Delirium: Evidence-Based Practice for 2019

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This is to acknowledge that Sarah A. Wingfield, M.D. has disclosed that she does not have any financial interests or other relationships with commercial concerns related directly or indirectly to this program. Dr. Wingfield will be discussing off-label uses in her presentation.

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Dr. Wingfield has been a faculty member at UT Southwestern since 2016. She founded and directs the UTSW Perioperative Optimization of Senior Health (POSH) program which is an interprofessional perioperative bridge program designed to improve the outcomes of high risk older adults undergoing elective surgical procedures at Clements University Hospital (CUH) and Zale Lipshy University Hospital (Zale). She also founded and directs the inpatient geriatrics consult service at CUH and Zale. She is involved in medical education as the director of the ambulatory geriatrics rotation for internal medicine interns and as a UT Southwestern Colleges mentor. Her particular interests include medical education, acute care geriatrics, perioperative care and complex surgical decision making in older adults.

Purpose and Overview:
The purpose of this lecture is to review delirium risk assessment, prevention, identification and management.

Educational Objectives:
At the conclusion of this lecture, listeners will be able to:

1) Recognize the morbidity and mortality associated with delirium
2) Discuss predisposing and precipitating factors for delirium and use these factors to assess patients' delirium risk
3) List evidence-based delirium prevention measures
4) Perform a rapid screening test for delirium in hospitalized older adults
5) Discuss the literature regarding the management of delirium

Background

Roughly 10,000 baby boomers have been turning 65 every day since January 1, 2011 and this trend will continue until 2030.[1] In 2016, there were 55.7 million adults over the age of 65 in the United States (17.2% of the population) and by 2050, there will be 104.6 million older adults (26.9% of the population).[2]

Older adults make up an even more significant proportion of patients who are admitted to the hospital. In 2010, older adults accounted for 38.7% of hospital discharges.[3] When geriatric patients are admitted to the hospital, they have unique vulnerabilities, referred to as "Hazards of Hospitalization"[4]. Delirium is one of these hazards. Just as serious as the entities of acute kidney failure and acute heart failure, delirium can be thought of as "acute brain failure."[5] The DSM-5 criteria define delirium as an acute disturbance of attention and cognition which tends to fluctuate over the course of a day.[6] It can lead to increased mortality, increased length of stay, pressure ulcers, falls and cognitive and functional decline.[5] Delirium costs the United States more than $164 billion annually[7] and can affect as many as 50% of older adults admitted to the hospital with the highest incidence in ICU, postoperative and palliative care settings.[5]

Delirium is prevalent and is associated with significant adverse outcomes. It is also preventable in 30-40% of cases.[8,9] National movements for quality in the care of geriatric patients have recognized the importance of delirium prevention as a quality measure including the American College of Surgeons National Surgical Quality Improvement Project (ACS NSQIP) Coalition for Quality in Geriatric Surgery (CQGS). The John A. Hartford Foundation and the Institute for Health Innovation (IHI) have launched the Age Friendly Health Systems Initiative (Figure 1) which seeks to create health systems that provide high quality care to geriatric patients by focusing on the 4Ms – Mobility, Medications, Mentation and What Matters.[10] Preventing and managing delirium addresses the mentation domain and also addresses what matters to patients and their families.

The increasing population of older adults within US hospitals who are at risk of developing delirium, a costly and morbid but preventable condition, creates an imperative for all providers in all specialties to be facile in delirium risk assessment, prevention, diagnosis and management.

