"Acute Pain Management in the Individual with Opioid Use Disorder"

Presented by:
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Webcast Questions and Answers
*(Answers are in **bold**)*

Questions:

1. Can you recommend additional resources for understanding withdrawal in Opioid Use Disorder?
   a. **Pergolizzi JV, Raffa RB Rosenblatt MH. Opioid withdrawal symptoms, a consequence of chronic opioid use and opioid use disorder: current understanding and approaches to management. *J Clin Pharm Ther.* 2020;45:892-903 https://onlinelibrary.wiley.com/doi/pdf/10.1111/jcpt.13114**
   b. **See the SAMHSA publication (TIP63: Medications for Opioid Use disorder chapter 2 2-12 and 2-30 – free download of PDF which has quite a bit of useful information and resources https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP21-02-01-002.pdf).**

2. When does gabapentin have a role?
   a. **Gabapentinoids (gabapentin and pregabalin) has a role as part of multimodal analgesia. It may provide benefit for the neuropathic component of pain in surgery and it may be antihyperalgesic and work to prevent central sensitization which can lead to chronic pain. Due to its synergistic effect it may reduce opioid use. There are wide variations in practice in terms of dosing/administration prior to surgery Studies have been performed in multiple surgeries which demonstrated efficacy. (Chang CY, Challa CK, Shah J, Eloy JD. Gabapentin in acute postoperative pain management. *Biomed Res Int*. 2014;2014:631756. doi:10.1155/2014/631756)(Chou et al Management of Postoperative pain a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee and Administrative Council https://www.jpain.org/action/showPdf?pii=S1526-5900%2815%2900995-5).**

3. As you say, methadone in the hospital for patients with OUD usually is about 40 mg/day to prevent/treat withdrawal. Patients in a methadone treatment program are often on doses > 100 mg/day. Is 40 mg enough for a patient on a dose like 100 mg/day?
   a. **To clarify, many hospitals have policies in place for when a patient is admitted and is on methadone maintenance therapy and the clinician is unable to verify the dose. In general most say methadone 40 mg daily is allowed until dose verification. If someone is on 100 mg daily of opioids due to the variable long half-life of methadone may not go through withdrawal. In addition the clinicians can supplement with immediate release opioids to**

prevent withdrawal. The caution with using higher doses of methadone if one has not verified dose is the long half-life, (can be upwards of 90 + hours) thus risk for overdose that may not manifest for days.

4. Is there a table for opioid conversions that includes buprenorphine? It would be useful for adding full agonist.
   a. **Mary Lynn McPherson, PharmD who is considered an expert on equianalgesic opioids removed buprenorphine from her tables of equianalgesic conversion due to the unique properties of buprenorphine. If you look at different sources, some say the equianalgesic t morphine is 1:30, others say 1:60 and yet others say 1:10. In the acute care situation it is best to start lower and increase as needed. Generally if the person is on buprenorphine you will need higher doses to overcome the buprenorphine on the mu-opioid receptor. Hydromorphone is recommended due to its receptor activation. A good overview article on buprenorphine and in this article is some equinalgesic conversions for low dose buprenorphine (transdermal and buccal) FDA approved for pain. (Case AA, Kullgren J, Anwar S, Pedraza S, Davis MP. Treating Chronic Pain with Buprenorphine-The Practical Guide. *Curr Treat Options Oncol*. 2021;22(12):116. Published 2021 Nov 18. doi:10.1007/s11864-021-00910-8 https://link.springer.com/article/10.1007/s11864-021-00910-8).**
5. How do manage acute pain with person with THC positive
   a. **If patient has been using cannabis on a regular basis they may experience some withdrawal symptoms which could include irritability and insomnia. If cannabis was being medically used to treat symptoms the person may have a return of those symptoms (such as anxiety or neuropathic pain). So treatment of acute pain may need to include treatment of the symptoms for which cannabis was utilized. If the cannabis was utilized recreationally may need to just treat symptoms associated with withdrawal. (Bonnet, U. & Preuss, U. W. (2017) The cannabis withdrawal syndrome: current insights. *Substance abuse and rehabilitation*. [Online] 89–37 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5414724/).**
6. Some pain doctors use pysch medications to treat pain, will they start an OUD with these then increase to something more potent to assist w/pain or depends on the medical issue?
   a. **Certain antidepressants such as serotonin norepinephrine reuptake inhibitors (duloxetine) are FDA approved for pain secondary to diabetic neuropathy, fibromyalgia and musculoskeletal pain and are often used off-label for other neuropathic conditions. However they are not a substitute for medications to treat opioid use disorder, but could be used in conjunction to medications for opioid use disorder. In addition buprenorphine is being studied for its possible efficacy in treating depression. (Serafini, G. et al. (2018) The efficacy of buprenorphine in major depression, treatment-resistant depression and suicidal behavior: A systematic review. *International journal of molecular sciences*. [Online] 19 (8), 2410–. https://mdpi-res.com/ijms/ijms-19-02410/article_deploy/ijms-19-02410-v2.pdf).**
7. During a recent in-service they spoke of using Mirtazapine (off label) and/or NAC for stimulant use, what are your thoughts?
   a. **From a systematic review (of only 180 total patients) "Conclusions and relevance: Mirtazapine probably results in a small reduction in continued methamphetamine use among cisgender men and transgender women with AMD, but probably does not improve patients' retention in treatment or depression symptom severity. (Naji, L. et al. (2022) Mirtazapine for the treatment of amphetamine and methamphetamine use disorder: A systematic review and meta-analysis. *Drug and alcohol dependence*. [Online] 232109295–109295.)**

