Treating the neuropsychiatric symptoms of dementia: A case based approach

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INTRODUCTION

It is estimated that about 90% of older adults with dementia experience neuropsychiatric symptoms.[1] These symptoms include but are not limited to agitation, aggression, delusions, and hallucinations. Neuropsychiatric symptoms are often treated with antipsychotics. However, the use of antipsychotics in the dementia population is associated with an increased risk of death, mostly due to cerebrovascular events. All antipsychotic medications (both first generation and second generation) have a Black Box Warning for increased mortality in elderly patients with dementia-related psychosis.

The Centers of Medicare and Medicaid Services (CMS) have taken steps to help reduce this risk with its initiative to decrease the rate of antipsychotic use for inappropriate indications by 15% in every nursing facility.[2] In September 2013, the American Psychiatric Association (APA) targeted five ways to decrease the inappropriate use of antipsychotics as first-line treatment for those with neuropsychiatric and behavioral symptoms associated with dementia.[3] APA specifically recommends non-pharmacologic interventions as first line therapy. The initiatives to decrease the use of antipsychotics by both CMS and APA highlight the importance of this health care issue in the elderly population.

THE CASE OF MR. SMITH

Mr. Smith is a 76 year old Caucasian male who was admitted to the psychiatric hospital from a local emergency room on Day 1 with a chief complaint of depression with suicidal ideation (SI) and aggression. He stated he was confused and wanted to kill himself by slitting his wrist. He presents with paranoia as he thinks someone is trying to kill him. Prior to hospitalization, he resided at a Nursing Home Center for one year and prior to the facility he lived with his wife in their private home. Shortly after entering the rehabilitation and nursing center, he began showing signs of aggression such as throwing a thermometer and grabbing another resident's arm. These behaviors were not characteristic of his usual demeanor while residing in the community with his wife.

Mr. Smith denies tobacco, alcohol, and illicit drug use. His past medical history includes multi-infarct dementia (dates and number of events unknown), mood disorder not otherwise specified, pernicious anemia, multiple subdural hematomas (dates unknown), acid reflux with a history of appendectomy, hyperlipidemia, coronary artery disease with a history of CABG, and hypertension. He also presented to the hospital with an acute community-acquired urinary tract infection (UTI), which was diagnosed at the emergency room and an antibiotic regimen was started. As for Mr. Smith's aggression during his hospital stay, he was emotionally labile on admission, yelling out for "hot coffee" and his wife. He also became physically aggressive towards staff, kicking and hitting nurses on his second day of admission. This aggressive behavior deescalated by day 5. He also experienced episodes of drowsiness and was noted to be sleeping through meals, mostly lunch and dinner. While in the hospital Mr. Smith began having periodic episodes of back pain, with a pain score of eight out of ten on two occurrences. He also experienced a ten out of ten pain attributed to emotional stressors, specifically missing his wife.

Patient reported Allergies: NSAIDs, cefuroxime, ciprofloxacin, haloperidol, hydromorphone, phenytoin, quetiapine and paroxetine

Table 1. Labs

Labs Day 1		Urinanalysis	Vitals Day 2
Glucose: 104	HGB: 11.5	Positive (culture	Temp: 98.2
Na: 141	HCT: 34.7	unknown)	Pulse Ox: 95
Cl: 103	MCV: 89	Day 4: Negative	RR: 20
K: 3.8	PLT: 236		BP: 114/65
CO_2: 28	WBC: 5.4		HR: 72
Ca: 9.5	AST: 14		Weight: 85.7 kg
BUN: 20	ALT:13		Hours of Sleep: 5.5
SCr: 0.9			
CrCL: 84.6			

