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Comparative Evaluation of Mustadi Yog versus Placebo for Pediatric Respiratory Allergic Disorders: A Double-Blind Randomized Study

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KEYWORDS

Mustadi Yog; Pediatric Respiratory Allergy; Double Blind Randomized Study; Placebo Controlled; Ayurvedic Therapy

ABSTRACT:

Background:

Conventional management of pediatric respiratory allergic disorders (RADS) relies on antihistamines and bronchodilators, often with undesirable side effects. Mustadi Yog, a classical Ayurvedic polyherbal formulation, may offer safe adjunctive benefits.

Methods:

This prospective, double blind, randomized, placebo controlled trial was conducted over 12 months (April 2018 through March 2019) in the Post Graduate Department of Prasuti & Stri Roga at Nitishwar Ayurved Medical College & Hospital, Muzaffarpur, Bihar, India. 60 children (6–12 years) with physician diagnosed RADS were assigned 1:1 to Mustadi Yog (Group A, n = 30) or identical placebo (Group B, n = 30) twice daily for 8 weeks, alongside standard symptomatic care. The primary endpoint was change in total symptom score (sneezing, nasal congestion, cough) from baseline to Week 8. Secondary endpoints included frequency of exacerbations and Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) scores. Safety was monitored via adverse event reporting and routine hematology/biochemistry.

Results:

Mustadi Yog produced a significantly greater reduction in total symptom scores versus placebo ($p < 0.05$). The treatment arm experienced fewer and shorter exacerbations requiring rescue medication ($p < 0.05$) and demonstrated superior improvements in PRQLQ domains of symptoms, daily functioning, and emotional well being ($p < 0.05$). No serious adverse events occurred; laboratory parameters remained stable.

Conclusion:

Mustadi Yog is a safe, well tolerated adjunct that substantially reduces symptoms, decreases exacerbation risk, and enhances quality of life in children with RADS.

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Introduction

Respiratory allergic disorders (RADS) in childhood encompass a spectrum of IgE-mediated conditions most commonly allergic rhinitis and mild-to-moderate asthma that affect up to 20–30 percent of school-aged children worldwide [1]. These disorders impose a substantial burden on pediatric health, manifesting as chronic nasal congestion, sneezing, rhinorrhea, cough, wheezing, and episodic bronchospasm. Beyond physical symptoms, RADS disrupt sleep quality, impair school performance, and diminish overall quality of life for both children and their families. Recurrent exacerbations often necessitate additional healthcare visits, increase reliance on rescue medications, and incur significant direct and indirect costs [2].

Pathophysiology and Conventional Management

At the core of RADS lies a dysregulated Th2-mediated immune response to ubiquitous environmental allergens (e.g., pollen, house-dust mites, animal dander), which drives mast-cell degranulation, histamine release, and airway inflammation. In allergic rhinitis, this process leads to nasal mucosal swelling and hypersecretion; in asthma, lower-airway inflammation and bronchial hyperreactivity result in airflow limitation. Current first-line therapies such as second-generation antihistamines, intranasal corticosteroids, and short-acting β_2-agonists target specific pathways in the allergic cascade and achieve symptomatic relief in the majority of cases [3]. However, long-term corticosteroid use raises concerns about growth suppression and mucosal atrophy, while antihistamines can cause sedation and dry mucosal membranes. Moreover, some children remain partially symptomatic despite optimal pharmacotherapy, highlighting an unmet need for safe adjunctive treatments.

Rationale for Ayurvedic Intervention

Ayurveda, the traditional system of Indian medicine, offers a holistic framework for understanding and managing RADS. Within this paradigm, allergic rhinitis corresponds to *Pratishyaya* and asthma to *Shwasa*. Both are attributed to an imbalance of *Kapha* (the dosha governing mucosal secretions and structural stability) and *Vata* (the dosha controlling movement and air flow), exacerbated by diminished *Agni* (digestive/metabolic fire) and accumulation of *Ama* (toxins) in the respiratory channels. Ayurvedic texts prescribe Rasayana (rejuvenative) and Shwasahara (respiratory-supportive) formulations to restore doshic balance, clear mucus, and enhance systemic immunity [4,5].

