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Hospice Palliative Care Program
Symptom Guidelines

Twitching/Myoclonus/ Seizures

Twitching/Myoclonus/Seizures

☐ 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 myoclonus, twitching or seizures. This guideline does not address disease specific approaches in the management of myoclonus, twitching or seizures.

Seizures may be the first indication of a brain tumour. They occur in up to 50% of palliative patients with a primary brain tumour[1] in 20% to 45% of patients with brain metastases,[2, 3] while up to 70% of patients with HIV infection can have seizures as a complication.[2] It is more difficult to control seizures in patients with primary brain tumours.[3]

☐ Definition of Terms

Twitching refers to an involuntary muscle contraction; it tends to be repetitive, unwanted, lacking obvious cause, and is not considered part of the normal operation of the body.[4]

Myoclonus is defined as involuntary single or irregularly repetitive movements of one part of the body associated with either muscle contraction (positive myoclonus) or brief loss of muscle tone (negative myoclonus).[5]

Simple partial seizures exhibit a normal level of consciousness; only a selective area of the cortex participates in the seizure (affecting partial motor, sensory, autonomic and affective functions). If these precede a generalized partial complex seizure they are called an “aura”.

Generalized tonic-clonic seizures start with a sudden loss of consciousness, followed by diffuse muscle rigidity and cyanosis. After one minute myoclonus and muscle fasciculations occur for one to two minutes, followed by the post-ictal phase.

Partial complex seizures combine focal symptoms with an altered state of consciousness. These are the most common type of seizures seen in palliative care adults. These can last on average three minutes and are followed by a post-ictal phase.[2]

Status epilepticus is a seizure lasting 5 minutes or repeated seizures one after another without regaining consciousness.[5, 6]

☐ Standard of Care

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

Recommendation 1 Assessment of Twitching/Myoclonus/Seizures

Ongoing comprehensive assessment is the foundation of effective management of twitching/myoclonus/seizures, 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: Twitching / Myoclonus / Seizures Assessment using Acronym O, P, Q, R, S, T, U and V

Onset	When did it begin? How long does it last? How often do they occur?
Provoking / **P**alliating	What brings it on? What makes it better? What makes it worse?
Quality	What does it feel like? Can you describe it? How do you feel afterwards?
Region / **R**adiation	What happens when you experience twitching or myoclonus or seizure?
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?
Treatment	What medications or treatments are you currently using? How effective are these? Do you have any side effects from the medications or treatments? What medications or treatments have you used in the past?
Understanding / **I**mpact on You	What do you believe is causing this symptom? How is this symptom affecting you and/or your family?
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 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 twitching/myoclonus/seizure 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 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 medication.

Determine if the patient is experiencing twitching, myoclonus or seizure and the underlying etiology to determine the interventions required.[7]

- Causes can be multifactorial.[5] Common causes include:
  - Brain tumours – primary or metastatic.[1-3, 5, 6, 8-10]
  - Metabolic causes (hyperglycemia, hyponatremia, renal or hepatic failure, and hypercalcemia).[2, 3, 5-11] Hypoglycemia is the most common metabolic cause of seizure activity. Hypoglycemia can be caused by prolonged seizure activity.[1]
  - Drug toxicity – opioid induced neurotoxicity.[1-3, 5-7, 10] Myoclonus or seizures caused by opioid toxicity are a late phase adverse effect.[9]
- Other causes are:
  - Alzheimer's Disease.[10]
  - Cerebral irritability of pre-death restlessness.
  - Creutzfeldt-Jacob disease.
  - Drug withdrawal (alcohol, barbiturates, benzodiazepines, opioids).[2, 6, 8, 10]
  - Encephalopathy.[6]
  - Hypoxia.[6, 8]
  - Infection[3, 6] – HIV toxoplasmosis, cryptococcus, tuberculosis, JC virus (progressive multi-focal leukoencephalopathy)[2, 3, 8, 10, 11] or CNS infection.[3, 10]
  - Intracerebral hemorrhage.[3, 5, 6]
  - Organic Brain Syndrome.[10]
  - Pre-existing epilepsy or seizure disorder.[5-8, 10]
  - Radiation-induced edema/necrosis.[3]
  - Stroke or transient ischemic attack.[7, 8, 10]
  - Trauma.[5, 11]
  - Twitching can be caused by; pinched nerve or nerve injury, stimulant abuse, Parkinson's disease, epilepsy, amyotrophic lateral sclerosis and benign fasciculation syndrome.

