The Pain of Addiction...
Opioid-Induced Hyperalgesia

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Opioid-Induced Hyperalgesia
(OIH)

A clinical phenomenon, characterized by increasing pain in patients that are receiving repeated doses of opioids...

History Opioid-Induced Hyperalgesia

As early as the 19th century, OIH was observed in patients receiving morphine for pain. In 1880, Rossbach noted that, “when dependence on opioids finally becomes an illness of itself, opposite effects like restlessness, sleep disturbance, hyperesthesia, neuralgia, and irritability become manifest.”
History Opioid-Induced Hyperalgesia

Pioneering studies by Himmelsbach and his coworkers during the 1930s and 1940s:

- Abrupt termination to a person who had been receiving daily doses of morphine produced symptoms that could be quantified.
- The intensity of this abstinence syndrome was related to the duration and magnitude of the dosing regimen and that certain signs only occurred after termination of a high dose regimen.
- Himmelsbach described opioid abstinence syndrome: "aching in bones, joints, muscles is probably the most common withdrawal symptom"

Research

Although direct and indirect experiments from animals and patients shows the evidence for opioid-induced analgesia, the clinical implications of this phenomenon continue to be unclear.

- Toxic metabolites
- Neuronal cell death
- P-glycoprotein inhibition
- Genetics

Definitions

Analgesia: Absence of sense of pain
Nociceptive: Causing pain
Agonist: A chemical substance capable of activating a receptor to induce a full or partial pharmacological response
Antagonist: A drug that counteracts the effects of another drug
Tolerance: Exposure to a drug induces changes that cause decreased response to drug’s effects over time
Sensitization: An increase in responsiveness upon repeated exposure to a stimulus
Risks related to Opioids

Physical dependence
Addiction
Overdose  Tolerance
Opioid-related side effects

*New*. Opioid Induced Hyperalgesia

Clinical Features of OIH

The common remark from patients is “Everything hurts”

- Severe allodynia
- Intractable, escalating pain on
- Delirium, mental status changes
- Increased doses results in increased pain
- Reducing dose or rotating opioid reversed symptoms in almost all patients

Early Identification is Key

OIH should be suspected when the opioid’s effect becomes less effective in absence of disease progression, especially if it is in conjunction with unexplained pain reports or diffuse allodynia unassociated with the original pain, and increasing pain with increasing doses

Tolerance vs. OIH:
- OIH produces diffuse, poorly defined pain
- OIH pain that extends to other areas from preexisting pain
- OIH worsens with increasing opioid dosage
Recent Evidence

- Animal Studies
- Human Studies
  - 2006 Prospective trial – long-acting morphine for patients with chronic low back pain resulted in measurable hyperalgesia within one month (Chu, 2006)

Common Culprit Medications

- Morphine is most common
- Dilaudid
- Oxycodone
- Less often with fentanyl or methadone

Barriers to Treatment

- Treating professionals often do not know about, recognize, or understand OIH
- False belief that opioids do not have a ceiling effect
- Family and patient need education
- Requires patience
In the News..

Protocols for Management of OIH

Subutex Protocol

Patients are induced with Subutex by administering the drug with gradual dose increments over 24 hours followed by stabilization doses. Based on severity, appropriate detoxification pathway is selected: Buprenorphine (Subutex) Pathway:
- 2mg SL Q3 hrs PRN for withdrawal symptoms
- Start Buprenorphine 2 mg SL (routine) as follows:

<table>
<thead>
<tr>
<th>7 DAY DETOX</th>
<th>5 DAY DETOX</th>
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<tbody>
<tr>
<td>2 mg SL at 0700, 1200, 1700 X 1 Day</td>
<td>2 mg SL at 0700, 1400, 2100 X 1 Day</td>
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<tr>
<td>2 mg SL at 0700, 1400, 2100 x 2 Days</td>
<td>2 mg SL at 0700, 1900 x 2 Days</td>
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<tr>
<td>2 mg SL at 0700, 1900 x 2 Days</td>
<td>2 mg SL at 0900 x 2 Days</td>
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5-Layer “Attack”

1. Hope/motivation
   - 1st visit/call
   - Immediate hope
   - Have been given the opposite

2. Detox - Buprenorphine
   - Detox – much easier/controls pain/positive antagonist

3. Use of Non-Opiates
   - NSAIDS (motrin)
   - Lidocaine
   - Heat/Ice
   - Muscle relaxants
   - Acupuncture
   - Tens Units
   - Anti-convulsants (lyrica)
   - SSRIs (cymbalta)
   - TCA’s (elavil)

4. Mind/Body
   - CBT
   - Yoga
   - Tai Chi
   - Meditation
   - Beach Walks

5. Live With It – Expectations

Treatment Works

- 90 day treatment protocol
- Mind/Body and Spirit
- 90 days to get the brain healing underway
- Levels of care
- Detox, inpatient rehab, partial, IOP, Aftercare
- Family education and healing
- MD-Program 90% success rate (treatment & Monitoring)
References

1) Angst MA, Clark JD: Opioid induced hyperalgesia. Anesth 2006; 104: 570-87
3) Davis MP, Shaiova LA, Angst MS: When opioids cause pain. 2007; 25: 4397-4398
4) Chang G, Chen L, Mao J: Opioid tolerance and hyperalgesia. 2007; 91: 199-211