Journal of Paediatrics and Child Health

Journal of Paediatrics and Child Health | RACP Specialists. Together

ORIGINAL ARTICLE OPEN ACCESS

Potentially Overlooked Risk for Neuropsychiatric Symptoms in Children: Montelukast Treatment

Seda Tunca[1] | Ozge Yilmaz[1] | Merve Ocalan[1] | Mustafa Arga[2] | Ozlem Cavkaytar[2] | Deniz Ozceker[3] | Mehmet Kiliç[4] | Fatma Duksal[5] | Demet Can[6] | Ozlem Sancakli[6] | Mehmet Şirin Kaya[6] | Nazli Ercan[7] | Nursen Cigerci Gunaydin[8] | Metin Aydogan[9] | Esen Demir[10] | Recep Sancak[11] | Sefika İlknur Kökcü Karadag[11] | Nihat Sapan[12] | Ahmet Ugur Demir[13] | Oznur Bilac[14] | Emine Dibek Misirlioglu[15] | Ahmet Turkeli[16] | Hasibe Artac[17] | Hatice Eke Gungor[18] | Haluk Cokugras[19] | Fazil Orhan[20] | Aysen Bingol[21] | Pinar Uysal[22] | Sennur Keles[23] | Aylin Kont Ozhan[24] | Tuba Tuncel[25] | Ozlem Keskin[26] | Elif Arik[26] | Öner Özdemir[27] | Ceren Can[28] | Nazan Altinel[28] | Koray Harmanci[29] | Yurda Simsek[30] | Derya Ufuk Altintas[31] | Serap Ozmen[32] | Nevin Uzuner[33] | Yakup Canıtez[12] | Hasan Yüksel[1]

Correspondence: Hasan Yüksel (hyukselefe@hotmail.com; hasan.yuksel@cbu.edu.tr)

Received: 6 February 2025 | **Revised:** 4 May 2025 | **Accepted:** 13 May 2025

Funding: The authors received no specific funding for this work.

Keywords: allergy | antihistamine | asthma | montelukast treatment | neuropsychiatric symptoms

ABSTRACT

Background: Montelukast is a leukotriene receptor antagonist commonly used in allergic diseases. In this study, we investigated the frequency, severity and risk factors for neuropsychiatric side effects and sleep disorders associated with montelukast in children.

Method: Children aged 6 months to 17 years prescribed montelukast for allergic rhinitis or asthma at 31 Paediatric Allergy and Immunology centres were enrolled in this cohort study. At enrollment, sociodemographic characteristics, prior diagnoses of neuropsychiatric diseases or sleep disorders, and indications for montelukast treatment were recorded, and the primary caregivers completed a baseline questionnaire about neuropsychiatric symptoms (insomnia, nightmares and depressed mood) of their children. All participants were followed up for 1 month, and a post-treatment follow-up questionnaire on neuropsychiatric symptoms was completed at the end of this period. Moreover, caregivers were instructed to contact the clinic if neuropsychiatric side effects or sleep disorders were observed during this period.

Results: Total of 1163 children were enrolled. There was a significant increase in the frequency of insomnia, nightmares, night terrors, drowsiness, behavioural problems, irritability, depressive mood, agitation, anxiety, hyperactivity, learning difficulties and headache during the 1 month period after montelukast treatment compared to the previous 1 month ($p < 0.001$ for all). Overall, caregiver reports of neuropsychiatric symptoms in children increased from 172 (14.8%) to 399 (34.3%) after 1 month of montelukast treatment ($p < 0.001$).

Conclusions: Montelukast treatment increases the risk of neuropsychiatric symptoms and sleep disorders in children with allergic diseases, especially if there is concomitant use of antihistamines.

1 | Introduction

Montelukast is a leukotriene receptor antagonist that binds with high affinity to the Cysteinyl leukotrienes (CysLT) type 1 receptor, which mediates bronchoconstrictor effects of CysLT, including LTB4, LTC4 and LTE4 [1, 2]. The major indications for prescription started as asthma and allergic rhinitis but have been expanded to include other diagnoses such as urticaria and

For affiliations refer to page 1293.

obstructive sleep apnea [2–4]. Although it was thought to be relatively safe during the first years in the market, now there are various reports regarding possible neuropsychiatric side effects associated with montelukast [5–8]. Research on adults reported that there was a significant increase in anxiety and insomnia in cases with asthma and allergic rhinitis [7]. Recent propensity score matched cohort study on electronic data of children on inhaled steroids reported that concomitant montelukast use was associated with increased anxiety, sleep and mood disorders [8]. Moreover, age has been reported to be an important risk factor for the development of neuropsychiatric side effects of montelukast treatment [9].

Considering the potential confounders on the development of sleep and neuropsychiatric symptoms, the risk associated with montelukast use may vary in different populations depending on socioeconomic status, indication and concomitant medications. Therefore, extrapolating the results of previous research from different settings and populations may lead to false clinical decisions on prescribing or de-prescribing montelukast.

The aim of this study was to evaluate the frequency and risk factors for the development of neuropsychiatric symptoms and sleep disorders in Turkish children with asthma or allergic rhinitis, which are the two most common indications for prescription in children.

2 | Materials and Methods

2.1 | Study Design and Ethics

This prospective observational cohort study evaluated the frequencies of neuropsychiatric symptoms and sleep disorders in children treated with montelukast. This study was approved by the Institutional Review Board (26.01.2021/674752) and the Medicines and Medical Devices Agency Review Board of Türkiye (21-AKD-10). Written informed consent was obtained from the caregivers of all the children.