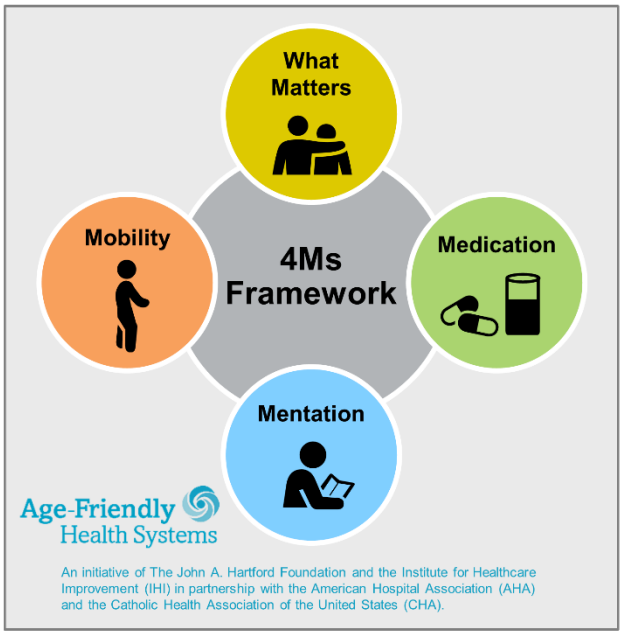

Figure 1: Age Friendly Health Systems

Delirium Risk Assessment

Delirium risk assessment is essential to help guide delirium prevention efforts. Delirium is a geriatric syndrome, which is a term used to describe a clinical entity with multiple causation and unified manifestation.[11] These multiple causative elements can be split into predisposing

factors and precipitating factors.[6] Predisposing factors are intrinsic to the patient and while they may be modified and addressed, they comprise the patient's baseline vulnerability to developing delirium. Precipitating factors are insults which may function independently or in combination to cause an episode of delirium. A patient with more predisposing and precipitating factors is at higher risk of developing delirium. Table 1 lists both predisposing and precipitating factors for delirium.

Table 1. Predisposing and Precipitating Factors for Delirium[5]

Predisposing Factors	Precipitating Factors
Dementia/Cognitive Impairment	Drugs (polypharmacy, psychoactive drugs, sedatives/hypnotics)
History of Delirium	Use of physical restraints
Functional Impairment	Use of a bladder catheter ("the one point restraint")
Sensory Impairment (Vision and/or Hearing)	Electrolyte Imbalances (Increased BUN:Cr ratio, abnormal Na, K, or glucose, metabolic acidosis)
Comorbidity or Severity of Illness	Infection
History of TIA or Stroke	Iatrogenic Events
Alcohol Misuse	Surgery
Older Age	Trauma
	Urgent admission

If a patient has several predisposing factors, this indicates high baseline vulnerability to delirium. For these patients, it may take a relatively small precipitating factor (ex. one dose of a sedative/hypnotic drug) to cause delirium. Alternatively, if a patient has few predisposing factors, it will take a very substantial insult to precipitate delirium.

When it is anticipated that an older adult will encounter an insult which may precipitate delirium (ex. hospital admission or surgery), it is essential to assess that patient's risk of developing delirium. Each patient should be evaluated for any potential predisposing factors which may make them more vulnerable to developing delirium. This will also help to prompt family education about the condition and initiation of multicomponent interventions for delirium prevention.

Delirium Prevention

Delirium is costly for the health care system and is associated with multiple adverse outcomes for older patients. Delirium is often incorrectly described as reversible and transient. In fact, some cases of delirium last for weeks or months[12] and there is evidence that delirium can have long term impacts on cognition.[13,14] A nested cohort study of 263 patients with Alzheimer's disease (AD) showed that 56% of patients with AD developed delirium during hospitalization and that patients who developed delirium experienced cognitive decline at twice the rate in the year following hospitalization compared to patients who did not develop

delirium after adjusting for severity of dementia, comorbidity and demographic characteristics.[14] This increased rate of cognitive decline lasted as long as 5 years after the hospitalization.

Given the severe consequences of delirium, it is essential that health care providers initiate interventions to prevent delirium in high risk patients. Delirium is multifactorial and therefore requires multicomponent interventions for prevention.

Any delirium prevention strategy begins with patient and family education. Once a patient is identified as being at high risk for delirium, this should be discussed with the patient and family. As delirium is associated with adverse outcomes, the risk of delirium should be routinely discussed as part of the informed consent process for any surgical procedure. The family can and should be encouraged to play an active role in delirium prevention. Family members should remain at bedside to offer reassurance and orientation to their hospitalized loved ones.