   b. **There is no effective treatments pharmacologic treatment at this time but in this older article " Promising signals have been observed for methylphenidate, naltrexone, bupropion and mirtazapine in subgroups of patients in reducing stimulant use (e.g. patients with less severe dependence at baseline and men who have sex with men), though none has produced an unambiguous, replicable signal of efficacy. (Brensilver, M. et al. (2013) Pharmacotherapy of amphetamine-type stimulant dependence: An update. *Drug and alcohol review*. [Online] 32 (5), 449–460.)**

8. Are you seeing the need for a higher concentration of naloxone with so much potent fentanyl and fentanyl analogs on the street? We are considering changing the concentration we dispense to pt's discharging. Also, is anyone dispensing fentanyl test strips to patients admitted with an overdose?
   a. **A higher dose of naloxone hydrochloride nasal spray to treat opioid overdose has received FDA approval. In addition to the previously approved 2-mg and 4-mg nasal sprays, an 8-mg spray is also available.**
   b. **In my current outpatient setting we are still prescribing the 4 mg dose. I have checked with our addiction colleagues and some are distributing two of the 4 mg doses**
   c. **I know of practices where fentanyl test strips are being given. This is most important in the setting of stimulant use where the person may not know/suspect fentanyl. For those using illicit opioids most are aware that illicit fentanyl is prevalent in most illicit opioids. In my own practice, I have not seen evidence of 'heroin' on a UDS (would either see 6 monoacetylmorphine shortly after use or the resulting metabolite methadone), but have only seen fentanyl/norfentanyl in those reporting 'heroin' use.**
9. Are you aware of any examples of management of patients with SUD in the palliative/hospice setting? Struggling to get providers to embrace harm reduction in the palliative setting, often resulting in unwillingness to prescribe opioids for symptom management.
   a. **I work in palliative and hospice medicine and it is rapidly changing. Just 5 years ago there was little talk about OUD/SUD. At this year's annual conference there were preconference on buprenorphine prescribing and multiple sessions on harm reduction. In my own setting most of the outpatient clinicians are waivered to prescribe buprenorphine although we only treat a few people. We do try to take a harm reduction approach. All patients prescribed opioids complete a risk screening, treatment agreement, have urine drug testing. This has resulted in safer prescribing, not discharge from the clinic. We may just change prescribing patterns (smaller amounts, less use of immediate use opioids, or transition to buprenorphine. There are some palliative care leaders that are boarded both in addiction medicine and palliative medicine so change is happening (see works by Julie Childers, Jessica Merlin, Katie Fitzgerald Jones, Janet Ho to name a few).**
10. What tool do you recommend to assess for over sedation? POSS or RASS and why?
   a. **It is usually an institutional choice and most often I have seen the RASS used in the ICU to assess level of sedation and the POSS used as part of PCA orders. Here is a study that may be of interest. Nisbet AT, Mooney-Cotter F. Comparison of selected sedation scales for reporting opioid-induced sedation assessment. *Pain Manag Nurs*. 2009;10(3):154-164. doi:10.1016/j.pmn.2009.03.001 "A descriptive survey-based study was undertaken to test the validity and reliability of three scales that are used to assess sedation during opioid administration for pain management: the Inova Health System Sedation Scale (ISS), the Richmond Agitation and Sedation Scale (RASS), and the Pasero Opioid-Induced Sedation Scale (POSS). The study was conducted in a large (830 beds) suburban level I trauma hospital with a**

