Brief Analysis on Naloxone for Patients on Chronic Opioid Therapy.

Naloxone is Effective, Well-Received and Underutilized.

Don Stader MD FACEP; Nate Novotny

Stader Opioid Consultants

Introduction

The life-saving opioid-reversal drug Naloxone is safe and efficacious for lay-person administration[1] and for patients taking opioids for chronic pain[2–4]. The CDC guideline for prescribing opioids for chronic pain advocates for co-prescribing Naloxone in a variety of cases (history of substance use disorder, high dose opioids, concomitant benzodiazepine prescription)[5]. This has resulted in a substantial increase in Naloxone dispensing rates nationally from 2012-2018; however, Naloxone dispensing rates to patients receiving high-dose opioid therapy remains low. In 2018, of the estimated 9 million patients who received high-dose opioid prescriptions only 406,203 of them were prescribed Naloxone—only 1 Naloxone prescription was given for every 69 high-dose opioid prescriptions[6]. Given that just over 1 in 3 overdose deaths involves a prescription opioid[7], there is a significant treatment gap that exists in providing naloxone to patients at risk for overdose on chronic opioid therapy.

Naloxone is Effective for Patients in Chronic Pain

A common misconception held by clinicians is that naloxone is only for patients who misuse opioids or have opioid use disorders. One survey of physicians found that there was a general lack of consensus about which patients should be receiving Naloxone, as it is generally thought of as an antidote for heroin overdose[8], but considered less in cases of prescription drug overdose. As previously stated, data from the CDC show as much as 36% of opioid-associated overdose deaths involve a prescription opioid as recently as 2017[6]. Other retrospective data from 2001-2007 indicate that over 60% of Americans who succumbed to opioid-involved overdoses were being treated for chronic pain. What's more, 49% of those people received a prescription for an opioid the same month they died[9]. In the same survey, several physicians felt that withholding the opioid prescription from at-risk patients was the superior option due to misconceptions that Naloxone gives patients a false sense of security and the belief that opioids are not effective for chronic pain[8].

While opioid prescribing has significantly decreased since peaking in 2012[10,11], opioids remain a frequently utilized medication for chronic pain, and patients on chronic opioid therapy warrant protection with naloxone. The benefits of providing naloxone to patients is significant. One study found that when Naloxone was integrated as part of physicians' routine care for patients at risk of an opioid

overdose, it resulted in a 50% decrease in opioid-associated deaths in a single year[3]. In another multicenter primary care study patients who received a naloxone prescription had 63% fewer opioid related ED visits after 1 year compared with patients who did not receive naloxone[17]. It is not only feasible to dispense Naloxone and educate chronic pain patients (and their families) on how to use it, it is efficacious and beneficial[12].

Naloxone Prescription are Well-Received by Patients and Do Not Increase Medical Legal Risk

A prominent theme amongst clinicians beginning to prescribe naloxone is the fear of offending patients, essentially conveying the message that they cannot be trusted with medication. One study showed that clinicians were concerned about stigmatizing their patients and it resulting in lower satisfaction ratings[8]. These concerns are not without merit[13], but virtually all studies on this topic show that dispensing Naloxone to at-risk patients and providing patient counseling is well received and a feasible strategy to destigmatize Naloxone and increasing access to it[14,15]. Furthermore, one qualitative study of Naloxone consumers, including chronic pain patients, found that stigma from healthcare providers actually contributed to fear of requesting naloxone[16]. The risk of offending a patient is presented in a non judgemental manner and less consequential than the risk of sending a patient home on a high-dose opioid without Naloxone. Mitigating the risk of developing a negative rapport with patients can be achieved with adequate counseling and framing of the situation as 'high risk medication' rather than 'a high risk patient'.

There have been concerns in the past that naloxone prescribing may increase medical legal risk if a patient has an adverse reaction to naloxone, if it is given to a patient using heroin or naloxone is misused. These risks of naloxone co-prescribing have been studied and do not increase medical liability[18]. Conversely, it is the opinion of several experts that with published recommendations from the CDC, FDA, AMA and WHO (to name a few organizations), that failure to prescribe or discuss naloxone with patients at risk of overdose may increase medical legal risk.

Compass Opioid Stewardship Program Recommends the Following to Clinicians:

+ Overdose education, safe storage and safe disposal should be provided to all patients on chronic opioid therapy
+ Naloxone should be prescribed to all patients on chronic opioid therapy.
+ In patients at high risk of overdose, clinicians should verify that a prescription is filled. This can easily be done by asking patients to bring their naloxone with them to their office visit.
+ Patients with children, pets or family members should be counseled on the risks of diversion and accidental overdose. Naloxone can improve safety for all members and guests of a household where opioids are present.

Conclusion

Dispensing rates of Naloxone have increased, but still remain low in patients who receive high-dose opioids for chronic pain. Naloxone is not exclusively for people who use opioids illicitly. Either through prescription or take-home Naloxone programs, it is medically appropriate and recommended to supply patients on opioid-therapy for chronic pain with Naloxone due to the risk of overdose and death. Through proper counseling, Naloxone is well-received by chronic pain patients and their families and can be life saving in the event of an accidental overdose.

