

Delirium Assessment and Management

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Overview

This review describes the rationale and evidence for the “IA-ADAPT: Improving Antipsychotic Appropriateness in Dementia Patients” pocket guide on delirium assessment and management.

Delirium, also known as “acute confusion,” is common in older adults with acute medical illnesses. People with dementia have a much greater risk of delirium because of their pre-existing cognitive impairment and sensitivity to stressors such as medical illnesses and medication side effects. About two-thirds of delirium cases occur in people with dementia [Inouye 2006]. Estimates of the prevalence of delirium in hospitalized older adults with dementia have ranged from 22% to 89% [Fick et al. 2002]. The rates of delirium in people with dementia are not as well characterized in other settings of care (e.g., home or nursing home) but can be assumed to be substantial when acute medical illness is present. One study of delirium in nursing home residents found that approximately 22% had delirium during a one-month observation period. Lower baseline cognitive scores were, as expected, associated with a higher risk of delirium [Culp et al. 2004].

Delirium is a state of acute cognitive impairment caused by a medical problem. In contrast to dementia, its onset is rapid (hours to days), severity often fluctuates throughout the day, and it is reversible. Particularly among persons with concurrent dementia, it is possible to have persistent symptoms of delirium for long period of time, even weeks to months, so in some cases the exact time of onset may be difficult to determine. Changes in the sleep-wake cycle are also common, such that a person may be quiet and subdued or asleep during the day and awake or agitated at night. Though delirium is primarily characterized by acute cognitive deficits, behavioral and psychiatric manifestations are common. Delirium may present as hypoactive, where the person appears over-sedated or subdued and is difficult to arouse. This is often overlooked or mistaken for depression. It may also present as hyperactive or agitated, or as some mix of hypoactive and hyperactive characteristics. Delirium is important to consider as a possible cause of problem behaviors and psychosis in people with dementia, given the high prevalence of delirium in people with dementia [Fick et al. 2002, Fong et al. 2009].

The current standard criteria for diagnosing delirium in the United States as of the time of this writing come from the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR). These are:

1. Disturbance of consciousness (i.e., reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention.
2. A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established, or evolving dementia.
3. The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.

4. There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.

Screening for Delirium

Delirium screening tests can be used by people without specific expertise in diagnosing delirium to help identify patients who may be suffering from delirium. These screening tests are not intended to diagnose delirium but rather to identify patients who might have delirium. Since delirium is often undetected, the regular use of screening tests in high-risk patients is recommended to help overcome under-diagnosis [Adamis et al. 2010]. As you might expect, some screening tests are too sensitive and identify patients as possibly being delirious who do not have delirium and some are not sensitive enough and miss identifying patients who actually have delirium. In general, patients with hypoactive delirium are more commonly missed with the screening tools that we currently have. The best screening tools include some sort of basic cognitive testing.

Our pocket guide provides a delirium screening tool adapted from several sources. The basic criteria match those of the short version of the Confusion Assessment Method (CAM) [Inouye 2003], which is included in the Minimum Data Set, version 3.0. The specific assessments for inattention and disorganized thinking are drawn from the Confusion Assessment Method for the ICU (CAM-ICU) [Ely et al. 2001]. These were selected for their ease of administration. More information can be found at the following website: www.icudelirium.org. There is some evidence that the CAM-ICU may not be particularly sensitive in detecting delirium in general medical patients [Neufeld et al. 2011]. Therefore, if a person passes the tests but still seems more confused than usual, further evaluation may be necessary to rule out delirium.

A first step in screening for delirium may be to ask a simple question to a caregiver who knows the person well, “Does this person seem more confused today than usual?” If not, then it may not be necessary to screen for delirium. If yes, then the person may have delirium and further evaluations should be performed. This question has been referred to as the Single Question in Delirium, or SQiD. It performed quite well in identifying or ruling out delirium in patients with cancer when compared to other screening tests and a psychiatrist interview [Sands et al. 2010].

