

Brief Commentary



How Much Is Too Much? Are Opioids Always the Answer to Pain?

Humair Rana, MD

From: Anesthesiology and Pain Management, University of Texas Southwestern, Dallas, TX

Address Correspondence:
Humair Rana, MD
5323 Harry Hines Blvd
Dallas, Texas 75390

E-mail:
: humair.rana@utsouthwestern.edu

Free full manuscript:
www.painphysicianjournal.com

A 28-year-old woman with homozygous sickle cell disease had numerous hospitalizations since childhood due to sickle cell pain crises. Her only other significant medical diagnoses were chronic eosinophilic pneumonitis and a history of deep venous thromboses in her extremities. Her pain was managed for the last several years by her primary care physician (PCP) with the use of increasing doses of numerous opioid medications including hydrocodone, hydromorphone, fentanyl, morphine, and methadone. In light of increasing hospitalizations related to difficulty in controlling her pain and her pulmonary disease, the option of hospice care was introduced by her PCP. The patient and her mother agreed to enter hospice and she was discharged from the hospital on morphine sulfate controlled release 120 mg/day, methadone 100 mg/day, hydromorphone 2 mg as needed every 4 hours, and Cymbalta 40 mg/day.

At home, she continued to have inadequate pain control and so her PCP admitted her to the hospital for end of life comfort care. Due to the extreme nature of her case, the hospital's ethics committee became involved; their recommendation was that not all treatment options had been exhausted and the suggestion of significant opioid induced hyperalgesia was raised. Based on these questions, a critical care physician was involved who consulted the pain service.

At this point, the patient was now on methadone 600 mg/day, a patient controlled analgesia device with hydromorphone, and both a ketamine (35 mg/hr) and midazolam (4 mg/hr) intravenous drip for sedation and comfort. Astoundingly, during our interview she was sitting in bed playing cards and only had one request—more medication. She reported pain throughout her entire body but noted it was worst in her low back and legs. She exhibited allodynia and her pain was exacerbated with even simple palpation. Her case was deliberated within the pain service team and several possibilities were raised. One possibility discussed was the development of a complex regional pain syndrome due to her vaso-occlusive disease process; however, she was trialed on clonidine and the bisphospho-

nate zoledronic acid with no improvement. Ultimately, we diagnosed her with significant opioid tolerance and opioid induced hyperalgesia. Our recommendation was to wean her off intravenous infusions slowly, place her on a stable dose of methadone and send her to a detoxification program to taper her opioid dose. After discussion with the patient, the primary team weaned her ketamine and midazolam drips to off and she was maintained on methadone 900 mg/day and gabapentin 2700 mg/day. She was referred to an outpatient methadone detoxification program and was to follow up in our chronic pain clinic.

She did not follow up in the pain clinic, but 6 months after her hospital discharge she was seen in our system's outpatient hematology clinic. She was noted to be off methadone and only on hydromorphone 10 mg orally every 6 hours and hydrocodone/acetaminophen 10/325 mg as needed for breakthrough pain with reported mild pain at that time. The patient did not return for follow up after that visit.

Discussion

Pain is a pervasive issue in health care; physicians often find themselves treating patients with complex

pain issues that may test their professional and ethical lines. It is our duty to address and treat pain; however, are there cases where we may be doing more harm than good?

This case presents a patient with a chronic pain state that was difficult to manage. She was placed on various medications over the years with what seemed to be little alleviation of her pain. The common thread was that she was consistently on what would be considered high dose opioids, greater than 200 milligrams of oral morphine equivalents a day. When we became involved, she was actually on greater than 20 grams of oral morphine equivalents a day. We know that opioids do not have a ceiling effect to their analgesic action, but rather are limited by physical side effects such as sedation and respiratory depression (1,2). However, the sheer dose of her opioids begs the question of whether there should be a threshold above which we do not venture without crystal clear clinical improvement. In a systematic review of opioid prescribing guidelines, it was recommended that patients on such high dose opioids (> 200 oral morphine equivalents) be referred to a specialist to evaluate appropriateness of further opioid therapy and went even further to question the appropriateness of this therapy at all (3). There is minimal supportive data for chronic use of opioids > 180 oral morphine equivalents in literature (4) and so its use could be considered unsubstantiated. We all need to learn when enough is enough and opioids have failed.

While this is a rare case, opioid use has undoubtedly increased dramatically over the past few decades (5-8). This trend is most likely due to the more accepted use of opioids for non-cancer pain and due to fundamental shifts in treatment guidelines as well (2,4,9-11). The increased prescription of opioids over this time has also seen a concomitant rise in patients entering substance abuse treatment programs and deaths related to opioids (6). Recently, these findings contributed to the Drug Enforcement Agency reclassifying hydrocodone products in an attempt to try and curb an epidemic of opioid abuse and misuse (12). Our patient did not appear to be abusing her opioids but was rather taking them as prescribed. There was minimal improvement in analgesia and escalations of opioids likely led to worsening of her pain state due to opioid-induced hyperalgesia. This belief was corroborated by the fact that her pain was diffuse, she did not appear to have any significant disease progression recently, and she was able to be maintained on much lower doses of opioids after her detoxification (13,14). In light of more liberal

opioid prescribing practices, clearly more education is needed amongst all physicians in opioid management and potential adverse effects such as opioid-induced hyperalgesia. The question of efficacy of chronic opioid therapy for non-cancer pain will continue on, but undoubtedly we should learn that opioid therapy can fail and can potentially lead to worse outcomes.