There are several evidence-based models for delirium prevention. One of the original models is the Hospital Elder Life Program (HELP) developed by Inouye in 1993.[8] This program provides targeted, protocol-driven interventions aimed at risk factors for delirium. Intervention protocols focus on providing orientation and therapeutic, cognitively stimulating activities for patients with cognitive impairment, implementation of a non-pharmacologic sleep protocol, encouraging mobility (ambulation or range of motion exercises in those who are non-ambulatory) three times per day, limiting tethers, addressing visual and hearing impairment and prevention of dehydration (Figure 2). In a controlled clinical trial using prospective individual matching to compare patients admitted to an intervention unit and two usual care units at a teaching hospital, the delirium rate was 15.0% in patients admitted to the usual care units and 9.9% in patients admitted to the intervention unit (matched odds ratio, 0.60; 95% CI 0.39-0.92).[8] HELP is now instituted in over 200 hospitals worldwide and a recent systematic review and meta-analysis of 14 studies demonstrated significant reductions in delirium incidence (OR 0.47, 95% CI 0.37-0.59), reduction in falls rate of 42% in three studies and 9 studies on cost savings revealed that the program saved $1600-3800 per patient in hospital costs and $16000 per person year in long term care costs in the year after an incident delirium.[15]

TABLE 1. RISK FACTORS FOR DELIRIUM AND INTERVENTION PROTOCOLS.

TARGETED RISK FACTOR AND ELIGIBLE PATIENTS	STANDARDIZED INTERVENTION PROTOCOLS	TARGETED OUTCOME FOR REASSESSMENT
Cognitive impairment*	Orientation protocol: board with names of care-team members and day's schedule; communication to reorient to surroundings	Change in orientation score
All patients, protocol once daily; patients with base-line MMSE score of <20 or orientation score of <8, protocol three times daily	Therapeutic-activities protocol: cognitively stimulating activities three times daily (e.g., discussion of current events, structured reminiscence, or word games)	
Sleep deprivation	Nonpharmacologic sleep protocol: at bedtime, warm drink (milk or herbal tea), relaxation tapes or music, and back massage	Change in rate of use of sedative drug for sleep†
All patients; need for protocol assessed once daily	Sleep-enhancement protocol: unit-wide noise-reduction strategies (e.g., silent pill crushers, vibrating beepers, and quiet hallways) and schedule adjustments to allow sleep (e.g., rescheduling of medications and procedures)	
Immobility	Early-mobilization protocol: ambulation or active range-of-motion exercises three times daily; minimal use of immobilizing equipment (e.g., bladder catheters or physical restraints)	Change in Activities of Daily Living score
All patients; ambulation whenever possible, and range-of-motion exercises when patients chronically non-ambulatory, bed or wheelchair bound, immobilized (e.g., because of an extremity fracture or deep venous thrombosis), or when prescribed bed rest		
Visual impairment	Vision protocol: visual aids (e.g., glasses or magnifying lenses) and adaptive equipment (e.g., large illuminated telephone keypads, large-print books, and fluorescent tape on call bell), with daily reinforcement of their use	Early correction of vision, ≤48 hr after admission
Patients with <20/70 visual acuity on binocular near-vision testing		
Hearing impairment	Hearing protocol: portable amplifying devices, earwax disimpaction, and special communication techniques, with daily reinforcement of these adaptations	Change in Whisper Test score
Patients hearing ≤6 of 12 whispers on Whisper Test		
Dehydration	Dehydration protocol: early recognition of dehydration and volume repletion (i.e., encouragement of oral intake of fluids)	Change in ratio of blood urea nitrogen to creatinine
Patients with ratio of blood urea nitrogen to creatinine≥18, screened for protocol by geriatric nurse-specialist		

*The orientation score consisted of results on the first 10 items on the Mini–Mental State Examination (MMSE).

†Sedative drugs included standard hypnotic agents, benzodiazepines, and antihistamines, used as needed for sleep.

Figure 2: HELP Non-Pharmacologic Delirium Prevention Protocol [8]

One study looked at whether a modified HELP intervention (mHELP) would reduce postoperative delirium and length of stay in older adults undergoing elective abdominal surgery.[16] The study was a cluster randomized controlled trial and 377 of 577 eligible patients were enrolled. The mHELP intervention consisted of 3 protocols which were administered by a nurse on a daily basis – orienting communication, oral and nutritional assistance and early mobilization. Patients in the intervention group received all 3 protocols daily and the control group received usual care. The study found that the group receiving the mHELP intervention had a 0.44 relative risk of delirium compared to the control group (95% CI 0.23-0.83, P = 0.008) and that those in the mHELP group had a LOS which was 2 days shorter than the control group (P=0.04).

