Providing Expert Analgesia: Case Studies

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Objectives

- Assess the patient with acute pain, including the impact of complicating factors such as substance use disorder or persistent pain
- Describe interventions to provide multimodal analgesia to the patient with acute pain
- Evaluate the effectiveness of the analgesic plan

The Problem

- **Substance use disorder is a BIG problem**
  - **Inadequate analgesia can trigger a relapse and create a new addiction**
- **Persistent Pain**
- **Acute on Persistent Pain**
- **Co-morbidities**
  - **Behavioral Health Issue**

Population of Patients

- Appropriately using prescribed opioids
- In recovery
  - Methadone (Dolophine)
  - Buprenorphine (suboxone)
  - Naltrexone (Vivitrol)
  - Active substance abusers
- Unauthorized use of prescribed medications
  - Opioids
  - Substitution therapy
- Planned or unplanned admission
- Acute on persistent pain
- Co-existing behavioral health issues

Assessment

- Requires a conversation
- Should be on going
- More than "just a number"
- Focus on function

ASPMN Position Statement

- **Use 10 step Universal Protocol approach for patients with persistent pain**
  - **Make a pain diagnosis with appropriate differential**
  - **Psychologic assessment, including risk of addictive disorder**
  - **Informed Consent**
  - **Treatment agreement**
  - **Pre/post intervention assessment of pain level & function**
  - **Appropriate trial of opioid therapy with or without adjunctive treatment**
  - **Reassessment of pain level & level of functioning**
  - **Regularly assess the "5As" of pain medicine**
  - **Periodically review pain diagnosis, coexisting conditions, including the presence of a SUD, & treatment plan**
  - **Documentation**

5 As

- A – analgesia
- A – activities of daily living
- A – adverse effects
- A – aberrant behavior
- A - affect

ASPMN RECOMMENDATIONS

Assessment

- Offer further assessment for possible substance use disorder for patients with illicit or non-prescribed illicit substances found on urine drug testing

Urine Tox Screening

- Screening test, confirmation may be needed
- Know what is on your lab panel
- Know your lab's thresholds
- Where any analgesics administered prior to obtaining sample?

Case Study -1

Assessment

Interventions

- Pharmacologic
  - Multimodal
    - opioid
    - Non-opioid
  - Pre-emptive
  - RTC vs. p.r.n.
  - route
- Non-pharmacologic

Multimodal Options

- Standard of care for all analgesia!
- Opioids
- NSAIDS
- Acetaminophen
- Gabapentin
- Ketamine
- Lidocaine infusions
- Regional
  - Blocks
  - Local anesthetics
  - PCEA
- Non-pharmacologic

ASPMN Position Statement Recommendations

- Consider multimodal & integrative therapy options
- Formal assessment tools & standard procedures are encouraged to guide individualized care & to limit legal liability

- (ASPMN, Sept. 2012)
- (Chou, APS, ASA, 2016)

Prescribing and Administering Opioid Doses Based Solely on Pain Intensity: A Position Statement by the American Society for Pain Management Nursing® 2016

- Prescribing opioid doses based solely on pain intensity is problematic for many reasons including that pain intensity ratings are completely subjective, cannot be measured objectively, and are not repeatable findings even within the same individual
- Many factors in addition to pain intensity influence opioid requirements
- There is no research showing that a specific opioid dose will relieve pain of a specific intensity in all patients

"Opioid Debt"

- **Patients physically dependent on opioids (methadone or buprenorphine) must be maintained on daily equivalence before ANY analgesic effect is realized with opioids used to treat acute pain**
- **Opioid analgesic requirements are often higher due to increased pain sensitivity & opioid cross tolerance**
- **Relapse to active drug use may be higher with inadequate pain management than with use of opioid analgesics**

Case Study 2

- Inadequate Pain Control following major abdominal surgery

Why Low-Dose Ketamine?

Shown in multiple studies to improve patient outcomes:

- **Reduce total opioid consumption during inpatient stay**
- **Decrease length of hospital stay**
- **Decrease opioid consumption post-discharge**
- **Earlier time to ambulation**
- **Decreased post-operative complications**

Other Benefits of Low-Dose Ketamine

- Works on different receptors than opioids
- An alternative when unresponsive to opioids
- Decreases central excitability
- Less sedation, preserved respiratory function
- Does not depress cardiovascular function, hepatic blood flow, or bowel function
- May help 'reset' opioid receptors so they are functional again

Mechanism of Action

- Ketamine inhibits the binding of excitatory amino acids, such as glutamate, to the NMDA receptors, thus blocking the transmission of painful stimuli.
- Pain relief happens at lower blood levels than loss of consciousness (sub-anesthetic doses produce analgesia)
- Ketamine is a controlled, class 3 substance

NMDA Receptor

***N*-methyl-D-aspartate receptor (NMDA)**

- **a glutamate receptor and ion channel protein found in nerve cells.**
- **It is activated when glutamate and glycine bind to it.**
- **This receptor has been shown to be involved in the development of chronic pain and opioid tolerance.**
- **Studies show that when the receptor is blocked with ketamine, average pain scores improve.**

Pharmacokinetics of Ketamine

Highly Lipid Soluble

- **Fast onset of action: 30 seconds**
- **Peak: 1 minute**
- **Duration: 60 minutes**
- **½ Life: 2-3 hours**