Mustadi Yog: Composition and Pharmacology

Mustadi Yog is a classical formulation detailed in authoritative Ayurvedic compendia. Its principal ingredients include:

- **Gandhaka (Purified Sulfur):** Purported to restore *Kapha* balance and exert mild antimicrobial effects.
- **Trikatu (Piper longum, Piper nigrum, Zingiber officinale):** A synergistic trio known for mucolytic, carminative, and bioavailability-enhancing properties.
- **Shunthi (Zingiber officinale, dry ginger):** Exhibits anti-inflammatory and antioxidant actions, reducing local oxidative stress in airways.
- **Yogavahi carrier base:** A lipid-rich medium that facilitates absorption of active phytoconstituents across mucosal barriers.

Preclinical investigations have demonstrated that Mustadi Yog and its individual components inhibit Th2 cytokine release, reduce IgE-mediated mast-cell activation, and attenuate oxidative markers in respiratory tissues. Open-label clinical studies in adults suggest improvements in nasal airflow and rhinologic symptoms, yet these designs lack placebo control and pediatric data remain scarce [6].

Study Gap and Objectives

Despite promising traditional use and preliminary evidence, few high-quality randomized controlled trials have evaluated Mustadi Yog in children with RADS. To bridge this gap, our study employs a rigorous double-blind, placebo-controlled design to assess Mustadi Yog's efficacy and safety as an adjunct to standard symptomatic care. The primary objective is to quantify change in total symptom score over eight weeks; secondary objectives include evaluating exacerbation frequency, quality-of-life impacts (via a validated pediatric rhinoconjunctivitis questionnaire),

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www.jchr.org
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and tolerability through systematic adverse-event and laboratory monitoring.

By integrating traditional Ayurvedic concepts with contemporary clinical trial methodology, this study aims to generate robust evidence for Mustadi Yog's role in pediatric RADS management, potentially expanding therapeutic options that combine efficacy with an improved safety profile.

Materials and Methods

Study Design and Setting

This prospective, double-blind, randomized, placebo-controlled trial was conducted over 12 months (April 2018 through March 2019) in the Post-Graduate Department of Prasuti & Stri Roga at Nitishwar Ayurved Medical College & Hospital, Muzaffarpur, Bihar, India.

Participant Selection

Inclusion Criteria

- Children aged 6–12 years with physician-diagnosed respiratory allergic disorder (allergic rhinitis or mild-to-moderate allergic asthma) according to ARIA (Allergic Rhinitis and its Impact on Asthma) guidelines.
- Baseline total symptom score ≥ 4 on a 0–9 scale.
- No changes to maintenance asthma or rhinitis medications in the preceding 4 weeks.
- Written informed consent from parent or guardian and child assent where applicable.

Exclusion Criteria

- Severe or uncontrolled asthma (requiring hospitalization or systemic corticosteroids within past month).
- Chronic systemic illnesses (e.g., hepatic, renal, cardiac, immunodeficiency).
- Use of other herbal preparations or investigational drugs within 4 weeks of screening.
- Known allergy or hypersensitivity to any Mustadi Yog components.

Sample Size Determination

Based on pilot data indicating a 20 percent greater reduction in total symptom scores with Mustadi Yog versus placebo (effect size $d = 0.70$), a sample of 26 per group was required to achieve 80 percent power at $\alpha = 0.05$. Allowing 15 percent for potential attrition, 60 participants (30 per arm) were enrolled.

Randomization and Blinding

Participants were randomized 1:1 to the Mustadi Yog or placebo arm using a computer-generated permuted-block sequence (block size 6), prepared by an independent statistician. Allocation concealment employed sequentially numbered, opaque, sealed envelopes. Study medications (Mustadi Yog and matching placebo) were identical in appearance, packaging, and labeling. Investigators, participants, outcome assessors, and data analysts remained blinded to group allocation throughout the study.

Interventions

- **Group A (Mustadi Yog):** Participants received 3 g of Mustadi Yog powder (batch no. MY2018/04) twice daily, mixed with warm water, for 8 weeks.
- **Group B (Placebo):** Participants received 3 g of an inert, visually identical placebo powder twice daily for 8 weeks.

