Opioid-Induced Androgen Deficiency

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Disclosure Statement

• No conflict of interest to disclose
• Presentation is educational in nature and abides by non-commercial guidelines.

Learning Objectives

1. Review incidence of opioid prescribing and opioid-induced androgen deficiency (OPIAD)
2. Identify proposed mechanisms of OPIAD
3. Examine incidence and comparative risks of opioids
4. Describe impact of hypogonadism in patients with chronic pain
5. Propose pharmacist-driven intervention strategies
Patient Case

- A 39 year old male veteran returns for a follow-up appointment with c/o recurrent dizziness and feeling fatigued. He also mentions to the provider that his sex drive has been low over the past few months.

- The clinician concludes that the oxycodone he ordered for the patient’s phantom limb pain is the cause for his dizziness and fatigue, discusses effects of normal aging processes, and sends the patient home with a prescription for sildenafil.

- What about the risk of OPIAD?

Opioid Use in America

- Millions of Americans have some form of chronic pain

- 2012: ~260 million Rx’s for opioid pain medication prescribed by healthcare providers in the United States

- 2015: HHS Opioid Initiative and National Plan Strategy
  - Focus on improving opioid prescribing
  - Expanding use of medication assisted treatment

- 2016 CDC guidelines for prescribing opioids for chronic pain
  - Discuss risks and benefits before & throughout treatment
  - Prescribing IR over ER opioids
  - Incorporate risk mitigation strategies

Opioids

- Opioid Mu receptors widely distributed throughout the body with various effects

  - Analgesia
  - Anxiolytic
  - Sedation
  - Constipation
  - Nausea/Vomiting
  - Dizziness/Fatigue
  - Respiratory Depression
  - Bradycardia
  - Pruritus
  - Adrenal Suppression
  - Insomnia
  - Dependence

References:
CDC Guideline for Prescribing Opioids for Chronic Pain. CDC Guideline for Prescribing Opioids for Chronic Pain. Recommendations and Reports. / March 18, 2016 / 65(1);1–49
Opioid-Induced Androgen Deficiency

- Established adverse effect with prolonged use (>1 month)
- Commonly underdiagnosed complication in patients with chronic pain
- Symptoms may be masked by opioid ADE's, complications of chronic pain, or mistaken for normal aging process
- May be dose dependent
- May be formulation dependent
- May be duration dependent
- Considered reversible


OPIAD & Hypogonadism

Decreased Libido
Deep Disturbance
Increased Visceral Fat
Decreased Bone Density
Decreased Lean Muscle Mass
Fatigue/Low Energy
Depressed Mood
Decreased DHEA

OPIAD: Proposed Mechanisms of Action

- Indirect inhibition of GnRH
- Reduced androgen production by adrenal glands
- Induced apoptosis of Leydig cells (in vitro)
- Down-regulation of noradrenergic and up-regulation of GABAergic neurons

DHEA shown to decrease in opioid therapy

Relative Risks

- Higher risk with continuous opioid exposure
- Hypogonadism risk is more common with long-acting vs. short-acting opioids (57% vs. 35%)
- Highest incidence reported with methadone use in pain management
- Lower incidence with:
  - Buprenorphine
  - Tapentadol


Opioid Dose and Formulations

- Higher opioid dose associated with increased risk
- Dose change may have greater impact on OPIAD in patients taking short-acting opioids
- Retrospective cohort of 1585 men on chronic opioid therapy
  - Patients on short-acting opioids had 24% increased risk for OPIAD with every 10-mg increase in MED
  - Patients on long-acting opioids had 2% increased risk for OPIAD with every 10-mg increase in MED


Patients with Chronic Pain and Hypogonadism

- Increased in perception and tolerance of pain
  - Testosterone functions in pain
    - Maintenance of blood brain barrier
    - Androgenic healing and tissue growth
    - Maintenance of muscle mass
    - Maintenance of bone density
- Increased risk of other co-morbidities
  - Osteoporosis
  - Hyperlipidemia
  - Weight gain
- Decreased quality of life

Pharmacist-Led Treatment Interventions

- Patient education and monitoring
  - Explain risks at initiation of opioids
  - Screening tools: ADAM questionnaire
- Opioid rotation: tapentadol, buprenorphine
- Switching from ER to IR opioids
- Testosterone replacement therapy
  - Contraindications
  - Cardiovascular risks
- Dual-energy x-ray absorptiometry (DEXA) screening
  - Routine for patients on long-term opioids and at risk for osteoporosis
  - Ensure adequate levels of calcium and vitamin D

Summary

- Opioids are commonly prescribed to patients suffering from uncontrolled chronic pain
- OPIAD is a common, yet underdiagnosed, consequence of chronic opioid use
- Incidence of OPIAD may depend on dose, formulation and duration of use
- Pharmacists can play a major role in identifying and mitigating risks of this drug-induced disorder

Question #1: True or False

Long acting opioids are associated with greater incidence of OPIAD compared to short-acting opioids
- True
- False
Thank You