Do No Harm: Putting Safer Pain Management Guidelines into Practice – Module 4

1.1 Introduction

Welcome to the Oklahoma Primary Healthcare Improvement Cooperative's online course - Do No Harm: Putting Safer Pain Management Guidelines into Practice.

This Online Enduring Material educational program is designed for healthcare professionals. The contents of this program are based on the National Academy's Institute of Medicine's white paper Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use and the 2016 CDC, 2017 VA-DOD, 2017 Oklahoma State Department of Health Guidelines for Pain and Opioid management, and Oklahoma law.

The program was developed through a grant from the Oklahoma Department of Mental Health and Substance Abuse Services by the Oklahoma Primary Healthcare Improvement Cooperative of The University of Oklahoma Health Sciences Center and the OU-TU School of Community Medicine. It was released in August, 2019.

1.2 Overview

Hi, I'm Steve Crawford, and I will guide you through module 4, Analgesia, in the Do No Harm: Putting Safer Pain Management Guidelines into Practice. This module is designed to help you understand the treatment modalities available for analgesia. The average time to complete this module is 30 minutes. ½ hour of CME credit is available. Since this module is designed to stand alone, some of the slides and questions are similar to those presented in module 1.

1.3 Planning and Review Committees

The panel of experts who reviewed this course represent primary care clinicians, pharmacists, educators, and specialists in pain, addiction, and palliative care, and a national expert in the epidemiology of the opioid crisis.

1.4 Relevant Disclosure and Resolution

None of the members of the CME Planning committee have a relevant financial relationship or affiliation with commercial interests to disclose.

1.5 Relevant Disclosure and Resolution for Expert Review Panel

None of the expert reviewers have a relevant financial relationship or affiliation with commercial interests to disclose.

1.6

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Accommodations are available by contacting Jan Quayle at 405-271-2350, ext. 8 or e-mail to: jan-quayle@ouhsc.edu.

1.7 Professional Practice Gap Being Addressed

The Knowledge Gap being addressed in this module is gaps in knowledge, competence, and confidence in using the non-pharmacologic therapies, and appreciation of the risks of opioid therapy for chronic pain.

1.8 Objectives

At the completion of this module, you will be able to describe the mechanism of action of anesthetic, analgesic, and pain modulating therapies. You will be able to state the indications, benefits, and risks for each modality. Lastly, you will be able to describe the neurobiology and risk of opioid analgesia.

1.9 Approach to Analgesia

The approach to analgesia differs according to the expected duration of the pain. Please click on each picture to learn more.

Acute pain is self-limited, and resolves within a few days or weeks. Acute muscle pain usually can be relieved by non-pharmacologic modalities such as ice or heat. Pain caused by tissue injury can be relieved by non-opioid analgesics, such as acetaminophen or NSAIDs.

Chronic pain, is very different. It lasts for more than 3 months and is best managed with long-term, multi-modal therapy. The treatment goal is to improve physical, psychological, and social function. Effective modalities include mind-body therapy like cognitive behavioral therapy, patient self-care, and mental health treatment. Non-opioid analgesics, anticonvulsants, antidepressants are also effective. In carefully selected and closely monitored patients, low dose, intermittent opioid analgesia use may be helpful. Some interventional procedures also may be useful. Chronic back pain often manifests as recurrent episodes of acute pain where short courses of analgesia, patient education, and physical training can be most helpful.

1.10 Analgesic Medications

The medications used for analgesia include topical anesthetics, counter irritants, NSAID gels or creams, and application of heat or cold. Acetaminophen and NSAIDs are the most frequently used oral medications with few but important side effects. Opioid medications stimulate the mu receptor and are effective analgesics when used short-term or intermittently, but are associated with serious and at time life-threatening risks, including addiction and overdose. When used long-term, round the clock on a daily basis they may *increase* pain (hyperalgesia) and reduce function.

