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- Hospice Palliative Care Program
Symptom Guidelines

Delirium/Restlessness

Delirium/Restlessness

□ Rationale

This guideline is adapted for inter-professional primary care providers working in various settings in Fraser Health, British Columbia and the Fraser Valley Cancer Center and any other clinical practice setting in which a user may see the guidelines as applicable.

□ Scope

This guideline provides recommendations for the assessment and symptom management of adult patients (age 19 years and older) living with advanced life threatening illness and experiencing the symptoms of delirium or restlessness. This guideline does not address disease specific approaches in the management of delirium or restlessness.

Delirium occurs in approximately 30% of palliative care patients⁽¹⁾ and 40% of advanced cancer patients.⁽²⁾ Terminal delirium reported in 88% of deaths.⁽³⁾ Terminal restlessness occurs in approximately 42% to 62% of dying patients.^(4, 5)

□ Definition of Terms

Delirium has been defined as a transient organic brain syndrome characterized by the acute onset of disordered attention and cognition, accompanied by disturbances of cognition, psychomotor behaviour and perception.⁽¹⁾

Types of Delirium:

- Hypoalert – hypoactive^(1, 3, 5, 6) often misdiagnosed as depression in the elderly.^(1, 6-10)
- Hyperalert – hyperactive.^(3, 5, 8-10)
- Mixed type – with fluctuations from hypoalert to hyperalert.^(5, 6, 8, 9)

Restlessness can be defined as an inability to relax or be still, the quality of being ceaselessly moving or active or a feeling of agitation expressed in motion.⁽³⁾

Terminal restlessness is best described as “agitated delirium in a dying patient, frequently associated with impaired consciousness” and non-purposeful movement.⁽⁹⁾

Confusion, altered mental state, cognitive impairment, acute brain syndrome, restlessness, dementia and delirium are often used interchangeably – although they have different meanings.⁽³⁾

□ Standard of Care

1. Assessment
2. Diagnosis
3. Education
4. Treatment: Nonpharmacological
5. Treatment: Pharmacological

Recommendation 1 Assessment of Delirium / Restlessness

Ongoing comprehensive assessment is the foundation of effective management of delirium or restlessness including interview, physical assessment, medication review, medical and surgical review, psychosocial review, review of physical environment and appropriate diagnostics (*see Table 1*). Assessment must determine the cause, effectiveness and impact on quality of life for the patient and their family.

Table 1: Delirium/Restlessness Assessment using Acronym O, P, Q, R, S, T, U and V

O Onset	When did it begin? How long does it last? How often does it occur?
P Provoking / Palliating	What brings it on? What makes it better? What makes it worse?
Q Quality	What does it feel like? Do you feel confused? Are you seeing or hearing anything unusual? How are you sleeping?
R Region / Radiation	Do you know what day/month/year it is? Do you know where you are right now? Can you tell me your full name?
S Severity	What is the intensity of this symptom (On a scale of 0 to 10 with 0 being none and 10 being worst possible)? Right Now? At Best? At Worst? On Average? How bothered are you by this symptom? Are there any other symptom(s) that accompany this symptom?
T Treatment	What medications or treatments are you currently using? How effective are these? Do you have any side effects from the medications/treatments? What medications or treatments have you used in the past?
U Understanding / Impact on You	What do you believe is causing this symptom? How is this symptom affecting you and/or your family?
V Values	What is your goal for this symptom? What is your comfort goal or acceptable level for this symptom (On a scale of 0 to 10 with 0 being none and 10 being worst possible)? Are there any other views or feelings about this symptom that are important to you or your family?

* Physical Assessment (as appropriate for symptom)

Recommendation 1 Assessment of Delirium/Restlessness continued...

