9:00 a.m. – 10:30 a.m.

INTERNATIONAL CONFERENCE ON OPIOIDS June 7-9, 2015

Intensive Training on ER/LA Opioids

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Extended-Release and Long-Acting (ER/LA) Opioids: Risk Evaluation & Mitigation Strategy (REMS)

OPIOID REMS RESOURCE:
TOOLS FOR EFFECTIVE MONITORING OF PATIENTS ON ER\LA OPIOIDS

opioid REMS resource

Co-provided by:

DANNEMILLER

CME
CONTINUING MEDICAL EDUCATION

Learning Objectives

- To apply communication strategies to strengthen relationships with patients and improve patient knowledge of their opioid treatment
- To adequately monitor patients on opioid therapy utilizing available resources, including Patient-Prescriber Agreements, and electronic Prescription Monitoring Programs

Acknowledgment

- Perry Fine
- Charles Argoff
- Michael Ashburn

Am College of Occupational and Environmental Medicine: Practice Guidelines for Opioids

- History, phys exam recommended, although no quality studies to support
- Screen patients
- Opioid trial
- Maximum MED of 50 mg, for most pts
- Use of an OTA
- Baseline and random UDS
- Discontinue if no functional improvement, noncompliance, side effects, or concurrent use of benzos
- Taper prior to discontinue

JOEM 2014; 56:e143

Informed Consent

- Obtain prior to initiating therapy
- Fosters communication between prescriber and patient
  - Discuss goals of treatment
  - Discuss expectations of provider and patient
  - Discuss risks of therapy/alternatives

Informed consent is a process, not a form

Patient-Prescriber Agreements (PPAs)

Used in conjunction with verbal or written informed consent

- Reviewed with patient
- Signed by both parties and a witness
  - Copy provided to patient and also retained by prescriber
- Purpose:
  - Provide patient with education about therapy
  - Highlight potential risks and benefits of therapy
  - Review treatment goals

Patient Opioid Treatment Agreement

http://www.consultantlive.com/sites/default/files/cl1422349.png

Wetherington B, Harned M, Sloan PA. KSA Annual Mtg 2015

Monitoring of Patients during Opioid Therapy

- Evaluate benefits vs. risks of continuing opioid treatment
  - Assess for addiction risk
- Evaluate the patient's status for necessity of continued opioid therapy
- Evaluate the patient for any changes in function from baseline after opioid therapy

Adverse Effects from Chronic Opioids

- **Typical: constipation, N&V, sedation**
- **Hyperalgesia**
- **tolerance**
- **Opioid overuse headache**
- **Restricted automobile driving?**
- **Immunosuppression**
- **Hypogonadism**
- **Tool for suicide-death from overdose**
- **Aberrant opioid-related behavior**
- **Rare: hypoglycemia, respiratory depression**
- **?central sleep apnea**
- **Death**

Benyamin R. Pain Physician 2008; 11:S105
Birthi, Nagar, Nickerson, Sloan. J Opioid Manage 2015; In Press.

Behaviors Predictive of Opioid Misuse

More predictive

- Selling prescription drugs
- Prescription forgery
- Stealing other patients drugs
- Injecting oral formulations
- Obtaining prescription drugs from street
- Abuse of illicit drugs
- Multiple unsanctioned dose escalations
- Recurrent prescription losses

Less predictive

- Aggressive complaining of need for higher doses
- Drug hoarding
- Requesting specific drugs
- Obtaining drugs from other providers
- Unsanctioned dose escalation 1-2 times
- Unapproved use of the drug to treat other symptoms

Passik SD. Oncology 1998; 12:517-521.

KENTUCKY

Kentucky.gov Kentucky

KASPER (KY All Schedule Prescription Electronic Reporting)
New on the KASPER Web site!
See the KASPER Trend Report Maps section below for a geographical representation of KASPER data regarding the dispensing of controlled substances in Kentucky.

What is KASPER? The Kentucky All-Schedule Prescription Electronic Reporting System (KASPER) tracks controlled substance prescriptions dispensed within the state. A KASPER report shows all scheduled prescriptions for an individual over a specified time period, the prescriber and the dispenser. Enhanced KASPER (eKASPER) Web-based access to KASPER data.

