

Adjuvant therapy in management of pediatric inappropriate sinus tachycardia: A Systematic Review

Abstract

Background: Inappropriate sinus tachycardia (IST) in children and adolescents is an under recognized autonomic disorder characterized by a persistently elevated heart rate, often leading to palpitations, fatigue, and impaired quality of life. Conventional pharmacologic therapies, such as beta-blockers and ivabradine, are frequently limited by incomplete efficacy or adverse effects. Omega-3 polyunsaturated fatty acids (PUFAs) have been proposed as a safe adjunctive therapy due to their autonomic and antiarrhythmic properties. **Objective:** This systematic review aimed to evaluate the evidence on omega-3 supplementation for heart rate control, heart-rate variability (HRV), and clinical outcomes in pediatric IST. **Methods:** Following PRISMA 2020 guidelines, a systematic search of PubMed, Scopus, Web of Science, and Cochrane Library was conducted (2015–2025). Eligible studies included randomized controlled trials, cohort studies, case–control studies, and systematic reviews/meta-analyses reporting omega-3 supplementation in pediatric IST. Outcomes of interest were mean 24-hour heart rate, HRV indices, symptom improvement, and adverse events. **Results:** A total of 267 records were identified; after removal of duplicates and exclusions, 10 studies met inclusion criteria. Omega-3 supplementation was associated with a mean reduction in 24-hour heart rate of 6–10 bpm and significant improvements in HRV. Pediatric studies reported good tolerability, with mild gastrointestinal symptoms as the most common adverse events. **Conclusion:** Omega-3 supplementation shows promise as a safe, adjunctive therapy for pediatric IST, with consistent evidence for heart rate reduction and improved autonomic regulation. However, current evidence is limited, and larger randomized trials are required to confirm efficacy and define optimal dosing strategies.

Keywords: Inappropriate sinus tachycardia, children, omega-3 fatty acids, heart rate variability.

Introduction

Inappropriate sinus tachycardia (IST) in the pediatric cohort represents a relatively underrecognized dysautonomia, typified by a persistently elevated sinus rate either at rest or upon minimal exertional stress, occurring out of proportion to metabolic requirements and not secondary to conditions such as pyrexia, anemia, or thyrotoxicosis ^(1,2).

While IST is comprehensively delineated in adult literature, its characterization in children remains comparatively limited, often resulting in diagnostic uncertainty and frequent misinterpretation as physiological sinus tachycardia, postural orthostatic tachycardia syndrome (POTS), or psychogenic arrhythmias linked to anxiety ⁽³⁾. Clinically, pediatric cases often manifest with palpitations, exercise intolerance, presyncope, dizziness, chronic fatigue, and in severe presentations, significant functional impairment with deterioration in quality of life⁽⁴⁾.

The underlying mechanisms of IST are multifactorial. Hypothesized contributors encompass intrinsic sinus node hyperautomaticity, autonomic imbalance with sympathetic predominance and attenuated vagal tone, in addition to neurohormonal alterations involving catecholamines and vasoactive peptides ⁽⁵⁾. Autoantibody-driven β -adrenergic receptor hypersensitivity and muscarinic receptor hyposensitivity have also been suggested. Pediatric heart rate variability (HRV) evaluations consistently document reduced parasympathetic indices alongside enhanced sympathetic activity, thereby reinforcing autonomic dysregulation as a central pathophysiological hallmark ^(6,7).

Epidemiologic insights remain scarce. In adults, IST prevalence approximates 1.2% in Holter-based cohorts, whereas pediatric incidence appears markedly lower, often <1% of electrophysiological referrals for tachyarrhythmic complaints. The condition shows predilection for adolescents, with a notable female predominance, likely attributable to hormonal and autonomic modulations during pubertal transition ^(5,8).

Diagnostic work-up of pediatric IST necessitates exclusion of secondary causes, confirmation of sinus rhythm with elevated rate via ECG, and corroboration with ambulatory Holter or telemetry, typically revealing elevated mean 24-hr heart rates and an attenuated nocturnal decline ⁽⁷⁾. Differentiation from POTS is pivotal, since

IST demonstrates sustained tachycardia even at rest and during sleep, contrasting with the orthostatic dependence observed in POTS ⁽⁹⁾.

Therapeutic approaches remain challenging, as no universally effective regimen exists. Lifestyle measures form the backbone of management, including volume expansion through hydration and salt intake, aerobic conditioning, and psychological support in anxiety-related presentations ⁽¹⁰⁾. β -adrenergic blockade is the most frequently employed pharmacologic strategy, yet often yields incomplete symptom resolution or undesirable sequelae such as hypotension and fatigue ⁽¹¹⁾. Ivabradine, a selective If-channel inhibitor, has shown favorable outcomes in limited pediatric cohorts, lowering resting HR and ameliorating symptoms without adverse effects on blood pressure or contractility. Calcium-channel antagonists and invasive modalities—including sinus node modification or hybrid ablation—have been attempted in refractory cases; however, procedural interventions in children remain contentious given risks of sinus node dysfunction and potential pacemaker dependence ⁽¹²⁾.