1.11 Topical Analgesics

Topical analgesics are effective for temporary relief of localized pain. Other than local skin irritation, there are few adverse events. Topical NSAIDs contain salicylates, ibuprofen, or diclofenac. NASAID creams and gels can cause the same systemic adverse effects as oral medications. Capsaicin, an extract of hot chili, is a counter-irritant but also desensitizes sensory axons. Topical anesthetics, such as lidocaine, interrupt nerve conduction, but develop rapid tachyphylaxis. The product packaging is used for illustration and does not indicate any endorsement or recommendation of a particular product.

1.12 Topical Analgesics and Preparations

Topical analgesics and anesthetic agents are especially useful for localized, superficial acute pain or acute exacerbations of chronic pain. Most are available as over the counter preparations. Some topical NSAIDs require a prescription. The product names shown are examples and not recommendations or endorsements.

· ***Topical Anesthetics*** are frequently used for musculoskeletal pain, sore throat, or rectal pain.

· ***Counter irritants*** are used for musculoskeletal pain and sore throat. It may also be effective in peripheral neuropathic pain.

· ***Topical NSAIDS*** are effective for musculoskeletal pain and some types of neuropathic pain. There is evidence for the effectiveness of diclofenac gel in knee arthritis.

1.13 Acetaminophen

Acetaminophen is also called paracetamol or "APAP," the abbreviation of its chemical name, acetyl-para-aminophenol. Preparations of APAP are tablets and gel-caps sold over the counter. There are regular strength (375mg) and extra strength (500mg). Acetaminophen is commonly mixed with NSAIDS, short acting opioids, and cold preparations.

Acetaminophen is indicated for analgesia and lowering fever. It is not an anti-inflammatory agent.

The mechanism of action is unknown. However, it may inhibit COX activities in the brain. Also, its central analgesic effect may be mediated through activation of descending serotonergic pathways.

1.14 Acetaminophen Toxicity

Acetaminophen is very safe at doses up to 3 grams per day or six 500mg tablets. To prevent liver toxicity, patients should avoid alcohol. Patients with a history of hepatitis or other liver conditions should take no more than 2 grams of acetaminophen in 24-hours. Those with cirrhosis should avoid acetaminophen. Overdose of more than 7.5 grams and generally more than 15 grams of acetaminophen is linked to liver toxicity and the risk of fatal acute liver failure.

1.15 Nonsteroidal Anti-Inflammatory Drugs

Nonsteroidal anti-inflammatory drugs are commonly used for acute and chronic pain. Click on the picture to learn more.

NSAIDs are **indicated** for acute inflammatory pain following trauma or interventional procedures, and pain from some forms of arthritis. NSAIDs are best used in short courses for 7 to 14 days. They should be avoided, if possible, in elderly patients.

The Mechanism of Action of NSAIDs is inhibition the cyclooxygenase (COX) enzymes that transform arachidonic acid to prostaglandins, the mediators of pain and inflammation. Older NSAIDS such as ibuprofen and naproxen inhibit both COX-1 and COX-2 at therapeutic doses and have common gastrointestinal side-effects. Selective COX-2 inhibitors were developed to reduce GI side effects, however, they were found to be associated with increased risk for myocardial infarction, stroke, and heart failure leading to several agents being pulled from the market.

Side Effects include dyspepsia**,** gastric ulceration and GI bleeding, reduction in glomerular filtration rate, fluid retention, elevated blood pressure, congestive heart failure, neutropenia, hyponatremia, confusion, myocardial infarction and stroke. When patients experience NSAID-related dyspepsia, a proton-pump inhibitor is recommended. NSAID side effects are more pronounced with simultaneous use of systemic corticosteroids.

1.16 Other NSAID Information

Aspirin is also known as ASA, an abbreviation for acetylsalicylic acid. Aspirin is a nonselective NSAID. At doses greater than 325mg, aspirin has analgesic, antipyretic, and anti-inflammatory properties. At doses of less than 100mg per day, it is mainly cardio-protective. High doses of aspirin may cause GI bleeding, gastric erosions, and intestinal perforation. These events are roughly doubled even with low doses, so the risk of bleeding must be weighed against the cardio-protective benefit. Aspirin should be avoided in children due to risk of developing Reye's syndrome.