2.2 | Study Population and Sampling

Patients aged 6 months to 17 years prescribed montelukast treatment for allergic rhinitis and/or asthma in 31 paediatric allergy and immunology centres across Türkiye were enrolled in this study. Inclusion criteria were as follows: prescription of montelukast treatment following a diagnosis of allergic rhinitis and asthma, not having used montelukast in the previous month. Exclusion criteria were: current diagnosis of and treatment for neuropsychiatric diseases such as schizophrenia, depression, epilepsy, mental retardation, mood disorder and attention deficit hyperactivity disorder by a psychiatrist; and chronic use of drugs associated with neuropsychiatric side effects and sleep disturbances such as antidepressants and psychostimulants.

2.3 | Data Collection

After enrollment of the subjects prescribed montelukast, sociodemographic characteristics of the patients, such as age, sex and birth history as well as past history of doctor-diagnosed neuropsychiatric diseases, sleep disorders, or family history of doctor-diagnosed neuropsychiatric diseases were recorded. Medications used in combination with montelukast were also recorded, as were the indications for and doses of montelukast. In addition, caregivers' responses to the neuropsychiatric symptoms in their children, such as insomnia, nightmares, depressed mood, night terrors, drowsiness, irritability, agitation, anxiety, hyperactivity, learning difficulties and headaches were also recorded by the researcher after the decision to prescribe montelukast to avoid selection bias. The caregivers were instructed to contact the researchers if their child showed any of the neuropsychiatric or sleep disturbance symptoms during the 1 month follow-up period. If none of these symptoms were observed, a follow-up visit was scheduled at the end of 1 month when the caregivers were questioned about noticing any neuropsychiatric symptoms, such as insomnia, nightmares, depressive mood, night terrors, drowsiness, irritability, agitation, anxiety, hyperactivity, learning difficulties and headaches in their children. Caregivers were also asked to rate the severity of these symptoms on a Likert scale ranging from 1 to 10, where 1 represented the least severe.

2.4 | Statistical Analysis

SPSS—25 version (The Statistical Package for Social Sciences) was used for all statistical analyses. Continuous variables such as age and time of adverse events are shown as the mean ± standard deviation, whilst categorical variables such as gender, diagnosis, family history, side effects and other medications used are given as percentages and numbers.

Logistic regression analysis was used to adjust for multiple variables that may have influenced the relationship between montelukast use and neuropsychiatric symptoms. The model included past neuropsychiatric symptoms or sleep disorders, age, sex, duration of illness, family history of doctor-diagnosed neuropsychiatric diseases, caregiver's educational level and other medications used by the participants that might influence the occurrence of neuropsychiatric symptoms as variables. The OR's and 95% CI's of the model findings were calculated as the relative risk estimates. $p < 0.05$ was considered statistically significant.

3 | Results

3.1 | Sociodemographic and Disease Characteristics

A total of 1542 patients were enrolled between June 2021 and June 2022. Amongst these, 379 patients were excluded because they did not complete the post-treatment follow-up questionnaire, were duplicate enrollments, or had missing data. The data of 1163 cases who met all the inclusion criteria and who completed the follow-up were included in the study (Figure 1).

The mean age of the patients included in the study was 91 ± 45 months. When the indications for montelukast were analysed, 39% of the patients had allergic rhinitis, 33% had asthma,