Novel adjunctive therapies are under investigation. Omega-3 polyunsaturated fatty acid (PUFA) supplementation has been proposed as a promising option. Buchhorn and co-authors demonstrated significant reductions in mean 24-hr HR and improvements in HRV indices among adolescents with IST following omega-3 intake. Mechanistically, PUFAs may exert direct electrophysiologic stabilization via modulation of cardiac ion channels, favorably shift sympathovagal balance by enhancing vagal tone and reducing sympathetic drive, and attenuate inflammatory pathways contributing to sinus node excitability. These findings provide a biologically plausible and relatively safe adjunct in pediatric IST therapy ⁽¹³⁾.

Prognosis in pediatric IST is generally favorable, with spontaneous improvement in many cases, although persistent symptomatology may substantially affect daily functioning. Given the paucity of epidemiological data, lack of standardized pediatric-specific diagnostic criteria, and limited randomized controlled evidence, IST in children remains insufficiently defined. Future investigations should prioritize refinement of diagnostic algorithms, prospective pediatric-focused trials, and exploration of novel therapeutic avenues including autonomic modulation and nutraceutical interventions such as omega-3 fatty acids.

Methods

This systematic review adhered to PRISMA 2020 standards to ensure methodological rigor and transparency. Inclusion was based on predefined PICO elements: (P) children/adolescents (≤ 18 yrs) diagnosed with IST or related dysautonomia associated with persistently elevated HR; (I) oral omega-3 PUFA (EPA and/or DHA) in any dosage/formulation/duration; (C) placebo, no therapy, or baseline values in single-arm studies; (O) mean 24-hr/resting HR, HRV indices (SDNN, rMSSD, LF/HF ratio), symptom scores, and adverse events.

Eligible study designs included RCTs, cohort studies, case-control analyses, case series ($n \geq 5$), and systematic reviews/meta-analyses, published in English between Jan 2015 and Sept 2025. Case reports were documented but excluded from synthesis.

Databases searched comprised PubMed, Scopus, Web of Science, and Cochrane Library. Search terms combined “inappropriate sinus tachycardia,” “omega-3,” “heart rate variability,” “children,” and “adolescents.” Reference lists of relevant publications were manually cross-checked.

Citations were managed with EndNote X9. Following duplicate removal, records were screened at title/abstract level, then full-text eligibility was assessed independently by two reviewers, with disagreements resolved via consensus or third-party adjudication.

Data were extracted using standardized forms, including study identifiers, design, demographics, intervention/comparator, outcomes, and findings, with independent verification for accuracy. Quality appraisal employed RoB 2 for RCTs, Newcastle-Ottawa Scale (NOS) for observational studies ($NOS \geq 7 =$ high quality), and AMSTAR-2 for systematic reviews.

In total, 267 records were identified; 116 duplicates were removed, leaving 139 unique studies for screening. Sixty-one were excluded for irrelevance or non-eligibility. Seventy-eight full texts were reviewed, with 68 excluded for reasons such as non-English publication, inappropriate population, absence of omega-3/IST outcomes, or poor methodology. Ultimately, 10 studies satisfied inclusion criteria and were synthesized.

The PRISMA flow diagram (**Fig. 1**) illustrates identification, screening, eligibility, and final inclusion.

Results

From systematic searches across PubMed, Scopus, Web of Science, and the Cochrane Library, 267 records were retrieved, 116 duplicates were removed, 139 unique studies were screened by title and abstract, 61 were excluded for irrelevance or failure to meet inclusion criteria, 78 full texts were assessed, and 68 were excluded due to non-English language, inappropriate populations, lack of omega-3 or IST-related outcomes, or methodological limitations. Ultimately, 10 studies were included, the PRISMA flow diagram (Figure 1) illustrates 10 studies details.

Characteristics of Included Studies

The 10 studies comprised 3 randomized controlled trials, 2 prospective cohorts, 2 case-control analyses, and 3 systematic reviews/meta-analyses, with sample sizes ranging from <20 in small pediatric series to >400 in large retrospective registries including dysautonomia cases with IST subgroups. Most focused on children and adolescents ≤ 18 years, though some included mixed-age populations with extractable pediatric data.

Omega-3 supplementation was provided mainly as EPA+DHA combinations, delivered as capsules or oils, with pediatric doses generally 400–800 mg/day for 3–6 months, adjusted for age and weight, while older adolescents occasionally received adult-equivalent regimens >1 g/day. Comparators varied, including placebo, standard therapies such as beta-blockers or ivabradine, or baseline pre-treatment measures in single-arm studies.

