PAIN MEDICINE CASE REPORTS

ISSN 2768-5152

Volume 7, Number 8, pp. 389-392

TRANSDERMAL BUPRENORPHINE IN THE TREATMENT OF CHRONIC ABDOMINAL PAIN SYNDROME

Om Dave, BS, Maryam Jowza, MD, and Daniel Nance, BS

Background: Centrally mediated abdominal pain syndrome (CAPS) is a condition that has traditionally been treated with first-line agents, such as tricyclic anti-depressants and serotonin and norepinephrine reuptake inhibitors. However, in the setting of pain refractory to these primary agents, there is little evidence in support of alternative regimens, especially opioid analgesics.

Case Report: This case examines the utility of weekly 10 mcg transdermal buprenorphine patches as an additional treatment modality for CAPS, specifically in the setting of a 27-year-old woman with intractable abdominal pain following a cholecystectomy. In < 1 week, the patient had significant improvement in pain control without any of buprenorphine's potential side effects.

Conclusion: Given the debilitating pain CAPS causes alongside the widespread economic burden it puts on both patients and hospital systems, transdermal buprenorphine can be a transformative approach to mitigating the consequences of this syndrome.

Key words: Abdominal pain, buprenorphine, opioids, chronic pain, interventional pain

BACKGROUND

Centrally mediated abdominal pain syndrome (CAPS) is a term used to describe a wide range of chronic abdominal pain symptoms, that do not fit the standard criteria of more well-studied, functional gastrointestinal disorders. Diagnostic requirements of CAPS include near-continuous abdominal pain, no correlation with physiological events (e.g., eating, defecating, etc), loss of daily function, absence of feigned pain, and lack of another more likely diagnosis. Its prevalence is between 0.5% to 2% in North America and it is most prominent among women in their 30s (1).

The greatest challenge associated with the treatment of CAPS is the vast differential encompassing abdominal pain and the paucity of any characteristic findings on imaging or laboratory studies. Given this poor understanding, the pathophysiology of this disease remains a topic of debate, especially given that suggested etiologies vary anywhere from postinfectious sequelae to the trauma of losing a loved one. However, one proposed mechanism for CAPS that has achieved an overall consensus is the role of visceral hypersensitivity (2).

Normally, the visceral afferent sensory neurons of the peripheral nervous system are recruited by various chemical, local, and mechanical stimuli to propagate pain information to the central nervous system via the dorsal horn of the spinal cord. There are specific nociceptors that respond to these diverse stimuli as well, and after

From: Department of Anesthesiology, UNC School of Medicine, Chapel Hill, NC

Corresponding Author: Om Dave, BS, E-mail: om_dave@med.unc.edu
Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.
Patient consent for publication: Consent obtained directly from patient(s).
Authors adhere to the CARE Guidelines for writing case reports and have provided the CARE Checklist to the journal editor.
Accepted: 2023-10-11, Published: 2023-12-31

prolonged intervals, it is suspected that peripheral sensitization may induce decreased pain thresholds in these patients. Furthermore, the chronic stimulation of nociceptors can also instigate long-term neuronal changes that lead to central sensitization, resulting in continual pain signaling, which is independent of peripheral stimuli (3,4).

Given the complex interaction of the central and peripheral nervous systems behind visceral hypersensitivity, there is no universally acknowledged management of CAPS, but the mainstay of pharmacologic treatment focuses on neuromodulation of suspected pathways. The 2 most conventional therapies initially utilized are tricyclic anti-depressants (TCAs) and serotonin and norepinephrine reuptake inhibitors (SNRIs), but evidence remains largely anecdotal for both (5). Opioids are also frequently given, but used judiciously, the potential for further gastrointestinal complications like constipation, ileus, distension, and biliary dysfunction (6). In this case, we will follow a 27-year-old woman who had CAPS refractory to an extensive multimodal pain regimen involving both TCAs and SNRIs, but resolved with the use of a weekly 10 mcg transdermal buprenorphine patch, a unique approach which has not been described in previous literature.

CASE PRESENTATION

Informed consent was obtained and CARE guidelines were followed for this case report.

The patient presented in this case is a 27-year-old woman with a past medical history of Ehlers-Danlos syndrome, anxiety, depression, idiopathic intracranial hypertension, endometriosis status post hysterectomy, and recent cholecystectomy. She was referred to the inpatient chronic pain consult service for evaluation of severe abdominal pain refractory to medical management. About 5 months prior to this admission, the patient began to develop sharp right upper quadrant pain, which initially only responded to hyoscyamine treatment. On further investigation, ultrasound imaging revealed distension of the gallbladder but no sign of gallstones. Given this distension and association of pain with meals, it was suspected that her pain was due to biliary colic. She subsequently underwent a laparoscopic cholecystectomy 2 months later. She tolerated the procedure quite well for 5 days prior to developing abdominal pain and severe abdominal distension without evidence of obstruction. She underwent extensive testing over the next month, including further imaging, esophagogastroduodenoscopy, colonoscopy, hepatobiliary iminodiacetic acid scan, and gastric emptying studies, to rule out gastrointestinal and hepatobiliary etiologies of disease, which ultimately revealed no indicators of acute disease. She was additionally started on nasogastric tube feeds and intravenous hydromorphone with no resolution in symptoms, prompting transfer of care to our facility.