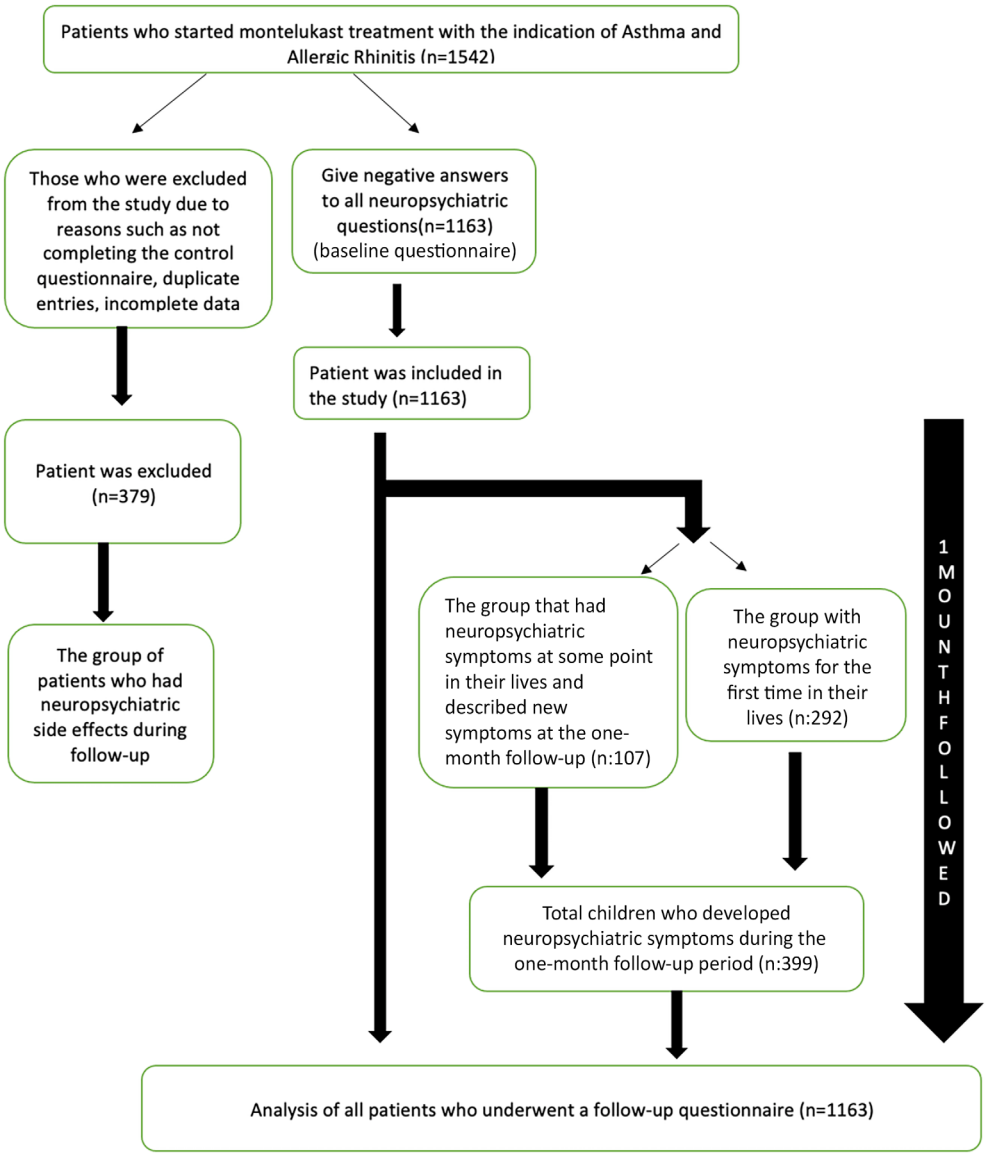


FIGURE 1 | A total of 1542 patients included in the study. Of these, 379 patients were excluded because they did not complete the follow-up questionnaire, were duplicate enrollments, or had missing data. The data of 1163 cases who met all the inclusion criteria and who completed the follow-up were included in the study. The 399 children developed neuropsychiatric symptoms but completed the follow-up questionnaire at the end of one-month follow-up.

and the rest had both diseases. The mean allergic disease duration was 27 ± 25 months.

A family history of neuropsychiatric disease was diagnosed by a physician in 4% of cases. The medications used during the month prior to enrollment were inhaled steroids (45%), inhaled salbutamol (36%) and antihistamines (36%) (Table 1).

3.2 | Neuropsychiatric Symptoms and Sleep Disorders at Enrollment and Follow Up

A previous history of doctor-diagnosed neuropsychiatric disease was observed in 2.1% patients however none of the participants had a current doctor-diagnosis that required treatment. "Neuropsychiatric symptom questionnaire" filled in by the caregiver at enrollment revealed that symptoms such as insomnia (3.4%), nightmares (2.3%), night terrors (1.6%), lethargy (2.2%), behavioural problems (3.2%), irritability (4.9%), depressive mood (2.7%), agitation (2.5%), anxiety (3.2%), hyperactivity (2.3%), learning disabilities (1.5%) and headache (2.2%) were present in study participants.

At the one-month follow-up, insomnia (12.1%), nightmares (14.2%), night terrors (10.8%), lethargy (10.6%), behavioural problems (12.1%), irritability (16.6%), depressive mood (9.3%), agitation (13.2%), anxiety (11.1%), hyperactivity (10.6%), learning disabilities (7.1%) and headache (8.9%) symptoms had increased significantly ($p < 0.001$) (Table 2).

Frequency of children with a neuropsychiatric symptom increased from 172 (14.8%) to 399 (34.3%) during the 1 month

period of montelukast use ($p < 0.001$). Table 3 shows the age distribution of the patients who experienced neuropsychiatric side effects and sleep disorders. Insomnia, drowsiness, depressive symptoms, anxiety, learning difficulties and headache were associated with older age, with a mean age of approximately 100–110 months (Table 3).

TABLE 1 | Demographics and patient characteristics of the study population.

Sociodemographic and clinical characteristic	
Age, mo[a]	91.4 (45.0)
Duration of allergic disease, mo[a]	27.5 (25.0)
Caregiver's education[b]	
<High school	364 (3.13)
High school	424 (36.5)
University	375 (32.2)
Family history of doctor-diagnosed neuropsychiatric disease[b]	45 (3.9)
Antihistaminic drug use[b]	
At baseline	423 (32.2)
At the post-treatment follow up visit	135 (11.6)
Adverse event[b]	
No	764 (65.7)
1	88 (7.6)
≥2	311 (26.7)

[a]Summarised as mean (standard deviation).
[b]Summarised as *n* (%).

Univariate analysis revealed that a previous history of neuropsychiatric illness in the child increased the frequency of all neuropsychiatric disorders during follow up. Moreover, family history of neuropsychiatric disorders was associated with an increased frequency of nightmares (20.1%), night terrors (11.1%), behavioural problems (15.6%), irritability (31.1%), agitation (20%), anxiety (20%) and hyperactivity (15.6%) following montelukast use.

3.3 | Multivariable Analysis of Association of Neuropsychiatric Symptoms With Montelukast Use

Multivariate logistic regression analysis with the model including age, duration of illness, previous history of neuropsychiatric illness in the child and caregiver, caregiver's educational status, and use of antihistamines at enrollment and during the study period revealed that montelukast use significantly increased the risk of neuropsychiatric symptoms (Table 4).

Amongst children who reported neuropsychiatric symptoms or sleep disorders in the past, headache and somnolence risk with montelukast use increased 9.2-fold and 8.2-fold, respectively. This was followed by nightmares, learning disabilities and behavioural symptoms, with adjusted risk ratios of 6.3 (95% CI, 2.8–13.5), 5.6 (95% CI, 1.7–16.0) and 5.3 (95% CI, 2.6–10.6), respectively (Figure 2A).