ASA Newsletter 2011; Dec: 18

Prescription Drug Monitoring Programs (PMPs)

- Online access of patient prescription history
- Powerful tool in discussing medication history with patient
  - Patient does not report certain agents to you
  - Patient pays for drug of abuse with cash at an unusual pharmacy
  - Alerts prescriber to risk of sedation with concomitant agents if not divulged otherwise

Case Study: Martha

A 78 year-old female who is a long-standing patient of yours with a history of breast cancer, lumbar fusion surgery, osteopenia and osteoporosis

- She has been maintained for the past 6 months on fentanyl patch 25 mcg/hour, and hydrocodone/acetaminophen 7.5/325 one tablet q6H for breakthrough.
- The past 3 visits she presents 1-2 weeks early for her prescription refills
- You query her and she tells you that she is just not feeling as much relief with her medicines and she is coming in early
- She appears sad and doesn't make eye contact with you, which is different for her
- You notice that an unkempt young couple has now started bringing Martha in to see you and your nurse remarks that they have been present during the past three visits

Case Study: Martha - Question

Which of the following is the next best step?

A. Speak with Martha about her opioids with the young couple present
B. Speak with the young couple privately about Martha
C. Recommend a urine drug screen on this patient well-known to you
D. Discharge Martha from your practice because of her non-compliance

Case Study: Martha

How should we proceed with this known patient?

- Recommend pill count
  - Martha tells you that she must have misplaced the bottle at home with the rest of her medicines that she gets from her internist and cardiologist
- Recommend urine drug screen
  - Drug screen comes back negative for opiates
- What should you now do?

Case Study: Martha

Discuss the immediate result with Martha

- Notify her that her urine drug screen was negative for her pain medication
- Given the agents she is taking, her urine drug screen should be positive. Further Gas Chromatography (GC) testing is also negative
  - Martha admits to you that the young couple are her neighbors who take her to her doctors' appointments and steal her opioid medications. She states that because of her condition, she is not able to drive to her and the neighbors have taken advantage of her

Case Study: Martha

What should be done next?

- Notify the social worker at your institution along with the Police Department to report elder abuse as well as drug diversion of the young couple

http://emedicine.medscape.com/article/805727-workup

Identifying and Managing Opioid Abuse and Diversion

- Assessing risk and aberrant behaviors
- Scheduled and random urine drug tests
- Prescription monitoring program access
  - Based on response, communication with pharmacies
- Assessing efficacy of pain control

The Role of UDT

- Goals of UDT in clinical practice
  - Provides documentation of treatment plan compliance by detecting presence of a particular drug/metabolites
  - Abnormal results may indicate diversion/abuse
- Reliability of results are a function of laboratory results/equipment
- Most important benefit: allows for discussion with patient regarding the use of agent

http://www.nhmrs.org/sites/default/files/Pdfs/UrineDrugTestingguide.pdf
http://www.pharmacomgroup.com/udt/udt5.pdf
Heit HA, Gourlay DL. *J Pain Symptom Manage*. 2004;27:260-267.
Dove B, Webster LR. *Avoiding Opioid Abuse while Managing Pain: a Guide for Practitioners*. North Branch, MN: Sunrise River Press; 2007.

Urine Drug Testing (UDT)

- Should be performed randomly
- Testing is performed with point-of-care followed by Gas Chromatography (GC)/Mass Spectrophotometry (MS)
- Prescribers should be aware of which agents may show up in the results based on drug metabolism
- Prescribers should be aware of the presence of false-positive and negative results

Synthetic/Semisynthetic Opioids

- Opiate assay testing detects morphine and codeine
  - synthetic opioids including methadone and fentanyl are not detected
  - semisynthetic opioids including oxycodone, hydrocodone, buprenorphine, hydromorphone are not reliably detected
- GC/MS will identify these medications

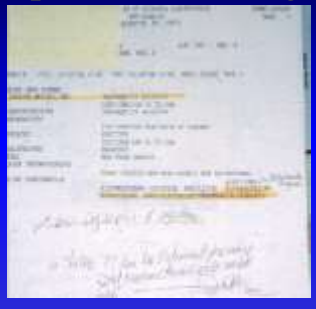
Heit HA, Gourlay D. *J Pain Sympt Manage*. 2004;27:260-267.

OXYCODONE

POTENTIAL URINARY ANALYTES
Oxycodone ~ Oxymorphone ~ Hydrocodone

Oxymorphone is a metabolite of oxycodone
Hydrocodone arises as an impurity in commercially manufactured oxycodone

Inappropriate Urine Drug Screen



Reisfield, GM, Sloan PA. J Opioid Manage 2007; 3:333-337

DETECTION TIME IN URINE WITH IMMUNOASSAY TECHNOLOGY

Drug Class	Detection Times
Amphetamines	1 to 2 days
Barbiturates	up to 2 days - up to 30 days after phenobarbital use
Benzodiazepines	Up to 3 days - up to 30 days after Diazepam or Chlordiazepoxide
Cocaine	2 to 4 days - heavy / chronic users 7 days, possibly longer
Ethanol (Alcohol)	2 to 4 hours
Marijuana (THC)	up to 5 days after occasional use - chronic users 30 days, sometimes longer
Methadone	2 to 3, up to 30 days
Opiates	2 days - heroin metabolite (6-AM) less than 8 hours
Phencyclidine	8 days Up to 30 days in chronic users

Gourlay DL, Heit HA. *Pain Med*. 2009;10 Suppl 2:S115-123.