On presentation to our facility, a thorough chart review of her medications was performed, and the treatment team gathered that the patient was treated with 600 mg gabapentin 4 times a day, 4 mg tizanidine 3 times a day as needed, 100 mg sertraline daily, 10 mg nortriptyline daily, 2 mg oral hydromorphone every 4 hours as needed, and 0.1 mg patient-controlled intravenous hydromorphone every 20 minutes as needed. Given the concern for potential serotonin syndrome, the treatment team elected to avoid TCAs and SNRIs and instead proceeded with a continuous ketamine infusion at 0.1 mg/kg/h. In addition to this regimen, the previously mentioned medications were continued.

She initially endorsed hallucinatory side effects on day one of ketamine infusion, but then reported significant improvement in pain and was able to tolerate solid foods again on day 2. However, by day 3, the patient reported sharp right upper quadrant pain with greater intensity than prior to this admission, increased from 8/10 to 9/10 based on the Numeric Rating Scale (NRS-11). In an effort to better address this pain, the ketamine infusion was titrated to a max dose of 0.2 mg/kg/h over the next 2 days to minimize risk of the hallucinatory side effects initially described. The patient continued to regress clinically and relayed that in addition to her severe abdominal pain, she was now experiencing frequent panic attacks in anticipation of her uncontrolled symptoms. Her oral hydromorphone as needed was increased to a 4 mg dose. At this point, the treatment team was at a crossroads and decided to discontinue the ketamine infusion and trial a 5 mcg/h buprenorphine patch in order to mitigate symptoms. This was chosen given a lack of appropriate remaining options and its success in addressing various other chronic pain conditions treated by the team. They were careful to discontinue intravenous hydromorphone and continued the rest of her ongoing medications without change.

For the first 3 days following initiation of the patch, the patient reported that her pain was present but stable, rather than continuing to worsen. On day 4, the patient turned a major corner in terms of pain control,

sharing that her pain was now 6/10 compared to the 9/10 based on the NRS-11 that she had consistently endorsed for the past week. She was visibly in better spirits and did not relay any symptoms or signs of withdrawal. The patient shared that this treatment was transformative for her pain, and she was amenable to increasing her buprenorphine patch to 10 mcg/h as we began to wean her off the oral hydromorphone regimen. By day 7, the patient was satisfied with the level of pain control she had attained with her patch and her ability to gradually tolerate more solid foods. She was discharged 4 days later after a full wean of her opioid medications and was sent home with a weekly 10 mcg/h transdermal buprenorphine patch in addition to her ongoing regimen of gabapentin, tizanidine, nortriptyline, and sertraline.

DISCUSSION

Buprenorphine is a partial agonist at the mu-opioid receptor in the central nervous system. As a partial agonist, it functions as a supraspinal analgesic with properties that plateau at higher doses. This significantly increases its safety profile in comparison to other standard opiates through its "ceiling effect," especially in the context of respiratory depression. Likewise, buprenorphine is a safer alternative for patients at risk of withdrawal symptoms given its high affinity for the mu-opioid receptor along with its slow-dissociation kinetics (7,8). It is also easier to administer than oral or intravenous opioids given that patches are switched weekly. This reduction in medication administration frequency causes fewer disruptions to patients' rest, while increasing adherence. Lastly, buprenorphine has been shown to be effective in the treatment of anxiety and depression, demonstrating that it can address some of the psychiatric components that may be contributing to CAPS (9-11).

Despite its potential, substantial drawbacks of buprenorphine must be recognized as well. It has a wide array of side effects, including, but not limited to, nausea, vomiting, headache, perspiration, orthostatic hypotension, sexual dysfunction, and urinary retention. Furthermore, buprenorphine's safety profile does not exclude it from risk of overdose when used in conjunction with other agents like benzodiazepines and alcohol. This holds true for the patch especially because it functions as an extended-release product, which means greater amounts of the drug remain present in the blood at any given time (8,12). However, it is paramount to note that several of these side effects and potential drug-drug interactions are also seen with both TCAs and SNRIs (13).

