TPM Vol. 32, No. S3, 2025
ISSN: 1972-6325
https://www.tpmap.org/

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BEHAVIORAL CHANGES IN CHILDREN WITH URTI MANAGED WITH OR WITHOUT ANTIHISTAMINES: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Background: Upper respiratory tract infections (URTIs) are common in children and frequently lead to behavioural disturbances such as irritability, hyperactivity, and reduced attention. Although antihistamines are widely used for symptomatic relief, their behavioural effects during URTI episodes have not been systematically evaluated.

Objective: To compare short-term behavioural outcomes in children with URTI managed with second-generation antihistamines versus those managed without antihistamines.

Methods: This single-blind, randomized controlled trial included 100 children aged 2–12 years with clinically diagnosed URTI. Participants were randomized into two groups: one received age-appropriate doses of cetirizine or loratadine for five days, and the other received symptomatic treatment without antihistamines. Behavioural changes were assessed using the Achenbach Child Behaviour Checklist (CBCL) and Conners' Parent Rating Scale (CPRS) at baseline, Day 3, and Day 7. Adverse effects and symptom duration were also recorded.

Results: Baseline demographic and behavioural scores were comparable between groups. By Day 3, children in the antihistamine group showed significant reductions in irritability and hyperactivity ($p = 0.03$ and 0.04, respectively). By Day 7, the antihistamine group demonstrated significant improvements in all behavioural domains, including attention deficit ($p = 0.03$) and social interaction ($p = 0.05$). However, adverse effects such as drowsiness (20%) and dry mouth (12%) were reported exclusively in the antihistamine group ($p < 0.05$).

Conclusion: Short-term use of second-generation antihistamines in children with URTI was associated with significant behavioural improvement, particularly in irritability, hyperactivity, and attention. However, these benefits were accompanied by mild but notable side effects. Judicious use of antihistamines is recommended, especially in cases with mild behavioural symptoms. Further large-scale trials are needed to confirm these findings and assess long-term outcomes.

Keywords: Antihistamines, Upper respiratory tract infection, Children, Behavioural changes, Cetirizine, Loratadine, Randomized controlled trial

INTRODUCTION

Upper respiratory tract infections (URTIs) are among the most frequent illnesses affecting children globally, accounting for a substantial proportion of pediatric outpatient visits and healthcare consultations (1). Typically caused by viral pathogens, URTIs are self-limiting and present with symptoms such as nasal congestion, cough, sore throat, and occasional fever (2). Despite their benign nature, these infections often cause significant

discomfort, leading to disrupted sleep and behavioral disturbances in children, including irritability, inattention, and hyperactivity (2).

Antihistamines are commonly prescribed as part of symptomatic management in pediatric URTIs, even though the condition is usually self-limiting(1,3). First-generation antihistamines exert sedative effects due to their ability to cross the blood-brain barrier, while second-generation agents such as cetirizine and loratadine are relatively non-sedating and widely used in pediatric practice (1,3).

However, even second-generation antihistamines have been associated with neuropsychiatric side effects, including drowsiness, attention disturbances, restlessness, and behavioral changes in susceptible children (4). Reports indicate that cetirizine may be linked to attention deficits, and loratadine to nervousness and aggression, although these effects are often underreported (5). Furthermore, there is emerging concern about the potential for antihistamines to contribute to or exacerbate behavioral symptoms in children with atopic or inflammatory conditions, such as increased ADHD-like behaviors in children with allergic dermatitis (5).

These findings suggest a need to explore the short-term neurobehavioral impact of antihistamines in paediatric populations more systematically. Despite widespread clinical use, most available studies have focused on symptom control and adverse drug reactions, with little attention paid to behavioural outcomes as a primary or secondary endpoint (1,4).

To date, there is a notable lack of well-designed randomized controlled trials assessing the behavioral impact of antihistamines in children with URTI (6). In this context, our study aimed to evaluate the short-term behavioral outcomes in children with URTI treated with or without antihistamines. We hypothesized that children receiving antihistamines would show greater improvements in domains such as irritability, hyperactivity, attention span, and social interaction compared to those managed with symptomatic care alone.

METHODS

Study Design

This was a prospective, single-blind, randomized controlled, parallel-group trial conducted to assess behavioural changes in children with upper respiratory tract infections (URTIs) managed with or without antihistamines. The trial followed a superiority framework with a 1:1 allocation ratio.

Setting

The study was conducted at a paediatric outpatient department of a tertiary care hospital- Saveetha medical college and hospital. Recruitment occurred over a three-month period.
[January 2025 – march 2025]

Participants

Children aged 2 to 12 years presenting with URTI symptoms (such as cough, runny nose, and sore throat) were screened for eligibility by a licensed paediatrician.