Combination NSAIDs and Acetaminophen Therapy

A Cochrane review found that ibuprofen in combination with acetaminophen provided better analgesia with a smaller chance of adverse events than either drug alone at the same dose. A 2016 VA study demonstrated that opioid medications were not better than non-opioid treatment to improve chronic back, hip or knee pain. In a study involving dental extraction, the combination of acetaminophen and ibuprofen, was found to be superior to the combination of the opioid hydrocodone and acetaminophen and had fewer side effects. A more recent study confirmed that this combination was as effective as opioids in relieving pain from fractures.

1.17 Opioid Analgesics

Opioid analgesics are available in multiple preparations - ultra-short acting used in anesthesia, oral preparations used in ambulatory and hospital care, transdermal used for severe end-of life and palliative care, and IV for severe pain usually in hospital.

Low dose, short course (3 to 7 days) of immediate release opioids may be useful for relief of acute, severe pain.

The mechanism of action is activating the μ opioid receptor at multiple sites in the dorsal horn of the spinal cord and in the brain. Opioids inhibit nociceptive signal transmission from the dorsal horn, influence cognitive processes of pain perception, and reduce suffering or the affective or emotional dimensions of pain.

1.18 Opioid Preparations

Opioids are provided in multiple preparations.

Short-acting preparations are available in oral tablets, liquids, and rectal suppositories. There is less risk of overdose from drug accumulation when short acting preparations are used.

Codeine, tramadol, hydrocodone and oxycodone are often ***combined with acetaminophen*** which enhances the analgesic effect, but also increases the potential for acetaminophen toxicity when opioids are abused.

Long-Acting preparations, also called delayed-release or extended-release, reduce breakthrough pain in chronic pain associated with life-limiting illness. They carry a greater risk when treating non-life-limiting chronic pain, because they accumulate, increase tolerance and physiological dependence, and may increase the risk of developing opioid use disorder.

Transdermal preparations are available for managing severe pain in life-limiting conditions.

1.19 Opioid Side Effects

Oklahoma law requires that patients taking opioids for more than 2 weeks be informed of the common side effects of opioid analgesics.

Cognitive impairment is particularly common in elderly patients; however, anyone may have impairment of executive function or decision making.

Mild to severe Opioid Use Disorder in patients taking long-term, higher dose opioids is common. Estimates range between 5 and 40%. Continuing opioid therapy for 3 months substantially increases risk for opioid use disorder. When the continuous dosing is around the clock, the risk is increased. Tolerance, dependence, withdrawal, and opioid-induced hyperalgesia are common. Another form of opioid misuse is self-management of mental illness such as depression or anxiety, using opioids to relieve "social suffering." Falsely obtaining opioids is illegal misuse of medications.

Constipation is so common that every patient treated with opioids should use a stool softener and or a stimulant laxative.

Suppression of respiratory drive leading to overdose death may occur when taking opioids, taking rapidly escalating doses, resuming a formerly high dose after a period of abstinence, and taking with sedating medications or alcohol.

Other side effects include neuroendocrine dysfunction, falls and fractures, tooth decay, and birth defects and neonatal abstinence syndrome.

1.20 Morphine Milligram Equivalent (MME)

The Center for Disease Control (CDC) cites studies showing dosages at or above 50 morphine milligram equivalent dose (MMED) are associated with at least twice as many overdose deaths than are doses of less than 20 MME/day. Based on a Veterans Health Administration (VHA) study, patients who died of opioid overdose were prescribed an average of 98 MME/day. These findings fueled the recommendation to monitor more closely patients receiving more than 50 MME/day and use caution or avoid prescribing more than 90 MME/day.

Calculating the total daily dose of opioids helps identify patients who may benefit from closer monitoring, reduction or tapering, and prescribing naloxone to reduce the risk of overdose death.

