Co-Morbid Cancer-Related Pain and Substance Use Disorder

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Learning Objectives

- To propose buprenorphine as an effective treatment for the management of cancer-related pain in patients with a current or past history of addiction.

Case Description

- **HPI:** A 36 y/o male with history of substance abuse disorder, depression, and non-seminomatous germ cell tumor with metastases to liver/multiple lymph nodes presented to Palliative Care for pain management.
- **Social History:** He was actively abusing 2 grams/day heroin, prescription opioids, THC, and alcohol. He was living in the San Fernando Valley with his mother who also struggled with substance abuse disorder. He was unemployed for several years and has been in jail several times for probation violations related to his drug use.
- **Assessment/Plan:** Due to his active substance abuse, he was deemed not a candidate for a potentially curative auto-stem cell transplant; he was instead started on paclitaxel, ifosfamide, and cisplatin for his germ cell tumor. For his substance abuse disorder and cancer-related pain, he was started on Suboxone (buprenorphine) 4mg every 6 hours, in addition to as-needed hydromorphone for breakthrough pain.
- **Outcome:** With aggressive behavioral therapy from the palliative care team, his situation improved to the point that he was able to get off all illicit drugs, as well as all PRN prescription opioids. His quality of life improved dramatically. The hospital is now planning to re-assess him for auto-stem cell transplant candidacy for potential cure.

Discussion

The Dual Diagnosis: Cancer-Related Pain and SUD

- Cancer patients are living much longer than before and therefore using opioids for longer periods of time; we can no longer assume inherent OUD protection from short-lived opioid use.
- A palliative care clinic study reported that although >90% of patients had a diagnosis of cancer, almost a third had no evidence of current disease.
- 2017 National Cancer Institute study on palliative care patients reported that almost ¾ had an abnormal or positive drug screen for non-medically prescribed substances.

The Case for Buprenorphine

- **It has a better safety profile than other opioids and has a decreased incidence of common opioid-related adverse effects:** It's availability in multiple non-oral routes (TD, SL, buccal, IV, IM, SC), helps avoid hepatic first-pass metabolism which increase its bioavailability and thus, enable lower buprenorphine doses. It does not significantly prolong the QT interval. There is a ceiling effect on opioid-induced respiratory depression and euphoria, without having a ceiling effect on analgesia. *OIRD can still occur in opioid-naïve patients in the acute pain setting. It is the only opioid not associated with increased fracture risk, and therefore considered a first-line opioid for the elderly. Compared to other opioids, it also causes less suppression of immune function, the gonadal axis, and testosterone levels.
- **Considered the safest opioid for patients with renal failure:** It is predominantly eliminated by the GI tract and does not lead to the accumulation of central-acting metabolites. There is a much lower risk of opioid-induced neurotoxicity compared to full mu-agonists.

- **It is effective in treating acute and chronic pain.** A 2015 Cochrane review on severe cancer-related pain found that 8 out of 11 studies demonstrated that buprenorphine was as effective or superior to the opioid comparison treatment. An average of 85% of patients experience "good to very-good" analgesia and there is only a 3% discontinuation rate. Additionally, a 2020 meta analysis revealed that buprenorphine has increased efficacy in neuropathic pain, compared to other opioids.
- **It is associated with less opioid-related analgesic tolerance development and can potentially be used to treat opioid-induced hyperalgesia.** This is due to its combination of prolonged mu- and kappa-receptor binding together with ORL-1 receptor activation that prevents central sensitization. Rotating from full mu-agonists to buprenorphine, even at high doses, may reduce the incidence of OIH through its anti-hyperalgesia effect. Studies report that after a withdrawal period of >12 hours, 86% of patients suffering from poorly controlled chronic pain on long term full mu-agonist opioids who were rotated to 8-32 mg SL/day buprenorphine experienced a significant benefit in analgesia and QOL.
- **It has concurrent anti-anxiety and anti-depressive properties due to its kappa-receptor antagonism:** A meta-analysis reported that depression and anxiety were prevalent in about half of chronic non-cancer pain patients and 1/3 of cancer pain patients.

The Underutilization of Buprenorphine

- Out of palliative care physicians, only 13% have completed DATA 2000 training. One study found that of all DATA 2000-certified clinicians, half are still only prescribing buprenorphine to 5 or fewer patients. Lack of definitive guidelines, experience, and provider education are the main reasons for this.

Implications

- The end goal is for all pain management providers to properly prescribe buprenorphine to treat their patients who have co-morbid conditions of OUD and pain.
- Definitive guidelines regarding the assessment and management of the growing dual diagnosis of cancer-pain and OUD need to be put in place within professional organizations.