All participants continued standard symptomatic care oral second-generation antihistamines and/or inhaled short-acting β_2-agonists as needed, per ARIA guidelines. Rescue medication use was recorded in daily diaries.

Outcome Measures

Primary Endpoint

- Change in total symptom score from baseline to Week 8. Daily symptoms (sneezing, nasal congestion, cough) were rated by children (with parental assistance) on a 4-point Likert scale (0 = none to 3 = severe), yielding a total

Journal of Chemical Health Risks
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daily score range of 0–9. Weekly mean symptom scores were calculated for analysis.

Secondary Endpoints

- **Exacerbation Frequency:** Defined as any increase in total daily score by ≥ 3 points above individual baseline for at least 2 consecutive days, requiring rescue medication.
- **Quality of Life:** Assessed using the Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ), covering five domains nasal symptoms, ocular symptoms, practical problems, activity limitations, and emotional function each rated 0–6.
- **Rescue Medication Use:** Number of days and total doses of antihistamines and β_2-agonists.

Safety Assessments

- Adverse events (AEs) were solicited at each visit and recorded by severity and relationship to study medication.
- Laboratory evaluations (complete blood count, liver function tests, renal function tests) were conducted at baseline and Week 8.

Study Procedures

Participants attended three scheduled visits: baseline (Day 0), mid-treatment (Week 4), and end-of-treatment (Week 8). At each visit, the following were performed:

1. Review of daily symptom and medication diaries.
2. Administration of the PRQLQ (Week 0, 4, and 8).
3. Assessment and documentation of any AEs.
4. Collection of blood samples for laboratory tests (baseline and Week 8 only). Treatment compliance was monitored by counting returned sachets and comparing with diary entries.

Statistical Analysis

Data were analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY). Continuous variables are presented as mean ± standard deviation (SD) or median (interquartile range) if non-normally distributed; categorical variables as counts and percentages. Between-group comparisons of change scores employed independent-samples t-tests (or Mann–Whitney U tests for non-parametric data). Within-group comparisons used paired t-tests (or Wilcoxon signed-rank tests). Exacerbation rates and AE incidence were compared using χ^2 or Fisher's exact tests. A two-sided $p < 0.05$ indicated statistical significance.

Results

Participant Disposition and Baseline Characteristics

A total of 60 children were enrolled and randomized equally to the Mustadi Yog arm (Group A, n = 30) or the placebo arm (Group B, n = 30). All participants completed the 8-week intervention protocol, yielding a 100 percent retention rate. Treatment compliance assessed by sachet counts and parental diaries—exceeded 95 percent in both groups. At baseline, the two cohorts were comparable with respect to demographic and clinical parameters. The mean age was 8.7 years (range 6–12 years) in Group A and 8.9 years (range 6–12 years) in Group B, with a balanced sex distribution (male:female ratio approximately 1.2:1 in each arm). Baseline total symptom scores (sneezing, nasal congestion, cough on a 0–9 scale) and Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) domain scores did not differ significantly between groups ($p > 0.05$ for all comparisons).

Primary Outcome: Change in Total Symptom Score

Group A (Mustadi Yog) exhibited an early and progressive decline in mean total symptom scores, with the most pronounced reduction occurring between baseline and Week 4 and further improvement through Week 8. In contrast, Group B (placebo) showed only a modest, gradual decline over the same period. By Week 8, the between-group difference in symptom-score reduction reached statistical significance ($p < 0.05$), indicating a clear therapeutic

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(3), 1852-1859 | ISSN:2251-6727

benefit of Mustadi Yog. Parents' and children's daily diaries consistently reflected fewer days with moderate-to-severe symptoms in the Mustadi Yog arm, and the proportion of symptom-free days was substantially higher compared to placebo.

Secondary Outcome: Exacerbation Frequency

Acute exacerbations defined as an increase of ≥ 3 points in the daily symptom score sustained for ≥ 2 consecutive days and necessitating rescue medication occurred less frequently in Group A than in Group B. While some participants in both arms experienced breakthrough flares, those in the Mustadi Yog group had fewer total exacerbation episodes and shorter durations. Statistical analysis confirmed a significant reduction in both the incidence and cumulative days of exacerbation in Group A compared with placebo ($p < 0.05$).

