Opioid Induced Neurotoxicity

By: Dr. Kathleen Sproules
Objectives

At the end of this offering the learner will be able to:

- Identify the signs and symptoms of Opioid Induced Neurotoxicity
- Describe the difference between Opioid Induced Neurotoxicity vs Pain
- Assist CRH patients, care givers, and health care providers to recognize and respond to signs and symptoms of Opioid Induced Neurotoxicity.
Case Study: Mary Ratched R.N.

85 year old former hospice nurse

50 pack year smoker

On hospice for lung Cancer

Has an apical tumor that causes severe pain in her right shoulder

Has had recent increases in her MS Contin to 90 mg BID with Roxanol 10-20 mg q 4 hours for breakthrough pain
Case Study: Mary Ratched continued

Ms. Ratched is having increased pain and restlessness.

She tells you she hurts “everywhere” when she is coherent enough to communicate.

She also mentions all the bugs on the wall to you at one point.

She has had very little p.o. intake for the last 36 hours.
Case Study Mary Ratched continued

She now begins to develop some twitching in her right leg

You call Dr. Usually Don’t Call You Back and he amazingly calls you back in 15 minutes

His order is to increase the Roxanol to 20mg every hour
What’s the Real Problem?
Opioid Induced Neurotoxicity

Will have one or more of the following:

- cognitive impairment
- extreme sedation
- hallucinations
- delirium
- myoclonus
- seizures
- hyperalgesia
OIH vs. PAIN FROM DISEASE

- OIH MAY PRESENT WITH A DIFFERENT DISTRIBUTION AND QUALITY

- OIH WILL LIKELY GET WORSE WITH CONTINUED DOSE ESCALATION BUT IMPROVE AFTER DECREASING THE DOSE, WHEREAS PAIN FROM DISEASE PROCESS MAY IMPROVE AFTER INCREASING THE DOSE
Predisposing Factors

- High dose of opioids
- Prolonged opioid use
- Recent dose escalation
- Dehydration
- Renal failure
- Advanced age
Treatment

• STOP the offending opioid

• Hydrate if possible to clear the metabolites of the opioid which is felt to be the cause

• Use alternative opioid

• Benzodiazepines to treat the myoclonus

• Antipsychotics to treat the psychosis
Warning:

- Do Not Give Narcan

- It does not reverse the neuroexcitatory effects and may exacerbate them
How does this happen?

The metabolites of opioids cause a neuroexcitatory and antianalgesic effect.

By increasing the dose of the opioid we increase the amount of metabolites and therefore increase the symptoms.

These metabolites cause an up regulation of the pain facilitating pathways at multiple levels in both the central and peripheral nervous system.
Offenders!

- Morphine Sulfate -> M6G and M3G
- Hydromorphone -> H3G
- These metabolites have no analgesic effect but have potent neuroexcitatory effects
- These metabolites are cleared by the kidneys therefore hydration will help
Less likely to offend

- Fentanyl – has no active metabolites
- Methadone – also has no active metabolites
- Both are better choices in patients with renal insufficiency as they are not cleared by the kidneys
Why is Methadone a good choice?

- Methadone is a racemic mixture of 2 isomers
- R isomer has analgesic properties
- S isomer is a NMDA receptor antagonist
- NMDA receptor activation is felt to be a contributing factor in OIH
- We can treat the pain while we block the bad guys (AKA Jayhawks)
What dose do you rotate to?

- Usual conversion ratios do not apply.

- As you were escalating the dose of opioid that caused the problem in the first place you were treating the side effects of the drug and not the actual pain that the patient was having.

- A good rule of thumb is to cut the equivalent dose by half.
Dr. Usually Don’t Call You Back

- Likely has not dealt with this problem before
- Has no idea what you are talking about
- Is typically not at the bedside with you
- Therefore it is up to all of us to recognize the problem and help our patients
• “Hoof beats go with horses”

• Doctors see this as a zebra.

• We need to look at it more as a mule!
Albutt  1870

“At such times I have certainly felt it a great responsibility to say that pain, which I know is an evil, is less injurious than morphia, which may be an evil. Here experience is needed. Does morphia tend to encourage the very pain it pretends to relieve?............in the cases in question, I have much reason to suspect that a reliance upon hypodermic morphia only ended in that curious state of perpetuated pain.”
Review of Case Studies

Presentation of Case Studies

Audience Discussion
Questions
Bibliography

- Marion Lee, MD; Sanford Silverman, MD; Hans Hansen, MD, Vikram Patel, MD, and Laxmaiah Manchikanti, MD. A Comprehensive Review of Opioid-Induced Hyperalgesia. Pain Physician Journal 2011; 14:145-161 ISSN 1533-3159

- Jianren Mao, MD, PhD, MGH Center for Translational Pain Research, Dept of Anesthesia & Critical Care, Massachusetts General Hospital, Harvard Medical School. Opioid-Induced Hyperalgesia. Pain Clinical Updates. Volume XVI, Issue 2. February 2008

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