Table 2. Medications

Home Medications	Daily Hospital Medications	PRN Hospital Medications
Amlodipine 10 mg PO QDay	Sulfamethoxazole/Trimethoprim DS 1 tab PO BID x 7 days	Lorazepam 0.5 mg PO Q6H PRN
Clonazepam 0.5 mg PO TID	Saccharomyces boulardii lyo 1 cap BID x 7 days	Trazodone 50 mg PO QHS PRN
Divalproex sodium 125 mg PO QHS	Cyanocobalamin 100 mcg PO QDay	Acetaminophen 650 mg PO Q4H PRN
Divalproex sodium 250 mg PO BID	Amlodipine 10 mg PO QDay	MgOH 30 ml PO QDay PRN (none)
Omeprazole 200 mg PO QDay	Famotidine 20 mg PO QDay	MgOH/AlOH 30 ml PO Q1H PRN (none)
Olanzapine 2.5 mg PO QDay	Pravastatin 20 mg PO QHS	Olanzapine 5 mg PO Q6H PRN (none)
Sulfamethoxazole/Trimethoprim DS 1 tab PO BID	Multivitamin 1 tab PO QDay	
Lorazepam 0.5 mg PO TID PRN	Folic acid 1 mg PO QDay	
	Olanzapine 2.5 mg PO QHS	
	Zolpidem 10 mg PO QHS	
	Clonazepam 0.25mg PO QDay	

DISCUSSION: ASSESSMENT OF AGGRESSION AND AGITATION

Disease Related Problems and Environmental Factors

Mr. Smith's agitation and aggression can be described as a symptom secondary to multi-infarct dementia. His level of agitation and aggression is mild to moderate as he is not harming himself or harming others. Mr. Smith did pose a threat to staff and himself at the beginning of his hospital stay showing physical aggression Mr. Smith's acute change in behavior can be explained by several triggers. The duration of his mental status change is unknown, but his wife reported he has been declining since he was living with her in the community. This impairment led to his placement in the nursing home. The recent change in environment, UTI, and acute pain episodes can be contributing to his neuropsychiatric symptoms, including agitation and aggression, as well as altered mental status. Changing environments from a familiar home setting with his wife to a skilled nursing facility filled with strangers and different daily activities has most likely negatively impacted his quality of life, resulting in changes in behavior. During his time at the nursing facility, Mr. Smith developed a complicated community acquired UTI that was diagnosed at the ER. In elderly patients with UTIs, a change in mental status is commonly seen as a presenting symptom and usually resolves with the treatment of the infection. For Mr. Smith, the severity of his behaviors diminished with the resolution of his UTI by day 5.

Another contributing factor to his agitation is his sporadic episodes of back pain. He denied pain on admission but later needed as needed doses of acetaminophen for complaints of pain. The first dose was given for "all-over aching pain" and for the other two occasions (day 5 and day 8) of acetaminophen use, Mr. Smith experienced severe back pain with an eight out of ten pain score. Nursing also noted that Mr. Smith experienced a ten out of ten emotional pain due to heartache and missing his wife. Although it is unclear if the medication relieved his pain, he was observed to be more at ease after the doses of pain medication. Thus, his uncontrolled back pain and emotional discomfort could have played a role in his development of agitation and aggression.

Medication Related Problems

Mr. Smith's previous treatment with olanzapine an indication of dementia, thus not in compliance with the FDA Black Box Warning as well as both CMS's and APA's recommendations for appropriate antipsychotic use. Using olanzapine chronically for the treatment of dementia places Mr. Smith at an increased risk for preventable death and other approaches should be utilized prior to antipsychotic therapy. The data for the use of this medication class in patients with dementia are for symptomatic management not treatment of dementia. Therefore, the long term use of olanzapine for the treatment of his dementia is inappropriate, highlighting the importance of documenting specific indications for antipsychotics in the dementia population.

Elderly patients are at an even greater risk for anticholinergic side effects. These effects include dry mucous membranes, constipation, dehydration, and possible delirium; he did not complain of any of these side effects. Currently, Mr. Smith is taking three different anticholinergic medications: olanzapine, trazodone, and famotidine. His anticholinergic burden score is a 3 according to the Anticholinergic Risk Scale, with olanzapine having the greatest burden. Those with a score of 3 or more are at the highest risk for anticholinergic adverse events.[4] He does not complain of thirst or dry mouth. However, he may already be

experiencing dehydration with a BUN/SCr of 22. These medications also place Mr. Smith at a greater risk for falls, self-harm and worsening agitation due to constipation discomfort, dizziness, confusion, impaired vision, and delirium. There are other viable alternatives to these anticholinergic agents that do not pose as great a risk, for example the use of calcium carbonate or a proton pump inhibitor for GERD and sleep hygiene techniques for insomnia instead of olanzapine.