The Urinator is small enough to hold in your hand and can be used many times- even shared with others.

"a specially designed 3 foot tube with on/off clip which may be routed along the body to the groin area to easily simulate the act of actual urination. It's virtually impossible to detect, even to those who may be standing around

Resources for Prescribers

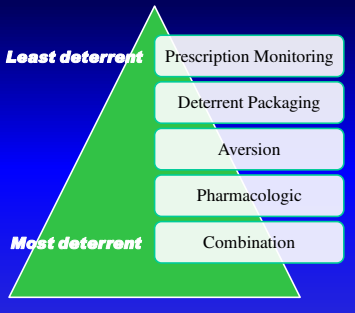
SAMHSA

MAIN WEBSITE: http://www.samhsa.gov/
TREATMENT CENTERS: http://findtreatment.samhsa.gov

MAIN WEBSITE:
http://www.drugabuse.gov
FOR HCPs:
http://www.drugabuse.gov/nidamed-medical-health-professionals

NIH National Institute on Drug Abuse
The Science of Drug Abuse & Addiction

Deterring Abuse



Aversion techniques include:
- Capsaicin – burning sensation
- Ipecac – emetic
- Bitrex® – bitter taste

Pharmacologic techniques include:
- Sequestered antagonist
- Bio-available antagonist
- Pro-drug

Pharmacological Solutions

- Abuse-Resistant Formulations
  - Decrease access to drug
  - Physical barrier (gels, shell, tamper-resistant)
    - Drug becomes unavailable when barrier is disrupted
- Abuse-Deterrent Formulations
  - Designed to alter impact of abuse
  - Pharmacologic barrier (drug with deterrent agent)
    - Deterrent in the form of an antagonist (naloxone) vs. irritant (capsaicin)
    - Deterrent not released under normal circumstances
    - Deterrent released only with formulation tampering

Deterrent Agents

- Targiniq ER
  - The FDA approved this oxycodone/naloxone agent (7/23/14)
    - Naloxone only released with tampering of the agent
      - Crushing and snorting pill
- Oxycontin
  - ER product that has been formulated to be difficult to crush/tamper
- Embeda
  - The FDA approved labeling for this ER morphine/naloxone agent (10/17/14)
    - This agent had been approved for use in 2009 but was withdrawn after manufacturing concerns (3/11)

http://blogs.fda.gov/fdavoice/index.php/2014/07/a-reminder-of-the-promise-and-limitations-of-abuse-deterrent-properties/
http://www.fda.gov/downloads/Drugs/DrugSafety/UCM179172.pdf

Definition of Terms

Misuse
- Use of a medication (for a medical purpose) other than as directed or as indicated, whether willful or unintentional, and whether harm results or not.

Abuse
- Any use of an illegal drug.
  The intentional self-administration of a medication for non-medical purpose, for example, altering one's state of consciousness.

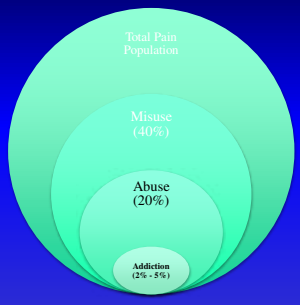
Diversion
- The intentional removal of a medication from legitimate and dispensing channels.

Addiction
- A primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations.
  Behavioral characteristics include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, craving.

Pseudoaddiction
- Syndrome of abnormal behavior resulting from under-treatment of pain that is misidentified by the clinician as inappropriate drug-seeking behavior.
  Behavior ceases when adequate pain relief is provided.
  Not a diagnosis; rather, a description of the clinical intention.

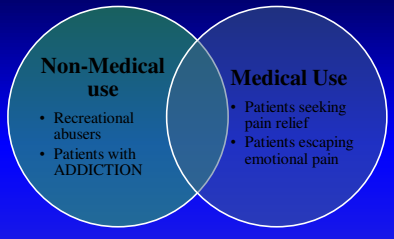
Katz NP, et al. *Clin J Pain.* 2007;23:648-660.