Antihistamine use at admission was independently associated with an increase in many neuropsychiatric side effects caused by montelukast treatment, including lethargy (OR = 1.6) (95% CI, 1.1–2.4), behavioural problems (OR = 1.5) (95% CI, 1.0–2.2), hyperactivity (OR = 1.5) (95% CI, 1.0–2.3), learning disability (OR = 1.7) (95% CI, 1.0–2.7) and headache (OR = 1.5) (95% CI, 1.1–2.6) (Figure 2B).

TABLE 2 | Frequency of neuropsychiatric symptoms reported before and after montelukast use in the study population.

	At baseline[a]	At follow up[a]	OR (95% CI)[b]	*p*[c]
Insomnia	40 (3.4)	141 (12.1)	3.9 (2.7–5.6)	<0.001
Nightmares	27 (2.3)	165 (14.2)	6.9 (4.6–10.5)	<0.001
Night terrors	19 (1.6)	126 (10.8)	7.3 (4.5–11.9)	<0.001
Drowsiness	26 (2.2)	123 (10.6)	5.2 (3.4–7.9)	<0.001
Behavioural problems	37 (3.2)	141 (12.1)	4.2 (2.9–6.1)	<0.001
Irritability	57 (4.9)	193 (16.6)	3.9 (2.8–5.3)	<0.001
Depressive mood	31 (2.7)	108 (9.3)	3.7 (2.5–5.6)	<0.001
Agitation	29 (2.5)	53 (13.2)	5.9 (3.9–8.9)	<0.001
Anxiety	37 (3.2)	129 (11.1)	3.8 (2.6–5.5)	<0.001
Hyperactivity	27 (2.3)	123 (10.6)	4.9 (3.3–7.6)	<0.001
Learning difficulties	18 (1.5)	83 (7.1)	4.9 (2.9–8.2)	<0.001
Headache	26 (2.2)	104 (8.9)	4.3 (2.8–6.69)	<0.001

[a]Reported as *n* (%).
[b]Odds ratio (95% confidence interval).
[c]Chi square test.

TABLE 3 | Age distribution of neuropsychiatric side effects and sleep disorders in the study cohort.

	Present[a]	Absent[b]	*p*[c]
Insomnia	**100.9 ± 47.0**	**90.1 ± 44.6**	**0.007**
Nightmares	89.3 ± 43.3	91.7 ± 45.3	0.27
Night terrors	85.6 ± 42.6	92.1 ± 45.3	0.15
Drowsiness	**103.2 ± 50.7**	**90.0 ± 44.2**	**0.006**
Behavioural problems	91.6 ± 42.8	91.4 ± 45.4	0.95
Irritability	93.5 ± 45.4	94.0 ± 45.0	0.48
Depression	**110.9 ± 49.8**	**89.4 ± 44.1**	**< 0.001**
Agitation	95.7 ± 42.7	90.7 ± 45.4	0.20
Anxiety	**104.9 ± 48.8**	**89.7 ± 44.3**	**< 0.001**
Hyperactivity	91.9 ± 43.8	91.3 ± 45.2	0.88
Learning difficulties	**105.7 ± 44.3**	**90.3 ± 44.9**	**0.003**
Headache	**110.1 ± 51.0**	**89.5 ± 44.0**	**< 0.001**

[a]Age mean ± standard deviation of participants with the symptoms (months).
[b]Age mean ± standard deviation of participants without the symptoms (months).
[c]Independent sample's *t* test.

TABLE 4 | Model findings for adverse event frequency at the follow-up visit.

	1 Adverse event OR (95% CI)	≥ 2 Adverse event OR (95% CI)
Age, mo[a]	0.9 (0.5–1.4)	1.0 (0.8–1.3)
Duration of allergic disease[a]	0.9 (0.7–1.1)	1.0 (0.8–1.1)
Caregiver's education		
<High school	1.1 (0.6–1.8)	1.2 (0.8–1.7)
High school	0.7 (0.4–1.2)	**1.4 (1.0–2.0)**
University	1	
Doctor-diagnosed neuropsychiatric disease in the family	1.5 (0.5–4.5)	**1.9 (1.0–3.7)**
Antihistaminic drug use at the baseline	1.0 (0.6–1.6)	**1.3 (1.0–1.7)**

Note: Model adjusted for age, allergic disease duration, caregiver's education status, neuropsychiatric symptoms in the family, and antihistamine drug use at baseline.
[a]Logarithmic transformations of age and allergic disease duration were performed.

4 | Discussion

The significant role of cysteinyl leukotrienes in the pathophysiology of allergic rhinitis and asthma has led to the widespread use of montelukast in the treatment of children with these diseases. The results of this study showed a marked increase in neuropsychiatric symptoms and sleep disturbances with montelukast treatment. The risk of these side effects is higher in children using concomitant antihistamines and in the ones with neuropsychiatric symptoms or sleep disorders in the past.

