Paradoxical Agitation and Urinary Retention from Quetiapine

Hampole, Ami DO; Tancredi, Nadia PharmD; Cohen, Robin MD

Marianjoy Rehabilitation Hospital
Now part of Northwestern Medicine

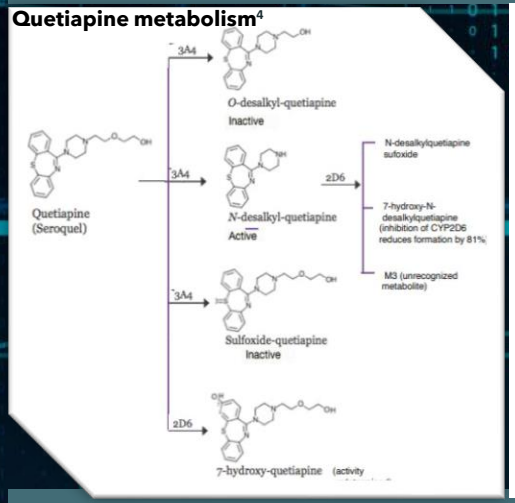
CASE DESCRIPTION

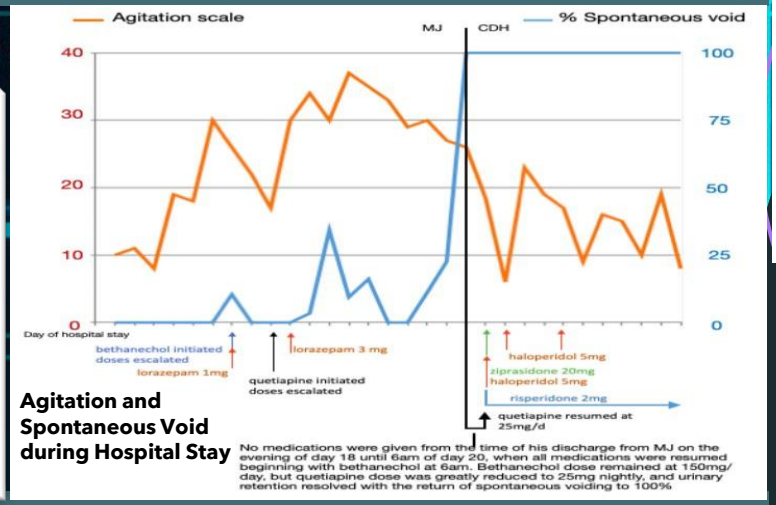
Following a month long acute hospital stay for alcohol and benzodiazepine encephalopathy, a 64-year-old male with PMH of CVA presented to acute inpatient physical rehabilitation with confusion and impaired gait. Rehab hospitalization was complicated by urinary retention, UTI, and nightly agitation. Following antibiotic treatment of UTI, urinary retention persisted. Patient required straight catheterization throughout the several-week hospitalization despite the addition and titration of tamsulosin, bethanechol, and finasteride. For agitation, which had failed conservative measures, quetiapine was prescribed and dose titrated upward. Agitation however, worsened. Patient became increasingly aggressive and was transferred to an acute care hospital for further management of severe agitation. Once quetiapine dose was markedly reduced, urinary retention resolved within 24-hours and agitation improved.

METHODS

Daily assessment of agitation was compared to degree of urinary retention (reported as % spontaneous voiding to total urine output) and doses of medications administered. Assessment of patient's orientation, cognition, behaviors and interventions aimed at reducing the observed agitation from daily nursing assessments were tallied and scored to quantify degree of agitation.

Quetiapine metabolism[4]



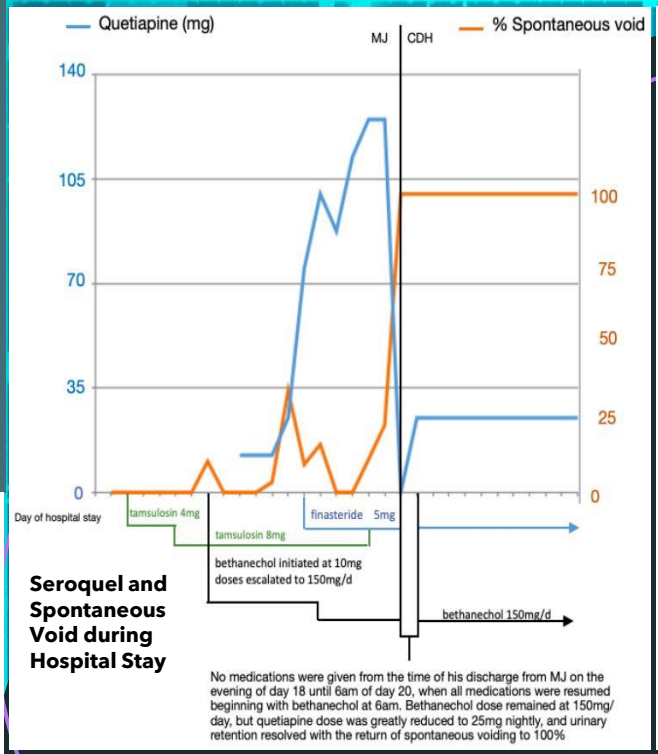


Agitation and Spontaneous Void during Hospital Stay

No medications were given from the time of his discharge from MJ on the evening of day 18 until 6am of day 20, when all medications were resumed beginning with bethanechol at 6am. Bethanechol dose remained at 150mg/day, but quetiapine dose was greatly reduced to 25mg nightly, and urinary retention resolved with the return of spontaneous voiding to 100%