The second step to screening for delirium is to conduct a brief cognitive assessment. We have recommended some simple tasks that evaluate sustained attention, since sustained attention often remains relatively intact in mild to moderate Alzheimer’s dementia but is impaired in delirium. In other types of dementia such as vascular dementia, attention impairments may be more common in earlier stages [McGuinness et al. 2010]. Attention may also suffer in later stages of Alzheimer’s disease in the absence of delirium, making changes more difficult to assess. Thus, these tests are far from perfect in determining whether deficits are due to delirium or dementia. They are most useful if providers are aware of the person’s usual capacity to perform these tasks and can determine whether their ability has changed. When the tests are performed, it is also useful to observe the person’s level of consciousness and communication patterns to help determine if these have changed from the person’s normal state.

One simple assessment of attention may involve asking the patient to name the months of the year and/or days of the week backwards, which may help detect inattention in patients with mild dementia. For people with moderate dementia, we have recommended asking them to count from 20 to 1 backwards. This is an easier task that many people with moderate dementia should be able to complete if they are not delirious. In severe dementia the assessment may need to be even simpler, such as determining whether the person is aware of the examiner or able to follow simple commands that they are usually able to follow.

Screening Tool

If it is determined that a more thorough screening exam for delirium should be conducted, the CAM-based screening tool on the pocket guide can be used. There are four basic domains assessed, which relate to the DSM-IV-TR criteria for delirium. The screen is considered positive for probable delirium if both of the first two criteria and at least one of the last two criteria are met. In other words, there has to be evidence of an acute onset and inattention, and either disorganized thinking or an altered level of consciousness.

1. Acute Onset:
 - Is there evidence of an acute change in mental status from the person's baseline?
 - This differentiates delirium from dementia. If the person's mental status changed quickly (i.e., they're more confused than usual), then the answer is yes.
2. Inattention
 - Does the person have difficulty focusing attention (i.e., easily distracted or can't follow what's being said)?
 - This could be evaluated using the previously discussed sustained attention tests, or by observation. The evaluator can also do the attention screening examination described in the pocket guide.
3. Disorganized Thinking
 - Is the person's thinking disorganized or incoherent, as evidenced by rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject?
 - Questions and commands to evaluate this domain are provided in the pocket guide. Each question counts for one point. The command counts for one point. Any combined score equal to or less than 4 is positive for disorganized thinking.
 - Disorganized thinking may be present in dementia with or without delirium, adding to the challenge of differentiating the disorders. It may be best to consider a change from the person's recent normal ability.
4. Altered Level of Consciousness
 - Is the patient anything other than alert, calm, and cooperative (at the current time)?
 - Delirium can be either hyperactive or hypoactive. So agitated or hyper-vigilant states may indicate delirium. A sedated or difficult to arouse state may also indicate delirium. Hypoactive delirium is more common in elderly patients.

- Psychomotor retardation, or sluggishness, slower than normal movement or responses, or staring into space, can also count as a ‘yes’ on this domain.

Ultimately, delirium can be challenging to assess in people with dementia, since they have cognitive problems even when they are not delirious. When uncertain, a good rule of thumb is to go ahead and perform a medical evaluation for possible causes of any acute change in mental status. Delirium symptoms may indicate problems ranging from mild infections to drug side effects to medical emergencies. Delirium is often caused by more than one medical problem, so it’s important to be thorough when evaluating possible causes.

Assessing Causes of Delirium

Delirium can be caused by just about any acute or uncontrolled medical condition or stressor, including infections, pain, sleep deprivation, dehydration, metabolic or electrolyte disturbances, constipation, and many others. Medications are also common contributors to delirium, especially psychoactive medications. People with dementia are at a high risk since their cognition is already impaired. People with sensory impairment such as visual or hearing impairment are also at a higher risk, so it is important to ensure that glasses and hearing aids are available and working if needed, and that ear wax is not causing hearing impairment [Inouye 2006, Gleason 2003, Fong et al. 2009, Fick et al. 2002].

Evaluation for Medical Conditions

The evaluation for medical conditions that may be causing delirium is perhaps unique only in that it needs to consider a large number of possible causes, since delirium is a non-specific symptom. As with any evaluation, it starts with a general review of systems and evaluation of the current status of any known medical conditions. Physical evaluation may initially focus on more common conditions such as pain, constipation, skin ulcers, or pneumonia, but should also rule out severe conditions such as myocardial infarction or stroke that would require immediate treatment. Reviewing current vitals can also give clues as to the cause of delirium. Elevated temperature and heart rate can indicate infection, while an elevated heart rate and low blood pressure may indicate sepsis. Laboratory evaluations such as a urinalysis, electrolytes, serum creatinine/blood urea nitrogen, blood glucose, and a complete blood count with differential are useful for evaluating infections or metabolic/electrolyte disturbances, which are common causes of delirium [Inouye 2006, Gleason 2003, Fong et al. 2009, Fick et al. 2002].