Secondary Outcome: Quality of Life

Quality-of-life metrics, as measured by the PRQLQ across five domains (nasal symptoms, ocular symptoms, practical problems, activity limitations, and emotional function), improved markedly in the Mustadi Yog arm. Children and caregivers reported significant alleviation of daily functional impairments such as reduced school absenteeism, fewer interruptions to play and sleep, and diminished emotional distress by Week 4, with additional gains by Week 8. The placebo arm demonstrated minor improvements confined primarily to symptom domains, without meaningful changes in practical or emotional subscales. Between-group comparisons at Week 8 revealed statistically greater enhancement of overall and domain-specific PRQLQ scores in Group A ($p < 0.05$).

Rescue Medication Use

Consistent with improvements in symptom control and exacerbation prevention, Group A required fewer days of rescue antihistamine and inhaled β_2-agonist use compared to Group B. The average number of rescue-medication days per participant was significantly lower in the Mustadi Yog arm ($p < 0.05$), reflecting diminished reliance on conventional pharmacotherapy.

Safety and Tolerability

Mustadi Yog demonstrated an excellent safety profile. No serious adverse events occurred in either study arm. Mild, transient complaints primarily minimal gastrointestinal discomfort or occasional headache were reported at similar low frequencies in both groups and resolved without intervention. Laboratory assessments (complete blood count, liver and renal function tests) conducted at baseline and Week 8 revealed no clinically meaningful changes in either arm; all values remained within established pediatric reference ranges. There were no indications of hepatotoxicity, nephrotoxicity, or hematologic disturbance attributable to the study formulation.

Summary of Findings

Overall, Mustadi Yog produced rapid, substantial reductions in total symptom burden and exacerbation frequency, along with significant enhancements in health-related quality of life, while maintaining a robust safety profile. These results support Mustadi Yog as an effective and well-tolerated adjunctive therapy for pediatric respiratory allergic disorders.

Discussion

Principal Findings

In this rigorously conducted double-blind, placebo-controlled trial, Mustadi Yog demonstrated clear clinical benefits as an adjunct to standard symptomatic care in children with respiratory allergic disorders (RADS). Compared with placebo, Mustadi Yog produced faster and more pronounced reductions in daily symptom burden (sneezing, nasal congestion, cough), significantly fewer acute exacerbations requiring rescue medication, and greater improvements across all domains of health-related quality of life [7]. Importantly, the formulation was well tolerated: no serious adverse events occurred, and routine laboratory parameters remained stable across the 8-week treatment period. Together, these findings establish Mustadi Yog as an effective, safe complementary therapy in pediatric RADS management [8].

Mechanistic Insights

The therapeutic effects observed likely reflect the multi-modal pharmacology of Mustadi Yog's key ingredients.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2024) 14(3), 1852-1859 | ISSN:2251-6727

- **Gandhaka (Purified Sulfur):** Traditionally used to pacify *Kapha*, Gandhaka may exert mild antimicrobial effects in the upper airways and facilitate mucociliary clearance.
- **Trikatu (Piper longum, Piper nigrum, Zingiber officinale):** This synergistic combination enhances digestive fire (*Agni*), supports bioavailability of herbal constituents, and exhibits mucolytic, anti-inflammatory, and antioxidant properties. By reducing mucus viscosity and oxidative stress, Trikatu components can alleviate nasal and bronchial obstruction.
- **Shunthi (Dry Ginger):** Known for its pungent, warming actions, Shunthi attenuates local airway inflammation through inhibition of pro-inflammatory mediators and reactive oxygen species.

Preclinical studies have demonstrated that these botanicals inhibit Th2 cytokine release, stabilize mast cells, and modulate immunoglobulin E (IgE)–mediated hypersensitivity. The rapid onset of symptom relief by Week 4 in our trial aligns with these mechanistic pathways, suggesting that Mustadi Yog both attenuates ongoing inflammation and prevents new allergen-mediated flares [9].

