Delirium

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FOR

UNIVERSITY OF MANITOBA CPD RURAL PROGRAM

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Have you met this patient?

- Leo Bonhoffer is a 74 year old man with pancreatic cancer
- Epigastric and mid-back pain
- Occasional nausea and vomiting
- Transferred in a hurry from community hospital (they need the bed) to your local hospice
- Opioid use has doubled in the 48 hours prior to transfer
- Hydromorphone 4 mg po Q4 H scheduled
- Hydromorphone 4 mg subcut Q2 H prn
- Methadone added 1 day prior to transfer: 1 mg po Q12H

Have you met this patient?

- Family very upset at poor pain control on morning of admission
- Transferring physician notes “variable confusion”
- Family agrees - patient sometimes picks at the air
- Patient admits to abdominal and back pain
- Visibly restless
- Oriented to person and place, not time
- BP 132/72, P 90, RR 18, T 36.8 C, O2 sats 96%
- Moderately tender fullness in upper abdomen

Have you met this patient?

- You diagnose delirium and inadequate pain control
- Switch oral hydromorphone 4 mg Q4 H to fentanyl patch 25 ug/H
- D/C scheduled oral hydromorphone 12 H after 1st patch applied
- Continue hydromorphone 4 mg subcut up to Q2 H prn
- continue dexamethasone 6 mg subcut Q am
- Continue methadone 1 mg po Q12 H
- Patient and family in agreement

Have you met this patient?

- Rx methotrimeprazine 6.25 mg subcut Q4 H scheduled & Q2 H prn
- To give for agitation or +ve CAM; Rx CAM Q shift and prn;
- Instructions given verbally to nurse, written in order sheet, and reiterated in progress note that prn hydromorphone should NOT be given for agitation/restlessness (only for pain the patient can localize)
- Patient calm & lucid by the end of that day and into the next pm
- Good pain control (day 1 & 2)

Have you met this patient?

- Day 2 evening shift starts at 15:30 – new nurse, looks at MAR, not chart
- Patient restless after sundown, calling out
- Hydromorphone 4 mg subcut prn given x 9 doses over next 24 H
- Day 3 -night nurse calls you in the wee hours – pain not controlled
- Special call to hospice
- On examination - patient grimacing with touch
- Admits to pain but can't say where it is

Delirium

- Acute confusion associated with global brain dysfunction
- “the clinical diagnosis of delirium is frequently missed by the healthcare team”[1]

1. Shirley Harvey Bush, Sallyanne Tierney, Peter Gerard Lawlor Clinical Assessment and Management of Delirium in the Palliative Care Setting Drugs (31 September 2017) 77:1623–1643
DOI 10.1007/s40265-017-0804-3

Prevalence and Incidence

- In one-third of patients ≥ 70 yrs. admitted to general medical wards (in half of these patients on admission and developing during hospitalization in the other half).
- Incidence in older adults of 15 to 25% after major elective surgery
- 50% after high-risk procedures (e.g. hip-fracture ORIF, cardiac surgery)
- Most ICU patients undergoing mechanical ventilation
- 10 to 15% of older adults in the emergency department[2]

2. Delirium in elderly people
Sharon K. Inouye, M.D., MPH, Rudi G. J. Westendorp, M.D., and Jane S. Saczynski, Ph.D.
Lancet. 2014 March 8; 383(9920): 911–922.
doi:10.1016/S0140-6736(13)60688-1.

Prevalence and Incidence

Inpatient palliative care settings

- delirium prevalence increases from 13–42% on admission to
- 88% in the last weeks–hours of life[1]

PCH residents presenting to ER

- 40% are delirious

Shirley Harvey Bush, Sallyanne Tierney,
Peter Gerard Lawlor
Clinical Assessment and Management of Delirium
in the Palliative Care Setting
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What's wrong with a little delirium?