In addition to examining medical conditions, it is important to evaluate the need for any restraining devices that might limit normal movement. Catheters, IV lines, and restraints should be removed if they aren’t necessary, or if the person is at risk of harming themselves by pulling out lines while confused. There is some evidence suggesting that restraints may worsen agitation and increase the risk of further cognitive worsening, so it is best to avoid them if possible [Flaherty and Little 2011].

DELIRIUM(S) is one mnemonic for remembering a number of common causes of delirium, further described in Table 1. Other mnemonics and more information on delirium can be found at the excellent website, www.icudelirium.org, from Vanderbilt University. The information is focused on delirium in the intensive care unit, but much is applicable to other settings.

Table 1. DELIRIUM(S): Mnemonic for Common Causes of Delirium

D	Drugs, Drugs, Drugs
E	Eyes, ears—poor hearing and vision are risk factors
L	Low oxygen states—myocardial infarction, acute respiratory distress syndrome, pulmonary embolism, congestive heart failure, chronic obstructive pulmonary disease
I	Infection, immobilization
R	Retention (of urine or stool), restraints
I	Ictal—seizures can cause delirium
U	Underhydration, undernutrition
M	Metabolic abnormalities
(S)	Subdural, sleep deprivation

Evaluating Medications

Determining the role of medications in delirium can be challenging. People with dementia are at a higher risk of drug-induced cognitive impairment. This has been illustrated by studies that have administered drugs such as anticholinergics to people with dementia and normal controls and examined their effect on cognition and other symptoms [Carnahan et al. 2004]. Medications may play a role in causing delirium in several ways.

1. Medications can directly impair cognition and be a primary cause of delirium. New drugs should especially be examined as possible causes. A new drug may also impair the metabolism of a medication that a patient has been taking for a while and increase its adverse impact on cognition.
2. Medications can impair cognition and lower the threshold at which other medical conditions or stressors will cause delirium. All medications should be carefully examined to determine if they might be contributing to cognitive impairment, even if they aren't a primary cause of the delirium. Delirium is often due to multiple causes, and medications may be contributing or predisposing factors.
3. Medications may induce electrolyte disturbances, metabolic disturbances, or other medical conditions that can lead to delirium.
4. Withdrawal from medications may cause delirium. Withdrawal from sedatives such as benzodiazepines or alcohol should be considered as a possible cause depending on the patient and circumstances.

Our pocket guide on drugs that can contribute to delirium or problem behaviors focuses on drugs that can have a direct adverse impact on cognition or psychiatric symptoms. It focuses on those medications for which substantial evidence suggests they can cause these problems. The list includes most psychoactive medications, including those that treat psychiatric disorders, anticonvulsants, and pain medications. It also includes steroids and certain cardiac medications (digoxin and antiarrhythmics) [Gray et al. 1999, Karlsson 1999].

The presence of a drug on this list does not necessarily mean that it should never be given to a patient with dementia, but rather that these drugs should be used with caution. If delirium does occur, the risk-benefit balance of their use should be considered. If discontinuation or dose reduction does not put the patient at risk of other problems, it is often a good choice. This is not always possible, however, particularly for opiates in people with pain or other drugs necessary for the treatment of serious medical conditions.

Case reports and other evidence suggest that a number of antibiotics, antivirals, and antifungals may cause cognitive or behavioral side effects [Gray et al. 2009]. The impact of these medications can be difficult to determine since they are often given to people with infections, and infections can cause delirium. However, the evidence is strong enough to consider them as potential causes.