The use of buprenorphine transdermal patches for CAPS in adults is not well-studied, which may be due to concerns of provoking narcotic bowel syndrome or opioid dependence following regular use. Additionally, it may take 2-3 days for full effects to be experienced, leading to pretherapeutic discontinuation by patients. However, transdermal buprenorphine patches have historically been used to achieve long-term chronic pain relief covering a broad range of etiologies (14). Similarly, buprenorphine is considered a safe, effective ameliorant of postoperative abdominal pain in adults and a prospective therapy for complex chronic abdominal pain in children (15,16).

The economic burden of CAPS is also worth considering in this discussion. An estimated 12 days of work are missed annually by those with a diagnosis of CAPS vs an estimated 4 days in those without the disease. Patients with CAPS average approximately 11 visits to a physician annually, compared to 2 visits for those without CAPS (2). Therefore, it is worth applying resources toward further understanding the role of transdermal buprenorphine for the management of chronic abdominal pain. Transdermal buprenorphine has the ability to play an integral role in how we treat CAPS, making it an ideal target for future studies to address and confirm via randomized controlled trials.

CONCLUSIONS

CAPS describes a wide range of chronic abdominal pain with no clear origin. It is a layered diagnosis involving a complex interaction of potential physiologic and psychologic components. Visceral hypersensitivity is one pathophysiologic mechanism that may be central to the experience of CAPS. It is considered to be primarily nociplastic in nature, and while there is no agreed-upon mainstay of treatment, most first-line therapies involve the administration of TCAs and SNRIs. In the setting of CAPS refractory to a multimodal pain regimen, this case demonstrates that transdermal buprenorphine may be a safe and efficacious pharmacologic therapy. It would be a significant relief economically for both patients and the health care system to reduce the excessive costs associated with extensive workups and redundant appointments for CAPS. If further studies can elucidate its application to CAPS, transdermal buprenorphine could be transformative in the lives of patients across the world who burden this pain and discomfort on a daily basis.

REFERENCES

1. Clouse RE, Mayer EA, Aziz Q, et al. Functional abdominal pain syndrome. *Gastroenterology* 2006; 130:1492-1497.
2. Drossman DA. Functional abdominal pain syndrome. *Clin Gastroenterol Hepatol* 2004; 2:353-365.
3. Delvaux M. Role of visceral sensitivity in the pathophysiology of irritable bowel syndrome. *Gut* 2002; 51(suppl 1):i67-i71.
4. Zhou Q, Verne GN. New insights into visceral hypersensitivity - clinical implications in IBS. *Nat Rev Gastroenterol Hepatol* 2011; 8:349-355.
5. Farmer AD, Aziz Q. Mechanisms and management of functional abdominal pain. *J R Soc Med* 2014; 107:347-354.
6. Camilleri M, Lembo A, Katzka DA. Opioids in gastroenterology: Treating adverse effects and creating therapeutic benefits. *Clin Gastroenterol Hepatol* 2017; 15:1338-1349.
7. Johnson RE, Fudala PJ, Payne R. Buprenorphine: Considerations for pain management. *J Pain Symptom Manage* 2005; 29:297-326.
8. Kumar R, Viswanath O, Saadabadi A. Buprenorphine. In: *StatPearls*. StatPearls Publishing, Treasure Island, FL 2022. Accessed 03/20/2023. www.ncbi.nlm.nih.gov/books/NBK459126/
9. Walter SA, Jones MP, Talley NJ, et al. Abdominal pain is associated with anxiety and depression scores in a sample of the general adult population with no signs of organic gastrointestinal disease. *Neurogastroenterol Motil* 2013; 25:741-e576.
10. Ahmadi J, Jahromi MS. Anxiety treatment of opioid dependent patients with buprenorphine: A randomized, double-blind, clinical trial. *Indian J Psychol Med* 2017; 39:445-449.
11. Serafini G, Adavastro G, Canepa G, et al. The efficacy of buprenorphine in major depression, treatment-resistant depression and suicidal behavior: A systematic review. *Int J Mol Sci* 2018; 19:2410.
12. Safety Information Butrans® (buprenorphine) Transdermal System CIII. Accessed 03/20/2023. https://butrans.com/patient/important-safety-information.html
13. Santarsieri D, Schwartz TL. Antidepressant efficacy and side-effect burden: A quick guide for clinicians. *Drugs Context* 2015; 4:212290.
14. Dankiewicz EH. Use of the low-dose buprenorphine patch: A response. *J Palliat Med* 2014; 17:379-380.
15. Vlok R, White L, Binks M, et al. Buprenorphine analgesia following major abdominal surgery: A systematic review and meta-analysis. *J Emerg Crit Care Med* 2019; 3:34.
16. Amin S, Dickerman M, Miller E, Levy C. Transdermal buprenorphine in children with complex chronic conditions: A case series. *Pediatrics* 2021; 147:550.