- increased frequency of falls[1]
- increased cognitive and functional impairment
- significant patient and family psychological distress
- associated with increased mortality

Delirium keeps bad company…

- Patients with delirium in the ICU are at 2–4 fold increased risk of death both in and out of the hospital.
- those who develop delirium on general medical or geriatric wards are at 1.5-fold increased risk for death in the year following hospitalization.
- patients with delirium in the emergency department have an approximately 70% increased risk of death during the first six months after the visit.
- Among older patients with dementia, delirium is associated with increased rates of cognitive decline, institutionalization, and mortality.

Must include…

- acute onset and fluctuating course of symptoms,
- inattention,
- impaired level of consciousness, and/or
- disturbance of cognition (e.g., disorientation, memory impairment, alteration in language).

Could include…

- disturbance in sleep-wake cycle,
- perceptual disturbances (hallucinations or illusions),
- delusions,
- psychomotor disturbance (hypo- or hyper-activity),
- inappropriate behaviour, and
- emotional lability.

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Table 1. Diagnostic Criteria for Delirium.

Source of Criteria
DSM-5*
The presence of delirium requires all the criteria to be met:
Disturbance in attention and awareness
Disturbance develops acutely and tends to fluctuate in severity
At least one additional disturbance in cognition
Disturbances are not better explained by a preexisting dementia
Disturbances do not occur in the context of a severely reduced level of arousal or coma
Evidence of an underlying organic cause or causes
Confusion Assessment Method (CAM)†
The presence of delirium requires features 1 and 2 and either 3 or 4:
Acute change in mental status with a fluctuating course (feature 1)
Inattention (feature 2)
Disorganized thinking (feature 3)
Altered level of consciousness (feature 4)

* The criteria are adapted from the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5).[5]
† The criteria are adapted from Inouye et al.[6]

Marcantonio ER.
Delirium in hospitalized older adults.
N Engl J Med.2017;377:1456-66.
[PMID: 29020579]

Tools for Detecting Delirium

1. *Behavioral checklists for delirium symptoms*
- DOS
- NuDESC
- NEECHAM (used in nursing-based studies).

2. *Tools for measuring delirium severity*
- Delirium Rating Scale (DRS and DRS-98)
- Memorial Delirium Assessment Scale (MDAS)

Confusion Assessment Method (CAM)

- validated in high quality studies including over 1000 patients
- sensitivity of 94%,
- specificity of 89%,
- and high inter-rater reliability

Risk Factors

- dementia or cognitive impairment
- functional impairment
- vision impairment
- history of alcohol abuse
- advanced age (> 70 years).
- Comorbidities (e.g., stroke, depression)

Precipitating Factors & Relative Risks

Risk Factor	RR
Psychoactive medication use	4.5
More than three medications added	2.9
Physical restraints	4.4
Bladder catheter	2.4
High BUN (dehydration)	2.0-2.9
Electroyte disturbance	3.4
malnutrition	4

Other Risk Factors…

- Infection
- Trauma
- Neurosurgery
- Sleep deprivation
- Any iatrogenic event

Final Common Pathway?

Many things adversely affect neurotransmission and/or cellular metabolism:

- Drugs
- Hypercortisolism
- Electrolyte disturbances
- Hypoxia
- Impaired glucose oxidation
- Relative cholinergic deficiency and/or dopamine excess

Management of Delirium

- Risk stratify
- Distressed patient = distressed (and angry) family
- Tell patients and family members what to expect
- Prevent delirium – eliminate or reduce risk factors
- In mild-moderate delirium – the paradigm is changing
- Severe delirium? – “Go big or go home”.