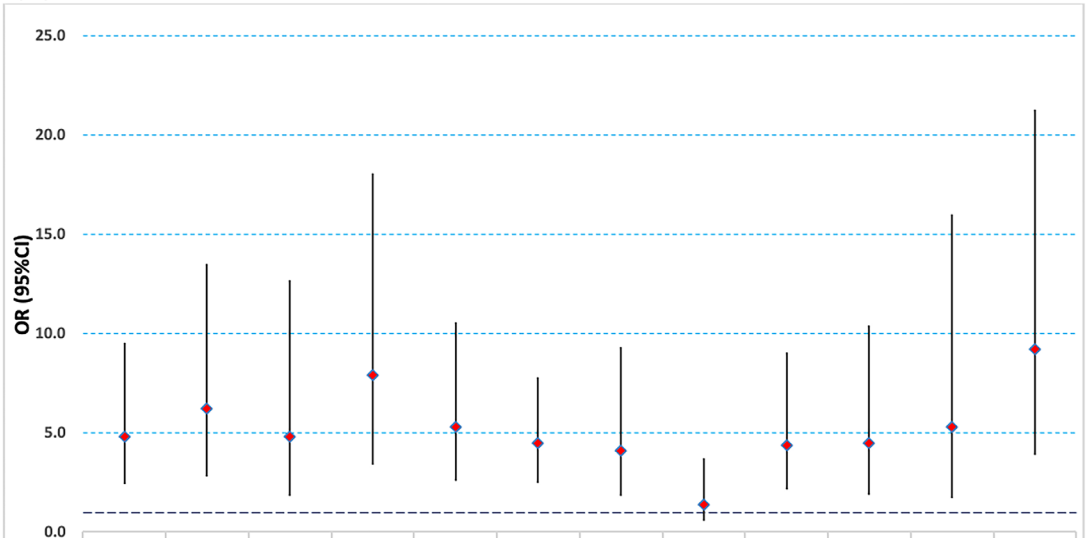
Montelukast acts by inhibiting the cysteinyl leukotriene receptor-1 expressed by inflammatory smooth muscle cells and endothelial cells in both the upper and lower respiratory tract mucosa [10, 11]. Unfortunately, montelukast is associated with a wide range of adverse drug reactions in children, including neuropsychiatric and gastrointestinal issues; however, these effects can be detected early with the awareness of clinicians [12, 13]. We therefore conducted this multicenter cohort study to evaluate the neuropsychiatric side effects and sleep disorders caused by the use of this popular medication for asthma and allergic rhinitis in Turkish children. Our data showed striking results in line with current warnings.

Overall, our results showed an increase of 2.3 folds in the risk of neuropsychiatric symptoms with montelukast use. In one retrospective cohort study of 106 subjects, Benard et al. showed that the rate of discontinuation of montelukast treatment due to neuropsychiatric side effects was 16% [11]. In another study, Wallerstedt et al. reported that 48 children reported anxiety, nervousness, hyperactivity, sleep disturbances and personality disorders as side effects in the side effect registry of 17945 children between 1998 and 2007 [14]. Furthermore, in a cohort study of 77473 adult patients using montelukast, a statistically significant increase in generalised anxiety disorder, insomnia and antidepressant prescriptions was observed in montelukast users compared to non-users [7]. In our study, nightmares, night terrors and irritability were the most common side effects, which increased in frequency with treatment.

Studies have shown that the concomitant use of montelukast with Inhaled Corticosteroids/Long-Acting Beta2-Agonists (ICS/LABA) is associated with an increased incidence of neuropsychiatric side effects. This has been indicated to occur as a synergistic effect, as no neuropsychiatric side effects were observed with ICS/LABA alone [15]. In our study, a similar synergistic effect was observed with pre-existing antihistamine use during enrollment, which caused an increase in side effects such as drowsiness, behavioural problems, hyperactivity, learning difficulties and headaches associated with montelukast use. Moreover, our results indicated that a previous history of neuropsychiatric symptoms at any time point before montelukast treatment increased the risk of these symptoms during treatment.

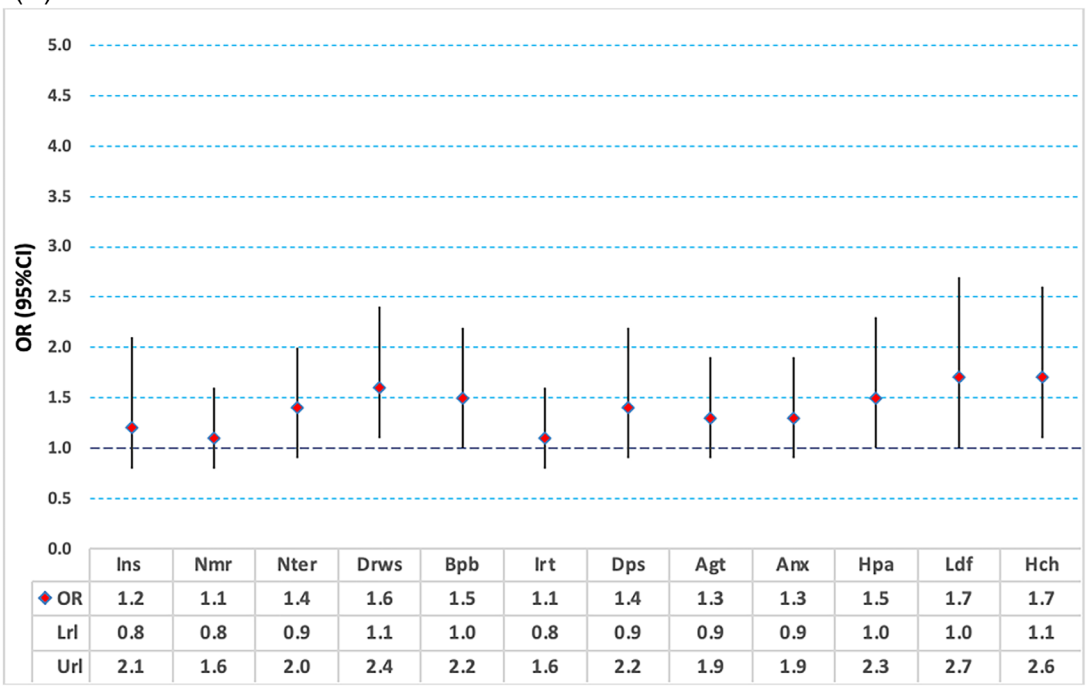
Using retrospective data from the Netherlands, the World Health Organisation reported that more than 75% of paediatric patients receiving montelukast treatment experienced nightmares within the first week [16]. Similar studies for children and adults in the US, Canada and Europe have similarly reported neuropsychiatric side effects associated with montelukast [14, 17–19] In our multicenter cohort study, it was found that the incidence of any neuropsychiatric side effects increased approximately 3-fold in the first month of montelukast treatment, in line with the literature. In contrast, in a prospective study conducted in adults in Denmark, the reasons for early discontinuation of montelukast use were investigated during a 19-year follow-up, with results showing that montelukast could be used for a longer period

