Delirium

KEY POINTS

- Delirium (with or without hallucinations) is commonly experienced by patients with advanced illnesses
  - Up to 80% of patients with advanced cancer develop delirium in the last days of life
- Delirium presents as an acute change in the patient's attention and awareness that was not previously there, with a fluctuating course
- Possible causes are many and the cause may be multifactorial and difficult to determine
- Delirium can be caused by opioids or the accumulation of opioid neurotoxic metabolites
- Patients with a prolonged hospitalization, particularly in ICU, with associated sleep deprivation and mechanical ventilation are at high risk of delirium

- Delirium is more common in younger children (<2 years of age) and in children with chronic neurological conditions, particularly while in ICU

ASSESSMENT

See comment on page 10

- Use of validated delirium screening tools may be helpful, e.g. Confusion Assessment Method
- Consider common medical triggers which may be treatable or modifiable, including:
  - Dehydration*
  - Poorly controlled pain or other symptoms
- Hepatic and renal failure*

**Can contribute to delirium by contributing to the accumulation of opioids and their metabolites*

- Urinary retention
- Infection, e.g. urinary tract infection
- Constipation
- CNS disease, e.g. brain metastasis, neurodegenerative conditions
- Biochemical imbalances, e.g. hypercalcaemia, hyponatremia
- Medications, particularly tricyclic antidepressants, corticosteroids, benzodiazepines, opioids, anticholinergics
- Hypoxia

- Children can be screened with the Cornell Assessment of Pediatric Delirium (CAPD) to identify delirium, which includes Developmental Anchor Points for young children (<2 years)

MANAGEMENT

Consider if the cause of delirium is identifiable and if the patient is well enough for intervention

- Management includes both environmental management and pharmacological management

Environmental Management

- Ensure an appropriate level of lighting (with changes for day and night)
- Provide reorientation with a calendar, clock, and verbal and written information
- Keeping noise to a low level
- Have family members present
- Ensure patient has their glasses and hearing aids to help provide normal sensory stimulation

- Discontinue drugs that may be causing the delirium
- Consider a trial of hydration if the patient's condition would tolerate this, which may help correct electrolyte disturbances and may reduce the accumulation of toxic opioid metabolites
- Correct electrolyte imbalances: hypercalcaemia may respond to hydration and/or to bisphosphonates such as **pamidronate 60-90 mg IV single dose**

Pharmacologic Management

- Pharmacological management includes:

1) Neuroleptics

- **Haloperidol** is commonly used
- **Chlorpromazine** may be more effective in cases of severe agitation
- Note: **Quetiapine** is the preferred agent for treatment of delirium in patients with Parkinson's disease as it is the least dopaminergic antipsychotic. Haloperidol should be avoided in these patients

Neuroleptic Agent	Dose	As Needed Dose	Route
Olanzepine	**2.5 mg qHS-BID, maximum dose of 10 mg/24hrs**	**1.25-2.5 mg q12h**	PO
Risperidone	**0.5-4 mg BID**	**1-2 mg q12h**	PO/SL
Quetiapine	**6.25-50 mg BID**	**12.5 mg q4-6h**	PO
Haloperidol	**0.5-2 mg BID, maximum dose of 5 mg/24hrs**	**0.5-1 mg q4-6h**	PO/Sub-cutaneous/IV
Chlorpromazine	**15-100 mg BID, maximum of 200 mg/24hrs**	**25-50 mg q4-6h**	PO/IV

2) Benzodiazepines

- Benzodiazepines should be used with caution as they can worsen delirium, and should not be used alone for the treatment of delirium

- **Lorazepam** or **midazolam** can also be used in situations where there is considerable agitation

Benzodiazepines	Regular Dose	As Needed Dose	Route
Lorazepam	**0.5-2 mg BID to QID**	**0.25-2 mg q4-6h**	PO/IV/PR
Midazolam	**5-60 mg/24h IV/ Subcutaneous infusion or 5-20 mg q4h**	**0.25-5 mg q1h**	Subcutaneous/ IV

3) Opioid rotation (if alternative opioids available)

- Opioid rotation (switching from one opioid to another) can be helpful for some patients who do not respond to the addition of neuroleptics or benzodiazepines
- In patients with significant renal impairment, metabolites from morphine can accumulate
- If an opioid rotation is performed, establish the equianalgesic dose from an equianalgesic table, and start the new opioid at 50% of the equianalgesic dose, if pain is well controlled; if pain is poorly controlled do not reduce the equianalgesic dose by 50% (See Appendix 3)
- The 50% dose reduction addresses incomplete cross tolerance which occurs between different opioids (see Pain section for more details)
- Repeated clinical assessments and consideration of patient-specific factors should always guide the approach to determining the new dose

- Try to prevent delirium by ensuring regular sleep and promote a sleep-wake cycle, by allowing natural light into the room during the day and making the room dark at night

- Promote reorientation by providing a clock, calendar, or verbal and written reorientation of the date and time for older children and teenagers
- Ensure familiar caregivers are present to reassure the child
- Provide familiar toys, stories, and activities
- **Haloperidol**
  - **>3 months of age: 0.01-0.02 mg/kg IV/PO q8h PRN (0.5-1 mg). For acute agitation: 0.025-0.05 mg/kg PO/IV; may repeat 0.025 mg/kg in 1 hour PRN**
  - **Usual onset of effect when selecting the appropriate route of administration: PO (2 hours), IV (3-20 minutes)**

- **If agitated delirium, consider the addition of:**
- **Lorazepam**
  - **0.025-0.05 mg/kg/dose (Maximum: 2 mg) AS SINGLE DOSE or q4-8h PO/SL/IV**
- **Midazolam**
  - **Oral: 0.25-0.5 mg/kg/dose (Maximum: 20 mg)**
  - **IN: 0.2-0.5 mg/kg/dose (Maximum: 10 mg, 5 mg per nostril)**
  - **Subcutaneous/IV bolus: 0.025-0.1 mg/kg/dose (Maximum: 10 mg)**
  - **Subcutaneous/IV infusion: 25-500 mcg/kg/hr**

- Benzodiazepines may worsen delirium or cause paradoxical reactions in some children

- **Clonidine (alpha-adrenergic agent)** can be helpful to promote sleep, with minimal side effects
  - **1-2 mcg/kg/dose PO q4-6h, may increase to a maximum of 4 mcg/kg/dose**
  - When initiating and titrating therapy, monitor for bradycardia and hypotension secondary to the alpha-2 agonist activity on the cardiovascular system
  - When discontinuing therapy, consider a wean over 3-7 days, as rebound hypertension, along with other withdrawal side effects (diaphoresis, headache, insomnia) may occur

PITFALLS/CONCERNS

- Antihistamines may cause paradoxical agitation and confusion
- Benzodiazepines can be useful in children in controlling agitation but at higher doses may worsen delirium for some children

PALLIATIVE TIPS

- Because of the high incidence of delirium in palliative care patients (up to 80% at end of life), regular screening is recommended using a delirium-specific screening tool (e.g. Confusion Assessment Method)
- Environmental modifications are key components of treatment
- If opioids are suspected as the cause of delirium, it is important to realize the symptoms may disappear after a few days of stable dosing of the opioid
  - Generally, opioid-related delirium is due to accumulation of neurotoxins in the setting of renal or liver failure

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