Anticholinergic medications may be particularly harmful for people with dementia. The cholinergic system is damaged in Alzheimer's disease and some other types of dementia. Challenge studies have shown that people with Alzheimer's disease are extremely sensitive to the cognitive deficits induced by anticholinergics. These drugs also appear to worsen psychotic and behavioral problems in some patients. Cholinesterase inhibitors are used to help maintain cognition in dementia, and work by reducing the breakdown of acetylcholine. Anticholinergics are likely to lessen or reverse any cognitive benefits of cholinesterase inhibitors since they block the effects of acetylcholine. Thus, anticholinergic medications are generally not recommended for use in people with dementia. The Beers criteria, an expert consensus statement on potentially inappropriate medications in older adults, support avoiding anticholinergics in people with dementia [Carnahan et al. 2004].

Anticholinergic medications include those used specifically for their anticholinergic effects (e.g., bladder and gastrointestinal antispasmodics, motion sickness medications, movement disorder medications). They also include medications with anticholinergic side effects for which the anticholinergic effect is not considered central to the therapeutic effect (e.g., antihistamines, tricyclic antidepressants, certain antipsychotics). Our pocket guide focuses on those medications that are known to have strong anticholinergic effects, or those that have been associated with delirium.

The pocket guide is not a comprehensive list of all medications that can cause cognitive impairment. It focuses on the worst or more common offenders, and serves as a starting point of a thorough medication review. Other medications to be aware of with potential to cause cognitive impairment include chemotherapy agents, cytokines, immunosuppressants, metoclopramide, and antihypertensives [Gray et al. 2009, Karlsson 1999, Dyrud 2004]. Since it is nearly impossible to list all medications that have been associated with cognitive or behavioral side effects, it is important to review potential side effects of any medication a delirious person is receiving and not rely solely on the pocket guide to identify such drugs.

Just because a drug can cause cognitive impairment does not mean that it is the cause for a given individual. However, it is usually best to err on the side of caution and discontinue any non-essential medication that may be causing harm to a delirious patient. To further explore the relationship between the drug and cognition, one might consider the relationship in time to the delirium (e.g., was the drug

started recently), whether cognition improves when the drug is discontinued or the dose is lowered, whether cognition worsens when it is added back or the dose is increased, and whether blood levels of drugs for which they are measured are in the toxic range.

Delirium Management

First and foremost, the main treatment for delirium is to identify and treat the underlying medical problems that are causing it. Managing symptoms of delirium is also important, but the only real treatment is to treat the underlying cause. Once the medical problem is brought under control, it may still take time for delirium to resolve [Inouye et al. 2006, Gleason 2003, Fong et al. 2009]. Since so many medical problems can cause delirium it is impossible to review their management here. Thus, this section focuses on symptom management strategies.

Non-Drug Management

Non-drug management strategies for delirium focus on optimizing function and orientation, maintaining a clear and calm environment, ensuring adequate nutrition and hydration, normalizing the sleep-wake cycle, and ensuring safety. Some strategies for each of these are listed below [Inouye 2006, Gleason 2003].

Optimizing function and orientation:

- Re-orient and reassure the person frequently.
- Re-introduce yourself regularly. Use consistent staff.
- Communicate slowly and clearly. Use simple, step by step instructions when providing care. Avoid jargon.
- Use an interpreter if necessary.
- Involve family in low-stimulating visits.
- Make sure glasses, hearing aids, and dentures are available. Remove ear wax if necessary.
- Maintain mobility and self-care ability to the extent feasible.

Maintain a calm and clear environment:

- Clock, calendar/date, and schedule clearly visible.
- Reduce excessive noise and alarms.
- Simplify the care area. Remove unnecessary objects, except familiar objects that may promote comfort.
- Consider a private room.
- Consider playing the patient's preferred music during the day.
- Lights on during the day.
- Maintain comfortable room temperature.
- Don't correct harmless misbeliefs. For example, if a patient talks about visiting with a friend earlier in the day (who did not visit), agree and ask how the visit went.

Ensure adequate nutrition and hydration:

- Monitor food intake. Offer easy to eat foods during times of wakefulness and clarity.
- Keep beverage of choice available and within reach. Avoid excessive caffeine as this may contribute to dehydration.

Normalize sleep-wake cycle:

- Keep lights on during normal waking hours. Open shades/curtains if a window is available to allow natural light exposure.
- Discourage naps.
- Allow uninterrupted sleep at night.

Maintain safety:

- Use sitters.
- Use non-drug strategies for agitation (e.g., music, massage, relaxation techniques).
- Avoid restraints. Remove unnecessary lines and catheters.