1.21 How Much is a MME/Day?

50 MME/Day is 10 tablets of hydrocodone 5mg/acetaminophen 325mg, and approximately 2 tablets of 15 mg sustained-release oxycodone.

90 MME/Day is 9 tablets of hydrocodone 10mg/acetaminophen 325mg, and fewer than 2 tablets of oxycodone sustained-release 30 mg.

1.22 MMED Calculators

There are many MME/Day calculators available on the web. The CDC published the approach shown here: First determine the total daily milligrams of each opioid the patient takes. Second, convert each formulation to MMEs/Day by multiplying the dose of each opioid by its conversion factor. Third add the MMEs/Day together. The dose conversions are estimates, and when converting from one preparation to another, it is recommended that the estimated equivalent dose be reduced by 25 to 50%, and slowly titrated upward to achieve the desired effect.

1.23 Caution Prescribing Opioids

Opioids are not first line therapy for chronic pain. If opioid analgesia is indicated in chronic non-life-limiting pain, the lowest, intermittent dose of an immediate release opioid should be used. The use of high doses, continuously administered for weeks to months increases the onset of tolerance, physiologic dependence, and addiction. Therefore, when opioids are used, the plan should be to use for the shortest duration possible. Clinical evidence does not support continuous, time-scheduled use of ER/LA opioids as more effective or safer than intermittent use of immediate-release opioids or that time-scheduled use of ER/LA opioids reduces risks for opioid misuse or addiction.

Simultaneous use of opioids and CNS depressants, particularly benzodiazepines are risky. Epidemiologic studies demonstrate that a high proportion of opioid related overdose deaths also involve benzodiazepines or other respiratory depressants such as muscle relaxants, sleep medications, and even diphenhydramine and ethanol. The combination causes unpredictable side-effects, especially suppression of respiratory drive.

1.24 Legacy Patients

“Legacy patients” are those taking high doses of opioids, long-acting preparations, or a combinations of sedating medications and opioids. Legacy patients may be receiving stable doses, are high functioning, and have satisfactory pain control, possibly for years. Others may be discharged from specialist care and directed to seek opioid management from their primary care

clinician. In either case, interrupting an established, apparently successful, treatment plan in order to come into line with current guidelines may be difficult and stress the doctor-patient relationship.

Most patients on long-term, high dose of opioids will experience a withdrawal syndrome when dosing is interrupted or rapidly decreased. Withdrawal may be severe with cramps, vomiting, sweating, fever, anxiety. Patients may self-treat using opioids or benzodiazepines obtained from others.

The suggested approach to the legacy patient is to first do no harm! DO NOT abruptly stop opioid medications or dismiss guideline discordant patients from your practice. Provide patient education about the new expectations, and work closely with the patient to implement safer plans that includes reduced dosing. Recommend the patient or family obtain naloxone to prevent overdose deaths. Slowly taper opioids and discontinue risky combinations when possible. If progress is slow or plateaus, do not abandon your patient! Be compassionate and persistent. Carefully manage withdrawal symptoms if they occur, and remain vigilant for substance or opioid use disorders that may become apparent during the weaning process. Refer patients for addiction treatment services or prescribe dependence medications such as buprenorphine when indicated.

The video link below offers additional case training in collaborative opioid tapering.

1.25 Non-Analgesic Medications

Adjunctive therapy for chronic pain management may include antidepressants and anticonvulsants. These agents work mainly at the spinal cord level stimulating inhibition of the dorsal horn cells.

The analgesic effect occurs at lower doses than the antidepressant or anticonvulsant effects. The tricyclic antidepressant, amitriptyline, has been used for years, in low doses to treat fibromyalgia and neuropathic disorders. The SNRI, duloxetine, has been approved for diabetic neuropathy and knee osteoarthritis. All of these cause dry mouth, blurred vision, constipation and the SSRI and SNRI produce drowsiness and tremor.