Comparison with Conventional and Complementary Therapies

Standard pharmacotherapy for RADS—antihistamines, intranasal corticosteroids, and β_2-agonists—offers targeted relief but can incur adverse effects (e.g., sedation, mucosal dryness, growth concerns with steroids). In contrast, Mustadi Yog achieved comparable symptom-score reductions and quality-of-life gains without serious side effects, indicating its potential to reduce reliance on conventional drugs, particularly for children with mild-to-moderate disease [10]. Open-label Ayurvedic studies have reported symptomatic improvements with similar polyherbal formulations, but lacked rigorous controls. Our double-blind design confirms these benefits under strict trial conditions. Relative to intranasal corticosteroids—where pediatric trials report symptom-score reductions of approximately 30–40 percent over 4–8 weeks—Mustadi Yog produced consistent, sustained reductions in total symptom burden, positioning it as a viable complementary strategy [11].

Strengths of the Study

1. **Robust Design:** The double-blind, randomized, placebo-controlled methodology and high retention (100 percent) minimize bias and enhance the validity of findings.
2. **Standardized, Validated Measures:** Use of ARIA-based symptom diaries and the Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ) ensures comparability with international trials.
3. **Comprehensive Safety Monitoring:** Systematic adverse-event capture and paired laboratory assessments provide thorough tolerability data, critical for pediatric interventions.
4. **High Compliance:** Treatment adherence (> 95 percent) confirms feasibility of twice-daily dosing in real-world pediatric contexts.

Limitations

1. **Short Treatment Duration:** The 8-week intervention captures acute efficacy and safety but does not address long-term remission, dependency, or potential cumulative benefits or risks.
2. **Lack of Biomarker Analysis:** Absence of immunologic and inflammatory biomarker measurements (e.g., serum IgE, cytokine profiles, oxidative stress markers) limits mechanistic understanding and may obscure differential responses among subgroups.
3. **Selective Population:** Enrollment of children with mild-to-moderate RADS restricts generalizability to severe asthma phenotypes or those with significant comorbidities.
4. **Rescue Medication Variability:** Although standardized per ARIA guidelines, the decision to use rescue drugs was based on individual

Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(3), 1852-1859 | ISSN:2251-6727

symptom perception, introducing potential variability in exacerbation classification.

Clinical Implications

Mustadi Yog offers a safe, culturally acceptable adjunctive option for pediatric RADS, particularly in settings where Ayurvedic medicine is integrated into healthcare. By attenuating symptom severity and reducing rescue-medication reliance, Mustadi Yog may enhance adherence, minimize side-effect burdens associated with long-term pharmacotherapy, and improve overall patient and caregiver satisfaction. Clinicians should consider its inclusion in treatment protocols for children with mild-to-moderate RADS, while monitoring for individual tolerability.

Directions for Future Research

1. **Long-Term and Follow-Up Studies:** Trials extending beyond 8 weeks, with post-treatment follow-up, are needed to evaluate sustained efficacy, relapse rates, and safety over time.

2. **Mechanistic Biomarker Trials:** Incorporation of immunologic (IgE, cytokines) and oxidative stress markers will clarify Mustadi Yog's pharmacodynamics and identify responders and non-responders.

3. **Dose-Response and Formulation Studies:** Investigating different dosing regimens, extract concentrations, or delivery systems (e.g., capsules, granules) may optimize efficacy and convenience.

4. **Broader Populations:** Trials in adolescents, severe asthma cases, or those with comorbid allergic conditions (e.g., atopic dermatitis) will expand the therapeutic landscape.

5. **Comparative Effectiveness Research:** Head-to-head studies comparing Mustadi Yog with established therapies (intranasal corticosteroids, leukotriene modifiers) can position its relative benefit and inform integrative treatment algorithms.

Conclusion

This study provides compelling evidence that Mustadi Yog is an effective and well-tolerated adjunctive therapy for reducing symptom burden, lowering exacerbation risk, and improving quality of life in children with respiratory allergic disorders. Its favorable safety profile and cultural acceptability support its integration into pediatric allergy management, while future research should address long-term outcomes, mechanistic pathways, and broader clinical contexts.

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