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RESEARCH ARTICLE

INOSITOL: AUGMENTING MANAGEMENT OF ADHD SYMPTOMS IN ADOLESCENTS

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ABSTRACT

Background: Attention-Deficit/Hyperactivity Disorder (ADHD) is a prevalent neurodevelopmental condition marked by inattention, hyperactivity, and impulsivity. While stimulant medications are considered first-line treatment, their use is frequently limited by adverse effects such as appetite loss, insomnia, and gastrointestinal discomfort. This has prompted growing interest in adjunctive therapies that offer symptom relief with improved tolerability. **Case Presentation:** We report the case of a 17-year-old male with combined-type ADHD and poor tolerance to multiple stimulant and non-stimulant pharmacotherapies. The patient experienced significant side effects with high-dose extended-release methylphenidate (Jornay PM), necessitating discontinuation. Following the introduction of inositol (4g three times daily) alongside a reduced stimulant dose (60 mg), the patient exhibited substantial improvement in attention, impulse control, and emotional regulation, as measured by the Conners Rating Scale. Notably, these improvements occurred without the previously experienced gastrointestinal side effects. **Discussion:** Inositol, a glucose isomer involved in neurotransmitter signaling and receptor modulation, may influence dopaminergic and serotonergic pathways implicated in ADHD. Its neuroprotective and mood-stabilizing properties suggest potential as a safe adjunctive treatment, especially in cases with stimulant intolerance or emotional dysregulation. **Conclusion:** This case highlights the potential benefit of inositol as a well-tolerated adjunct to stimulant therapy in adolescents with ADHD. Further controlled studies are warranted to evaluate its efficacy and define its role in the broader management of treatment-resistant ADHD.

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INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common neurodevelopmental disorders in adolescents, affecting an estimated 5–10% of youth globally (1). It is characterized by persistent inattention, hyperactivity, and impulsivity patterns that significantly impair academic performance, interpersonal relationships, and emotional regulation (1). Stimulant medications, such as methylphenidate and amphetamines, are the standard of care. Although these medications are generally effective, their side effect profile, particularly at higher doses, often includes adverse effects such as appetite suppression, insomnia, and emotional blunting, which can ultimately lead to treatment discontinuation (2,3). These limitations have sparked increasing interest in alternative or adjunctive treatments that target the underlying neurobiology of ADHD while aiming for a more favorable safety profile (4). Inositol, a naturally occurring glucose isomer found in high concentrations in the brain, has demonstrated promise in the treatment of anxiety and mood disorders (5). It modulates intracellular signaling pathways associated with dopamine, norepinephrine, and serotonin, neurotransmitters implicated in ADHD pathophysiology (5). Despite its well established role in mood regulation, inositol's potential in ADHD has received limited attention. This report describes the case of an adolescent with ADHD who demonstrated symptomatic improvement on stimulant therapy but was unable to continue at the prescribed dosage due to adverse effects like appetite loss, insomnia, and GI distress, which prevented complete symptom control of hyperactivity and impulsivity. The introduction of inositol alongside a reduced stimulant dose resulted in equivalent, if not greater, improvement in symptoms without the burden of side effects. This case underscores the potential of inositol as a safe and well-tolerated adjunctive treatment. It supports further investigation into its role in the management of neurodevelopmental disorders such as ADHD.

CASE PRESENTATION

A 17-year-old adolescent male with a diagnosis of attention-deficit/hyperactivity disorder (ADHD), combined type, presented with longstanding symptoms of inattention, difficulty focusing and concentrating, and daily challenges with procrastination, home management, and organization.

Table 1. Average Conners rating parent/teacher t-score for ADHD symptoms

	Baseline	6 months	12 months	18 months	24 months
Inattentive	75	60	72	58	48
Hyperactive	78	62	75	55	46
Executive function	70	55	68	55	50

Table 2. Neurotransmitters and affected brain areas in ADHD

Neurotransmitters	Affected Part of brain	Affected functions
Dopamine	Prefrontal cortex, striatum	Inattention, poor executive function
Norepinephrine	Locus ceruleus, frontal cortex	Attention regulation, alertness
Serotonin(secondary)	Limbic system, raphe nuclei	Mood, impulsivity, comorbid anxiety

Table 3. Role of inositol in ADHD symptoms

Mechanisms of Inositol action	Neurotransmitter/Process	ADHD symptom Addressed
IP3/DAG second messenger	Dopamine, Serotonin	Inattention, impulsivity
Serotonin receptor sensitivity	5-HT1A, 5-HT2A	Mood, aggression
Dopamine signaling modulation	D1/D2 receptors	Attention, motivation
Neuro-protection	Oxidative stress reduction	Cognitive preservation

