Opioid Induced Myoclonus

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Myoclonus Defined

Is it:
A. Uncontrolled twitching and jerking
B. Distressful
C. A symptom requiring more precise assessment
D. Caused by opioids and nonopioids
E. All of the above

Description

“The term myoclonus is used to describe uncontrollable twitching and jerking of various muscle groups, most frequently in the extremities.”

FOR MORE INFO...

What We Do Know about OIM

Dose related and unpredictable
All routes of administration
Complicates pain assessment in nonverbal /nonresponsive patients
Occurs independent pf age, gender, or PS

Pain Management Goals

Adequate relief
Safety
Reasonable timeframe
Minimize side effects
Convenient and least noxious means available

FOR MORE INFO...
WHO guidelines, AHQR, NCCN, etc

Sophie

42 year old female
MBC (visceral and brain), HER2+, ER/PR+
Pain meds:
Pathophysiology of OIM

Proposed neuropathology:
- Spinal motor neurons
- Metabolic pathways
- Role of opioids

Spinal Motor Neurons

Two distinct descending pathways may modulate opioid toxicity:
- Dorsolateral funiculus pathway modulating seizure activity
- Ventral funiculus pathway influencing myoclonic activity
Targeted therapy to enhance the modulating mechanism of these pathways

Spinal Motor Neurons

Disruption of central cortical inhibitory/excitability pathways
- Inhibition of Renshaw cells
- Antiglycinergic effect
Opioid and nonopioid binding sites
Pathologic changes in spinal column

Opioid Receptors

- Mu, delta and kappa receptor sites
- ORL 1
  - Opioid receptor-like
  - Ligand precursor is a molecule that plays a role in pain transmission

Metabolic Pathways

Liver and first pass
- Glucuronidation of MSO$_4$
- Uridinediphosphate glucuronyl transferases (UDPGT)
Renal insufficiency
Calcium and potassium

Role of Opioids

Poorly understood
Neuroexcitatory metabolites of opioids
Change in pH of cerebrospinal fluid
Toxicity of other adjuvant drugs
Facing the Facts

Where is the patient on the palliative care continuum?
Opioid related or other related causes?
Patient goals?
Patient risk factors influencing the opioid related SEs?
What management strategies?

Patient Factors

Hydration status
Patient goals, palliative care continuum
Metabolic changes addressed
Liver or renal
Drug-induced:
  - Can any drugs be withdrawn?
Comorbidities mimicking OIM

Management Approaches

Opioid dose reductions
Symptomatic management of AEs
Opioid Rotation (OR)
Switching route

Sophie

End of life care: focus on comfort
Reversible causes should be addressed and treated
Medications contributing to myoclonus
  - Changes?
Metabolic issues/comorbidities

Pain Management Goals

Early recognition of rapid dose escalation
Individual titration of opioid
  - Reduce AEs, optimize pain relief
Implement adjuvant drugs to treat symptoms

Symptomatic Management

Recommendations are empirical and/or anecdotal!
  - Muscle relaxants
  - Benzodiazepines
  - GABA antagonists
  - Valproic acid

FOR MORE INFO...

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**Muscle Relaxants**
- Baclofen
- Dantrolene
- Modafinil

**Benzodiazepines**
- Diazepam (out of favor)
- Lorazepam
- Clonazepam
- Midazolam

**Benzodiazepines con’t.**
- Midazolam
  - short half-life
  - CI
- Lorazepam
  - longer duration of anticonvulsant effect
  - versatility

**GABA antagonists**
- Gabapentin 600 mg BID
  - Minimal binding to plasma proteins
  - Not metabolized by the liver

**Valproic acid**
- Only anticonvulsant recommended
- 125-250 mg TID
- Can be increased to a total of 1500 mg/d administered in 3 divided doses

FOR MORE INFO...
- O’Mahoney S, Coyle N, Payne R (2001) Oncology
Other interventions

- NMDA inhibitors
- Haloperidol
- Alpha adrenergic agents in spinal analgesia

Opioid Rotation

- Not well understood
- Goal: decrease AEs and increase analgesia
- May open the therapeutic window
- Requires that the clinician understand equianalgesic dosing

Opioid Rotation

- Can minimize polypharmacy
- Outcomes are variable and unpredictable
- Lack of skill among clinicians
- Need to be conservative
- MSKCC: 3 days per drug

Opioid Rotation

- Tables are just guidelines
- Monitor patient closely during switchover period
- Titrate to clinical effect
- Start new opioid at 30-50% less than anticipated dose

Switching the Route

- Conflicting data
  - No evidence to support that route increases or decreases the incidence of myoclonus
  - Route of MSO₄ is related to incidence of myoclonus
  - Oral increases risk suggesting metabolites play a role

Sophie

- What are your recommendations?
- Dose reduction
- Symptom management
- Opioid rotation
- Route switch
Summary

More research needed to define optimal management
MOA for drug induced myoclonus
Management of drug-induced SEs
Chronic and malignant pain populations