Non-pharmacologic, multicomponent interventions have also been shown to be effective in preventing delirium in the intensive care unit (ICU). The ABCDEF Bundle (**A**ssess, prevent, and manage pain; **B**oth spontaneous awakening and breathing trials; **C**hoice of analgesia and sedation; **D**elirium assess, prevent, and manage; **E**arly mobility and exercise; **F**amily engagement/empowerment) was created by the ICU Liberation Collaborative to facilitate implementation of the Society of Critical Care Medicine Pain, Agitation and Delirium (PAD) guidelines. This bundle was studied in a prospective, multicenter cohort study which included over 15,000 patients in 68 ICUs nationally.[17] Patients who received complete bundle

performance were less likely to develop delirium (adjusted OR 0.60, 95% CI 0.49-0.72, P<0.0001), were more likely to be discharged from the ICU and they were less likely to die or be discharged to a facility other than home.

While not every practice location will have the resources to implement these evidence-based programs in their entirety, individual clinicians should work with their interprofessional teammates to implement the components of these models for their patients who are at high risk of delirium. Clinicians should also advocate for implementation of delirium prevention strategies at a health system level to improve care for all hospitalized older adults.

There are many high risk medications which increase the risk of delirium in older adults. A list of medications which increase the risk of delirium is provided in Table 2. Table 3 provides a list of common medications with strong anticholinergic properties. Clinicians should endeavor to avoid these medications when possible in older adults who are admitted to the hospital. However, it is important to recognize that some of these medications are associated with withdrawal syndromes. Medications which can cause withdrawal should not be discontinued abruptly because withdrawal of psychoactive medications can precipitate or worsen delirium.

Table 2. Medications which may induce or worsen delirium[18]

Medications which may induce or worsen delirium
Anticholinergics (see table 3)
Antipsychotics
Benzodiazepines
Corticosteroids
H2 receptor antagonists (cimetidine, famotidine, nizatidine, ranitidine)
Meperidine
Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics (eszopiclone, zaleplon, zolpidem)

Table 3. Medications with strong anticholinergic properties.[18] Adapted from 2019 AGS Beers Criteria®

Class	Common Medications in the Class
Antidepressants	Amitriptyline, Doxepin, Nortriptyline, Paroxetine
Antiemetics	Prochlorperazine, Promethazine
Antihistamines (1st Generation)	Diphenhydramine, Hydroxyzine, Meclizine, Dicyclomine, Hycosamine
Antimuscarinics	Oxybutynin, Solifenacin, Tolterodine, Trospium
Antipsychotics	Olanzapine
Antispasmodics	Atropine, Scopolamine
Skeletal Muscle Relaxants	Cyclobenzaprine

Delirium Identification

Not all cases of delirium can be prevented. Close monitoring and use of an objective screening tool is required to identify cases of delirium. Delirium is very challenging to recognize. It can be difficult to ascertain a patient's cognitive baseline, especially when no collateral information is available. By definition, delirium waxes and wanes over the course of a day. Delirium is a clinical diagnosis and the presentation often varies. Clinical features include acute onset and fluctuating course, inattention, impaired consciousness, disturbance of cognition, disturbances in the sleep-wake cycle, hallucinations/illusions, delusions, psychomotor disturbances, inappropriate behavior and emotional lability.[5]

Patients may be classified as having hypoactive, hyperactive or mixed delirium based on their clinical symptoms. Patients with hypoactive delirium are sedated and lethargic. Those with hyperactive delirium are restless, agitated and may have hallucinations or delusions. Patients with mixed delirium have features of both hyperactive and hypoactive delirium. Hyperactive delirium is the most easily recognizable form but hypoactive delirium has been associated with worse outcomes including higher rates of mortality.[19]

The gold standard for diagnosis of delirium is the DSM-5 criteria.[6] However, there are validated screening tools which can also be used at the bedside. The most commonly used screening tool is the Confusion Assessment Method (CAM).[20] The CAM consists of 4 criteria: (1) Acute onset and fluctuating course, (2) inattention, (3) disorganized thinking and (4) altered level of consciousness. In order to screen positive for delirium, patients must meet criteria (1) and (2) and either (3) or (4). It has a sensitivity of 94% and a specificity of 89% with high interrater reliability. There have been multiple iterations of the CAM. The 3D-CAM is a 3-minute screening test for delirium. In a prospective validation study including 201 participants with a mean age of 84 years, the 3D-CAM was found to have a sensitivity of 96% and specificity of 86% in patients with dementia and a sensitivity of 93% and specificity of 96% in patients without dementia.[21] An overview of the 3D-CAM assessment is shown in Figure 3.