Another learning point in this case is that complex patients such as this often benefit from earlier involvement of specialists, allowing for more experienced providers to weigh in on treatment and consider alternative therapies. It is unclear in our case whether a pain specialist was involved with the patient on an outpatient basis. With rescheduling of hydrocodone containing products and some pain specialists focusing more on interventional management, changes in referral patterns are to be expected. One concern in our current health care system is that some pain specialists are practicing "defensive" medicine due to medico-legal liability concerns (15,16). Consequently, specialists may refer chronic pain patients that are only being medically managed back to their PCPs (17), possibly on high doses of opioids. This shift in the treatment pattern is concerning as it may lead to suboptimal care due to increased burden on PCPs and disparities in experience with chronic opioid management (16). PCPs who have limited time with patients and who may be inexperienced with chronic opioid management may feel pressured to increase opioid doses to avoid being accused of inadequately treating pain (15,18). This situation would lead to inappropriate increases in opioid prescription and potentially increased adverse effects. We realize it would be impractical for all chronic pain patients managed with opioids to be seen by specialists indefinitely. Along with increased pain management education, a proposed solution would be for improved systems between PCPs and pain specialists that would allow for more intercommunication.

In summary, a case is presented of opioid escalation to such levels that the patient was placed on hospice care due to the belief that her disease state was untreatable. Her management raises significant issues related to chronic opioid pain management. Certainly, there is a need for improved education amongst all physicians regarding chronic opioid management and complications that may ensue. More data is needed regarding how to optimize opioid management for chronic non-cancer pain while minimizing potential short-term and long-term adverse effects. There is also a need for improved relationships amongst pain specialists and PCPs in order

to provide more optimal care to patients. In the face of health care reforms and changes in pain management practice, all physicians must remember one of the most

important old adages—first do no harm.

REFERENCES

1. Ballantyne JC. Opioids for chronic non-terminal pain. *South Med J* 2006; 99:1245-1255.
2. Chou R, Fanciullo GJ, Fine PG, Adler JA, Ballantyne JC, Davies P, Donovan MI, Fishbain DA, Foley KM, Fudin J, Fudin J, Gilson AM, Kelter A, Mausekopp A, O'Connor PG, Passik SD, Pasternak GW, Portenoy RK, Rich BA, Roberts RG, Todd KH, Miaskowski C; American Pain Society-American Academy of Pain Medicine Opioids Guidelines Panel. Opioid treatment guidelines: Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain* 2009; 10:113-130.
3. Nuckols TK, Anderson L, Popescu I, Diamant AL, Doyle B, Di Capua P, Chou R. Opioid prescribing: A systematic review and critical appraisal of guidelines for chronic pain. *Ann Intern Med* 2014; 160:38-47.
4. Ballantyne JC, Mao J. Opioid therapy for chronic pain. *N Engl J Med* 2003; 349:1943-1953.
5. Caudill-Slosberg MA, Schwartz LM, Woloshin S. Office visits and analgesic prescriptions for musculoskeletal pain in US: 1980 vs 2000. *Pain* 2004; 109:514-519.
6. Center for Disease Control and Prevention. Prescription Painkiller Overdoses in the US. 2011. www.cdc.gov/vitalsigns/PainkillerOverdoses/index.html
7. Sullivan MD, Edlund MJ, Fan MY, Devries A, Brennan Braden J, Martin BC. Trends in use of opioids for non-cancer pain conditions 2000–2005 in commercial and Medicaid insurance plans: The TROUP study. *Pain* 2008; 138:440-449.
8. Trescot AM, Glaser SE, Hansen H, Benyamin R, Patel S, Manchikanti L. Effectiveness of opioids in the treatment of chronic non-cancer pain. *Pain Physician* 2008; 11:S181-S200.
9. American Pain Society and American Academy of Pain Medicine. Guideline for the management of acute and chronic pain in sickle cell disease. 1999. <http://ampainsoc.org/education/guidelines/sickle-cell-guideline>
10. Rosenblum A, Marsch LA, Joseph H, Portenoy RK. Opioids and the treatment of chronic pain: Controversies, current status, and future directions. *Exp Clin Psychopharmacol* 2008; 16:405-416.
11. Trescot AM, Helm S, Hansen H, Benyamin R, Glaser SE, Adlaka R, Patel S, Manchikanti L. Opioids in the management of chronic non-cancer pain: An update of American Society of the Interventional Pain Physicians' (ASIPP) guidelines. *Pain Physician* 2008; 11:S5-S62.
12. Drug Enforcement Administration. Schedules of Controlled Substances: Rescheduling of Hydrocodone Combination Products From Schedule III to Schedule II. 2014. www.deadiversion.usdoj.gov/fed_regs/rules/2014/fr0822.htm
13. Mao J. Opioid-induced abnormal pain sensitivity: Implications in clinical opioid therapy. *Pain* 2002; 100:213-217.
14. Silverman SM. Opioid induced hyperalgesia: Clinical implications for the pain practitioner. *Pain Physician* 2009; 12:679-684.
15. Furrow BR. Pain management and provider liability: No more excuses. *J Law Med Ethics* 2001; 29:28-51.
16. Giordano J. Changing the practice of pain medicine writ large and small through identifying problems and establishing goals. *Pain Physician* 2006; 9:283-285.
17. Schofferman J. Interventional pain medicine: Financial success and ethical practice: An oxymoron? *Pain Med* 2006; 7:457-460.
18. Von Korff M, Deyo RA. Potent opioids for chronic musculoskeletal pain: Flying blind? *Pain* 2004; 109:207-209.