random convenience sample of 96 medical-surgical nurses. The study reports: measures of reliability and validity of each scale and significant findings related to correct nursing score and selected actions; nurses' ratings of each scale in terms of combined ease of use; information provided by the scale to inform clinical decisions; and nursing confidence measures. Both the RASS and the POSS demonstrated adequate measures of reliability and validity for measurement of sedation during opioid administration for pain management. However, the POSS scored higher in combined measures of ease of use, nursing confidence, and usefulness of information provided to make clinical decisions. The POSS also yielded the highest percentage agreement with the correct score and correct nursing actions chosen by the nurse among the three scales tested. Study results have clinical significance for accuracy of clinical assessments and subsequent actions on behalf of patients experiencing advancing sedation during opioid analgesia. The POSS can be recommended as a superior sedation scale for the measurement of sedation during opioid administration for pain management."

11. What do you think for ibuprofen for chronic pain management for this population?
    a. **Nonsteroidal anti-inflammatory drugs can be helpful in the management of chronic pain, especially if related to musculoskeletal pain. One must assess the risk in older adults and those with cardiovascular risks, risks for gastrointestinal toxicity and renal risks.** **Ho, K. Y. et al. (2018) Nonsteroidal anti-inflammatory drugs in chronic pain: Implications of new data for clinical practice. *Journal of pain research*. [Online] 111937–1948. https://www.dovepress.com/getfile.php?fileID=44655.**
12. If a patient had severe pain and required high dose opioid medication, how much would you taper in terms of MME before resuming Buprenorphine for discharge
    a. **The patient would have to be moderate withdrawal to start buprenorphine in the traditional manner if the buprenorphine was discontinued. Thus the reason not to discontinue. There are multiple ways to restart buprenorphine using 'micro-induction' or 'low dose initiation' which can take between 3-7 days and would require involvement of the clinician. In our own setting there is an order set for micro induction.** **Robbins, J. L. et al. (2021) Buprenorphine Microdose Induction for the Management of Prescription Opioid Dependence. *Journal of the American Board of Family Medicine*. [Online] 34 (Suppl), S141–S146. https://www.jabfm.org/content/jabfp/34/Supplement/S141.full.pdf.**
13. Can you talk about the role of ketorolac (Toradol) for post op pain? Why is it not more readily available particularly for surgeries where only 2-3 days of severe post op pain are expected?
    a. **Ketorolac is an effective NSAID as part of multimodal analgesia and can be an effective part of post-operative pain management. In an article about safety concerns "As an inhibitor of cyclooxygenase, ketorolac use has raised clinical concern including particular controversy regarding its potential effects on bone healing, postoperative kidney function and perioperative bleeding." Maslin B, Lipana L, Roth B, Kodumudi G, Vadivelu N. Safety Considerations in the Use of Ketorolac for Postoperative Pain. *Curr Drug Saf*. 2017;12(1):67-73. doi:10.2174/1574886311666160719154420.**
14. If we continue buprenorphine while giving full agonist opioid pain medications, are we teaching our patients that they can easily breakthrough the mu receptor blockade of buprenorphine and subtly making relapse more likely?
    a. **I am not sure it is 'more likely'. As you know methadone is a pure mu-agonist so one can readily use other opioids on top of methadone. The potential safety measure may be that if the person is going daily to an opioid treatment program to obtain methadone then they may**

be urine tested more frequently. What is hoped is that if someone agrees to treatment with buprenorphine it is because they may want to treat the OUD. In reality once someone has been using drugs for a period of time they will readily tell you they are using the drugs to prevent withdrawal as they may not be getting the 'high' anymore. Additionally one can hope that if the buprenorphine is blocking the mu-agonist receptors the other opioids have to compete for receptors and may decrease the risk for over sedation.