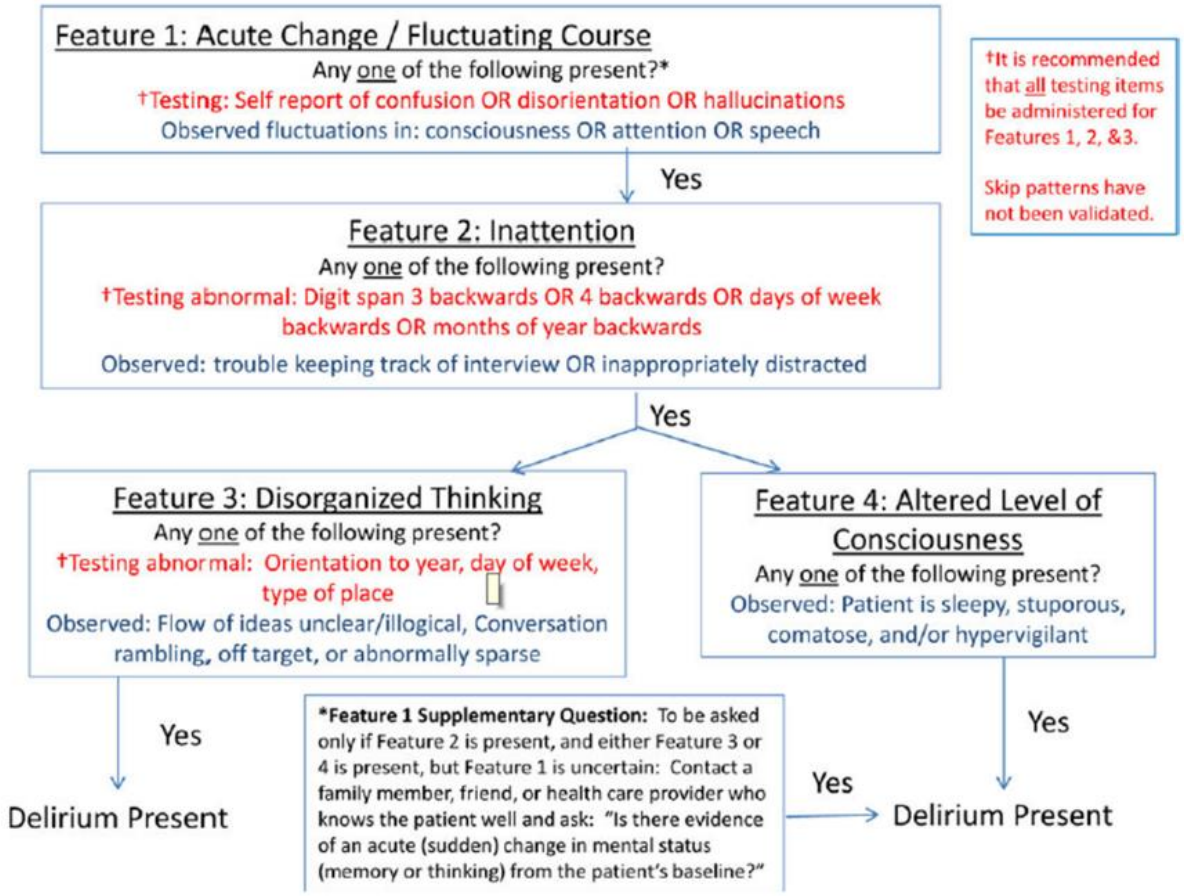

Figure 3: 3D CAM Diagnostic Algorithm[21]

Analyzing data from the 3D-CAM validation study, the single mental status test item with the best test characteristics was "months of the year backwards" with a sensitivity of 83% and a specificity of 69%.[22] The 2 items with the best test characteristics were "months of the year backwards" and "what is the day of the week?" with a sensitivity of 93% and a specificity of 64%. There is ongoing research to determine even more rapid methods to diagnose delirium.

