

Things We Do For No Reason™: Use of Antipsychotic Medications in Patients with Delirium

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Inspired by the ABIM Foundation's Choosing Wisely® campaign, the "Things We Do for No Reason™" (TWDFNR™) series reviews practices that have become common parts of hospital care but may provide little value to our patients. Practices reviewed in the TWDFNR™ series do not represent "black and white" conclusions or clinical practice standards but are meant as a starting place for research and active discussions among hospitalists and patients. We invite you to be part of that discussion.

CASE

An 86-year-old woman with mild dementia falls at home while preparing a meal. Her son brings her to the emergency department for excruciating pain in her right hip. X-rays reveal a fractured right femur that requires open reduction and internal fixation. On the first postoperative day, she does not participate in therapy and sleeps most of the day. Overnight, a nurse observes her calmly speaking to a hallucination of a family member in the room and picking at the tape around her peripheral intravenous catheter (PIV) causing the PIV to fall out twice. Her vital signs are temperature 36.7°C, pulse 82 beats per minute, respirations 12 breaths per minute, blood pressure 143/72 mm Hg, and pulse oximetry of 99% on room air. She is hypoactive, distractedly picks at her clothing and PIV, inattentive, and unable to say the day of the week or count months backward. Nursing asks for haloperidol for her delirium.

WHY YOU MIGHT THINK ANTIPSYCHOTICS FOR DELIRIUM ARE HELPFUL

Delirium is an acute change in cognition characterized by inattention typically associated with disorganized thinking and/or alteration in consciousness.¹ Delirium occurs in almost 25% of hospitalized patients, and clinicians have a limited pharmacologic armamentarium to treat it, given the absence of benefit for acetylcholinesterase inhibitors and concern that benzodiazepine medications cause/exacerbate delirium.^{2,4} Another treatment option is antipsychotic medications which block dopamine since dopamine excess is a key element in the neurotransmitter

pathophysiology of delirium.⁵ A small 2005 trial of haloperidol prophylaxis in hip fracture patients found that haloperidol reduced the overall severity and duration of delirium.⁶ Based in part on this trial, a 2007 Cochrane Systematic Review concluded that antipsychotics "may reduce severity and duration of delirium episodes and shorten length of hospital stay in hip surgery."⁷ Another study in 2010 demonstrated a 55% faster decline in total Delirium Rating Scale-Revised 98 (DRS-R-98) scores in patients on a general/medical-surgical floor receiving quetiapine treatment compared to those who received placebo.⁸

Studies show that 10%-30% of patients receive antipsychotics at some point during their hospitalization, usually for delirium.^{9,10} Variability in antipsychotic prescribing patterns not explained by patient characteristics suggests the local culture may influence antipsychotic prescribing practices when evidence from randomized controlled trials is sparse or conflicting.¹⁰

WHY ANTIPSYCHOTIC MEDICATIONS ARE NOT HELPFUL IN PATIENTS WITH DELIRIUM

While few studies have demonstrated positive effects of antipsychotics in delirium treatment, the overall evidence is not persuasive. The results of some studies have not been reproduced while only the positive effects rather than the adverse side effects of antipsychotic medications were highlighted in other articles. For instance, the 2005 hip fracture delirium prophylaxis trial found there was no difference in the incidence of delirium in patients on postoperative day one.⁷ Furthermore, the 2010 quetiapine study was underpowered for the primary outcome of lower DRS-R-98 scores. Importantly, there was no significant difference in severity of delirium between treatment (quetiapine) and placebo groups on days one, three, or 10.¹⁰ These studies show that antipsychotics were neither effective at preventing delirium or in reducing its severity compared to placebo. In 2016, a systemic review in the *Journal of the American Geriatric Society* included both of the above studies in addition to 17 other studies to assess the efficacy of antipsychotics in preventing and treating delirium. This analysis concluded that antipsychotics did not change the length of delirium or length of stay.¹¹ In addition, the absence of convincing evidence of antipsychotics benefits in postoperative delirium has led the American Geriatrics Society to recommend: "The prescribing practitioner should not prescribe antipsychotic... medications for the treatment of older adults with postoperative delirium who are not agitated and threatening substantial harm to self or others."¹²

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There is a paucity of data speaking directly to whether antipsychotics reduce patient distress. A recent randomized controlled study compared haloperidol, risperidone, and placebo for delirium treatment in palliative care and hospice patients. With treatment, the patients in the antipsychotic arms demonstrated slightly more severe delirium and a significantly higher incidence of extrapyramidal symptoms (EPS) than the patients receiving placebo.¹³