Medications to Manage Delirium Symptoms

Antipsychotics

Antipsychotics are the mainstay of treatment to manage distressing hallucinations, delusions, or agitation that can occur in delirium. It is not necessary to treat all delirious patients with antipsychotics, but the drugs may be helpful for those with distressing psychotic or agitated symptoms. Some providers support use of antipsychotics in hypoactive delirium, in which the patient appears sedated rather than agitated, but this is controversial and may expose the patient to the risks of antipsychotics unnecessarily [Fong et al. 2009].

Haloperidol has been used extensively to manage symptoms of delirium, and is often a good choice unless the patient is at high risk of extrapyramidal side effects. Other antipsychotics can also be used [Fong et al. 2009]. We recommend caution with those that are more sedating or have significant anticholinergic effects, such as olanzapine or quetiapine, as it is possible that these could worsen delirium in some patients [Lim et al. 2006, Sim et al. 2000, Huang and Wei 2010]. However, there is little evidence from clinical trials suggesting one antipsychotic is safer or more effective than another for delirium management [Fong et al. 2009].

Antipsychotics should be started at low doses, such as those recommended in the pocket guides, and titrated to effect. The dose should be minimized in elderly patients to avoid side effects. The total dose required to provide symptom control can be used as a guide for scheduled dosing, if deemed necessary, which can be titrated down and discontinued as the delirium resolves. It is not necessary to continue antipsychotic treatment after the delirium has resolved, though some clinicians recommend continuing or tapering the antipsychotic for 5-7 days after symptom resolution to prevent rebound delirium. Response to and need for antipsychotic treatment should be evaluated at least every 24 hours during a delirium episode [Gleason 2003].

Benzodiazepines and Other Sedative-Hypnotics

Benzodiazepines are not usually recommended to manage delirium. They may worsen confusion and prolong delirium since they impair cognition and can cause over-sedation. The same applies to other sedative hypnotics and sleep medications, most of which can impair cognition. Non-drug strategies are preferred to promote sleep [Fong et al. 2009]. If non-drug strategies are ineffective low dose melatonin might be tried, e.g., 2.5-10 mg. Evidence for this strategy is limited and inconclusive, but some observations suggest it may be effective and safe for some patients with delirium and circadian rhythm disturbances [de Jonghe 2010].

If the delirium is due to alcohol or sedative-hypnotic withdrawal, then a benzodiazepine is the drug of choice. Other drugs such as antipsychotics or anticonvulsants are also sometimes used, but usually as adjuncts to benzodiazepines. Signs of alcohol or sedative-hypnotic withdrawal include increased blood pressure, increased heart rate, increased temperature, nausea, vomiting, sweating, tremor, anxiety, insomnia, and agitation. Seizures, hallucinations, or illusions may also occur [Bayard et al. 2004]. A full review of alcohol or sedative hypnotic withdrawal is outside of the scope of this website, so readers should refer to other resources if they need more information.

Cholinesterase Inhibitors

Cholinesterase inhibitors are not recommended as first-line treatments for delirium. While benefits have been reported in some cases, such as in anticholinergic overdose or Lewy body dementia, the evidence is too weak to support their regular use for delirium. Randomized controlled trials conducted to date have not supported the efficacy of cholinesterase inhibitors in delirium [Grover et al. 2011]. One randomized controlled trial testing the addition of rivastigmine to haloperidol for delirium in the intensive care unit found an increased risk of mortality with rivastigmine compared to placebo (22% vs. 8%) [van Eijk et al. 2010].

Further study is necessary before cholinesterase inhibitors can be considered safe or effective for the treatment of delirium. On the other hand, there is little reason to recommend discontinuation of a cholinesterase inhibitor that a delirious patient was already receiving for dementia, unless side effects are a concern.

Summary

Delirium is a state of acute cognitive impairment caused by a medical condition, and people with dementia are at high risk. Delirium should be considered as a possible cause of new psychiatric or behavioral disturbances in a person with dementia. The treatment for delirium is to manage the underlying medical condition that caused it. Medications should be reviewed in delirious patients to ensure that they are not causing or contributing to the delirium. Non-drug strategies can be used to manage many cases of delirium. If drug therapy is necessary, antipsychotics are usually the drugs of choice.

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