A Case of Major Depressive Disorder in an adolescent patient exacerbated by Montelukast

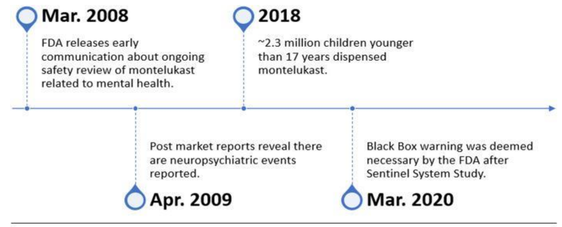
Samuel Polhemus MD; Samantha Fleck MD; Christopher Rogers MD

The Medical Center of Aurora

Background

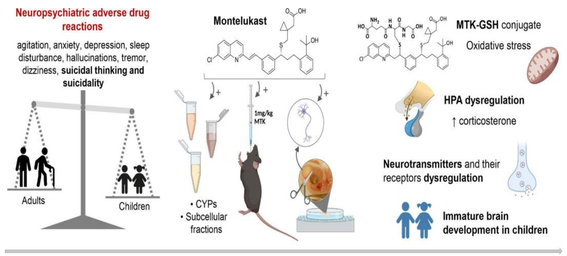
Following post-market reports of increased neuropsychiatric events of Montelukast, the FDA issued a black box warning in March of 2020.[1] This black box warning has since been studied and there have been mixed results between various publications. Many studies have demonstrated a strong correlation between Montelukast and recommend caution/monitoring for neuropsychiatric effects.[2–4] Some studies have demonstrated that this correlation is not as strong as some research suggests and that there may not be any increased risk of suicide as well.[5–8] Although the mechanism of action is not entirely understood, one study theorized that the mechanism behind this is that Montelukast interferes with glutathione detoxification and interacts with neurotransmitter/neurosteroids in the HPA axis.[9] Due to the conflicting evidence and relatively recent issuing of the black box warning in 2020 this case report is necessary to bring to light an example of an adolescent patient who was having significant depressive symptoms suspected to be worsened by Montelukast and improved significantly when it was discontinued.

Figures



FDA, US Food and Drug Administration

Abdelkader et al.



Marques et al.

Case

2020-2021:
- With the isolation due to COVID and transition to online school parents noted an onset of depressive symptoms during this time including more isolation, less socialization with the family/peers, and more irritability
- At this time patient was 13 years old
- March of this time patient was brought by his parents to the pediatrician and was started on Fluoxetine.

2021:
- Due to concerns for patient's ongoing allergic rhinitis/asthma symptoms he was started at this time on Montelukast; per parents report they were not informed of black box warning

2021-2022:
- After a brief symptom remission, his mood symptoms returned and persisted for the following year despite increases in Fluoxetine

2023:
- Patient continues to have severe mood symptoms, but no hospitalizations or suicide attempts. Consistently low mood and depressive symptoms
- During this time he was switched to Escitalopram

2023:
- Patient is transferred to a psychiatric NP and was placed on Aripiprazole and Bupropion XR; Escitalopram discontinued
- He continues to demonstrate consistent depressive symptoms

2023:
- ER visit for a Panic attack and severe depression with SI

September 2023:
- Started IOP

2023:
- He is transferred to the outpatient clinic where first author initiated care of patient
- At that time he was on Aripiprazole 5mg daily as well as Bupropion extended release 150mg
- Initial treatment plan was to initiate psychotherapy and discontinue abilify as bupropion had not been properly titrated and augmentation did not seem appropriate yet
- Bupropion increased to 300mg

2023:
- Despite increase in Bupropion symptoms continue; initial plan was to continue medication for two more weeks, but parents called the day after the appointment and were curious about Montelukast and neuropsychiatric black box warning they found while researching his medications; parents were informed to contact pediatrician and request alternative agent to see if Montelukast was exacerbating symptoms
- Within 3 days of discontinuing Montelukast patient demonstrated significant improvements in both subjective, self-reported symptoms as well as observed behaviors by parents

2023:
- Patient continuing to demonstrate symptom remission despite no further changes in medications after stopping montelukast

Discussion

Although this patient's case is still ongoing, his significant improvement regarding his self-reported depression symptoms as well as observed behaviors at home within 3 days after discontinuation is suspicious for at least an exacerbating effect by montelukast. The pharmacokinetics of montelukast demonstrate a short half-life (approx. 4.5 hours) but given the suspicion for cause via metabolites it is difficult to know for certain how impactful montelukast was.[9,10] This report is also limited by the history and symptoms being almost exclusively self-report by the patient and his parents. He is still being seen in the outpatient clinic and the plan is to taper Bupropion extended release to see if symptoms remain in remission without any medication treatment. Other considerations for his diagnosis and confounding variables are hypothyroidism/organic depression which was not seen on labs. Additionally there may have been a placebo-effect of stopping montelukast as well as the possible benefit of increasing Wellbutrin; however, the rapid and significant nature of his symptom improvement is inconsistent with the usual onset time of Wellbutrin and placebo would unlikely lead to sustained remission.

Conclusion

Providers should be asking about neuropsychiatric side effects after the initiation of montelukast and psychiatric prescribers should be aware to monitor for patients on Montelukast. It is worth considering discontinuation of montelukast in children and adolescents presenting with new-onset psychiatric symptoms or worsening and treatment resistance of pre-existing symptoms. More research is needed into the risk of this reaction occurring as well as the pathophysiology that may be causing it.

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