The CAM-ICU was developed to assess delirium in patients who are intubated and unable to verbally respond to mental status questions.[23] The CAM-ICU uses the same basic CAM framework but provides specific examples of how to test each key feature of delirium in a patient who is unable to speak. For example, to test inattention, the examiner asks the patient to "squeeze my hand every time you hear me say the letter A" and then reads out "SAVEHAART". The patient is considered inattentive if they squeeze on a letter other than A or if they do not squeeze on an A. Altered level of consciousness is assessed using a Richmond Agitation Sedation Scale (RASS) score of anything other than 0 (alert and calm) and Disorganized thinking is assessed using a series of yes or no questions. For example, "Squeeze my hand for yes – will a stone float on water?"

Every hospitalized patient should be assessed for delirium at least once a day. It is important not to "make excuses" for patients. For example, if items on the screening test are positive, it is important to record them as such instead of attempting to explain away the

abnormalities by stating that the patient is in the hospital, sick, elderly, just received pain medication or did not sleep the night before the evaluation. Remember that sleep disturbance is an abnormality associated with delirium.

It is often very challenging to distinguish cognitive manifestations of delirium in patients who have an underlying dementia. In this situation, it is very important to have collateral information from informants who are familiar with the patient's baseline mental status. Given that delirium has multiple adverse outcomes associated with it, in cases where the diagnosis is questionable because of lack of collateral information or lethargy to the point where the patient is unable to complete an interview, delirium should be assumed until proven otherwise.[5]

Management

The first step in managing the delirious patient is to identify and treat underlying medical causes. Common precipitating factors for delirium are electrolyte imbalances, medications, impaired oxygenation, pain, sleep deprivation and infection.[5] Other medical emergencies may also present as delirium. For example, in an older adult, pulmonary embolism may present as delirium rather than with shortness of breath or chest pain. Overall, the laboratory and imaging evaluation should be targeted based on the clinical assessment. Neuroimaging, lumbar puncture and electroencephalography are not required in all patients with delirium. Neuroimaging is indicated for older adults with new focal neurologic deficits, patients who have had a fall or head trauma, those with decreased consciousness for unknown reasons or those with fever and concern for encephalitis.[24] If meningitis, encephalitis or subarachnoid hemorrhage is suspected, a lumbar puncture should be performed. Electroencephalography should be performed if there is concern for occult seizures.

It is important to remember that not all cases of delirium are rapidly reversible after the underlying cause is treated. One systematic review found that up to 45% of patients who developed delirium were still delirious at hospital discharge.[12] Patients may be persistently delirious for weeks or months after their initial episode. The same systematic review found that the proportion of patients who were persistently delirious at 1, 3 and 6 months after their initial episode was 33%, 26% and 21% respectively. This essential fact, along with the waxing and waning nature of delirium, must be explained to family members. Families often think that once their loved one appears to be less confused, the episode of delirium is over and then they become extremely distressed when the symptoms return later the same day. It is also important to remember that not all episodes of delirium are rapidly reversible as a member of the treatment team. There is no "silver bullet" which will completely resolve delirium. Once it occurs, careful attention must be paid to non-pharmacologic measures of treatment to allow the brain to heal.

<u>Non-pharmacologic management</u>

Multicomponent non-pharmacologic measures are the mainstay of treatment for delirium.[25] There are several predisposing and precipitating factors which can be addressed non-pharmacologically. Also, non-pharmacologic measures can prevent complications of delirium and decrease agitation in patients with hyperactive delirium. See table 4 for a list of non-pharmacologic measures used to manage delirium.

Implementation of non-pharmacologic measures for the management of delirium should be performed by an interprofessional team. No single healthcare team member is able to be at the bedside 24 hours per day to implement all of these interventions. Each team member can play a role in addressing the patient's delirium. For example, the nursing assistant helps the patient to eat breakfast, the nurse encourages the patient to take a drink of water each time she is in the room and engages the patient in cognitively stimulating conversation, the physical therapist gets the patient out of bed to walk in the hallway and the physician prescribes a suppository after the nurse notes that the patient has not had a bowel movement in three days.