In addition to the anticholinergic medications increasing Mr. Smith's risk of falls, he is also taking clonazepam, as needed lorazepam, and zolpidem, which are all listed in The Beers Criteria for Inappropriate Medications for Older Adults.[5] The clonazepam is a home medication, which he was taking for an unknown duration of time. Older adults are particularly sensitive to benzodiazepine and non-benzodiazepine hypnotics, especially longer-acting agents like clonazepam, because they have a decreased metabolism of the medications resulting in accumulation. Mr. Smith's increased exposure to chronic long-acting clonazepam puts him at a high risk for cognitive impairment, delirium, falls, fractures, and behavioral disinhibition. Mr. Smith's subdermal hematoma head wounds show evidence of a past history of falls, making him more likely to fall again. Therefore, a conservative approach should be taken with benzodiazepine therapy and a shorter acting agent may be more appropriate, if needed at all.

TREATMENT APPROACH AND PLAN

Non-Pharmacologic Options

The first line therapy for neuropsychiatric symptoms in patients with dementia is non-pharmacologic modalities as recommended by APA and CMS. In the unit where Mr. Smith resides, the available interventions include music therapy, recreational therapy, purposeful activities, and vibroacoustic therapy. These non-pharmacologic modalities should be utilized as interventions during agitated episodes and prior to triggers of agitation as well as part of his daily care. Environmental modifications, such as large clocks and a regular daily routine, should be utilized to prevent further escalation of neuropsychiatric symptoms due to an abrupt change in environment as he is now in a hospital setting. To address his emotional pain of missing his wife, a large picture of her should be placed in his room to help console and redirect him during these episodes.

Pharmacologic Options

First, it is important to address Mr. Smith's primary agitation-trigger: his episodic back pain. Mr. Smith's allergy or intolerance of NSAIDs limits the options for pain management. As previous use of acetaminophen eased Mr. Smith's pain, prophylactic dosing of acetaminophen before possible painful activities such as physical therapy would be appropriate. This medication poses potential hepatic toxicity, thus the total daily amount should not exceed 3 grams. Mr. Smith does not have an underlying liver disorder and his liver enzymes are currently within normal limits.

The available medications that have shown some efficacy in the treatment of agitation/aggression in dementia include selective-serotonin reuptake inhibitors, cholinesterase inhibitors, second generation antipsychotics, and mood stabilizers. Valproate and carbamazepine are the mood stabilizers that have been studied for the treatment of these target symptoms. The use of valproate is not recommended, due to lack of efficacy and significantly higher adverse drug reactions (ADRs). There is also currently not enough data to support the use of carbamazepine due to mixed study results, making mood stabilizers a last line treatment. The cholinesterase inhibitors, donepezil and galantamine, may provide some benefit as evidence shows small improvements in the target symptoms, but clinical significance is unknown. Mr. Smith does not have a compelling indication for cholinesterase inhibitors because he has vascular dementia not Alzheimer's dementia.

Low-dose risperidone, olanzapine and aripiprazole are the only antipsychotics that have shown benefit in the treatment of neuropsychiatric symptoms. Risperidone (1mg/dose) improved the overall behavioral and psychiatric symptoms of dementia and olanzapine (5-10 mg/dose) improved aggression/agitation, hallucinations, and delusions.[1] Aripiprazole (5-15 mg/dose) improved overall neuropsychiatric symptoms in those with Alzheimer's type dementia.[6] During his olanzapine therapy at the nursing home there was no documentation of adverse effects. However, during his hospital stay he is experiencing episodes of drowsiness possibly due to olanzapine therapy causing him to sleep through meals, which is negatively impacting his nutritional status. As mentioned previously, the use of antipsychotics in patients with dementia poses an increased risk of cerebrovascular-related mortality. Mr. Smith has multiple risk factors that increase his likelihood of cerebrovascular accidents (CVA),including age greater than 75, gender, hyperlipidemia, hypertension, and a history of stroke(s).Therefore, the use of antipsychotics are not an appropriate choice for him as he is already at an increased

risk of developing a CVA and antipsychotics can further increase this risk.

