

Risks of Opioid and Sedative Prescription in an Elderly Patient

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Story from the Front Lines:

A man in his 70s with mild cognitive impairment and a history of recurrent DVT on lifelong warfarin was evaluated in an orthopedics clinic. He had undergone total knee replacement 6 weeks prior. The patient reported poor pain control overall since the surgery; he had initially been trialed on short-acting hydrocodone and was discharged post-operatively on short-acting hydromorphone. Imaging did not demonstrate any signs of hardware misalignment or failure. His serum creatinine was 1.0 and glomerular filtration rate (GFR) was estimated to be $>60 \text{ mL/min/1.73m}^2$. The patient also reported difficulty sleeping at night due to uncontrolled pain, and reported that he had received benefit from zolpidem in the past as a sleeping aid. The actual amount of hydromorphone the patient was taking daily was not reported, but the patient had been prescribed a 2 week supply of hydromorphone 2 months prior to this appointment. He had not been on any opioids prior to surgery. Given uncontrolled pain on short-acting agents, the patient was prescribed sustained-release morphine 15mg twice daily. He was also prescribed zolpidem 5mg at bedtime as needed for sleep.

Six days after initiating these medications the patient's wife called to report that he was acting abnormally. Primary care follow-up was arranged for one week after this phone call though in the interim was evaluated at an emergency department for increased somnolence and generalized weakness. Computed tomography of the head was negative and ultimately the patient was discharged home from the emergency room with recommendations to limit opioids and stop zolpidem. At his subsequent follow-up in primary care clinic, morphine and zolpidem were stopped and he was changed to short-acting oxycodone for pain control. Further administration of zolpidem or other sleep aids was discouraged. His symptoms resolved completely and was able to taper off opioid pain medications over the following month.

Teachable Moment:

The patient presented above was elderly with mild cognitive impairment (MCI), each of which increases his risk of adverse effects from sedating medications. In this clinical vignette, we outline multiple ways in which this patient was placed at increased risk for falls and other adverse events.

Zolpidem is a sedative hypnotic, which can cause excessive daytime sedation and confusion, especially in those who are elderly. A review in the Journal of Hospital Medicine found that inpatient use of zolpidem was a strong and independent driver of fall risk.¹ A fall in this patient on warfarin could have been catastrophic. In 2016 the FDA published revised safety guidelines for the prescription of opioids along with benzodiazepines or other sedating medications, citing the risk of excessive sedation, respiratory depression, and death.²

Additionally, the prescription of long-acting opioids at excessive dosage placed him at increased risk of sedation and other adverse outcomes. As prescribed, his hydromorphone prescription (2mg every four hours as needed) would equate to a dose of 48 oral morphine equivalents (OMEs) daily. However, the patient was only prescribed a 2 week of this dosage 2 months prior to his visit; he was unlikely taking a full 48 OMEs daily. It is therefore likely that the patient was placed on long-acting morphine at a much

higher effective dose (30 OMEs) than what he had previously been receiving. Additionally, although his estimated GFR was normal, the GFR is known to decrease physiologically with age and the renal clearance of sustained-action morphine may have been somewhat reduced compared to a younger individual.³

Finally, more urgent triage of the patient's and family's concerns at the primary care office could have avoided an unnecessary emergency room visit with neuroimaging. Recognition of the compounded adverse effects of opiates and sedatives in the elderly could have led to more rapid triage of the patient's complaints. Given the high risk of falls, and possible death due to sedation and respiratory depression, earlier follow up than one week would be advised in similar cases in the future.

Concomitant usage of opioids and sedating hypnotics should be avoided when possible, especially in elderly individuals or those at higher risk of falls and other medication-related adverse events. Careful history taking regarding opioid usage should be encouraged to avoid overmedicating individuals when dose adjustments are made.

References:

- 1: Kolla BP, Lovely JK, Mansukhani MP, Morgenthaler TI. Zolpidem is independently associated with increased risk of inpatient falls. *J Hosp Med.* 2013;8(1):1-6.
- 2: FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning. Food and Drug Administration Web site. <http://www.fda.gov/Drugs/DrugSafety/ucm518473.htm>. Accessed September 27, 2017.
- 3: Raman M, Middleton RJ, Kalra PA, Green D. Estimating renal function in old people: an in-depth review. *Int Urol Nephrol.* 2017. Epub September 15, 2017.