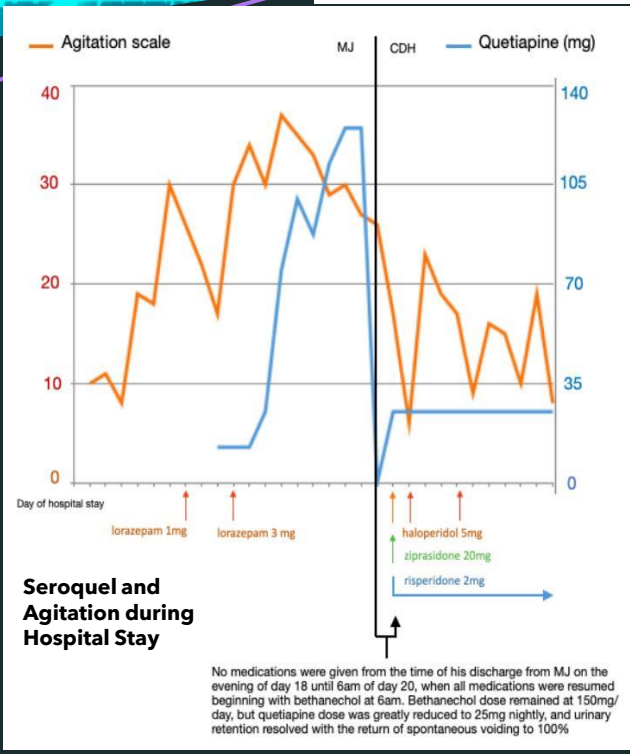
DISCUSSION

Devoid of antimuscarinic blockade, quetiapine is preferred for delirium given its effectiveness and tolerability. Metabolism by isoenzyme CYP3A4 produces the active metabolite norquetiapine, which differs significantly from quetiapine in that it possesses potent muscarinic blockade.[1] Norquetiapine is metabolized by CYP2D6. Roughly 10% of the population have little or no active CYP2D6 enzyme and are termed "poor metabolizers."[3] Antagonism at muscarinic receptors by norquetiapine is responsible for the anticholinergic adverse effects associated with quetiapine including urinary retention and delirium.[5] We hypothesize that the patient described here is a poor metabolizer at CYP2D6 which results in elevated levels of norquetiapine, causing urinary retention and anticholinergic delirium from muscarinic blockade.



Seroquel and Spontaneous Void during Hospital Stay

No medications were given from the time of his discharge from MJ on the evening of day 18 until 6am of day 20, when all medications were resumed beginning with bethanechol at 6am. Bethanechol dose remained at 150mg/day, but quetiapine dose was greatly reduced to 25mg nightly, and urinary retention resolved with the return of spontaneous voiding to 100%



Seroquel and Agitation during Hospital Stay

No medications were given from the time of his discharge from MJ on the evening of day 18 until 6am of day 20, when all medications were resumed beginning with bethanechol at 6am. Bethanechol dose remained at 150mg/day, but quetiapine dose was greatly reduced to 25mg nightly, and urinary retention resolved with the return of spontaneous voiding to 100%

CONCLUSION

Quetiapine is commonly used in the acute inpatient rehabilitation setting to reduce acute agitation. In this case, quetiapine's use resulted in significant urinary retention and a paradoxical worsening of agitation. This case demonstrates the importance of recognizing adverse reactions when they occur, in order to avoid the cycle of poly-pharmacy, dose escalation, and behavioral deterioration.

SOURCES

1.Almeida F, Albuquerque E, Murta I. Delirium Induced by Quetiapine and the Potential Role of Norquetiapine. Front Neurosci. 2019;13:886. doi:10.3389/fnins.2019.00886

2.Grimm SW, Richtand NM, Winter HR et al. effects of cytochrome P450 3A modulators ketoconazole and carbamazepine on quetiapine pharmacokinetics. Br J Clin Pharmacol 2006;61:58-69

3.Mora F, Molina JD, Zubillaga E, López-Muñoz F, Álamo C (2015) CYP450 and Its Implications in the Clinical Use of Antipsychotic Drugs. Clin Exp Pharmacol 5: 176. doi:10.4172/2161-1459.1000176

4.National Center for Biotechnology Information. PubChem Substance Record for SID 387163760, 139079-39-3, https://pubchem.ncbi.nlm.nih.gov/substance/387163760

5.López-Muñoz F, Alamo C. Active metabolites as antidepressant drugs: the role of norquetiapine in the mechanism of action of quetiapine in the treatment of mood disorders. Front Psychiatry. 2013;4:102. doi:10.3389/fpsyt.2013.00102