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General

Evaluating the use of sublingual sufentanil in patients with buprenorphine treatment who are undergoing ambulatory surgery: A Prospective Case Report

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Introduction

Opioid use disorder is a chronic illness with significant morbidity and mortality. Opioid agonists, like buprenorphine, are commonly used to prevent relapse. Recent changes in buprenorphine legislation are expected to increase prescription and guidelines recommend its continuation during the perioperative period for many patients. However, buprenorphine's strong affinity for mu receptors can complicate perioperative pain management, requiring high doses of analgesics and increasing risks like respiratory depression. A newly FDA-approved sublingual sufentanil system, with higher mu receptor affinity, may offer a solution.

Case Presentation

A series of three cases with patients undergoing outpatient surgery procedures while continuing buprenorphine treatment are presented.

Management and Outcomes

Sublingual sufentanil was effective in lowering pain with no adverse effects for the buprenorphine patients undergoing surgery with general anesthesia without a missed dose.

Conclusion

Further research is needed to make conclusive remarks on the efficacy of this treatment, but the quick onset and effective treatment make this route worthwhile to consider.

INTRODUCTION

Despite widespread public awareness programs and pain management recommendations, opioid use disorder (OUD) remains a significant medical challenge.[1] Opioid use disorder is a chronic illness with considerable mortality and morbidity.[2] One of the long-term management options to avoid opioid use relapse is to include an opioid agonist (methadone or buprenorphine) in the management regime.[3,4] The number of Medicaid-covered prescriptions for buprenorphine-containing products for treatment has increased 5-fold from 2011 to 2018.[5] More recently in 2021, guidelines for buprenorphine have changed such that providers no longer need additional training or licensure to prescribe buprenorphine, so prescriptions numbers and access to this medication are expected to increase further. Therefore, the number of patients at risk for uncontrolled pain due to receptor saturation by buprenorphine is a worthwhile concern to explore.

Recommendations for perioperative treatment of patients on suboxone have varied in recent years, with many discussions on a need for discontinuation or tapering of dose due to the potential for pain control difficulties.[1] Recent guidelines have pivoted to suggest that buprenorphine should be continued if possible (particularly for low-pain procedures). Postoperative pain management can be achieved with the focused utilization of regional anesthesia and IV non-opioid anesthesia where applicable and opioids acting as a supplement. Nevertheless, conversion to methadone or morphine is noted as an option to avoid difficulties for challenging patient populations.[6] A multimodal approach to analgesia and communication with the prescribing provider is recommended.[7] There is a known concern that increased IV medication and increased opioid need to achieve pain control can lead to adverse effects

such as nausea, respiratory depression, and more. Furthermore, the need for this intervention may increase patient length of stay and require increased monitoring. One potential medication that may assist with such issues is sufentanil.

Numerous studies have shown the success of sublingual sufentanil in postoperative pain management for non-opioid tolerant patients. Overall, a literature review of the sublingual sufentanil tablet found it to be an excellent treatment for chronic pain patients, reducing the need for IV medication.[8] The sublingual sufentanil tablet was approved by the FDA in 2018. Out of the commonly used opioids, it is the only one that has a higher affinity (K_i =0.138) of the mu receptor than buprenorphine (K_i =0.2157). It also outcompetes hydromorphone, morphine, and fentanyl (K_i =0.3654,1.168, 1.346, respectively).[9] Since it is able to outcompete at the receptor level, it has the potential not to require exorbitant elevated doses to be effective. In non-opioid tolerant patients, it has shown great success. A randomized, placebo-controlled study of SST for pain management after abdominal surgery showed that 30 mcg of sublingual sufentanil significantly reduced pain intensity when compared to the placebo group.[10] A similar study using 15 mcg of SST to treat pain after knee or hip arthroplasty showed similar results, also for non-opioid tolerant patients. Both studies indicated an increased rate of nausea for those not in the placebo group.[11] A retrospective chart review of 61 patients undergoing outpatient plastic surgery showed that 30 mcg SST, administered twice due to the length of the case, significantly lowered PACU opioid administration.[12] Furthermore, the use of PCA sublingual sufentanil has faster onset and greater patient and nurse satisfaction than morphine PCAs. Additionally, those receiving sublingual sufentanil experienced less oxygen desaturation below 95% (p=0.028).[13] While no research is currently available on the efficacy of sublingual sufentanil in opioid-tolerant patients, we present a series of 3 cases at Montefiore Medical Center of patients undergoing outpatient surgery procedures without pausing their buprenorphine treatment.

CASE PRESENTATION

ETHICAL CONSIDERATIONS

Patient written consent was obtained for the novel application of sublingual sufentanil in patients on buprenorphine. The study was sponsored by AcelRx Pharmaceuticals and IRB-approved by Einstein IRB. All three patients enrolled received standardized general anesthesia, as per site protocol. Then, the sublingual sufentanil tablet system was used to place the tablet.