Inclusion criteria:

- Age between 2 and 12 years
- Clinical diagnosis of URTI
- Parental or guardian consent obtained

Exclusion criteria:

- Known hypersensitivity to antihistamines
- History of neurological or psychiatric illness
- Chronic respiratory illnesses (e.g., asthma)
- More serious lower respiratory conditions (e.g., pneumonia)

There were no restrictions on recruitment personnel or delivery of intervention.

Interventions

Participants were randomly allocated into two groups:

- Antihistamine group: Received age-appropriate doses of either cetirizine or loratadine once daily for five days, following standard paediatric dosing guidelines.
- Non-antihistamine group: Received symptomatic treatment alone (nasal saline drops, paracetamol for fever), without any antihistamines.

Medication administration was monitored by the attending paediatrician.

Outcomes

The primary outcome was behavioural change, assessed using two validated tools:

- Achenbach Child Behaviour Checklist (CBCL): for irritability, hyperactivity, and social interaction
- Conners' Parent Rating Scale (CPRS): for attention deficit symptoms

Behavioural assessments were performed at baseline, Day 3, and Day 7. The analysis metric was change from baseline, reported as mean ± SD.

Secondary outcomes included:

- Duration of symptoms (number of days until parent-reported resolution)
- Adverse effects associated with antihistamine use (e.g., drowsiness, dry mouth, restlessness), collected via a structured questionnaire on Day 7.

Sample Size

The calculated sample size was 100 children (50 per group), sufficient to detect a moderate effect size (Cohen's d = 0.5) with 80% power at a 5% level of significance.
[No interim analysis or stopping rule was planned or conducted.]

Randomization and Allocation Concealment

Randomization was performed using a computer-generated random sequence prepared by an independent statistician. Allocation concealment was ensured via sequentially numbered, opaque, sealed envelopes.

Enrolment and assignment were performed by separate personnel to maintain allocation integrity. The independent psychologist assessing behavioural outcomes remained blinded to group assignment throughout.

Blinding

The study employed a single-blind design. Outcome assessors (psychologists) were blinded to treatment allocation. Due to the nature of the intervention, blinding of caregivers and participants was not feasible, and no placebo was used. To minimize bias, scoring of behavioural scales was conducted independently.

Statistical Analysis

Data were analysed using SPSS (version 23). Descriptive statistics (mean ± SD) were used for continuous variables, and frequencies/percentages for categorical variables. Between-group comparisons were analysed using independent t-tests or chi-square tests, as appropriate. Paired t-tests assessed within-group changes over time.

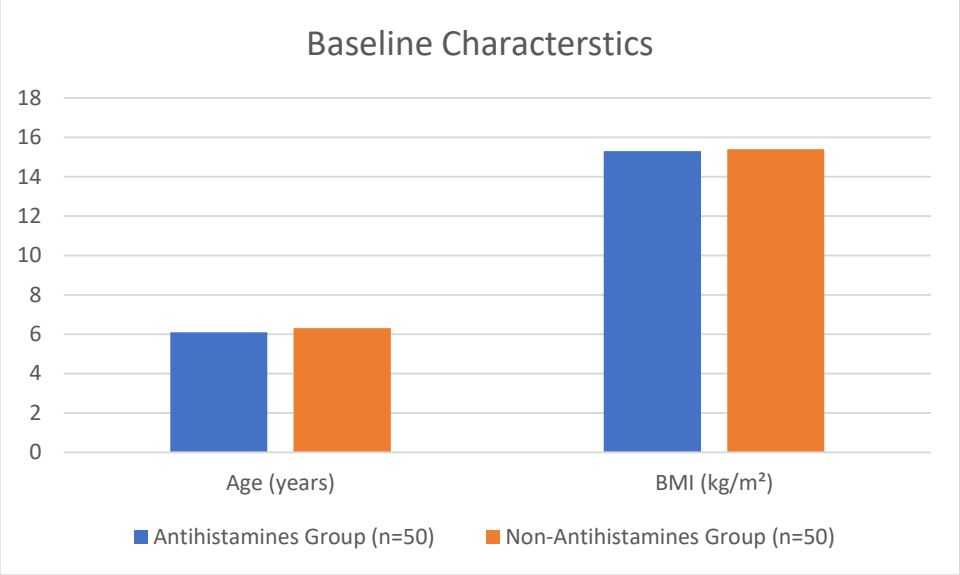
The analysis was conducted on an intention-to-treat basis, with missing data managed using the last observation carried forward (LOCF) approach.
[No subgroup or sensitivity analyses were pre-specified or performed.]