15. What about nano-curcumin/boswellia? I'm using this personally (along with quality CBD, topical DMSO) to AVOID NSAIDS as well as opioids.
    a. **Many people do use supplements for treatment and are effective. Unfortunately because they are not FDA approved it is more difficult to get them into standard practice.**
16. What do you think about ordering Tylenol and NSAIDS around the clock instead of prn? I find when they are ordered prn, they are not given regularly.
    a. **In many postoperative pain sets the Tylenol and NSAIDs are ordered around the clock and should be as they are opioid sparing especially when used around the clock alternating between an NSAID and APAP. If they are ordered PRN then it makes it very difficult as the prescriber would have to put indications for each such as give APAP first for mild pain and if not effective give Ibuprofen and then if pain is moderate or severe give an opioid. And many order sets use these directions based on dosing to numbers in terms of severity which is not the most appropriate way to dose PRN opioids. Pergolizzi JV, Magnusson P, LeQuang JA, et al. Can NSAIDs and Acetaminophen Effectively Replace Opioid Treatment Options for Acute Pain?. *Expert Opin Pharmacother*. 2021;22(9):1119-1126. doi:10.1080/14656566.2021.1901885.**
17. Could you talk briefly about the use of buprenorphine in end of life settings?
    a. **Buprenorphine is an effective analgesic and can be used at end of life if the person still has the ability to utilize sublingual or transmucosal formulations. If more analgesic is required one can utilize immediate release hydromorphone. If the person is unable to continue buprenorphine as cannot use sublingual, one can transition to a full mu- opioid agonist. Be aware however that it will take up to 3 days before the buprenorphine disassociates from the mu opioid receptor and so higher dose opioids may be needed prior to the disassociation of the buprenorphine and there is a risk of increased sedation once the buprenorphine disassociates. Jones KF. Buprenorphine Use in Palliative Care. *J Hosp Palliat Nurs*. 2019;21(6):540-547. doi:10.1097/NJH.0000000000000598.**
18. Have you been using ketamine for patients in the hospital/ acute pain and receiving Vivitrol, and outcomes?
    a. **I personally have not but ketamine would make the most sense if the patient has received vivitrol injection the effects are there for about 28 days and it may require up to 20 x the opioid dose to overcome the naltrexone. Ketamine has been successfully utilized in some surgeries as an analgesic agent nd with someone on Vivitrol, all non-opioid methods of pain control should be attempted. Here is an editorial that addresses this issue. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1336752/pdf/bmj33200132.pdf Also you can review the advansky, B. M. et al. (2015) Role of Ketamine in Acute Postoperative Pain Management: A Narrative Review. *BioMed research international*. [Online] 2015749837–10. https://downloads.hindawi.com/journals/bmri/2015/749837.pdf; Wenzel, J. T. et al. (2016) Managing Opioid-Tolerant Patients in the Perioperative Surgical Home. *Anesthesiology clinics*. [Online] 34 (2), 287–301. https://www-clinicalkey-**

com.dartmouth.idm.oclc.org/service/content/pdf/watermarked/1-s2.0-S1932227516000069.pdf?locale=en_US&searchIndex=.

19. Can you discuss the use of ketamine for pain management in the acute care setting?
    a. **Ketamine is an anesthetic with multiple mechanisms but of great interest is its role as NMDA antagonist which in simple terms may decrease hyperexcitability along the pain pathway and blunt the potential to develop central sensitization and thus chronic pain. It may also reduce the risk of opioid tolerance. Studies in terms of efficacy have been varied but it is being increasingly used in many settings as an opioid sparing agent.** Radvansky, B. M. et al. (2015) Role of Ketamine in Acute Postoperative Pain Management: A Narrative Review. *BioMed research international*. [Online] 2015749837–10. https://downloads.hindawi.com/journals/bmri/2015/749837.pdf; Wenzel, J. T. et al. (2016) Managing Opioid-Tolerant Patients in the Perioperative Surgical Home. *Anesthesiology clinics*. [Online] 34 (2), 287–301. https://www-clinicalkey-com.dartmouth.idm.oclc.org/service/content/pdf/watermarked/1-s2.0-S1932227516000069.pdf?locale=en_US&searchIndex=.
20. Are there any mu agonists that will displace suboxone on receptors if someone has pain that has exceeded the suboxone ceiling?
    a. **Previously it was thought that once all mu-receptors were saturated with suboxone that other opioids could not displace the suboxone, but it appears that the binding is not a static process. Per recent articles and clinician experience, we now know that breakthrough opioids can be effective. In terms of mu opioid binding receptor activity hydromorphone appears to be more effective than morphine and oxycodone when used with buprenorphine. A good review article is A good overview article on buprenorphine** Case AA, Kullgren J, Anwar S, Pedraza S, Davis MP. Treating Chronic Pain with Buprenorphine-The Practical Guide. *Curr Treat Options Oncol*. 2021;22(12):116. Published 2021 Nov 18. doi:10.1007/s11864-021-00910-8 https://link.springer.com/article/10.1007/s11864-021-00910-8.