References

1. Walley AY, Xuan Z, Hackman HH, et al. Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. *BMJ*. 2013;346:f174. doi:10.1136/bmj.f174
2. Vondrackova D, Leyendecker P, Meissner W, et al. Analgesic Efficacy and Safety of Oxycodone in Combination With Naloxone as Prolonged Release Tablets in Patients With Moderate to Severe Chronic Pain. *The Journal of Pain*. 2008;9(12):1144-1154. doi:10.1016/j.jpain.2008.06.014
3. Albert S, Brason FW II, Sanford CK, Dasgupta N, Graham J, Lovette B. Project Lazarus: Community-Based Overdose Prevention in Rural North Carolina. *Pain Medicine*. 2011;12(suppl_2):S77-S85. doi:10.1111/j.1526-4637.2011.01128.x
4. DePriest AZ, Miller K. Oxycodone/Naloxone: Role in Chronic Pain Management, Opioid-Induced Constipation, and Abuse Deterrence. *Pain Ther*. 2014;3(1):1-15. doi:10.1007/s40122-014-0026-2
5. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. *MMWR Recomm Rep*. 2016;65. doi:10.15585/mmwr.rr6501e1er
6. Guy GP, Haegerich TM, Evans ME, Losby JL, Young R, Jones CM. Vital Signs: Pharmacy-Based Naloxone Dispensing — United States, 2012–2018. *MMWR Morb Mortal Wkly Rep*. 2019;68(31):679-686. doi:10.15585/mmwr.mm6831e1
7. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and Opioid-Involved Overdose Deaths - United States, 2013-2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(5152):1419-1427. doi:10.15585/mmwr.mm675152e1
8. Binswanger IA, Koester S, Mueller SR, Gardner EM, Goddard K, Glanz JM. Overdose Education and Naloxone for Patients Prescribed Opioids in Primary Care: A Qualitative Study of Primary Care Staff. *J Gen Intern Med*. 2015;30(12):1837-1844. doi:10.1007/s11606-015-3394-3
9. Olfson M, Wall M, Wang S, Crystal S, Blanco C. Service Use Preceding Opioid-Related Fatality. *AJP*. 2018;175(6):538-544. doi:10.1176/appi.ajp.2017.17070808
10. Chen L, Vo T, Seefeld L, et al. Lack of Correlation Between Opioid Dose Adjustment and Pain Score Change in a Group of Chronic Pain Patients. *The Journal of Pain*. 2013;14(4):384-392. doi:10.1016/j.jpain.2012.12.012
11. Reuben DB, Alvanzo AAH, Ashikaga T, et al. National Institutes of Health Pathways to Prevention Workshop: The Role of Opioids in the Treatment of Chronic Pain. *Ann Intern Med*. 2015;162(4):295-300. doi:10.7326/M14-2775
12. Coe MA, Walsh SL. Distribution of naloxone for overdose prevention to chronic pain patients. *Preventive Medicine*. 2015;80:41-43. doi:10.1016/j.ypmed.2015.05.016
13. Mueller SR, Koester S, Glanz JM, Gardner EM, Binswanger IA. Attitudes Toward Naloxone Prescribing in Clinical Settings: A Qualitative Study of Patients Prescribed High Dose Opioids for Chronic Non-Cancer Pain. *J Gen Intern Med*. 2017;32(3):277-283. doi:10.1007/s11606-016-3895-8
14. Behar E, Bagnulo R, Coffin PO. Acceptability and feasibility of naloxone prescribing in primary care settings: A systematic review. *Preventive Medicine*. 2018;114:79-87. doi:10.1016/j.ypmed.2018.06.005

15. Smith JO, Malinowski SS, Ballou JM. Public perceptions of naloxone use in the outpatient setting. *Ment Health Clin*. 2019;9(4):275-279. doi:10.9740/mhc.2019.07.275
16. Green TC, Case P, Fiske H, et al. Perpetuating stigma or reducing risk? Perspectives from naloxone consumers and pharmacists on pharmacy-based naloxone in 2 states. *Journal of the American Pharmacists Association*. 2017;57(2, Supplement):S19-S27.e4. doi:10.1016/j.japh.2017.01.013
17. Coffin PO, Behar E, Rowe C, et al. Nonrandomized Intervention Study of Naloxone Coprescription for Primary Care Patients Receiving Long-Term Opioid Therapy for Pain. *Ann Intern Med*. 2016;165(4):245-252. doi:10.7326/M15-2771
18. Davis CS, Burris S, Beletsky L, Binswanger I Md Mph Ms. Co-prescribing naloxone does not increase liability risk. *Subst Abus*. 2016;37(4):498-500. doi:10.1080/08897077.2016.1238431

This material was prepared by the Iowa Healthcare Collaborative, the Opioid Prescriber Safety and Support contractor, under contract with the Centers for Medicare & Medicaid Services (CMS), an agency of the U.S. Department of Health and Human Services. Views expressed in this material do not necessarily reflect the official views or policy of CMS or HHS, and any reference to a specific product or entity herein does not constitute endorsement of that product or entity by CMS or HHS.

Developed in collaboration with Stader Opioid Consultants.