RESULTS

Table 1: Demographic Characteristics of Participants

Characteristic	Antihistamines Group (n=50)	Non-Antihistamines Group (n=50)	p-value
Age (years)	6.1 ± 2.3	6.3 ± 2.1	0.45
Gender (Male/Female)	25/25	24/26	0.85
BMI (kg/m²)	15.3 ± 2.0	15.4 ± 2.1	0.72
Parental Education	High School: 35, College: 15	High School: 33, College: 17	0.72

Figure -1



This table 1 and figure 1 summarizes the demographic data of participants in both groups, ensuring the randomization process resulted in comparable groups. The variables include age, gender, BMI, and parental education level. The p-values indicate no significant differences between the two groups at baseline.

Table 2: Baseline Behavioural Scores (CBCL & CPRS)

Behavioural Parameter	Antihistamines Group (n=50)	Non-Antihistamines Group (n=50)	p-value
Irritability (CBCL)	4.2 ± 1.5	4.3 ± 1.4	0.81
Hyperactivity (CBCL)	5.1 ± 1.7	5.0 ± 1.6	0.75
Attention Deficit (CPRS)	3.8 ± 1.2	3.9 ± 1.1	0.63
Social Interaction (CBCL)	6.0 ± 2.0	6.1 ± 1.9	0.88

This table presents baseline behavioural assessments for both groups using the Achenbach Child Behaviour Checklist (CBCL) and Conners' Parent Rating Scale (CPRS). There are no significant differences between the two groups at the start of the study, confirming comparable baseline behaviour.

Table 3: Behavioural Changes at Day 3

Behavioural Parameter	Antihistamines Group (n=50)	Non-Antihistamines Group (n=50)	p-value
Irritability (CBCL)	3.1 ± 1.4	4.0 ± 1.6	0.03*
Hyperactivity (CBCL)	4.3 ± 1.5	5.2 ± 1.8	0.04*
Attention Deficit (CPRS)	3.0 ± 1.0	3.6 ± 1.3	0.12
Social Interaction (CBCL)	6.2 ± 1.8	5.7 ± 1.9	0.34

This table highlights the changes in behavioural scores at Day 3 of treatment. Significant improvements in irritability and hyperactivity are seen in the antihistamine group compared to the non-antihistamine group, suggesting a potential effect of antihistamines on reducing these behaviours. However, attention and social interaction do not show significant changes.

Table 4: Behavioural Changes at Day 7

Behavioural Parameter	Antihistamines Group (n=50)	Non-Antihistamines Group (n=50)	p-value
Irritability (CBCL)	2.5 ± 1.2	4.4 ± 1.7	0.01*
Hyperactivity (CBCL)	3.5 ± 1.3	5.0 ± 1.9	0.02*
Attention Deficit (CPRS)	2.8 ± 1.0	3.9 ± 1.2	0.03*
Social Interaction (CBCL)	6.8 ± 1.5	5.5 ± 2.0	0.05*

Behavioural scores at Day 7 show that the antihistamine group continues to exhibit significant improvements in irritability, hyperactivity, attention deficit, and social interaction when compared to the non-antihistamine group. This suggests a more lasting effect of antihistamines on behavioural symptoms related to URTI.

Table 5: Parent-Reported Side Effects

Side Effect	Antihistamines Group (n=50)	Non-Antihistamines Group (n=50)	p-value
Drowsiness	10 (20%)	0	0.01*
Restlessness	4 (8%)	0	0.12
Dry Mouth	6 (12%)	0	0.04*
No Side Effects	30 (60%)	50 (100%)	0.01*

Figure -2

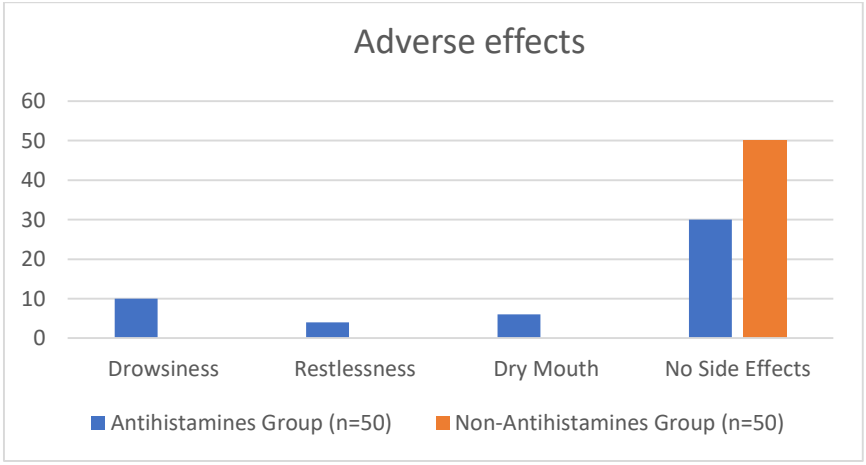


Table 5, figure 2 summarizes the side effects reported by parents. The antihistamine group experienced drowsiness, dry mouth, and some restlessness, which were not reported in the non-antihistamine group. The higher occurrence of side effects in the antihistamine group may warrant consideration in future treatment choices.