(A)



	Ins	Nmr	Nter	Drws	Bpb	Irt,	Dps	Agt	Anx	Exa	Ldf	Hch
OR	4.8	6.2	4.8	7.9	5.3	4.5	4.1	1.4	4.4	4.5	5.3	9.2
Lrl	2.4	2.8	1.8	3.4	2.6	2.5	1.8	0.5	2.1	1.9	1.7	3.9
Url	9.6	13.5	12.7	18.1	10.6	7.8	9.3	3.7	9.1	10.4	16.0	21.3

(B)



	Ins	Nmr	Nter	Drws	Bpb	Irt	Dps	Agt	Anx	Hpa	Ldf	Hch
OR	1.2	1.1	1.4	1.6	1.5	1.1	1.4	1.3	1.3	1.5	1.7	1.7
Lrl	0.8	0.8	0.9	1.1	1.0	0.8	0.9	0.9	0.9	1.0	1.0	1.1
Url	2.1	1.6	2.0	2.4	2.2	1.6	2.2	1.9	1.9	2.3	2.7	2.6

FIGURE 2 | (A) Model findings of neuropsychiatric side effects or sleep disorders reported in the National Montelukast Cohort in allergic children due to the past reporting of these events. Amongst children who reported neuropsychiatric symptoms or sleep disorders in the past, headache and drowsiness (somnolence) were associated with the highest increase in occurrence risk with montelukast use (9.2-fold and 8.2-fold increase in risk, respectively). Increase in the risk of nightmares, learning disabilities and behavioural symptoms were also observed (Adjusted risk ratios of 6.3, 5.6 and 5.3, respectively). Ins: Insomnia, Nmr: Nightmare, Nter: Night terror, Drws: Drowsiness, Bpb: Behavioural problems, Irt: Irritability, Dps: Depressive mood, Agt: Agitation, Anx: Anxiety, Exa: Excess activity, Ldf: Learning difficulty, Hch: Headache, Lrl: Lower range limit, Url: Upper range limit, OR: Odds Ratio. (B) Model findings of neuropsychiatric side effects or sleep disorders reported in the National Montelukast Cohort in allergic children due to antihistaminic drug use at the baseline. Antihistamine use at admission independently was associated with an increase in many neuropsychiatric side effects caused by montelukast treatment, including lethargy (OR = 1.67), behavioural problems (OR = 1.59), hyperactivity (OR = 1.55), learning disability (OR = 1.77) and headache (OR = 1.59). Ins: Insomnia, Nmr: Nightmare, Nter: Night terror, Drws: Drowsiness, Bpb: Behavioural problems, Irt: Irritability, Dps: Depressive mood, Agt: Agitation, Anx: Anxiety, Exa: Excess activity, Ldf: Learning difficulty, Hch: Headache, Lrl: Lower range limit, Url: Upper range limit, OR: Odds Ratio.

in asthma patients with concurrent use of inhaled steroids. Montelukast received a patent in 2012; the prescription of the medication as well as the indications have increased since then. However, the appearance of adverse events has also increased, leading to early discontinuation [20]. In our study, we aimed to emphasise these adverse effects.

The major strength of this study was its cohort design, which reduced information bias and allowed us to make causal inferences. Furthermore, the multicenter participation allowed us to include children from different regions of Türkiye. The primary limitations of the study include the absence of a placebo group, increased awareness of caregivers regarding side effects and reliance on self-reported questionnaires, which may introduce information bias. We consulted with the paediatric psychiatrist on our research team when developing the data collection instruments to mitigate this.

In conclusion, this study demonstrates that montelukast treatment may increase the risk of neuropsychiatric symptoms and sleep disorders in children with asthma and allergic rhinitis. The risk of these side effects is heightening amongst those concurrently receiving antihistamines and those with a prior history of such symptoms. Clinicians prescribing montelukast need to weight these risks, ensure appropriate patient and family counselling, and establish a plan for close monitoring. The development of a structured risk–benefit assessment matrix prior to initiating treatment may be beneficial to guide clinicians before starting this treatment.