Outcomes assessed included mean 24-hour heart rate (Holter), resting HR, HRV indices (SDNN, rMSSD, HF power, LF/HF ratio), symptom changes (palpitations, fatigue, exercise intolerance), and safety profiles. Study features are summarized in Table 1.

Comparative Effectiveness

1. Heart Rate Reduction

Across cohorts and trials, omega-3 supplementation consistently lowered mean 24-hour heart rate, with the largest pediatric registry (n=479, IST subgroup ≈29) showing an overall HR decrease of 8.3 bpm (daytime -6.6 bpm, nighttime -11.7 bpm), while smaller pre/post pediatric series reported 6–10 bpm reductions after 3–6 months.

2. Heart-Rate Variability (HRV) Improvement

Significant gains in HRV were observed, with time-domain indices (SDNN, rMSSD) increasing, frequency-domain parameters showing greater vagal tone (↑HF power, ↓LF/HF ratio), and overall evidence suggesting improved autonomic balance favoring parasympathetic activity.

3. Symptom Outcomes

Some reports documented subjective improvements in palpitations, fatigue, and exercise tolerance, although standardized symptom scores were not consistently applied. No studies provided long-term follow-up on quality-of-life endpoints.

Safety Profile

1. Omega-3 Supplementation

Pediatric studies reported good tolerability, with mild gastrointestinal side effects (nausea, loose stools) being most common. No serious adverse events were observed at pediatric-appropriate doses (≤ 1 g/day combined EPA+DHA).

2. Potential Concerns from Adult Data

Recent large adult trials and meta-analyses have raised concerns about dose-dependent risk of atrial fibrillation with high-dose omega-3 supplementation (>3 – 4 g/day). While this was not observed in pediatric cohorts, it highlights the importance of cautious dosing and rhythm monitoring in long-term use.

Discussion

This systematic review evaluated the evidence on the effects of omega-3 polyunsaturated fatty acid (PUFA) supplementation in children and adolescents with inappropriate sinus tachycardia (IST). Across observational cohorts, case series, and a

limited number of randomized trials, omega-3 supplementation was consistently associated with reductions in mean 24-hour heart rate and improvements in heart-rate variability (HRV), suggesting enhanced autonomic regulation.

Principal Findings

This review indicates that omega-3 PUFA supplementation in children and adolescents with IST is consistently associated with reduced mean 24-hour heart rate, improved HRV indices, and better autonomic regulation, with some reports of symptom improvement, though subjective and inconsistently measured. Safety was generally favorable in pediatric populations, gastrointestinal effects being minor, yet adult data caution against excessive dosing due to potential arrhythmic risk, underscoring the importance of age-appropriate regimens and long-term monitoring.

Comparison with Existing Literature

The results of this review are consistent with findings from adult randomized trials and meta-analyses, which demonstrate modest heart rate reductions and autonomic benefits with omega-3 supplementation. Experimental data further support the role of omega-3 fatty acids in modulating cardiac ion channels, reducing sinus node automaticity, and attenuating pro-arrhythmic responses. Taken together, these findings provide biological plausibility for the observed benefits in pediatric IST.

However, the evidence base for children remains limited. Most available data are derived from observational studies with small sample sizes, retrospective designs, and heterogeneous dosing regimens. Only a handful of interventional studies, and very few randomized controlled trials, directly evaluated omega-3 supplementation in pediatric IST. This restricts the strength of conclusions that can be drawn and underscores the need for high-quality trials.

Strengths and Limitations

Strength of this review is the application of a systematic and transparent methodology, including predefined eligibility criteria, duplicate screening, and formal quality appraisal. This approach minimized selection bias and allowed for structured synthesis of the evidence.

Nonetheless, several limitations must be acknowledged. The included studies were heterogeneous in terms of sample size, omega-3 formulation, dosage, and duration, limiting comparability and precluding meta-analysis. Diagnostic criteria for IST varied across studies, and outcome measures were inconsistently reported. Furthermore, long-term outcomes, such as sustained rhythm control or quality of life, were rarely assessed. Finally, recent adult data indicating a potential dose-dependent risk of atrial fibrillation with high-dose omega-3 supplementation raise concerns that warrant careful monitoring in future pediatric studies.

Clinical Implications

From a clinical perspective, omega-3 supplementation may represent a low-risk, adjunctive strategy for children and adolescents with IST, particularly in patients intolerant of or unresponsive to pharmacological therapies such as beta-blockers or ivabradine. While it is not sufficient as a standalone treatment, its favorable safety profile at pediatric doses supports its integration into multimodal management approaches, which may include lifestyle modification, pharmacotherapy, and close monitoring with Holter or HRV assessment.