Prevalence of Misuse, Abuse, and Addiction



Webster LR, Webster RM. *Pain Med.* 2005;6:432-442.

Problematic Use of Opioids and Why?

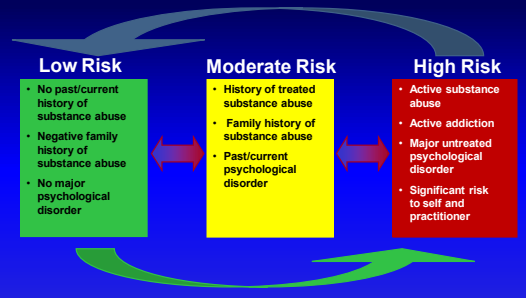


Aberrant Behavior Risk Factors

BIOLOGICAL	PSYCHOLOGIC	SOCIAL
• Age ≤ 45 years • Male>Female • Family history of prescription drug or alcohol abuse • Tobacco Use	• Substance use disorder • Preadolescent sexual abuse (in women) • Major psychiatric disorder (e.g., personality disorder, anxiety or depressive disorder, bipolar disorder)	• Prior legal problems • History of motor vehicle accidents • Poor family support • Involvement in a problematic subculture

Katz NP, et al. *Clin J Pain.* 2007;23:103-118; Manchikanti L, et al. *J Opioid Manag.* 2007;3:89-100.
Webster LR, Webster RM. *Pain Med.* 2005;6:432-442.

Identify and Stratify



Webster LR, Webster RM. *Pain Med.* 2005;6:432-442.

10 Principles of Universal Precautions

1. Diagnosis with appropriate differential
2. Psychological assessment
3. Informed consent
4. Treatment agreement
5. Pre-/post-intervention assessment of pain level and function
6. Appropriate trial of opioid therapy adjunctive medication
7. Reassessment of pain score and level of function
8. Regularly assess the "Four A's" of pain medicine: *Analgesia, Activity, Adverse Reactions, and Aberrant Behavior*
9. Periodically review pain and comorbidity diagnoses, including addictive disorders
10. Careful, Accurate and thorough documentation

Courtney DL, Heit HA. *Pain Med.* 2009;10 Suppl 2:S113-123.
Courtney DL, et al. *Pain Med.* 2007;8(2):197-212.

Principles of Responsible Opioid Prescribing

Treatment Plan

- Key points resolved before initiating opioid therapy
  - Diagnosis established and treatment plan developed
  - Risk level characterized
  - Single provider care or need to refer to pain management/addiction specialists
- Non-opioid modalities considered
  - Non-invasive and interventional techniques
  - Behavioral strategies
  - Pain rehabilitation program

Principles of Responsible Opioid Prescribing

Prescribers should periodically review:

- Drug choice, dose, and route of administration
- Anticipation and management of adverse effects
- Therapeutic outcome assessment
- Patient-provider agreements
- Consultations of specialists as needed

Medical Records

Maintain current, accurate and complete records

- Medical history & physical examination
- Diagnostic, therapeutic, lab results
- Evaluations/consultations
- Treatment objectives
- Discussion of risks/benefits
- Treatment and medications
- Instructions/agreements
- Periodic reviews
- Discussions with and about patients

Fishman SM. *Pain Med.* 2006;7:360-362. Federation of State Medical Boards of the United States, Inc. *Model Policy for the Use of Controlled Substances for the Treatment of Pain.* 2004.

Considerations

- What is conventional practice for this type of pain or pain patient?
- Is there an alternative therapy that is likely to have an equivalent or better therapeutic index for pain control, functional restoration, and improvement in quality of life?
- Does the patient have medical problems that may increase the risk of adverse effects?
- Is the patient likely to manage the opioid therapy responsibly?
- What is the risk of misuse, abuse, addiction and diversion?
- Who can I treat without assistance of a specialist?
- Who should I not treat but instead refer/consult to a specialist?

Fine PG, Portenoy RK. *Clinical Guide to Opioid Analgesia.* Vendome Group, New York, 2007.

Differential Diagnosis of Aberrant Drug-Taking Attitudes and Behavior

- Addiction (out-of-control, compulsive drug use)
- Pseudoaddiction (inadequate analgesia)
- Other diagnosis
  - Organic mental disorder
    - Confusion secondary to medical causes
  - Depression/anxiety/situational stressors
    - self-medication
  - Personality disorder
    - Impulsive entitled behavior
  - Chemical coping
- Criminal intent (diversion)

Passik SD, Kirsh KL. *Curr Pain Headache Rep.* 2004;8:289-294.