- **Ketamine is metabolized by the liver cytochrome P450 enzyme system**

Possible Adverse Effects

- **Hallucinations**
- **Psychosis**
- **Vivid Dreams**
- **Nystagmus**
- **Sedation**
- **Diaphoresis**
- **Nausea**
- **Vomiting**
- **Lacrimation**
- **Salivation**
- **Increased intraocular/intracranial pressure**

Note: These symptoms are usually not seen with low-dose infusions

Contraindications

- High risk coronary or vascular disease
- Uncontrolled hypertension
- Elevated intracranial pressure
- Elevated intraocular pressure
- Globe injuries
- **History of psychosis or severe PTSD**
- Sympathomimmetic Syndrome
- Moderate to severe hepatic dysfunction
- Recent liver transplantation
- Porphyria or related disease
- **Recent history of ETOH or drug abuse**
- Untreated seizure disorder

Case Study - 3

- Difficult to control pain following orthopedic patient in patient with pre-existing chronic pain

Case Study - 4

- Pain in a patient using buprenorphine

Buprenorphine

- Parenteral & transdermal approved for pain
  - NOT addiction treatment
  - Cannot be used off-label
- Sublingual approved for addiction
  - NOT pain treatment
  - Can be used off-label

Buprenorphine

- Binds tightly to the mu opioid receptor
- Does not “turn on” the receptor as completely as a full mu agonist opioid
- Sublingual tablets (film) require at least 20 minutes for effect

Buprenorphine

- Half life is about 37 hours
  - –Analgesic half life is shorter
  - –3 doses per day needed to treat pain (Vadivelu,2014)

Buprenorphine Strategies: Options

- Continue buprenorphine maintenance therapy & titrate short-acting opioid analgesics (for pain of short duration)
- Divide buprenorphine dose to every 6-8 hours
- Discontinue buprenorphine maintenance therapy 72 hours prior & use opioid analgesics
- Discontinue buprenorphine, treat opioid dependence with methadone & use short acting opioids to treat pain

Probuphine

- Approved May 2016 by FDA
- Subdermal implant
- Provides effect for 6 months, then removed
- $5,940
- (suboxone films $3,184 for 6 months)

Buprenorphine (Sublocade)

- Monthly sq. injection
- 2017 FDA approval
- Indicated for patients on a stable dose of buprenorphine for a minimum of 7 days
- Treatment of moderate to severe opioid use disorder

Case Study - 5

- Post-operative pain in a patient using methadone

Methadone (Dolophine)

- Multiple analgesic mechanisms of action
  - Active at mu, delta & kappa opioid receptors
  - NMDA receptor antagonist
  - Serotonin & norepinephrine reuptake inhibitor
- Analgesic option for syndromes poorly responsive to other opioids
- Used for maintenance therapy to reduce craving & prevent withdrawal

Methadone: Clinically Important Characteristics

- **Highly lipophilic**
  - **85% oral bio-availability**
  - **Readily crosses blood-brain barrier**
- **Highly protein bound**
- **Wide distribution**
  - **Slow elimination**
  - **Long, highly variable half-life (5-100+ hours, average 20)**
- **Duration of action**
  - **Initial dosing: 4-6 hours**
  - **8-12 hours with accumulation**
  - **Methadone (Dolophine) maintenance dosed every 24 hours does not provide analgesia beyond 6-8 hours**
- **Wide individual variability in pharmacokinetics & response**
- **Potential to prolong QTc**

Methadone

- Chronic pain
  - Significant tolerance is often seen in patients with past history of opioid abuse, may require higher doses
  - High doses of methadone for chronic pain has been seen to result in serious side effects (Vadivelu, 2014)
- Maintenance
  - Higher risk of toxicity, due to low therapeutic index with higher risk of accidental OD & methadone poisoning
  - Possesses NMDA blocking properties, can alter central pain processing, (Vadivelu)

Methadone: Acute Pain & Maintenance Therapy

- Continue the once daily dose through peri-operative period (Stromer)
- To treat pain may need 1-5 x higher dose & shorter intervals
- Substitution with fentanyl for methadone for the patient on methadone maintenance, better to use oxycodone or hydromorphone, not morphine due to metabolites
- Avoid mixed agonist/antagonist (butorphanol) they will precipitate withdrawal
- Evaluation effect carefully.
- Risk of cumulative effect & OD

Naltrexone (Vivitrol)

- Option for Maintenance Opioid Therapy
- Monthly injection
- Oral daily
- Must be off opioids for 7 days prior to starting
  - Peak plasma 2-3 days
  - Begins to decline in 14 days
- Has no analgesic properties

Naltrexone (Vivitrol)

- Issue if acute pain management needed
- Can overcome blockade with 6-20x usual opioid dose without significant respiratory depression or sedation
  - Must monitor patient very closely
- Optimal discontinue oral 72 hours prior to elective surgery
- IM depot discontinue 1 month prior to elective surgery

Evaluation

- Starts with a reasonable goal
- Good assessment, reassessment
  - What is the pain due to?
  - Injuries?
  - Complications?
  - Withdrawal?
- Focus on function
- Ongoing
- Coordinated transfer of care

Conclusion

- Assessment is essential
- Multimodal approach
- Use ALL resources
  - Social worker
  - Behavioral health
  - Outpatient providers
  - Pharmacist
- Treat patient with respect

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