Onset:

- Has an acute onset.^(1, 7, 11, 12)
- Can fluctuate and be preceded by subtle changes.^(3, 5, 7, 13)

Signs and Symptoms of Delirium:

- Affected reasoning – irrelevant or rambling thinking, abnormal conceptualization and altered insight with anosognosia.^(2, 6, 13, 14)
- Agitation.^(1, 6, 7, 11, 13, 15)
- Altered level of consciousness.^(1, 5-7)
- Anger.^(1, 3, 5, 6, 11, 16)
- Anxiety.^(1-3, 5, 6, 13, 14, 16)
- Attention disturbances.^(1, 5, 7)
- Delusions – poorly organized and characterized by paranoid features.^(3, 5, 6, 8, 11-14, 16)
- Depression.^(1, 3, 6, 13, 14, 16)
- Disorientation to time, as well as place and person (in more severe cases).^(1, 5, 7, 13)
- Disturbance of sleep – wake cycle.^(3, 5-7, 11, 15)
- Emotionally labile.^(1, 5, 6, 13)
- Enhanced startle reflex.⁽³⁾
- Hallucinations^(5, 6, 8, 11, 12, 17) often visual^(1, 6, 13) or tactile but not auditory (this is more common with schizophrenia).^(1, 3, 6, 16)
- Irritability.^(5, 6, 13)
- Language abnormalities – lack fluency and spontaneity, conversation may be prolonged and interrupted by long pauses or repetitions, inability to find the correct word, may be characterized by ‘passé partout’ words, perseveration, stereotypes and clichés. Writing abilities are affected early and more severely than other language related skills.^(6, 7, 13, 14, 16)
- Lethargy.^(1, 16)
- Memory impairment.⁽¹⁾

Recommendation 1 Assessment of Delirium/Restlessness continued...

- Miosis – occurs with opioid toxicity.^(1, 2, 6, 16)
- Mydriasis – occurs with anticholinergic toxicity.⁽³⁾
- Myoclonus.^(1, 5, 6, 11, 13, 15, 16)
- Nightmares.^(1, 17)
- Restlessness.^(1, 5, 6, 11, 15)
- Seizures.^(11, 15)
- Tachypnea – occurs with sepsis, hypoxemia or manifestations of a central process.^(1, 3, 6)
- Tremors – typical in alcohol withdrawal.^(3, 5, 6)

Delirium is reversible in approximately 50% of patients with advanced disease.^(3, 7)

Delirium is likely to be more reversible on first occurrence. It is more unlikely with second and subsequent occurrences.^(1, 6, 13)

However, factors associated with irreversible delirium are: hypoxic encephalopathy, metabolic factors (hypercalcemia, hyponatremia, renal insufficiency) or non-respiratory infection.⁽²⁾ Delirium may not be reversible in the last 24 to 48 hours of life.^(7, 18)

Laboratory Studies:

WBC, serum electrolytes, urea, creatinine, creatinine clearance, glucose, liver function tests, ammonia, thyroid hormone, TSH, adrenal function, blood and urine cultures, blood gases, EEG, pulse oximetry.^(3, 5, 7)

Recommendation 2 Diagnosis

Management should include treating reversible causes where possible and desirable according to the goals of care. The most significant intervention in the management of delirium or restlessness is identifying underlying cause(s) and treating as appropriate. While underlying cause(s) may be evident, treatment may not be indicated, depending on the stage of the disease.

Whether or not the underlying cause(s) can be relieved or treated, **all** patients will benefit from management of the symptom using education or medications.

Recommendation 2 Diagnosis continued...

Identifying the underlying etiology of the delirium or restlessness is essential in determining the interventions required. Under-diagnosing is a problem in delirium.^(1-3, 5, 7)

The decision to carry out investigations must be weighed against the value which will be gained from the results and the expected improvement from treatment based on those tests, as well as the morbidity and ‘usefulness’ of pursuing investigations in a patient who may be deteriorating quickly and close to death.^(2, 3, 5) A number of assessment tools exist to assist in assessment of delirium.^(6, 7)

DSM IV criteria for diagnosing delirium due to a general medical condition:^(2, 5, 13, 14, 16)

- Disturbance of consciousness with reduced ability to focus, sustain and shift attention.
- Change in cognition (such as memory deficit, disorientation, language disturbances or perception disturbances not better explained by a pre-existing stabilized or evolving dementia).
- The disturbance develops over a short period of time and tends to fluctuate during the course of the day.
- 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.