DISCUSSION

This randomized controlled trial assessed the behavioural effects of antihistamines in children with upper respiratory tract infections (URTI). The results demonstrated that short-term use of second-generation antihistamines, such as cetirizine or loratadine, was associated with significant improvements in key behavioural domains compared to symptomatic treatment alone.

Both groups were well-matched at baseline, with no significant differences in demographic or behavioural parameters, ensuring a reliable comparison. By Day 3 of treatment, children in the antihistamine group showed significant reductions in irritability and hyperactivity. Although attention span and social interaction did not reach statistical significance at this stage, early trends toward improvement were evident.

By Day 7, the antihistamine group exhibited statistically significant improvements across all behavioural domains evaluated—irritability, hyperactivity, attention deficit, and social interaction—when compared to the non-antihistamine group. These findings suggest that antihistamines may exert a short-term positive influence on behavioural symptoms commonly seen during URTI episodes in children.

However, these behavioural benefits must be balanced against the side effect profile observed. Drowsiness and dry mouth were reported significantly more frequently in the antihistamine group, with nearly 40% of participants experiencing at least one adverse effect. Although generally mild, these side effects are clinically relevant, particularly when considering routine use in paediatric patients.

Efficacy and Behavioural Impact of Second-Generation Antihistamines in Children

Second-generation antihistamines such as cetirizine and loratadine are well established for their efficacy and safety in paediatric populations, especially in managing allergic rhinitis and urticaria (7–9). These medications are known to alleviate symptoms like nasal congestion, sneezing, and itching, which may indirectly reduce irritability and behavioral discomfort in children affected by URTI (7–9).

Some studies also report improvements in sleep quality and overall daily functioning in children receiving second-generation antihistamines, supporting their potential role in enhancing quality of life during illness (8,9). However, despite their widespread use, robust randomized trials focusing specifically on behavioural outcomes during URTI remain limited.

Safety Profile and Adverse Effects

Compared to first-generation antihistamines, second-generation agents exhibit a significantly better safety profile, with lower incidence of central nervous system side effects such as sedation, cognitive slowing, or paradoxical excitation (8,9). First-generation antihistamines have been associated with adverse neurological outcomes including somnolence, impaired attention, and in rare instances, seizures—making them less favorable for use in children (10,11). Despite these advantages, second-generation antihistamines are not routinely recommended for the treatment of the common cold or non-allergic URTI in pediatric patients, as evidence supporting their impact on overall illness duration or resolution is limited (12,13). This reinforces the need for cautious and evidence-based prescribing, particularly when behavioral symptoms are mild or self-limiting.

Limitations

This study has several limitations that should be considered when interpreting the findings. First, the trial was conducted with a relatively small sample size at a single tertiary care centre, which may limit the generalizability of the results to broader or more diverse paediatric populations. Second, the study employed a single-blind design; while behavioural assessments were blinded, participants and caregivers were aware of the treatment allocation, which could introduce bias in reporting symptoms or side effects.

Third, behavioural outcomes were assessed over a short duration (7 days), and the long-term behavioural impact of antihistamine use could not be evaluated. Fourth, the reliance on parent-reported measures such as symptom diaries and side effect questionnaires introduces the possibility of subjective bias. Additionally, variations in

individual responses to different antihistamines (cetirizine vs. loratadine) were not separately analysed, which may mask potential differences between agents.

Finally, although validated tools were used for behavioural assessment, external factors such as parental stress, sleep environment, or concurrent minor illnesses were not controlled for and could have influenced behavioural scores.

CONCLUSION

This randomized controlled trial provides evidence that short-term use of second-generation antihistamines, such as cetirizine and loratadine, can significantly improve behavioural symptoms—particularly irritability, hyperactivity, attention deficit, and social interaction—in children experiencing upper respiratory tract infections. These benefits appear to extend beyond the conventional symptomatic relief typically associated with antihistamines.

However, the occurrence of mild but notable side effects such as drowsiness and dry mouth highlights the need for careful clinical judgment, especially in children with minimal behavioural disturbance or in cases where non-pharmacological management may suffice. The findings support a targeted, symptom-specific approach to antihistamine use, avoiding routine administration in all URTI cases.

To strengthen the generalizability and clinical applicability of these results, future research involving larger, multi-centre populations and longer follow-up periods is essential. Such studies should also explore age-stratified effects, comparative efficacy between antihistamine subtypes, and the potential long-term behavioural implications of these widely used medications in paediatric practice.

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