A 58-year-old male taking 4 mg of suboxone daily presenting for a prostatic urethral lift was given 975 mg acetaminophen in preop. The patient reported taking his daily dose of suboxone at 10:00 AM. General anesthesia was induced and 30 mcg of sublingual sufentanil was administered following induction. No opioids were given intraoperatively. The procedure began at 16:35 and ended at 16:45. The patient spent 1.5 hours in PACU and reported a pain score of zero. The following day, the patient reported no pain, no adverse events, and no missed suboxone doses. No additional medication was needed for pain.

A 52-year-old biological female taking 8 mg suboxone daily for pain management presented for bilateral breast reduction mammoplasty was given 975 mg acetaminophen in preop. She reported taking her buprenorphine the day before at an unknown time. General anesthesia was induced and 100 mcg of fentanyl and 75 mg of 2% lidocaine were given. 30 mcg of sublingual sufentanil was administered shortly after. Her procedure began at 13:20 and ended at 17:56. She remained hemodynamically stable with no vitals excursions observed. During the 2.5-hour PACU stay, she reported a pain score of 0 at all check-ins. She was discharged home with no opioids and continued her suboxone use with no missed doses. No follow-up contact was made.

A 45-year-old female taking 12 mg suboxone twice a day presenting for a vaginal sling for stress incontinence was given 975 mg acetaminophen in preop. She reported taking her suboxone prescription at an unknown time prior to coming to the hospital. General anesthesia was induced with an additional 100 mg of 2% lidocaine and 200 mcg of fentanyl. 30 mcg sublingual sufentanil was administered shortly after. Her procedure began at 12:13 and ended at 13:12. In PACU, the patient reported a pain score of 8 which quickly increased to 10 within half an hour. The attending anesthesiologist administered an additional dose of 30 mcg sublingual sufentanil and followed with 800 mg of IV ibuprofen 30 minutes later. The patient stated she felt better after 30 minutes and, after an hour, reported a pain score of 2. The patient was discharged home after spending 2.25 hours in PACU with satisfactory pain management and a prescription for 500 mg acetaminophen PRN and 6 times a day oxycodone 5 mg immediate-release tablet. During the follow-up call, the patient stated pain medications were ineffective and her pain was now at a five. Suboxone use was continued.

CONCLUSION

While the results of the 3 cases cannot be taken as conclusive evidence of sublingual sufentanil's efficacy in opioid-tolerant patients, it demonstrates an important option for pain management for patients on varying doses of suboxone. All three patients treated had no adverse effects, tolerated recovery room pain well, and reported little to no pain the day after surgery with no need for large doses of opioids. The contrasting minimal need for analgesia is novel as the majority of previous case reports present a high level of difficulty and complication when treating patients on buprenorphine. One case report stated that postoperative pain control of a 50-year-old male with McArdle's disease on suboxone treatment was very difficult, requiring a hydromorphone PCA at 0.8 mg with a 15-minute lockout. The patient was transferred to oral opioids after his pain plateaued at 3/10 two days after surgery. Suboxone use had to be stopped but was restarted 2 months after surgery.[14] Another case report states that pain management was not

successful until buprenorphine was stopped, requiring over 70 mg of intravenous hydromorphone as well as oral opioids to keep pain tolerable prior to the discontinuation.[15] Finally, a 41-year-old male undergoing revision spine surgery showed the need for high-dose opioids and dexmedetomidine therapy to control pain postoperatively. While they were successful in lowering at-rest pain, the patient had to be closely monitored in the ICU and still had a 5/10 pain score when out of bed.[16] Even when stopping buprenorphine and transitioning to hydromorphone 5 days in advance of surgery, a multimodal approach for pain management was still needed in a patient undergoing removal of vaginal mesh and cystoscopy.[17]

While it is difficult to compare the expected pain from the varied procedures discussed in reports, the end results are worth noting. Pain management using sublingual sufentanil is fast, effective, and minimally invasive allowing for repeat dosing if needed. Its pharmacological profile allows for doses to be kept low, which limits the risk of adverse events such as respiratory depression. The treatment of acute pain plays a major role in preventing chronic pain development.[18] While the patients on buprenorphine are already being treated for pain, preventing further chronic pain development in addition to their baseline helps keep medication doses constant and prevent quality of life changes.

Overall, further research is needed to attest to the efficacy of sublingual sufentanil in opioid-tolerant patients. However, the case report presented speaks for the benefit of individual consideration and implementation due to excellent pain management and lack of adverse events seen.

DISCLOSURES

All authors except Dr. Naum Shaparin and Dr. Karina Gritsenko report no disclosures. Dr. Naum Shaparin reports receiving research funding from AcelRx Pharmaceuticals, Averitas Pharma, and Heron Therapeutics. Dr. Karina Gritsenko reports being a consultant for Pacira Biosciences and Grunenthal Pharmaceuticals.

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