Causes of Delirium: usually multi-factorial^(5, 6, 8, 11)

- **Neoplastic**
 - Primary tumour of brain.^(6, 11, 13)
 - Metastases.^(1, 6, 11, 13)
 - Tumour burden or location.⁽³⁾
- **Infection/inflammatory** – pneumonia and urinary tract infection^(1-3, 6, 7, 10, 12-14, 16, 18), other causes of sepsis.

Recommendation 2 Diagnosis continued...

- **Metabolic** – hypercalcemia, uremia, hypoglycemia, hyperglycemia, or hyponatremia.
(1, 3, 7, 10, 11, 13, 14, 16)
- **Drug Effects**
 - **Idiosyncratic:**
 - Anti-cholinergic drugs.^(6, 11, 13)
 - Anticonvulsants.⁽¹⁸⁾
 - Antidepressants.
 - Antiemetics.^(6, 13)
 - Antihypertensives.^(6, 13)
 - Antiviral.^(6, 7, 13)
 - Chemotherapy – vinca alkaloids, methotrexate, cisplatin, bleomycin, procarbazine.^(11, 13, 18)
 - Corticosteroids.⁽¹⁾
 - H₂ antagonists.^(1, 3, 6, 13, 18)
 - Neuroleptics.⁽³⁾
 - Opioids.^(3, 11, 15)
 - **Overdosage:**
 - Due to physical deterioration.⁽³⁾
 - Due to metabolic causes.^(1, 3)
 - Accidental.^(3, 13, 16)
 - Intentional – alcohol abuse.^(3, 18)
 - **Drug withdrawal:**
 - Alcohol.⁽¹⁶⁾
 - Barbiturates.
 - Benzodiazepines.^(3, 18)
 - Nicotine.⁽³⁾
 - Opioids.^(1, 2, 6, 13)
 - Steroids.^(1, 6)

Recommendation 2 Diagnosis continued...

- **Cardiopulmonary** – cerebral hypoxia, hypercapnia, or cerebrovascular disease.^(3, 10)
- **Discomfort** – pain, constipation, urinary retention, or dehydration.^(1, 6, 7, 11-13, 16, 19)
- **Endocrine dysfunction** – thyroid and adrenal.^(1, 6, 7, 13, 18)
- **Liver failure.**^(6, 11, 14, 18)
- **Malnutrition** – thiamine or folate or vitamin B12.^(1-3, 6, 7, 13, 16)
- **Psychosocial or Psychiatric Causes:** grief⁽¹⁸⁾, sensory deprivation⁽⁷⁾ or overload⁽⁷⁾ or social isolation.⁽⁷⁾
- **Renal failure.**^(1, 11, 13, 15, 19)
- **Trauma** – convulsion, subdural hematoma, or hemorrhage.^(1-3, 13, 16, 18)
- **Visual or hearing impairment.**⁽¹⁸⁾

Causes Contributing to Restlessness:

Physical – pain, constipation, bladder retention, hypoxia, metabolic, organ failure, fever.^(3, 4)

Drug effect – Extrapyrarnidal effects, akathisia, opioid-induced neurotoxicity.⁽³⁾

Psychosocial – personal suffering, existential anguish, interpersonal conflict, spiritual journey, worry, grief.^(3, 4)

Psychiatric – delirium of any cause, dementia, anxiety disorder.^(1, 6, 13)

Imminently dying – any combination of above with altered, fluctuating and declining state of consciousness.^(3, 13, 16)

Recommendation 3 Education

- It is important to explain to the family that the symptoms are caused by the illness, are not within the patient’s control, will fluctuate^(1, 2, 6, 7, 13, 14, 16) and the patient is not going ‘insane’.^(13, 14) Include the family in decision making, emphasizing the shared goals of care.⁽¹⁴⁾ Report hallucinations that become threatening.⁽¹²⁾
- Patients may have comforting hallucinations – common in hypoactive delirium.^(3, 13)
- Instruct the family to provide gentle, repeated reassurance^(3, 7, 13) and avoid arguing with the patient.^(2, 3, 13, 16)
- If communication is difficult encourage the family to be present in a calming way.^(2, 4)