Author Contributions

Seda Tunca: submitting author, writing – original draft, investigation, writing – review and editing, resources, software. **Ozge Yilmaz:** methodology, writing – review and editing, writing – original draft, resources, formal analysis, supervision, investigation. **Merve Ocalan:** investigation. **Mustafa Arga:** investigation. **Ozlem Cavkaytar:** investigation. **Deniz Ozceker:** investigation. **Mehmet Kiliç:** investigation. **Fatma Duksal:** investigation. **Demet Can:** resources. **Ozlem Sancakli:** investigation. **Mehmet Şirin Kaya:** investigation. **Nazli Ercan:** investigation. **Nursen Cigerci Gunaydin:** investigation. **Metin Aydogan:** investigation. **Esen Demir:** investigation. **Recep Sancak:** investigation. **Sefika İlknur Kökcü Karadag:** investigation. **Nihat Sapan:** investigation. **Ahmet Ugur Demir:** formal analysis, supervision, data curation, software. **Oznur Bilac:** conceptualization, supervision, resources, validation. **Emine Dibek Misirlioglu:** investigation. **Ahmet Turkeli:** investigation. **Hasibe Artac:** investigation. **Hatice Eke Gungor:** investigation. **Haluk Cokugras:** investigation. **Fazil Orhan:** investigation. **Aysen Bingol:** investigation. **Pinar Uysal:** investigation. **Sennur Keles:** investigation. **Aylin Kont Ozhan:** investigation. **Tuba Tuncel:** investigation. **Ozlem Keskin:** investigation. **Elif Arik:** investigation. **Öner Özdemir:** investigation. **Ceren Can:** investigation. **Nazan Altinel:** investigation. **Koray Harmanci:** investigation. **Yurda Simsek:** investigation. **Derya Ufuk Altintas:** investigation. **Serap Ozmen:** investigation. **Nevin Uzuner:** investigation. **Yakup Canıtez:** investigation. **Hasan Yüksel:** corresponding author, supervision, data curation, software, project administration, conceptualization, validation, visualisation, writing – review and editing, funding acquisition, methodology.

Affiliations

[1]Pediatric Allergy and Immunology, Celal Bayar University Faculty of Medicine, Manisa, Turkey | [2]Pediatric Allergy and Immunology, Istanbul Medeniyet University Faculty of Medicine, İstanbul, Turkey | [3]Pediatric Allergy and Immunology, Istanbul Prof. Dr. Cemil Taşçıoğlu City Hospital, İstanbul, Turkey | [4]Pediatric Allergy and Immunology, Firat University Hospital, Elazig, Turkey | [5]Pediatric Allergy and Immunology, Konya City Hospital, Konya, Turkey | [6]Pediatric Allergy and Immunology, Behçet Uz Children's Hospital, İzmir, Turkey | [7]Pediatric Allergy and Immunology, SBU Gülhane Training and Research Hospital, Ankara, Turkey | [8]Pediatric Allergy and Immunology, Tekirdağ Namık Kemal University Faculty of Medicine, Merkez, Turkey | [9]Pediatric Allergy and Immunology, Kocaeli University Faculty of Medicine, Kocaeli, Turkey | [10]Pediatric Allergy and Immunology, Ege University Faculty of Medicine, Izmir, Turkey | [11]Pediatric Allergy and Immunology, Ondokuz Mayıs University Faculty of Medicine, Samsun, Turkey | [12]Pediatric Allergy and Immunology, Uludağ University Faculty of Medicine, Bursa, Turkey | [13]Chest Diseases, Hacettepe University Faculty of Medicine, Ankara, Turkey | [14]Child Psychiatry, Celal Bayar University Faculty of Medicine, Manisa, Turkey | [15]Pediatric Allergy and Immunology, Ankara City Hospital, Ankara, Turkey | [16]Pediatric Allergy and Immunology, Kütahya SBU Evliya Çelebi Training and Research Hospital, Kütahya, Turkey | [17]Pediatric Allergy and Immunology, Konya Selcuk University Faculty of Medicine, Konya, Turkey | [18]Pediatric Allergy and Immunology, Kayseri City Hospital, Kayseri, Turkey | [19]Pediatric Allergy and Immunology, Istanbul University Cerrahpasa Medical Faculty Hospital, İstanbul, Turkey | [20]Pediatric Allergy and Immunology, Karadeniz Technical University Faculty of Medicine, Trabzon, Turkey | [21]Pediatric Allergy and Immunology, Akdeniz University Faculty of Medicine, Antalya, Turkey | [22]Pediatric Allergy and Immunology, Aydin Adnan Menderes University Faculty of Medicine, Aydın, Turkey | [23]Pediatric Allergy and Immunology, SBU Antalya Training and Research Hospital, Antalya, Turkey | [24]Pediatric Allergy and Immunology, Mersin University Faculty of Medicine, Mersin, Turkey | [25]Pediatric Allergy and Immunology, Izmir Katip Celebi University Tepecik Training and Research Hospital, Izmir, Turkey | [26]Pediatric Allergy and Immunology, Gaziantep University Şahinbey Research and Application Hospital, Gaziantep, Turkey | [27]Pediatric Allergy and Immunology, Sakarya University Training and Research Hospital, Sakarya, Turkey | [28]Pediatric Allergy and Immunology, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey | [29]Pediatric Allergy and Immunology, Eskişehir Osmangazi University Faculty of Medicine, Eskisehir, Turkey | [30]Bursa Private Practice—Yurda Şimşek, Bursa, Turkey | [31]Pediatric Allergy and Immunology, Çukurova University Faculty of Medicine, Adana, Turkey | [32]Dr Sami Ulus Obstetrics and Gynecology Child Health and Diseases Education Arş Child Allergy and Immunology, Ankara, Turkey | [33]Pediatric Allergy and Immunology, Dokuz Eylül University Faculty of Medicine, İzmir, Türkiye

Ethics Statement

This study was approved by the Institutional Review Board (26.01.2021/674752) and the Turkish Medicines and Medical Devices Agency Review Board (21-AKD-10).

