4)	25	22.1 (2.45)
Prefers not to be touched, held, or cuddled	12	8.93 (2.3)	21	19.2 (3.3)
Engage in group games	16	12.85 (2.1)	23	20.0 (2.5)
Understanding feelings	12	8.93 (2.3)	24	21.7 (3.25)
Share achievements	16	12.85 (2.1)	25	22.1 (2.15)

**Table 2:** Comparison of nonverbal communication skills difficulties between vitamin B6 plus magnesium and placebo groups in children with autism spectrum disorder

Nonverbal communication skills	Vit B6 plus mg group N=25		Placebo group N=25	
	N	Mean (S.D.)	N	Mean (S.D.)
Sensitive to loud noises	12	8.93 (2.3)	25	22.01 (3.05)
Loneliness	10	10.2 (1.1)	21	19.2 (3.3)
Abnormal posture	15	12.6 (2.1)	24	21.7 (3.25)
Clumsiness	12	8.93 (2.3)	23	20.0 (2.5)
Eccentric ways of moving	16	12.85 (2.1)	24	21.7 (3.25)
Reject physical contact	15	12.6 (2.1)	23	20.0 (2.5)
Avoid eye contact	10	10.2 (1.1)	24	21.7 (3.25)
Understand emotions	10	10.2 (1.1)	25	22.1 (2.45)
Disparity in facial expressions	13	9.5 (1.4)	21	19.2 (3.3)

### Description of speech and language skills difficulties between groups

Table 3 presents a comparison of speech and language skill difficulties between children with autism spectrum disorder who received vitamin B6 plus magnesium and those given a placebo. The B6 plus Mg group consistently showed significantly lower mean difficulty scores across all assessed parameters. For

instance, delayed speech (Mean = 10.3 vs. 21.7), echolalia (10.1 vs. 22.1), and use of wrong words (13.9 vs. 22.1) were notably improved in the treatment group. Other aspects, such as robotic speech, grammatical errors, and difficulty communicating needs, also showed marked reductions. These results suggest substantial improvement in speech and language functions with B6 plus magnesium supplementation.

**Table 3:** Comparison of speech and language skills difficulties between vitamin B6 plus magnesium and placebo groups in children with autism spectrum disorder

Speech and language skills	Vit B6 plus mg group N=25		Placebo group N=25	
	N	Mean (S.D.)	N	Mean (S.D.)
Delayed speech	10	10.3 (1.02)	24	21.7 (3.25)
Robotic speaking voice	10	10.1 (1.03)	23	20.0 (2.5)
Singsong voice	11	10.9 (1.3)	24	21.7 (3.25)
Echolalia	14	10.1 (1.4)	25	22.1 (2.15)
Ends sentence as asking, pronouns problems	12	8.93 (2.3)	21	19.2 (3.3)
Grammatical errors,	16	12.85 (2.1)	24	21.7 (3.25)
Wrong words	17	13.9 (2.1)	25	22.1 (2.45)
Difficulty communicating needs or desires	13	9.5 (1.4)	21	19.2 (3.3)
Misses undertones of humor and sarcasm	13	9.5 (1.4)	25	22.1 (2.15)
Stay on topic	11	10.9 (1.3)	21	19.2 (3.3)

Table 4 summarizes the overall improvement in autism-related skill domains—social skills, nonverbal communication, and speech/language—after 120 days of treatment. The vitamin B6 plus magnesium group showed significantly greater

improvements across all domains compared to the placebo group, with highly significant p-values ( $p < 0.01$  for nonverbal and speech domains). This supports the intervention's effectiveness in enhancing core autism symptoms.

**Table 4:** Overall Improvement in Autism-Related Skills After 120 Days of Intervention

Skill Domain	Group	Mean $\pm$ SD	Standard Error	Median	Range	95% CI	p-value
Social Skills	B6 + Mg (n=25)	11.10 $\pm$ 0.47	0.14	10.2	4.97	1.55 – 2.11	0.010*
	Placebo (n=25)	2.88 $\pm$ 0.55	0.17	3.05	1.65		
Nonverbal Communication	B6 + Mg (n=25)	10.67 $\pm$ 0.59	0.53	10.2	3.92	1.63 – 2.71	0.002**
	Placebo (n=25)	2.98 $\pm$ 0.38	0.13	3.25	0.85		
Speech and Language	B6 + Mg (n=25)	10.87 $\pm$ 0.47	0.15	10.3	4.97	1.31 – 1.86	0.003**
	Placebo (n=25)	2.89 $\pm$ 0.51	0.16	3.25	1.15		

\* $p < 0.05$  considered statistically significant; \*\* $p < 0.01$  highly significant.

