

A case report on montelukast and fexofenadine induced depression and nightmares

CHRISTEENA MARY VIJI ^{1,*}, THOMAS JACOB ABRAHAM ², HARIKRISHNAN S ³

¹ Pharm D Intern Nazareth College of Pharmacy, Othara, Kerala, India.

² Associate Professor, Department of General Medicine, Believers church medical college hospital, Thiruvalla, Kerala, India.

³ Clinical Pharmacist Believers Church Medical College Hospital, Kerala, India.

World Journal of Biology Pharmacy and Health Sciences, 2025, 21(02), 111–113

Publication history: Received on 19 December 2024; revised on 31 January 2025; accepted on 02 February 2025

Article DOI: <https://doi.org/10.30574/wjbphs.2025.21.2.0114>

Abstract

Depression and nightmares are caused by Montelukast. Montelukast is a selective leukotriene receptor antagonist (LRTA) and US-FDA issued a black box warning in 2020. In this case report, a 14 year old female was prescribed a combination of Tab. Montelukast and Tab. Fexofenadine for the treatment of bronchial asthma exacerbations. After this, she started experiencing multiple episodes of depression and nightmares. The patient was asked to avoid Montelukast after which the patient's condition improved and she was started on MDI Formoterol fumarate and Budesonide powder for inhalation and Tab. Desloratadine for further management. After stopping the drug, her condition improved. This case report underlines the importance of monitoring for rare but serious side effects of leukotriene receptor antagonist and highlights the need for further research into their mechanisms and risk factors.

Keywords: Montelukast; Depression; Nightmare; Bronchial asthma; Fexofenadine

1. Introduction

Dream disturbances, such as nightmares, along with psychiatric conditions like hallucinations, aggressive behaviour, depression, and suicidal thoughts or behaviours were not reported in Montelukast clinical trials^[2-5]. A nightmare is a long, intensely distressing dream, often centred around attempts to escape threats to survival, safety, or physical well-being. However, according to the product labelling, nightmares are categorized as an uncommon adverse drug reaction (ADR), occurring at a frequency of $\geq 1/1000$ to $< 1/100$ ^[1].

Depressive disorder, or depression, is a common mental health condition which can happen to anyone. It is characterized by low mood, loss of pleasure or interest in activities for long periods of time^[18]. Depression is an uncommon adverse drug reaction (ADR) occurring at a frequency of $\geq 1/1000$ to $< 1/100$ people taking the medication^[7].

2. Case report

A 14-year-old female came to the Department of General Medicine with complaints of tiredness and dyspnoea on 26th August 2024. She had bronchial asthma since her childhood and frequent exacerbations since November, 2023. She also had complaints of dust allergy and was unable to tolerate scents and paint smell. She was started on treatment for bronchial asthma with Tab. Montelukast and Tab. Fexofenadine 10/120 mg once a day at night time on 24th June 2024. She developed depression and nightmares while on treatment with Tab. Montelukast and Tab. Fexofenadine 10/120 mg. She experienced nightmares and depressive episodes with a feeling of weakness. Upon consultation, the patient had depressive episodes and nightmares frequently. Tab. Montelukast and Tab. Fexofenadine was withdrawn and the patient was started on MDI Formoterol fumarate and Budesonide powder for inhalation 400 1 puff 2 times a day and Tab. Desloratadine 5 once a day at bedtime. Now her condition has improved.

* Corresponding author: CHRISTEENA MARY VIJI

Upon evaluation at our Adverse Drug Reaction (ADR) Monitoring Center, the causality was determined to be “probable” using the WHO-UMC Causality Assessment Scale^[12]. The type of ADR was classified as “Type B” according to the Rawlins–Thompson^[9] classification and was assessed as “Level 3, Moderate” in terms of severity based on Hartwig’s scale. As per the WHO criteria, the seriousness of the reaction was categorised as “nonserious,” and the outcome of the reaction was “Recovering.” In addition, according to the Schumock and Thornton scale, the ADR was deemed “nonpreventable” As per Naranjo’s adverse drug reaction probability assessment scale it is “probable” ADR. The assessment of causality and other attributes of the ADR was conducted using established scales.

3. Discussion

Tab. Montelukast and Tab. Fexofenadine are leukotriene receptor antagonists (LTRAs) and non-sedating H1 receptor antagonists respectively^[19]. When Tab. Montelukast and Tab. Fexofenadine 10/120 mg was administered to this patient for the treatment of exacerbations of bronchial asthma, after which the patient experienced depression and nightmares. After withdrawal of the drug, the patient’s condition improved which indicates that the drug may have caused depression and nightmares^[6,7]. However, Vigibase shows a total of 32,506 ADRs reported. Amongst them, 10,977 are psychiatric disorders. Depression was reported in 2,265 ADRs and nightmares in 1,607 ADRs^[17]. Depression and nightmares should be carefully assessed and closely monitored in children receiving montelukast, as these symptoms may develop during the treatment.

4. Conclusion

Although Montelukast is marked beneficial but the adverse neuropsychiatric drug reactions are more prevalent than those documented in the literature. The health professional should focus on collecting the patient’s history regarding previous exposure to the drug and drug provocation testing. They should also emphasize on the management of the adverse effects.