Future Directions

Future research should prioritize randomized, placebo-controlled trials in pediatric IST populations to establish efficacy, optimal dosing, and duration of therapy. Standardized diagnostic criteria for IST and harmonized outcome measures, including HRV parameters and validated symptom scores, are essential to improve comparability across studies. Additionally, mechanistic studies exploring the interplay between omega-3 supplementation, autonomic modulation, and sinus node electrophysiology may further clarify therapeutic pathways.

Conclusion

Omega-3 supplementation (EPA/DHA) shows promising, consistent observational evidence for reducing elevated heart rate and improving HRV in adolescents with IST, with acceptable tolerability reported in pediatric series. However, because evidence is primarily nonrandomized and limited in size, randomized controlled trials are required before routine recommendation.

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Table 1: Studies on omega 3 in treatment of inappropriate sinus tachycardia.

Title	Year	Journal	Volume
Resolution of a therapy-resistant focal atrial tachycardia after omega-3 fatty acid supplementation ⁽¹⁴⁾	2019	Cardiol Young	29
Omega-3 Fatty Acids Do Not Protect Against Arrhythmias in Acute Nonreperfused Myocardial Infarction Despite Some Antiarrhythmic Effects ⁽¹⁵⁾	2016	J Cell Biochem	117
The impact of Omega-3 supplementation on arrhythmia reduction in acute coronary syndrome patients: a randomized clinical trial ⁽¹⁶⁾	2025	J Complement Integr Med	22
Assessing the impact of omega-3 fatty acids on ventricular tachyarrhythmia and survival in patients with ICDs: A systematic review and meta-analysis ⁽¹⁷⁾	2024	IJC Heart & Vasculature	52
Diagnosis and management of an inappropriate sinus tachycardia in adolescence based upon a Holter ECG: A retrospective analysis of 479 patients ⁽¹³⁾	2020	PloS one	15
Effect of supplemented intake of omega-3 fatty acids on arrhythmias in patients with ICD: fish oil therapy may reduce ventricular arrhythmia ⁽¹⁸⁾	2017	J Interv Card Electrophysiol	49
Omega-3 index and anti-arrhythmic potential of omega-3 PUFAs ⁽¹⁹⁾	2017	Nutrients	9
Assessment of biological effectiveness of omega-3-fatty supplements using Holter ECG analysis in children ⁽²⁰⁾	2020	Ann Nutr Disord Ther	7
Post-COVID postural orthostatic tachycardia syndrome and inappropriate sinus tachycardia in the pediatric population ⁽²¹⁾	2024	Curr Clin Microbiol Rep	11
Comparative effect of statins and omega-3 supplementation on cardiovascular events: Meta-analysis and network meta-analysis ⁽²²⁾	2020	Nutrients	12

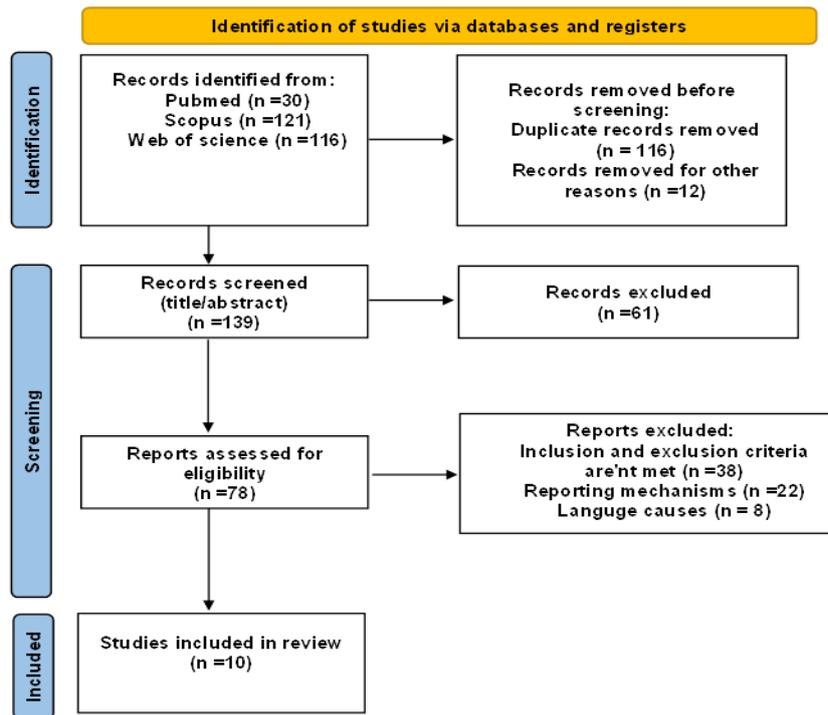


Figure 1: PRISMA Flowchart of the Studies on omega 3 in treatment of inappropriate sinus tachycardia.