Although they are well-tolerated, antidepressants in general do not appear to be very effective in treating neuropsychiatric symptoms. Citalopram is the only antidepressant that has shown to be beneficial in the treatment of neuropsychiatric symptoms.[7] However, citalopram can potentially increase the risk of myocardial infarction (MI) and QTc prolongation.[8] According to the Framingham risk assessment, Mr. Smith has a 20% or greater risk of having an MI in the next 10 years as he already has coronary artery disease and has had symptomatic carotid artery disease resulting in multiple strokes. However, the risk of citalopram appears to be lower than other antidepressants such as paroxetine.[8] Furthermore, in a recent study comparing citalopram and risperidone, citalopram 20 mg daily had similar efficacy in reducing neuropsychiatric symptoms as risperidone and had a significantly lower side effect burden with no incidence of MI or QTc prolongation.[9] The risk of MI with citalopram is dose dependent and would not likely occur at a lower dose of 20 mg. Mr. Smith's is also at a high risk of having a recurrent stroke. The incidence of antipsychotics increasing risk of a cerebrovascular events is much higher than citalopram's risk of MIs.[1,9] Therefore, citalopram 20 mg daily is both safe and effective and would be a viable option for Mr. Smith, as he also has the compelling-indication of depression.

Treatment Plan

Non-pharmacologic therapy will be initiated as first-line. Music therapy, the Somatron chair, and/or purposeful activities should be used at the onset of unknown agitation and in anticipation of agitation triggers. Daily routine for Mr. Smith including meals at the same time and orienting environmental modifications (e.g., large clock, wife's photo in room, name on door and other labeled areas) to help decrease agitation due to environmental changes should be continued. The standing order of olanzapine should be discontinued.

After the initiation of these non-pharmacologic interventions, Mr. Smith's neuropsychiatric symptoms are expected to improve. However, if Mr. Smith continues to show signs of uncontrolled agitation/aggression, citalopram 20 mg daily should be initiated. The full benefit of citalopram is expected to occur after at least two weeks of therapy. Therefore, olanzapine 5 mg every 6 hours as needed will be available for incidences of severe agitation, which is defined as physically harming himself and/or others. Mr. Smith should be monitored for the resolution of agitation, aggressive behavior, depression and changes in mood. He should also be monitored for the adverse effects of confusion, gastrointestinal upset, sedation, and chest pain.

REFERENCES

1. Sink KM, Holden KF, Yaffe K. Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence. JAMA. 2005;293(5):596-608. DOI: 10.1001/jama.293.5.596. PubMed PMID: 15687315.
2. Nursing home initiative on behavioral health & antipsychotic medications [Internet]. Baltimore, MD: Centers of Medicare and Medicaid Services; 2012; cited Feb 2013. Available from: http://www.youtube.com/watch?v=U1_rpOobwbM&list=UUhHTRPxz8awulGaTMh3SAkA&index=3&feature=plcp.
3. Choosing Wisely [Internet]. Arlington, VA:The American Psychiatric Association; 2013; cited Sept 2013. Available from: http://www.psychiatry.org/choosingwisely
4. Rudolph JL, Salow MJ, Angelini MC, McGlinchey RE. The anticholinergic risk scale and anticholinergic adverse effects in older persons. Arch Intern Med. 2008;168(5):508-13. DOI: 10.1001/archinternmed.2007.106. PubMed PMID: 18332297.
5. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2012;60(4):616-31. DOI: 10.1111/j.1532-5415.2012.03923.x. PubMed PMID: 22376048.
6. De Deyn PP, Drenth AFJ, Kremer BP, Oude Voshaar RC, Van Dam D. Aripiprazole in the treatment of Alzheimer's disease. Expert Opin Pharmacother. 2013;14(4):459-74. DOI: 10.1517/14656566.2013.764989. PubMed PMID: 23350964.
7. Pollock BG, Mulsant BH, Rosen J, Sweet RA, Mazumdar S, Bharucha A, et al. Comparison of citalopram, perphenazine, and placebo for the acute treatment of psychosis and behavioral disturbances in hospitalized, demented patients. Am J Psychiatry. 2002;159(3):460-5. PubMed PMID: 11870012.
8. FDA Drug Safety Communication. Revised recommendations for Celexa (citalopram hydrobromide) related to a potential risk of abnormal heart rhythms with high doses. March 28th 2012. Accessed March 2014.
9. Pollock BG, Mulsant BH, Rosen J, Mazumdar S, Blakesley RE, Houck PR, et al. A double-blind comparison of citalopram and risperidone for the treatment of behavioral and psychotic symptoms associated with dementia. Am J Geriatr Psychiatry. 2007;15(11):942-52. DOI: 10.1097/JGP.0b013e3180cc1ff5. PubMed PMID: 17846102.

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