Side effects such as EPS, aspiration pneumonia, and arrhythmia are concerns when using antipsychotics for delirium treatment.¹⁴ A systematic review and meta-analysis found the difference in EPS incidence between patients treated for delirium with antipsychotics versus no intervention ranged from no difference to over 10%.¹¹ In addition to EPS, patients receiving antipsychotics in a cohort study were at increased risk for aspiration pneumonia compared to patients who did not receive antipsychotics (adjusted odds ratio = 1.5, 95% CI = 1.2-1.9).¹⁵ These serious side effects led the Food and Drug Administration (FDA) to issue a black box warning for antipsychotic treatment in dementia-related psychosis. Most importantly, the FDA warns that there is an increased risk of death.¹⁶

WHAT YOU SHOULD DO INSTEAD OF USING ANTIPSYCHOTICS

In the first-line management of delirium, hospitalists should address underlying modifiable contributions to the condition with attention to medications, pain, electrolytes, ischemia, infection, alcohol withdrawal, and reducing invasive lines. For example, two studies demonstrated a decrease in delirium severity and duration of palliative care in patients by treating delirium triggers, such as dehydration, electrolyte abnormalities, or infection, rather than using antipsychotics.^{13,17} Furthermore, hospitalists should review the medication list carefully and look for opportunities to deprescribe sedative/hypnotics and anticholinergics.

In addition, hospitalists should implement the core elements of the nursing delirium protocol from the Hospital Elder Life Program (<http://www.hospitalelderlifeprogram.org/>). The program focuses on orientation, hydration, mobility, sensory aids, and an environment conducive to sleep.¹⁸ When not representing an acute threat to the patient or staff, hospitalists should manage transient agitation from blood draws or vital sign checks by having staff members deescalate and re-approach the intervention later. While multicomponent nonpharmacologic interventions have more robust evidence for prevention of delirium than for treatment, they are low risk and still recommended for the patient with established delirium.^{19,20}

A delirious patient picking at PIVs should prompt clinicians to re-evaluate the need for continued PIV access. If still necessary, experience suggests that PIVs can be protected with a combination of well-taped gauze extending from wrist to shoulder with any attached tubing exiting out of reach behind the shoulder. Also “beneficial distraction” with a task or “activity vest” that consists of an apron with zips, ties, and buttons designed to provide harmless objects can occupy the patient’s hands.

WHEN IT IS HELPFUL TO USE ANTIPSYCHOTICS FOR DELIRIUM

The literature does not provide clear evidence for when the use of antipsychotics is warranted. Antipsychotics may have a role for patients who are having severe psychotic symptoms posing an acute safety risk. In those situations, the American Geriatrics Society recommends using the “lowest effective dose for the shortest possible duration to treat patients who are severely agitated or distressed, and are threatening substantial harm to self and/or others...only if behavioral interventions have failed or are not possible.”¹² In those patients who are having an acute myocardial infarction, consider atypical antipsychotics since haloperidol carries a small increased risk of mortality in that patient population.²¹

RECOMMENDATIONS

- Address underlying modifiable contributions to the delirium paying attention to medications, pain, electrolytes, ischemia, infection, alcohol withdrawal, and reducing invasive lines. Deprescribe sedative/hypnotic and anticholinergic medications.
- After addressing modifiable risk factors, attempt behavioral interventions for continuous problematic behaviors or symptoms of delirium.
- Reserve antipsychotics for cases where the patient poses an immediate danger of self-harm or harm to others. Treat for the shortest possible duration with the lowest effective dose of antipsychotic.

CONCLUSION

Returning to our case presentation, the hospitalist should not prescribe antipsychotic medications since there is no immediate risk of harm and antipsychotics do not treat hypoactive delirium. Delirium is a complex condition requiring a review of multifactorial causes. The hospitalist should investigate and address modifiable contributions. Furthermore, the hospitalist can make the PIV less accessible to deter the patient’s efforts to remove it and offer a distracting activity. Resolution of delirium, in all its forms, is still best achieved by treating the underlying etiology. The use of antipsychotics for treatment of patients with delirium in the absence of severe agitation and potential for self-harm or harm to others is not supported by the current body of literature as it is more likely to cause an adverse event than it is to improve the symptoms.

Do you think this is a low-value practice? Is this truly a “Thing We Do for No Reason?”™ Share what you do in your practice and join in the conversation online by retweeting it on Twitter (#TWDFNR) and liking it on Facebook. We invite you to propose ideas for other “Things We Do for No Reason”™ topics by emailing TWDFNR@hospitalmedicine.org.

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