Identifying Patients at Risk for Opioid Abuse and Diversion

- Predictive tools
- Aberrant behaviors
- Urine drug testing
- Prescription monitoring programs
- Severity and duration of pain
- Communication
  - Patient, pharmacist, social support/network

Patient Education Document

www.er-la.opioidrems.com/IwgUI/rems/pdf/patient_counseling_document.pdf

Patient/Family Education Proper Use of ER/LA

- Medication should be taken as prescribed
- Discuss product-specific information
- Encourage review of medications at each visit
- Medication guide from pharmacy should be reviewed by patients
- Review AEs and recommend immediate call to prescriber if AEs occur.
  - report serious AEs to the FDA: www.fda.gov/downloads/Safety/MedWatch/HowToReport/DownloadForms/UCM082725.pdf or **1-800-FDA-1088**
- Discuss risks of falls, danger of operating heavy machinery and driving an automobile

DA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. Available at www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf
The ER/LA Opioid Analgesics Risk Evaluation & Mitigation Strategy. *Selected Important Safety Information. Abuse potential & risk of life-threatening respiratory depression.* www.erlopioidrems.com/IwgUI/rems/pdf/important_safety_information.pdf

Patient/Family Education Proper Use of ER/LA

- Do NOT crush, chew tablets, capsules
- Do NOT tear, grind, crush patches
  - The above actions may lead to overdose and death.
  - Some agents may able to be sprinkled on applesauce or administered via a feeding tube for patients unable to swallow.
  - Product insert MUST be consulted.
- In the event of overdose of a patient, child or pet inadvertently ingesting an opioid, poison control/emergency services MUST be immediately notified.
  - Confusion, slurring of speech
  - Feeling faint or dizzy
  - Difficulty waking up from sleep
  - CALL 911!
  - Call National Poison Hotline 1800-222-1222.

FDA. *Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics.* 8-28-2012. www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM311290.pdf

Patient/Family Education Proper Use of ER/LA

- Store ER/LA in a secure location away from pets, visitors, children
- Selling ER/LA is against the law
- Sharing ER/LA can lead to death and other AE in others
- Always dispose of safely

Patient/Family Education Proper Use of ER/LA

- Medications should only be taken by the patient
- Misusing drugs = abusing illicit street drugs
- Be aware of using alcohol while taking prescription ER/LA opioids as death may occur

Ape-Hall P, et al. *J Sch Nurs*. 2008;24(suppl):S1-16. Paulozzi LJ, et al. *Pain Med*. 2012;13:87-95. Webster LR, et al. *Pain Med*. 2011;12 Suppl 2:S26-35.

Patient/Family Education

- Encourage parents on ER/LA to speak with their teenage children about these agents, and the safe use of these drugs
- Perform regular pill counts
- Keep pills in a secure location
- Promptly and properly discard expired/unused medications

Disposal of ER/LA Opioids

- Take-back days
  - A safe, convenient, and responsible means of disposing of prescription drugs, while also educating the general public about the potential for abuse of medications
    - Http://www.deadiversion.usdoj.gov/drug_disposal/takeback
- Drop boxes
  - Secure and Responsible Drug Disposal Act of 2010 that expands efforts to safely dispose of otherwise unused controlled substances
    - http://rxdrugdropbox.org/
    - www.americanmedicinechest.com/
    - www.takebacknetwork.com/local_efforts.html

www.deadiversion.usdoj.gov/drug_disposal/

Disposal of ER/LA Opioids

If the drop box/take back is not available:

- Place unused drug in a sealable bag out of it's original container mixed with unpalatable substances (coffee/tea grounds, kitty litter, garbage)
  - Remove patient identification information along with drug label when discarding medicine vials
- Flush pills/patch down toilet
  - Ensure that patch is folded and adheres to itself

Drugs Recommended for Disposal by Flushing FDA (2013)

- Buprenorphine: Suboxone
- Fentanyl: Abstral, Actiq, Fentora, Onsolis
- Morphine products: Avinza, Embeda, Kadian, Morphine, MS Contin,
- Hydromorphone: Exalgo
- Methadone
- Oxymorphone: Opana, Opana ER
- Oxycodone: Oxecta, Oxycodone, Oxycontin
- Tapentadol: Nucynta

http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/ucm186187.htm#MEDICINES

Summary

Monitoring patients who are taking ER/LA opioids

- Patient-provider agreements
- Urine drug tests
- Prescription drug monitoring programs
- Excellent record keeping
- Recognize signs for concern