Recommendation 3 Education

Myoclonus may disrupt sleep, make coordinated movements difficult and be bothersome to patients or families.[7] Patients and families should be educated about improving sleep hygiene. Information about normal sleep and sleep hygiene can be found on the Canadian Sleep Society website at: **http://www.css.to/sleep/normal_sleep.pdf**

Advice to family for seizure at home:[3, 8]

- Try to make sure that the patient does not fall or bump into any sharp objects.
- Do not attempt to restrain the patient.
- Do not try to force anything into the patient's mouth.
- When the seizure stops, turn the patient onto his/her side.
- The patient will be sleepy for a while after the seizure.
- If the seizure does not stop by itself in about 5 to 10 minutes or if another seizure occurs soon after the first, call for medical assistance.
- Do not shout or expect verbal commands to be obeyed.[3]

Seizures are frightening to the patient and family. Take time afterward to explore concerns of the patient and family and offer honest reassurance.[1, 3] Address questions such as:[8]

- Will the patient swallow his/her tongue or choke to death during a seizure?
- Will there be permanent brain damage from a seizure?
- Will seizures hasten death?

Recommendation 4 Treatment: Nonpharmacological

During the seizure:

- Clear the area of hard or sharp objects to prevent injury during the seizure.[3, 8]
- Maintain airway by lifting up the patient's chin.[8]
- When seizure is over, place in stable side position (recovery position) until he/she is alert.[8, 11]
- Draw blood test for laboratory investigation[8] (if the patient in hospital and thought to be necessary).
- Administer oxygen for patients with status epilepticus.[8]

Recommendation 5 Treatment: Pharmacological

Twitching/Myoclonus:

- All opioid analgesics can produce myoclonus. Mild and infrequent myoclonus is common. If the dose cannot be reduced due to persistent pain, consider opioid rotation or symptomatic treatment.[7, 9, 12, 13] Hydration should be considered[14] *(See Fraser Health Hospice Palliative Care Symptom Guideline for Dehydration).*
- When myoclonus is severe or there is concern that generalized seizures can occur there is limited evidence to support the use of baclofen, diazepam, clonazepam, midazolam, valproic acid or dantrolene sodium.[9] Consider opioid rotation.[2]
- Benzodiazepines are the primary symptomatic treatment.[7] Lorazepam is often used as it can be given orally, SL or S.C.. Clonazepam and valproic acid also have been used for the treatment of myclonus.[3]
- Midazolam can be used for terminal restlessness and myoclonus (especially due to opioid toxicity).[8]

Seizure:

- If a seizure has occurred and recurrence is likely, then treatment is warranted.[5]
- Prophylactic anticonvulsant therapy in patients with brain tumours or metastases is controversial. It has not been shown to provide an advantage in seizure control.[1-3]
- Seizure prophylaxis should be instituted after the first seizure.[8]
- Clonazepam can be used for the temporary treatment of seizures not controlled by ongoing therapy.[2] Start with clonazepam 0.5 mg PO t.i.d., and then increase by 0.5 mg every 3 days until symptoms are controlled. Abrupt withdrawal of clonazepam after long-term use may precipitate status epilepticus taper dosage instead.[8]
- Although diazepam has been the benzodiazepine of choice for status epilepticus, recent evidence indicates that lorazepam may be more beneficial because it provides longer control of seizures and produces less cardiorespiratory depression.[16]
- Gabapentin can be used for adjuvant therapy of partial seizure and tonic-clonic seizures.[1] Starting dose is 300 mg t.i.d. to q.i.d PO with maintenance dose of 900 to 3600 mg per day PO.[1]
- Midazolam can be given I.V. or S.C. or PO, with the quickest onset by I.V. route. I.M. route is not recommended. Use lower dose in older adults (1 to 2 mg).[2]
- Phenobarbital is effective in both partial and generalized tonic-clonic seizures.[2]
- Phenothiazines should be avoided in patients in whom cerebral irritation is a potential problem.[15]
- Consider starting or increasing dexamethasone PO or S.C. in seizures from brain tumour or metastasis.[5] Dexamethasone should not be the only drug used, even if only one seizure has occurred.[5]

