Exercising Pharmacologic Restraint with Intravenous Olanzapine

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Problem Identification

Agitation is a challenging symptom to manage in elderly patients with neuropsychiatric impairment, where commonly used agents can confer excessive sedation and worsening confusion. Here, we identified an index case of IV olanzapine administered for management of agitation in an elderly patient, resulting in a dense hypoactive delirium with symptoms of anticholinergic toxicity. This was the first time we observed parenteral olanzapine administration in our hospital, and it raised concerns for patient safety. We highlight a second case of IV olanzapine use in an elderly woman with dementia which necessitated medical admission for persistent hypoactive delirium and urinary retention. On review with our pharmacy, we learned that IV olanzapine was approved for use within our hospital system and had widespread adoption despite our concerns for its safety profile; particularly in medically ill, elderly patients managed on general medical units.

Aims

- To improve patient safety when managing agitation and delirium.
- To encourage a thoughtful clinical review before administering IV olanzapine to neuropsychiatrically vulnerable adults.
- To review the process of approval and ongoing monitoring of psychotropic drug safety in our hospital system.

Cases

Case 1 (10/2020): 85-year-old female with past medical history of hypertension, irritable bowel syndrome, depression, and anxiety presented with increased confusion, bizarre behavior, and religious delusions. Found to have UTI (UA with 2+ LE, 20 WBC), CT brain demonstrated microvascular changes, and her remaining labs were otherwise normal. While admitted to medicine, she received as needed quetiapine, IV antibiotic treatment of her UTI, followed by multiple PRNs for agitation including IV olanzapine 5 mg, IV haloperidol 5 mg x2, and quetiapine 25 mg. Following this, she was stuporous for an entire day. After her excessive sedation lifted, she approximated her baseline and was able to be discharged to her family.

Case 2 (10/2021): 71-year-old female with past medical history of of normal pressure hydrocephalus status post shunt, moderate dementia thought to be multifactorial (NPH and vascular contributions), and hyperlipidemia who presented with 4 months of worsening paranoid delusions, hallucinations and wandering. In the emergency department, she was given a total of 5 mg IV olanzapine combined with 1 mg IV lorazepam. She then required medical admission for persistent hypoactive delirium and urinary retention. After two days of excessive sedation and need for intermittent urinary catheterization, she transferred to inpatient geriatric psychiatry for further management of her presenting symptoms.

Literature Review

- We reviewed the existing literature on the use of IV olanzapine. The majority of this literature comes from ED and ICU settings in the treatment of acute agitation and/or to achieve sedation. To our knowledge, there are no RCTs that have examined the use of IV olanzapine on general medical floors. Further, there are no studies examining IV olanzapine use specifically for patients with dementia or delirium.

- A retrospective cohort study by Martel et al evaluated safety and efficacy of IV olanzapine over a 7 month period in an ED setting. The median age of the study population was 38 and neuropsychiatric diagnoses were broad-ranging. 10% of patients required treatment for hypoxia, and rates of respiratory complications were high in patients requiring additional sedation. Of note, the primary goal of olanzapine use in this study was to achieve sedation, which may differ from the goal of antipsychotic use in delirium or dementia management.

- A prospective observational study by Cole et al evaluated IV versus IM olanzapine use for acutely agitated patients in the ED with respiratory depression as a primary outcome, which occurred in 3.7% of patients with IV use and 2.0% with IM use. Of note, no formal statistical analysis was done. The authors concluded that IM and IV olanzapine are safe for use in the ED setting.

- A well designed RCT by Chan et al evaluated IV olanzapine vs droperidol adjunct to IV midazlolam for acutely agitated patients. The proportion of patients adequately sedated at 10 minutes was similar between the droperidol and olanzapine groups (66.1% vs 67.9%). The authors concluded that both agents decreased time to adequate sedation versus midazlolam alone.

Investigations and Interventions

- We met with pharmacy leadership to learn about the process by which an agent is added to the formulary in our hospital and learned that:

  (1) A physician can make a request. Notably, the request does not specify route of administration (PO vs IM vs IV).

  (2) The pharmacy itself can make a medication request based on drug use trends, comparison to peer hospital usage, which can then advance through pharmacy internal committees.

- The pharmacy will review ongoing use of medication and route of administration for a variety of reasons including SafetyNet reports filed by staff following adverse patient events, recurrent need for pharmacy interventions, and FDA warnings. Our pharmacy is currently in the process of reviewing its formulary.

- During the early waves of the COVID-19 pandemic, there were shortages of medications typically used in the ICU for sedation and agitation management as these agents were deployed at high rates and above average doses in COVID patients. This led to liberalization of off label use of more atypical sedating agents including IV olanzapine in the ICU setting. We suspect that medical residents gained comfort using this agent in the ICU, which led to more widespread use within the ED and general medical floors as they moved through their various training sites throughout the academic year.

- We have submitted a request to initiate a review process with the pharmacy with the goal of creating restrictions and/or electronic order set warnings for the use of IV olanzapine in medically frail, neuropsychiatrically vulnerable adults in non ICU settings. We aim to reduce excessive sedation, anticholinergic burden, and prolonged hospital stays.

Conclusions

- The existing body of literature on the use of IV olanzapine relates primarily to the treatment of acute agitation or sedation in ED and ICU settings. The data has several limitations, most notably lack of generalizability.
- Data exists to suggest that IV olanzapine is an effective sedative, which supports our concern that it can precipitate or perpetuate hypoactive delirium in elderly patients.
- The two cases we presented highlight the lack of existing evidence to support IV olanzapine use in elderly patients, in cases of delirium or dementia, and on the general medical floors.
- We investigated how pharmacologic agents are approved for use in our hospital and identified targets for interventions to promote a more thoughtful clinical review before ordering this agent parenterally.
- We learned that typical agents used in the ICU setting for sedation and agitation management were in short supply during the COVID-19 pandemic, leading to liberalized use of sedating agents including IV olanzapine, which likely encouraged its use beyond the ICU setting to general medical floors.

Future Directions

- Collect and analyze data on IV olanzapine use regarding patient demographics, med-surg unit location, credentials/ training level of ordering provider, co-occurring diagnoses, length of stay and concomitant benzodiazepine administration to identify further areas for targeted interventions
- Improving core delirium lecture series for medical residents to highlight evidenced based practices for delirium/agitation management in elderly populations and articulating risks/ benefits of commonly used agents.
- Ongoing work with pharmacy to create restrictions that promote safe use of IV olanzapine in vulnerable populations/non-ICU settings.

References

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