Table 4. High-Risk Drugs in Delirium and Potential Substitutes.*

Drug	Mechanism of Adverse Effect	Substitutes or Alternative Strategies	Comments
Benzodiazepines	CNS sedation and withdrawal	Nonpharmacologic sleep protocol[36]	Associated with delirium in hospitalized patients; if patient is already taking, maintain or lower dose, but do not discontinue abruptly
Opioid analgesics (especially meperidine)	Anticholinergic toxicity, CNS sedation, and fecal impaction	Local and regional analgesic measures; nonpsychoactive pain medications (e.g., acetaminophen and NSAIDs) around the clock; reserve opioids for breakthrough and severe pain	Consider risks versus benefits, since uncontrolled pain can also cause delirium; patients with renal insufficiency are at elevated risk for adverse effects; naloxone can be used for severe overdoses
Nonbenzodiazepine sedative hypnotics (e.g., zolpidem)	CNS sedation and withdrawal	Nonpharmacologic sleep protocol[36]	Like other sedatives, these agents can cause delirium
Antihistamines, especially first-generation sedating agents (e.g., doxylamine and diphenhydramine)	Anticholinergic toxicity	Nonpharmacologic sleep protocol,[36] pseudoephedrine for upper respiratory congestion, and nonsedating antihistamines for allergies	Patients should be asked about the use of over-the-counter medications; many patients do not realize that drugs with names ending in "PM" contain diphenhydramine or other sedating antihistamines
Alcohol	CNS sedation and withdrawal	If patient has a history of heavy intake, monitor closely and use benzodiazepines for withdrawal symptoms	The history taking must include questions about alcohol intake
Anticholinergics (e.g., oxybutynin and benztropine)	Anticholinergic toxicity	Lower the dose or use behavioral approaches for urinary incontinence (e.g., scheduled toileting)	Delirium is unusual at low doses
Anticonvulsants (e.g., primidone, phenobarbital, and phenytoin)	CNS sedation	Use an alternative agent or consider stopping if patient is at low risk for seizures and has no recent history of them	Delirium can occur despite therapeutic drug concentrations
Tricyclic antidepressants, especially tertiary amines (e.g., amitriptyline, imipramine, and doxepin)	Anticholinergic toxicity	Serotonin-reuptake inhibitors, serotonin–norepinephrine reuptake inhibitors, and secondary amine tricyclics (e.g., nortriptyline and desipramine)	Newer agents (e.g., duloxetine) are as effective as tertiary amines for adjuvant treatment of chronic pain
Histamine H_2–receptor blockers	Anticholinergic toxicity	Lower the dose or substitute antacids or proton-pump inhibitors	Anticholinergic toxic effects occur primarily with high-dose intravenous infusions
Antiparkinsonian agents (e.g., levodopa and amantadine)	Dopaminergic toxicity	Lower the dose or adjust dosing schedule	Dopaminergic toxic effects occur primarily in advanced disease and at high doses
Antipsychotics, especially low-potency typical antipsychotics (e.g., chlorpromazine and thioridazine)	Anticholinergic toxicity as well as CNS sedation	Discontinue entirely or, if necessary, use low doses of high-potency agents	Carefully consider risks vs. benefits of use in delirium
Barbiturates	CNS sedation and severe withdrawal syndrome	Gradual discontinuation or benzodiazepine substitution	In most cases, barbiturates should not be prescribed; avoid inadvertent or abrupt discontinuation

* In older adults, the risks and benefits of all medications should be considered carefully. Adverse effects should be monitored whenever any medication is started or the dose is adjusted. CNS denotes central nervous system, and NSAIDs nonsteroidal antiinflammatory drugs.

Marcantonio ER. Delirium in hospitalized older adults. N Engl J Med. 2017;377:1456-66. [PMID: 29020579]

Management of Delirium

- removing anticholinergic and psychoactive medications;
- family or companion involvement for reorientation and comfort;
- Non-pharmacologic approaches to sleep and relaxation;
- creating a quiet, soothing, warm environment; and
- attending to pain[2]

Management of Mild to Moderate Delirium

Antipsychotics are associated with:

- increased delirium symptoms;
- and reduced patient survival.
- Large dose, old, low-potency worst (e.g. chlorpromazine, thioridazine)
- Small doses of high-potency antipsychotics better
- E.g. haloperidol (Haldol) 1 mg subcut or p.o. Q8H;
- In palliative setting, consider methotrimeprazine (Nozinan) e.g 6.25 mg starter dose

Hospital Elder Life Program (HELP)

- reorientation,
- therapeutic activities,
- reduction of psychoactive medications,
- early mobilization,
- promoting sleep,
- maintaining hydration and nutrition, and
- providing vision and hearing adaptations.[3]

3. Inouye SK, Bogardus ST Jr, Charpentier PA, Leo-Summers L, Acampora D, Holford TR, et al. A multicomponent intervention to prevent delirium in hospitalized older patients. N Engl J Med. 1999 Mar 4; 340(9):669–76. [PubMed: 10053175

Management of Severe/refractory Delirium

- Persistent confusion/agitation?
- Go big or go home
- Nozinan dose increases beyond 25 mg Q4H unlikely to help
- Consider snowing with midazolam
- Consider phenobarbital
- Frequent, in-person reassessment
- Aggressive dose adjustment

Management of Delirium

- Pharmacologic management (severe agitation or psychosis only)
- Reserve for patients with severe agitation, which will result in interruption of essential medical therapies
- Start low doses and titrate until effect achieved;
- haloperidol 0.25–0.5 mgs. po/IM
- BID preferred; atypical antipsychotics close in effectiveness.
- *BID=twice daily; CBC=complete blood count; IM=intramuscular; mgs=milligrams; po=by mouth; PRN=as needed medicatio

Management of Delirium

- Address sensory impairment; provide eyeglasses, hearing aids, interpreters
- Maintain safe mobility • Avoid use of physical restraints, tethers, and bed alarms, which can increase delirium and agitation
- Ambulate patient at least 3 times per day; active range-of-motion
- Encourage self-care and regular communication
- Normalize sleep-wake cycle • Daytime: Discourage napping, encourage exposure to bright light
- Facilitate uninterrupted period for sleep at night
- Quiet room at night with low level lighting; nonpharmacologic sleep protocol

Management of Delirium

The adverse effects of antipsychotic medications include:[4]

- Sedation
- Hypotension
- Falls
- Parkinsonism
- Q-T interval prolongation
- Aspiration pneumonia

4. Christina Reppas-Rindlisbacher MD, Lesley Wiesenfeld MD MHCM, Nathan M Stall MD PhD
Antipsychotic medications for older adults with delirium admitted to hospital
CMAJ 2023 August 14; 195:E1038.
doi: 10.1503/cmaj.230227

Management of Delirium

Medication adjustments:

- Reduce or remove psychoactive medications (e.g., anticholinergics, sedative- hypnotics, opioids);
- lower dosages;
- avoid PRNs
- Substitute less toxic alternatives

Use nonpharmacologic approaches for sleep and anxiety:

- music, massage, relaxation techniques

Management of Delirium

- Antipsychotic medication are commonly used in hospital for the management of patients with delirium
- Antipsychotic medication should not be used as standard treatment for delirium
- Antipsychotic medications may be considered for patients with delirium experiencing severe agitation or distress
- Assessment of individual risks and benefits is warranted prior to used given serious adverse effects
- Frequent reassessment of treatment should be undertaken for dose reduction or discontinuatiion[4]

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Management of Delirium

- Address acute medical issues
- Treat problems identified in work-up (e.g., infection, metabolic disorders)
- Maintain hydration and nutrition
- Treat hypoxia
- Reorientation strategies
- Encourage family involvement; use sitters as needed

Lancet. Author manuscript; available in PMC 2015 March 08. Author Manuscript Inouye et al. Page 27

Overcoming Barriers to Change

Critical factors for initiating and sustaining HELP include:

- gaining internal support;
- ensuring effective champions;
- maintaining program fidelity while adapting to local circumstances;
- documenting positive outcomes; and
- obtaining long-term funding and resources.[2]

Thank you!