Table 4. Non-pharmacologic measures of delirium management

Family Education – Encourage family to remain at bedside, bring familiar and reassuring objects from home	Avoid tethers (ex. telemetry, Foley catheters, continuous pulse oximetry, etc) and restraints
Frequent reorientation- Keep white boards up to date, make sure clocks in the room are working	Discontinue high risk medications
Encourage an adequate sleep-wake cycle – Keep lights on and shades up during the day, discourage daytime napping, lights off and TV off at night to facilitate sleep, avoid night time interruptions	Avoid and address constipation and urinary retention
Encourage oral intake of food and fluids	Address sensory impairment
Address pain	"T-A-DA" Method – Tolerate, Anticipate, Don't Agitate[25]
Encourage mobility – Out of bed at least three times per day	

The non-pharmacologic measures noted in Table 4 are also meant to prevent some of the complications of delirium. For example, delirium increases the risk of pressure ulcers and functional decline. Encouraging mobility helps to prevent these issues. Patients who are delirious may have poor oral intake because they are too inattentive to eat the meal that is sitting in front of them. Paying careful attention to their oral intake helps the medical team to prevent dehydration and malnutrition.

The next aspect of delirium care that the non-pharmacologic measures address is behavioral management. Agitation and aggression may be seen in patients with hyperactive delirium. Unaddressed pain, constipation and urinary retention may all trigger episodes of agitation and aggression. Patients with delirium may not be able to verbally express their needs and therefore are unable to localize and inform the medical team of physical symptoms such as pain. These physical symptoms may then manifest as "agitation." Addressing the underlying cause of the behavior is likely to be more successful than medicating the patient with a sedating medication to stop the behavior. Encourage family members to remain at bedside to calm fearful patients and prevent behaviors from escalating.

The "T-A-DA" method encourages those caring for patients with delirium to address challenging behaviors with the framework **T**olerate (behaviors which are not dangerous to the patient or others), **A**nticipate (the patient's needs and meet them) and **D**on't **A**gitate.[26]

Pharmacologic management

Pharmacologic agents are frequently used for the management of delirium although no agents have been approved for delirium treatment by the United States Food and Drug Administration (FDA). Two classes of medications, antipsychotics and benzodiazepines, are frequently used off label for management of delirium and their use will be discussed here.

Benzodiazepines are sometimes used to treat symptoms of agitation in the setting of delirium. These medications should not be used as a first line treatment in the management of delirium.[24] There is evidence that benzodiazepines may precipitate delirium[17] and that they may worsen or prolong episodes of delirium. Benzodiazepines are indicated if the delirium is secondary to alcohol or benzodiazepine withdrawal.

Antipsychotics are also frequently used to manage delirium but they have significant side effects. First generation antipsychotics (ex. haloperidol) are associated with extrapyramidal effects, anticholinergic side effects, tardive dyskinesia, neuroleptic malignant syndrome, QT prolongation, orthostatic hypotension and sudden death. Compared to first generation agents, second generation agents (ex. quetiapine, risperidone, ziprasidone and olanzapine) are associated with a lower incidence of extrapyramidal symptoms. All of these medications have been associated with an increased risk of mortality in patients with dementia and therefore have been given a Black Box warning by the FDA for use in dementia related psychosis. In a retrospective case-control study which included over 90,000 patients 65 years or older with a diagnosis of dementia in the Veterans Health Administration, patients receiving haloperidol had an increased mortality risk of 3.8% compared to matched nonusers with a number needed to harm (NNH) of 26 over 180 days of follow-up.[27] Patients taking second generation antipsychotics also had increased mortality compared to medication nonusers. Risperidone was associated with a 3.7% increased risk of mortality (NNH of 27), olanzapine 2.5% (NNH of 40) and quetiapine 2.0% (NNH of 50). There was a dose-response relationship with mortality risk in patients treated with the second generation antipsychotics.

These data are important because patients with dementia are at increased risk of developing delirium and dementia superimposed on delirium may be difficult to distinguish from behavioral and psychological symptoms secondary to dementia. In the previously mentioned study, a significant proportion of the patients on an antipsychotic had experienced an episode of delirium within the prior 12 months (haloperidol 44.2%, olanzapine 39.6%, quetiapine 42.8%, risperidone 43.0%).[27]