Recommendation 5 Treatment: Pharmacological continued...

Seizure continued...

- Response to pharmacological therapy is individualized and highly variable. The dose should be titrated to clinical response rather than to a specific serum level.[1]

Status Epilepticus:

- Status epilepticus should be controlled, even in the unconscious patient near death, because of the distress that continuous seizures cause to the patient's family.[8]
- Lorazepam is the drug of choice for status epilepticus.[2, 5] Preferred routes are I.V. or rectally, I.M. is not recommended.[2] Do not infuse faster than 2 mg per minute.[2]
- Phenytoin should be used in benzodiazepine refractory status epilepticus by I.V. infusion. In older adults use a lower dose (15 mg per kg).[2] Check serum phenytoin level after 10 to 14 days of therapy and again if seizures occur.[8]

Twitching or Myoclonus:

- Consider opioid rotation –e.g., morphine to hydromorphone or fentanyl.[14]

Use:

- Clonazepam - starting dose 0.5 to 1 mg PO or S.C. at bedtime or b.i.d. if necessary.
- Lorazepam - 0.5 to 2 mg SL or S.C. q4h or p.r.n.
- Diazepam - 2.5 to 5 mg PO or rectally q12h p.r.n.

Simple Partial Seizure:

Use:

- Lorazepam 1 to 2 mg SL or S.C. STAT then 1 to 2 mg q4h to q6h.
- Phenytoin SR capsules 300 mg PO daily[1] or (100 mg t.i.d. if using liquid). Titrate dose.[5]

For Generalized Tonic/Clonic Seizures:

Initial management with:

- Lorazepam 4 to 8 mg I.V. or S.C. or SL STAT[3, 5] then 2 to 4 mg q4h to q6h.
- Diazepam 10 mg STAT,[3] repeated q15min (maximum 30 mg in 8 hours) until settled.
- Phenobarbital 80 to 120 mg S.C. q15min until settled.
- Phenytoin 10 to 15 mg per kg I.V. STAT, at 25 to 50 mg per minute.[3]

Recommendation 5 Treatment: Pharmacological continued...

For Generalized Tonic/Clonic Seizures continued:

Then start on:

- Phenobarbital 80 to 240 mg S.C. q12h with 120 mg q1h S.C. p.r.n. OR as a continuous S.C. infusion at 1200 mg per 24h (end stage care).[3, 15]
- Midazolam 5 mg S.C. STAT then 1 to 4 mg per hour by continuous S.C. infusion to manage the seizures.
- Phenytoin 300 mg daily PO at bedtime.[8]
- Valproic Acid - 20 mg per kg loading dose followed by 3 to 5 mg per kg per min infusion[5] or liquid rectally.

For Status Epilepticus: [5]

First line:

- Lorazepam 2 to 8 mg I.V. or S.C. or SL STAT then q10 to 20 min until controlled OR Midazolam 5 to 10 mg S.C. OR Diazepam 10 to 20 mg I.V. or rectally (if available).
- Phenytoin 50 mg per min I.V. until seizure stops or maximum 20mg per kg per 24 hours.
- Valproic acid loading dose 20 mg per kg then 3 to 5 mg per kg per min infusion.

Failing control:

- Phenobarbital 120 mg S.C. or I.V. and titrating to control.

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 twitching/myoclonus/seizure 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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