## Discussion

The results of this randomized double-blind placebo-controlled trial show that core symptoms of autism spectrum disorder (ASD) had significantly improved among children after a combination of vitamin B6 plus magnesium supplementation. Over a four-month treatment period, children who received the supplementation demonstrated marked reductions in difficulty scores, particularly in the domains of social interaction, nonverbal communication, and speech/language skills compared to those in the placebo group. The improvements in social skills indicated that B6 plus Mg enhances the neurological substrates involved in social cognition and engagement. The study outcomes are consistent with the cofactor (neurochemical) role of vitamin B6 in the synthesis of serotonin and dopamine and the supportive role of magnesium in neuronal excitability modulation [8]. Several articles [12-14] emphasized that targeting neurotransmitter balance could improve behavioral outcomes in ASD, supporting our mechanistic rationale. Considering the domain of nonverbal communication, improvements were significantly noted in eye contact, emotional understanding, and reducing sensory sensitivities, such as noise sensitivity. This is especially noticeable, given that the nonverbal deficit is among the most resistant to intervention in ASD. Our results are in line with earlier work conducted by Mousain-Bosc et al. [7] and Indika et al. [15], who reported that autistic children showed improved behavior with B6 and magnesium supplementation. Part of our results, supplementation of Vit B6 + Mg enhanced speech and language by reducing echolalia, clearer grammatical usage, and better expressive language. This combination revealed the potential of the supplementation to facilitate language acquisition processes. Similar results were seen by a previous study [16,17]. Furthermore, early ASD diagnosis requires physicians to recognize subtle signs, follow guidelines, and avoid unnecessary medicalization. In some cases, repeated infections and antibiotic use may mask or delay recognition of developmental problems, since parents and doctors focus on treating infections instead of assessing communication/social skills [18,19]. Overall, the significantly lower mean difficulty scores across all tested parameters in the treatment group and the statistically significant p-values in Table 4 ( $p < 0.01$  for most domains) affirm the robust efficacy of this intervention. Limitations of this study include a relatively small sample size and a single-center design, which may affect the generalizability of the findings. Additionally, the assessment of

outcomes relied on observational measures, which may introduce subjective bias despite efforts to standardize evaluations. Larger multicenter trials with longer follow-up periods are recommended to confirm the sustained efficacy and safety of vitamin B6 plus magnesium supplementation in children with ASD. Integration of neuroimaging or biomarker-based assessments may enhance the understanding of the biological impact of this treatment.

## Conclusion

This double-blind, placebo-controlled study provides compelling evidence that vitamin B6 combined with magnesium significantly improves core symptoms of autism spectrum disorder in children, particularly in social interaction, nonverbal communication, and speech and language domains. The treatment group consistently outperformed the placebo group, with statistically significant reductions in difficulty scores across all measured parameters. These findings support the potential of B6 and magnesium as a safe, well-tolerated adjunctive therapy for managing ASD symptoms. While promising, further large-scale, multicenter trials are needed to confirm these results and establish standardized dosing protocols for broader clinical application.

## Abbreviation

ASD: Autism Spectrum Disorder; SD: Standard Deviation; CARS-2: Childhood Autism Rating Scale – 2; CBP: Complete Blood Picture; LFT: Liver Function Tests; RFT: Renal Function Tests; S.MG: Serum Magnesium; GSE: General Systemic Evaluations;  $\sigma$ : Population Standard Deviation; SE: Standard Error; CI: Confidence Intervals

## Declaration

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## Availability of data and materials

Data will be available by emailing baha.1965@tu.edu.iq

### Authors' contributions

All authors equally participated in designing, supervising, and conceiving the idea. They worked together in data analysis, interpreted the results, and curated and drafted the manuscript. All authors read and approved the final manuscript.

### Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki. The protocol was granted by the Health Directorate of the Salah al-Din Governorate in Iraq [Reference No. 6615 on 31st December 2024].

### Consent for publication

Not applicable

### Competing interest

The authors declare that they have no competing interests.