Compliance with ethical standards

Acknowledgments

We express our gratitude to the ADR Monitoring Centre operating under Pharmacovigilance Programme of India (PvPI) at Believers Church Medical College Hospital, Thiruvalla, Kerala, for their generous assistance in reporting this ADR.

Disclosure of conflict of interest

There are no conflicts of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

- [1] Watson S, Kaminsky E, Taavola H, Attalla M, Yue QY. Montelukast and Nightmares: Further Characterisation Using Data from VigiBase. *Drug Safety*. 2022 Jun;45(6):675–84.
- [2] Kelsay K. Assessing risk: Data from montelukast clinical trials. *Journal of Allergy and Clinical Immunology*. 2009 Oct;124(4):697–8.
- [3] Holbrook JT, Harik-Khan R. Montelukast and emotional well-being as a marker for depression: Results from 3 randomized, double-masked clinical trials. *Journal of Allergy and Clinical Immunology*. 2008 Oct;122(4):828–9.
- [4] Philip G, Hustad C, Noonan G, Malice MP, Ezekowitz A, Reiss TF, et al. Reports of suicidality in clinical trials of montelukast. *The Journal of Allergy and Clinical Immunology* [Internet]. 2009 Oct 1 [cited 2020 Mar 26];124(4):691–696.e6. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/19815114>
- [5] Philip G, Hustad CM, Marie-Pierre Malice, Noonan G, Ezekowitz A, Reiss TF, et al. Analysis of behavior-related adverse experiences in clinical trials of montelukast. 2009 Oct 1;124(4):699–706.e8.
- [6] Calapai G, Casciaro M, Miroddi M, Calapai F, Navarra M, Gangemi S. Montelukast-Induced Adverse Drug Reactions: A Review of Case Reports in the Literature. *Pharmacology*. 2014;94(1-2):60–70.

- [7] Haarman MG, van Hunsel F, de Vries TW. Adverse drug reactions of montelukast in children and adults. *Pharmacology Research & Perspectives* [Internet]. 2017 Sep 20;5(5). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5625152/>
- [8] Donmez Y, Karaer I. Does short-term montelukast treatment cause sleep problems or psychiatric problems in children? A preliminary study. *Annals of Medical Research*. 2020;27(10):2654.
- [9] Lo CWH, Pathadka S, Qin SX, Fung LWY, Yan VKC, Yiu HHE, et al. Neuropsychiatric events associated with montelukast in patients with asthma: a systematic review. *European Respiratory Review: An Official Journal of the European Respiratory Society* [Internet]. 2023 Sep 30 [cited 2023 Sep 30];32(169):230079. Available from: <https://pubmed.ncbi.nlm.nih.gov/37758273/>
- [10] Marques CF, Marques MM, Justino GC. The mechanisms underlying montelukast's neuropsychiatric effects - new insights from a combined metabolic and multiomics approach. *Life Sciences* [Internet]. 2022 Dec 1;310:121056. Available from: <https://www.sciencedirect.com/science/article/pii/S0024320522007561>
- [11] Aldea Perona A, García-Sáiz M, Sanz Álvarez E. Psychiatric Disorders and Montelukast in Children: A Disproportionality Analysis of the VigiBase®. *Drug Safety*. 2015 Nov 30;39(1):69–78.
- [12] The use of the WHO-UMC system for standardized case causality assessment The use of the WHO-UMC system for standardized case causality assessment Why causality assessment? [Internet]. Available from: <https://www.who.int/docs/default-source/medicines/pharmacovigilance/whocausality-assessment.pdf>
- [13] Adverse drug reactions [Internet]. Clinical Gate. 2015. Available from: <https://clinicalgate.com/adverse-drug-reactions/>
- [14] Paljarvi T, Forton JT, Thompson C, Luciano S, Herttua K, Fazel S. Neuropsychiatric diagnoses after montelukast initiation in paediatric patients with asthma. *Thorax*. 2024 Nov 22;thorax-2024-221590.
- [15] Uğur Altaş, Zeynep Meva Altaş, Fırat Öz, Mehmet Yaşar Özkars. Evaluation of Neuropsychiatric Effects of Montelukast–Levocetirizine Combination Therapy in Children with Asthma and Allergic Rhinitis. *Children (Basel)*. 2023 Jul 28;10(8):1301–1.
- [16] Al-Shamrani A, Alharbi S, Kobeisy S, AlKhater SA, Alalkami H, Alahmadi T, et al. Adverse Drug Reactions (ADRs) of Montelukast in Children. *Children*. 2022 Nov 21;9(11):1783.
- [17] VigiAccess [Internet]. www.vigiaccess.org. Available from: <https://www.vigiaccess.org/>
- [18] World. Depression [Internet]. Who.int. World Health Organization: WHO; 2019. Available from: <https://www.who.int/health-topics/depression>
- [19] Mahatme M, Dakhale G, Tadke K, Hiware S, Dudhgaonkar S, Wankhede S. Comparison of efficacy, safety, and cost-effectiveness of montelukast-levocetirizine and montelukast-fexofenadine in patients of allergic rhinitis: A randomized, double-blind clinical trial. *Indian Journal of Pharmacology*. 2016;48(6):649.