These behaviors were more pronounced in less structured settings, such as home and non-school environments. At school, he also struggled with concentration, completing/ initiating/and sustaining tasks. Diagnosis of ADHD was confirmed with the Conners Rating Scale and a comprehensive psychiatric evaluation. Previous medication trials for this adolescent with ADHD included dexmethylphenidate, methylphenidate, d- and l-amphetamine, guanfacine, and atomoxetine with poor tolerance and repeated side effects. The most recent pharmacotherapy involved extended-release methylphenidate (Jornay PM), which was gradually titrated from 20 mg to 100 mg. However, this regimen led to severe gastrointestinal side effects, including persistent diarrhea and frequent bathroom use, ultimately resulting in discontinuation of the medication. Given the patient's limited tolerability to multiple prior treatments, his parents expressed growing frustration with the continued introduction of new medications. As an alternative approach, inositol was introduced at a dose of 4 grams three times daily, in combination with extended releasemethylphenidate at a reduced dose of 60 mg. Following the addition of inositol, both the patient and his family reported notable clinical improvements. Specifically, the patient demonstrated enhanced emotional regulation, fewer and less intense behavioral outbursts, and improved impulse control, all of which were reflected in improved scores on the Conners Rating Scale (Table 1). He also reported feeling less irritable and more capable of managing interpersonal stressors, although some residual difficulties persisted within the family dynamic. Importantly, his ADHD symptoms remained minimal in structured settings, highlighting the significant influence of environmental factors on his overall presentation. This case highlights the potential utility of inositol as a safe and well-tolerated adjunctive intervention for adolescents with ADHD who are unable to tolerate stimulants. The observed behavioral and emotional regulation improvements support further investigation into its role in complex, treatment-resistant cases.

DISCUSSION

Attention-deficit/hyperactivity disorder (ADHD) is increasingly recognized as a complex neurodevelopmental condition involving dysregulation of catecholaminergic and serotonergic signaling, particularly within the prefrontal cortex and associated cortico-striatal networks. These brain regions are responsible for executive function, attention control, emotional regulation, and impulse inhibition—domains frequently impaired in individuals with ADHD. Neuroimaging studies have demonstrated delayed cortical maturation and functional hypoactivity in the dorsolateral prefrontal cortex, anterior cingulate cortex, and basal ganglia structures such as the caudate nucleus. These findings align with the core symptoms of ADHD: inattention, hyperactivity, and impulsivity (Table 2). Inositol, a naturally occurring cyclic polyol found abundantly in the brain, plays a vital role in intracellular signaling through the phosphoinositide (PI) cycle. This pathway yields second messengers such as diacylglycerol (DAG) and inositol triphosphate (IP3), which regulate calcium signaling, protein kinase C activity, and receptor sensitivity. These mechanisms are essential for synaptic plasticity and neurotransmitter regulation, particularly for dopamine, serotonin, and norepinephrine, all implicated in ADHD pathophysiology (6). Preclinical and clinical studies have demonstrated that inositol may enhance dopaminergic and serotonergic receptor responsiveness, especially at D1, D2, 5-HT1A, and 5-HT2A receptors, without necessarily increasing extracellular neurotransmitter levels (5). This receptor-level modulation may improve attention and reduce impulsivity, offering a more stable neurochemical environment without the stimulant-induced peaks and troughs. Moreover, given serotonin's role in emotional regulation and impulsive behavior, inositol may be particularly beneficial in adolescents with combined-type ADHD or co-morbid mood symptoms (7,8). In addition to its effects on neurotransmission, inositol may offer neuroprotective benefits by reducing oxidative stress and stabilizing mitochondrial function, factors increasingly recognized as relevant in the neurobiology of ADHD (9). These properties may contribute to long-term cognitive resilience and emotional stability (Table 3). This case demonstrates the potential utility of inositol as an adjunctive treatment for ADHD in adolescents with stimulant intolerance. Initial Conners Rating Scale assessments confirmed the diagnosis of ADHD, combined type, with significant hyperactivity and impulsivity. Despite dose optimization, Jornay PM (methylphenidate) was discontinued due to intolerable gastrointestinal side effects. Reassessment with the Conners Rating Scale for ADHD after reintroducing a lower

dose of Jornay PM alongside inositol showed marked improvement in symptoms, supporting its adjunctive role. While inositol lacks robust evidence in ADHD, its mood-stabilizing and anxiolytic effects, observed in depression and anxiety disorders, may benefit emotional dysregulation in ADHD (10,11). This case, along with limited anecdotal reports, suggests inositol could be a viable option for patients with incomplete responses or adverse effects to standard therapies. Further controlled studies, incorporating structured rating scales like the Vanderbilt or Conners are needed to validate its efficacy and optimal use in ADHD management.

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