Montelukast-Induced Behavioral Problems in a Child With Bronchial Asthma

Hadik Al Jouhar Kunnath, MD; Padinharath Krishnakumar, MD; and Rajith Ravindren, MD

Montelukast is a cysteinyl leukotriene receptor antagonist that is US Food and Drug Administration approved to treat asthma, seasonal allergic rhinitis, and exercise-induced bronchoconstriction. Montelukast works by binding to the leukotriene receptors (D4, C4, and E4) in the lungs and prevents bronchoconstriction and inflammation.[1]

Neuropsychiatric events such as aggressive behavior, anxiousness, depression, disorientation, disturbance in attention, memory impairment, obsessive-compulsive symptoms, hallucinations, insomnia, and suicidal thoughts have been described with the use of montelukast.[2,3] We report a case of a 6-year-old boy who developed acute behavioral disturbances after being prescribed montelukast prophylaxis for bronchial asthma.

Case Report

A 6-year-old boy presented to the psychiatry clinic with a 2-week history of school refusal, temper tantrums, irritability, and verbal and physical abuse. The child would run away from home for trivial issues. He insisted that his mother accompany him to the classroom and would throw tantrums if she did not. No psychosocial precipitating factors were reported. He was a temperamentally easy child with good academic performance. He had a history of childhood asthma with an exacerbation 3 weeks ago. He was prescribed montelukast for this recent episode of asthma.

We made a provisional diagnosis of unspecified behavioral disorder and began behavior therapy. However, there were no improvements in the child's symptoms. On one occasion, the child ran away from the therapy room and threw a tantrum continuously for 1 hour. The absence of any behavioral issues until 6 years of age and the lack of any recent psychosocial stressors prompted the treating team to look for other possible causes. The child's symptoms were found to temporally correlate with the use of montelukast prescribed for the recent asthmatic episode. The medicine was discontinued under pediatric supervision, and the behavioral symptoms completely subsided in 1 week.

Discussion

A temporal association with behavioral problems indicates the causal role of montelukast in this patient's adverse event. A Naranjo Adverse Drug Reaction Probability Scale[4] score of 6 indicates a probable causal association of montelukast with the adverse outcome.

Many hypotheses have been made to explain the neuropsychiatric side effects of montelukast. One of them states that the side effects are caused by the creation of a glutathione conjugate during the drug's metabolism and the ensuing decrease in glutathione availability, which is crucial for regulating oxidative stress in brain cells. Another explanation based on metabolomic studies states that montelukast causes dysregulation of the hypothalamic-pituitary-adrenal axis. This in turn alters the neurosteroid pathways and levels of neurotransmitters.[5] Children are more prone to these side effects due to insufficient brain maturation.

Studies have also found interactions between montelukast and genes linked to psychiatric diseases such as *HTR2A, KALRN*, and *HCRT*. These interactions are also considered a potential mechanism for the neuropsychiatric side effects of montelukast.[6]

In conclusion, while montelukast is a generally safe medicine, it has the potential to generate neuropsychiatric side effects that doctors may miss in the absence of close surveillance. Early recognition and management can reduce morbidity and costs for patients and the mental health system.

Article Information

Published Online: September 5, 2024. https://doi.org/10.4088/PCC.24cr03750

Prim Care Companion CNS Disord 2024;26(5):24cr03750

Submitted: March 28, 2024; accepted June 6, 2024.

To Cite: Kunnath HAJ, Krishnakumar P, Ravindren R. Montelukast-induced behavioral problems in a child with bronchial asthma. *Prim Care Companion CNS Disord*. 2024;26(5):24cr03750.

Author Affiliations: Department of Psychiatry, Institute of Mental Health and Neurosciences, Kozhikode, India (Kunnath, Krishnakumar, Ravindren); Centre for Interdisciplinary Brain Sciences, Institute of Mental Health and Neurosciences, Kozhikode, India (Ravindren).

Corresponding Author: Ravindren Rajith, MD, Department of Psychiatry, Institute of Mental Health and Neurosciences, Medical College Campus, Kozhikode, India 673008 (rajith@imhans.ac.in).

Relevant Financial Relationships: None.

Funding/Support: None.

Patient Consent: Informed written consent was obtained from the patient's father to publish the case report, and information has been de-identified to protect anonymity.

References

1. Wermuth HR, Badri T, Takov V. *Montelukast*. StatPearls Publishing; 2022.
2. Ducharme FM, Bénard B, Vinet B, et al. Neuropsychiatric adverse drug reactions in children initiated on montelukast in real-life practice. *Eur Respir J*. 2017;50(5):1702135.
3. Clarridge K, Chin S, Eworuke E, et al. A boxed warning for montelukast: the FDA perspective. *J Allergy Clin Immunol Pract*. 2021;9(7):2638–2641.
4. Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther*. 1981;30(2):239–245.
5. Marques CF, Marques MM, Justino GC. The mechanisms underlying montelukast's neuropsychiatric effects-new insights from a combined metabolic and multiomics approach. *Life Sci*. 2022;310:121056.
6. Umetsu R, Tanaka M, Nakayama Y, et al. Neuropsychiatric adverse events of montelukast: an analysis of real-world datasets and drug–gene interaction network. *Front Pharmacol*. 2021;12:764279.