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. K. Kelsay, "Assessing Risk: Data From Montelukast Clinical Trials," *Journal of Allergy and Clinical Immunology* 124, no. 4 (2009): 697–698.

2. A. Nayak, "Review of Montelukast for the Treatment of Asthma and Allergic Rhinitis," *Expert Opinion on Pharmacotherapy* 5, no. 3 (2005): 679–686.

3. T. Ji, T. Lu, Y. Qiu, et al., "The Efficacy and Safety of Montelukast in Children With Obstructive Sleep Apnea: A Systematic Review and Meta-Analysis," *Sleep Medicine* 78 (2021): 193–201.

4. D. G. Rayner, M. Liu, A. W. L. Chu, et al., "Leukotriene Receptor Antagonists as Add-On Therapy to Antihistamines for Urticaria: Systematic Review and Meta-Analysis of Randomized Clinical Trials," *Journal of Allergy and Clinical Immunology* 154 (2024): 996–1007.

5. L. Sampson and J. M. Portnoy, "Joint Statement on FDA Investigation of SINGULAIR from the ACAAI and AAAAI," *European Annals of Allergy and Clinical Immunology* 40, no. 2 (2008): 64.

6. W. Storms, T. M. Michele, B. Knorr, et al., "Clinical Safety and Tolerability of Montelukast, a Leukotriene Receptor Antagonist, in Controlled Clinical Trials in Patients Aged > or = 6 Years," *Clinical and Experimental Allergy* 31, no. 1 (2001): 77–87.

7. T. Paljarvi, J. Forton, S. Luciano, et al., "Analysis of Neuropsychiatric Diagnoses After Montelukast Initiation," *JAMA Network Open* 5, no. 5 (2022): e2213643, https://doi.org/10.1001/jamanetworkopen.2022.13643.

8. T. Paljarvi, J. T. Forton, C. Thompson, S. Luciano, K. Herttua, and S. Fazel, "Neuropsychiatric Diagnoses After Montelukast Initiation in Paediatric Patients With Asthma," *Thorax* 80, no. 1 (2024): 9–15, https://doi.org/10.1136/thorax-2024-221590.

9. Z. Ou, Y. Han, W. Zhuang, Y. Xiao, S. Cai, and X. Zhang, "Post-Marketing Safety Concerns With Montelukast: A Pharmacovigilance Study Based on the FDA Adverse Event Reporting System," *International Journal of Clinical Pharmacology and Therapeutics* 62, no. 11 (2024): 497–506, https://doi.org/10.5414/CP204560.

10. M. Peters-Golden and W. R. Henderson, "Role of Leukotrienes in Allergic Rhinitis," *Annals of Allergy, Asthma & Immunology* 94, no. 6 (2005): 609–618.

11. B. Benard, V. Bastien, B. Vinet, R. Yang, M. Krajinovic, and F. M. Ducharme, "Academic Chair in Clinical and Knowledge Transfer Research on Childhood Asthma at the Sainte-Justine University Health Center," *European Respiratory Journal* 50 (2017): 1700148.

12. E. G. Dixon, C. E. Rugg-Gunn, V. Sellick, I. P. Sinha, and D. B. Hawcutt, "Adverse Drug Reactions to Leukotriene Receptor Antagonists in Children With Asthma: A Systematic Review," *BMJ Paediatrics Open* 5 (2021): 1206.

13. C. Ekhart, F. van Hunsel, V. Sellick, and T. de Vries, "Neuropsychiatric Reactions With the Use of Montelukast," *BMJ* 376 (2022): e067554, https://doi.org/10.1136/bmj-2021-067554.

14. S. M. Wallerstedt, G. Brunlöf, A. Sundström, and A. L. Eriksson, "Montelukast and Psychiatric Disorders in Children," *Pharmacoepidemiology and Drug Safety* 18, no. 9 (2009): 858–864.

15. A. Aldea Perona, M. García-Sáiz, and E. Sanz Álvarez, "Psychiatric Disorders and Montelukast in Children: A Disproportionality Analysis of the VigiBase," *Drug Safety* 39, no. 1 (2016): 69–78.

16. M. G. Haarman, F. van Hunsel, and T. W. de Vries, "Adverse Drug Reactions to Montelukast in Children and Adults," *Pharmacology Research & Perspectives* 5, no. 5 (2017): 341.

17. G. T. Schumock, L. T. Stayner, R. J. Valuck, M. J. Joo, R. D. Gibbons, and T. A. Lee, "Risk of Suicide Attempt in Asthmatic Children and Young Adults Prescribed Leukotriene-Modifying Agents: A Nested Case-Control Study," *Journal of Allergy and Clinical Immunology* 130, no. 2 (2012): 368–375.

18. S. D. Glockler-Lauf, Y. Finkelstein, J. Zhu, L. Y. Feldman, and To, T, "Montelukast and Neuropsychiatric Events in Children With Asthma: A Nested Case-Control Study," *Journal of Pediatrics* 209 (2019): 176–182.e4.

19. G. Cereza, N. G. Doladé, and J. R. Laporte, "Nightmares Induced by Montelukast in Children and Adults," *European Respiratory Journal* 40, no. 6 (2012): 1574–1575.

20. R. I. Farah, P. Damkier, A. Christiansen, and D. P. Henriksen, "Early Discontinuation of Montelukast Treatment; A Danish Nationwide Utilization Study," *Basic & Clinical Pharmacology & Toxicology* 123, no. 1 (2018): 78–83.