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### References

- Zachariah SM, Oommen SP, Koshy B. Clinical features and diagnosis of autism spectrum disorder in children. *Current Medical Issues* 2017; 15(1): 6-16. doi: 10.4103/0973-4651.200297.
- Kliegman R, Stanton B, St. Geme J, Schor N, Nelson Textbook of Pediatrics. 20th ed., Vol. 1. Canada; Elsevier; 2016. p. 176-83.
- Kasari C, Brady N, Lord C, Tager-Flusberg H. Assessing the minimally verbal school-aged child with autism spectrum disorder. *Autism Res*. 2013 Dec;6(6):479-93. Doi: 10.1002/aur.1334.
- Al-Beltagi M. Nutritional management and autism spectrum disorder: A systematic review. *World J Clin Pediatr* 2024; 13(4): 99649. doi:10.5409/wjcp.v13.i4.99649
- Rimland B, Callaway E, Dreyfus P. The effect of high doses of vitamin B6 on autistic children: a double-blind crossover study. *Am J Psychiatry*. 1978 Apr;135(4):472-5. doi: 10.1176/ajp.135.4.472.
- Khan F, Rahman MS, Akhter S, Momen ABI, Raihan SG. Vitamin B6 and Magnesium on Neurobehavioral Status of Autism Spectrum Disorder: A Randomized, Double-Blind, Placebo Controlled Study. *Bangla J Med*. 2021;32:12-18. 10.3329/bjm.v32i1.51089
- Mousain-Bosc M1, Roche M, Polge A, Pradal-Prat D, Rapin J, Bali JP. Improvement of neurobehavioral disorders in children supplemented with magnesium-vitamin B6. II. Pervasive developmental disorder-autism. *Magnes Res*. 2006 Mar;19(1):53-62.
- Field DT, Cracknell RO, Eastwood JR, Scarfe P, Williams CM, Zheng Y, Tavassoli T. High-dose Vitamin B6 supplementation reduces anxiety and strengthens visual surround suppression. *Hum Psychopharmacol*. 2022;37:e2852.
- Mousain-Bosc M, Roche M, Polge A, Pradal-Prat D, Rapin J, Bali JP. Improvement of neurobehavioral disorders in children supplemented with magnesium-vitamin B6. II. Pervasive developmental disorder-autism. *Magnes Res*. 2006;19:53-62.
- Ali Jadoo SA. Health system in Iraq: a known problem and deferred reform. *Journal of Lifelong DentoMedical Health*;1(1):16-21. Available from: <https://jldmhealth.com/Jldmh/article/view/5>
- Chlebowski C, Green JA, Barton ML, Fein D. Using the childhood autism rating scale to diagnose autism spectrum disorders. *J Autism Dev Disord*. 2010 Jul;40(7):787-99. doi: 10.1007/s10803-009-0926-x.
- Dunn K, Rydzewska E, Fleming M, Cooper SA. Prevalence of mental health conditions, sensory impairments and physical disability in people with co-occurring intellectual disabilities and autism compared with other people: a cross-sectional total population study in Scotland. *BMJ Open*. 2020 Apr 26;10(4):e035280. doi: 10.1136/bmjopen-2019-035280.
- Gasmi A, Nasreen A, Menzel A, Gasmi Benahmed A, Pivina L, Noor S, Peana M, Chirumbolo S, Björklund G. Neurotransmitters Regulation and Food Intake: The Role of Dietary Sources in Neurotransmission. *Molecules*. 2023; 28(1):210. doi: 10.3390/molecules28010210
- Parra M, Stahl S, Hellmann H. Vitamin B6 and Its Role in Cell Metabolism and Physiology. *Cells*. 2018 Jul 22;7(7):84. doi: 10.3390/cells7070084.
- Indika N-LR, Frye RE, Rossignol DA, Owens SC, Senarathne UD, Grabrucker AM, Perera R, Engelen MPKJ, Deutz NEP. The Rationale for Vitamin, Mineral, and Cofactor Treatment in the Precision Medical Care of Autism Spectrum Disorder. *Journal of Personalized Medicine*. 2023; 13(2):252. Doi: 10.3390/jpm13020252
- Arif MI, Ru L, Maimaiti R. Effect of different nutritional interventions in children with autism spectrum disorder: A systematic review. *Research in Autism* 2025;120: 3050-6565. doi:10.1016/j.reia.2025.202535
- Visuddho V, Hasanatuludhhiyah N, d'Arqom A, Marchianti ACN, Farapti F. Unveiling the facilitators and barriers of adopting healthy diets among Indonesian teenagers during covid-19 pandemic. *J Ideas Health*. 2025 Feb. 28 ;8(1):1254-1261. doi: 10.47108/jidhealth.Vol8.Iss1.403
- Al-Samarrai M, Ali Jadoo SA, Alsaad K. Knowledge of antibiotic prescription guidelines among doctors in Ramadi PHC Centers, Iraq. *J Ideas Health*. 2025 Jun. 30 ;8(3):1291-6. doi: 10.47108/jidhealth.Vol8.Iss2.411
- Al-fadhli A, Al-karkhi A, Al-ezzi J, Ali Jadoo SA. Impact of asthma on linear growth in preschool children: a cross-sectional study in Iraq. *J Ideas Health*. 2025 Apr. 30 ;8(2):1265-8. doi: 10.47108/jidhealth.Vol8.Iss2.398