Recommendation 4 Treatment: Non-pharmacological

- Watch for the sun downing effect (nocturnal confusion)^(1-3, 6, 13, 14, 16) as it is often the first symptom of early delirium.^(2, 3, 6, 18)
- Provide a calm, quiet environment and help the patient reorient to time, place and person (visible clock, calendar, well known object).^(5, 6, 14, 18)
- Presence of a well known family member is preferred.^(4-6, 13)
- Provide a well lit, quiet environment.^(2-7, 13, 14, 16) Provide night light.⁽¹⁾
- Keep visitors to a minimum to prevent over stimulation^(1, 13) and minimal staff changes⁽¹³⁾ and room changes.⁽⁷⁾
- Correct reversible factors – dehydration^(6, 11, 19) nutrition⁽¹¹⁾ alteration in visual or auditory acuity (provide aids)^(5, 18) sleep deprivation.^(3, 7)
- Avoid the use of physical restraints, catheterization or other impediments to ambulation.⁽³⁾
- Encourage activity if patient is physically able.⁽¹³⁾

When Mildly Restless Provide:

- Observation^(3, 5) and relaxation techniques (massage, tub baths, gentle music) as applicable.⁽¹⁴⁾

Recommendation 5 Treatment: Pharmacological

- Correct reversible factors – infection, constipation, pain, withdrawal, drug toxicity.^(10, 13) A firm diagnosis may only be attainable in less than half of cases.⁽¹³⁾
- Review medications; consider opioid rotation to reverse neurotoxicity,^(1, 2, 8, 13) discontinue unnecessary drugs or prolong the dosing interval for necessary drugs.⁽³⁾
- If a patient is developing sun downing effect (confusion in the evening),⁽¹¹⁾ psychotropic drugs have a place in treatment.
- Anticipate the need to change treatment options if agitation develops – particularly in cases where patient, family and staff safety may become threatened.^(5, 18)
- Benzodiazepines may paradoxically excite some patients^(10, 15) and should be avoided unless the source of delirium is alcohol or sedative drug withdrawal, or when severe agitation is not controlled by the neuroleptic.⁽¹⁰⁾ Examples of neuroleptic drugs include haloperidol and methotrimeprazine.
- If patient has known or suspected brain metastases a trial of corticosteroids is worthwhile.⁽⁶⁾ Dexamethasone 16 to 36 mg PO daily in the morning.⁽⁶⁾

Medication Used for Mild Restlessness

- Haloperidol 0.5 to 1.5 mg PO t.i.d.⁽³⁾ The parenteral dose should be 50% of the oral dose.^(3, 5)
- Lorazepam 1 to 2 mg S.C. should be used as an adjunct only on a p.r.n basis only until the neuroleptic provides control.⁽³⁾

Medication Used for Delirium and Agitation In Terminal Illness

- **Restless & Confused but Cooperative**
 - Haloperidol 1.5 to 5 mg PO or S.C. q4h to q8h.⁽³⁾
 - Methotrimeprazine 10 to 15 mg for mild and up to 50 mg for severe delirium q4h to q6h.⁽³⁾
- **Delirium with Paranoia, Confusion and/or Aggression**
 - Haloperidol 10 mg S.C. or I.V. q30 to 60 min until relief then maintenance dose is 50% of amount to achieve control (usually between 1.5 to 20 mg per day divided into one to three doses).⁽³⁾
 - OR**
 - Methotrimeprazine 10 to 50 mg S.C. q30min until relief then 10 to 50 mg PO or SL or S.C. q4h to q8h.⁽³⁾
 - OR**
 - Chlorpromazine 50 to 100 mg I.M. or rectally or I.V. q1h until relief then 12.5 to 50 mg PO or I.V. q4h to q12h.⁽⁴⁾

Consider palliative sedation when all other measures have failed.⁽¹⁸⁾

□ References

Information was compiled using the CINAHL, Medline (1996 to April 2006) and Cochrane DSR, ACP Journal Club, DARE and CCTR databases, limiting to reviews/systematic reviews, clinical trials, case studies and guidelines/protocols using delirium/restlessness terms in conjunction with palliative/hospice/end of life/dying. Palliative care textbooks mentioned in generated articles were hand searched. Articles not written in English were excluded.

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