Multiple studies have found that a significant portion of patients who are started on an antipsychotic during an acute episode of delirium are continued on it at the time of discharge. One prospective cohort study of 500 ICU patients with acute respiratory failure and/or shock found that 208 (42%) were started on an antipsychotic during their ICU admission.[28] These patients were more likely to have had delirium than patients who were not started on antipsychotics (93% versus 61% $p < 0.001$). Of the 208 patients who were started on antipsychotics, 172 ultimately survived to hospital discharge and 42 (24%) of those patients were discharged from the hospital with a new prescription for the antipsychotic. A

retrospective chart review of 487 geriatric inpatients newly started on an antipsychotic during their hospitalization revealed that 147 (30.2%) of those patients were discharged on the antipsychotic.[29] The majority of those patients had a diagnosis of delirium (82.3%). The discharge summaries of only 15 (12.4%) of the patients discharged on antipsychotics with a diagnosis of delirium discussed a plan for discontinuation of the antipsychotic. The majority of the patients (12, 80%) whose discharge summaries mentioned a plan for antipsychotic discontinuation had been followed during their admission by a geriatric or psychiatry inpatient consult service.

These medications are high risk and have multiple side effects but are they efficacious in treatment of delirium? A Cochrane Review published in June 2018 found 9 studies with 727 participants addressing the use of antipsychotics for the treatment of delirium with 4 trials comparing the antipsychotic with placebo and 7 trials comparing a first generation with a second generation antipsychotic. The review concluded that the overall quality of the data was poor but based on these studies, antipsychotics did not reduce delirium severity, resolve symptoms or decrease mortality.[30]

A randomized, double-blind, placebo-controlled trial published in the New England Journal of Medicine in 2018 examined whether antipsychotic medications are effective in the treatment of ICU delirium. Patients with acute respiratory failure or shock and hypoactive or hyperactive delirium were assigned to receive IV boluses of haloperidol (max dose 20 mg daily), ziprasidone (max dose 40 mg daily) or placebo. The study found that haloperidol or ziprasidone versus placebo had no significant effect on the number of days alive without delirium or coma during the 14-day study period. There were also no significant between group differences for the secondary endpoints of 30-day and 90-day survival, time to freedom from mechanical ventilation, and time to ICU and hospital discharge.[31]

Major professional organizations have recognized the lack of evidence for efficacy of antipsychotics in the treatment of delirium. The American Geriatrics Society and the American College of Surgeons Clinical Practice Guideline for Postoperative Delirium in Older Adults recommends using antipsychotic medications in the lowest effective dose for the shortest duration possible only in patients who are severely agitated or distressed and are posing a danger to themselves or others.[25] The guideline also states that these medications should only be considered after non-pharmacologic methods have failed. The 2018 Society of Critical Care Medicine Clinical Practice Guidelines for the Management of Pain, Agitation and Delirium in Adult Patients in the ICU (PADIS guidelines) recommend against routine use of antipsychotics for treatment of delirium in critically ill patients.[32] Use of antipsychotics in patients with delirium was designated as a Choosing Wisely ®: Things We Do for No Reason by the Society of Hospital Medicine.[33]

Antipsychotics and other pharmacologic agents should only be used to manage symptoms of delirium which place the patient or others at risk or when behaviors are preventing necessary, life-saving care. If they are used, it is essential to have a discussion with the patient's family members regarding risks and benefits of using these medications.

Conclusions

In conclusion, delirium is an acute disorder of attention and cognition which is common in older adults admitted to the hospital. It is associated with multiple adverse outcomes

including increased mortality, falls, pressure ulcers, functional and cognitive decline. It is costly to the health care system. Despite the personal and monetary costs of delirium, it frequently goes unrecognized. Delirium prevention is possible and up to 30-40% of delirium cases may be preventable with multicomponent, non-pharmacologic measures. There are validated, rapid bedside screening tests available for delirium and delirium screening should be performed at least daily on all older adults admitted to the hospital.

Following identification and management of the underlying cause of an episode of delirium, non-pharmacologic treatment measures should be instituted. There are no FDA approved medications for the treatment of delirium. Use of antipsychotic medications in delirium has not been shown to resolve delirium or reduce delirium severity. These medications are associated with many adverse drug effects including increased mortality in patients with dementia. Low dose antipsychotic medications for the shortest possible duration of time may be used in patients who are severely agitated, distressed and/or pose a danger to themselves or others. If an antipsychotic is started in the hospital for delirium it should be discontinued prior to discharge from the hospital. If discontinuation is not possible, there should be explicit instructions for discontinuation in the patient's discharge summary.

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