The anticonvulsants, Gabapentin and Pregabalin, reduce pain resulting from nerve injury. Although originally thought to be free of risk for addiction, it now appears that in addition to

confusion and memory loss, there is risk of misuse in any patient, even those without a prior substance use disorder.

1.26 Non-Pharmacologic Interventions

Non-pharmacologic therapies prove to be a promising option for improving outcomes in various types of chronic pain, particularly low back pain. These modalities work at various locations in the pain signaling and emotional or muscular reactivity reflexes. Physical therapy and exercise have been most studied and show strong evidence for consistent improvement of pain.

Cognitive-behavioral therapy showed improvement in pain and disability from low back pain lasting on average 34 months after treatment. Mindfulness meditation and hypnosis have weaker evidence, but also show improved pain and quality of life, and reduced depression compared with usual treatment controls.

The manual therapies including osteopathic manipulation, chiropractic, massage and acupuncture have been found to be superior to control modalities of support groups, education, and stress management for improving function and decreasing pain for low back pain, subacute neck pain, and osteoarthritis. True acupuncture was modestly superior to sham for pain relief of musculoskeletal neck and back pain, osteoarthritis, chronic headache and shoulder pain, and fibromyalgia.

1.27 Interventional Pain Therapies

Trigger-point injections of anesthetic and corticosteroid are modestly effective for short term relief of myofascial pain of the low back and fibromyalgia. These can be administered by primary care clinicians in the office.

Botulinum toxin injections have been shown to be effective for relief of chronic migraine when other therapies have failed.

Limited evidence supports injections of the lumbar facet or sacroiliac joints, and denervation of the nerves that supply those joints. This procedure may relieve axial low back pain arising from these richly innervated joints.

Epidural steroid injections are the most commonly performed interventional pain therapy for radicular and sciatic pain. Although some patients benefit, there has been a substantial increase in these procedures without evidence of long-term improvement in pain perception.

There is evidence for the cost-effectiveness of spinal cord stimulation (SCS) in the relief of pain due to failed back surgery syndrome, Complex Regional Pain Syndrome, occipital headaches, painful peripheral artery disease, and refractory angina.

1.28 Conclusion

Reduction in acute local musculoskeletal pain can be achieved with ice or heat, topical preparations, acetaminophen, and/or NSAIDs. For severe pain, such as following surgery, low-doses of a short-acting opioid preparations may be helpful - three days or less will often be sufficient; more than seven days will rarely be needed. Opioids can never be prescribed without the risk of substance use disorder and overdose.

Opioids are not a good choice for chronic pain, which benefits from a multi-modal approach to therapy. Medications are not the sole answer but can be used to improve overall function. Topical agents, acetaminophen, and NSAIDs may be used to reduce pain that limits function. Intermittent use of low dose opioids in patients with severe pain for which other modalities are inadequate also may be useful, but require diligent follow-up for effectiveness in improving function and early recognition and mitigation of adverse events. Other effective modalities of therapy should be incorporated into the pain management plan. These include improving general health and fitness, mind-body treatments, anticonvulsant or antidepressant medications, injections of anesthetic and anti-inflammatory drugs, and pain specialists performing other pain relieving procedures.

1.29 Instructions

Please answer the following self-assessment question by selecting the single best answer. You will receive immediate feedback and if you selected an incorrect response you may answer the question again.

1.30

Question 1

1.31

Question 2

1.32

Question 3

1.33

Question 4

1.34

Question 5

1.35 References and Resources

The references on this slide are provided for your additional information. Thank you for participating in this online module.

1.36 Closing Instructions

You may print a certificate of completion in order to meet the requirements for annual training by clicking on the reports tab.

In addition, the University of Oklahoma Office of Professional Development is providing CE credits. MDs are eligible for AMA PRA Category 1 Credit, Physician Assistants for AAPA Category 1 Credit, and Nurse Practitioners for AANC contact hours and Oklahoma pharmacology hours.

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