Clinical and Program Note

The Implementation of Buprenorphine/Naloxone in College Health Practice

Peter A. DeMaria, Jr, MD, FASAM; Ashwin A. Patkar, MD

Abstract. Opiate abuse and dependence have become important concerns for college healthcare providers. The passage of the Drug Addiction Treatment Act of 2000 and the approval of the combination buprenorphine/naloxone for office-based treatment of opiate dependence have increased the options available for college students and their healthcare providers. The authors review the pharmacology of buprenorphine/naloxone and discuss how it can be implemented in college health practice. They also present a case report.

Keywords: buprenorphine, clinical medicine, naloxone, opiate dependence, other drugs

wo recent developments have changed the options available to patients and clinicians for the treatment of opiate dependence. In 2000, the Drug Addiction Treatment Act (DATA) was signed into law.¹ It permits qualified physicians, defined as those holding specialty certification in the addictions or those who have completed an 8-hour training program, to prescribe schedule III-, IV-, and V-approved medications in their offices for the treatment of opiate dependence. In 2002, the US Food and Drug Administration (FDA) approved a sublingual formulation of buprenorphine alone and a sublingual formulation of buprenorphine combined with naloxone for the treatment of opiate dependence. Because the combination buprenorphine/naloxone is the preferred agent for treating opiate dependence, we focus on its use in this article.

Several researchers have tried to better identify the opiate use problem among college students. Investigators for the CORE Study of Alcohol and Drug Use who studied 38,857 undergraduate students at 89 colleges in 2003 found that 1.7% of students reported opiate use at least once in the past year and 0.8% had used an opiate in the 30 days prior to completing the survey.² In the 2004 Monitoring the Future Study, a longitudinal survey of 8th-, 10th-, and 12th-graders nationwide, OxyContin use among 12th-graders rose from 4.0% in 2002 to 4.5% in 2003, and to 5.9% in 2004.³ McCabe et al⁴ investigated the illicit use of prescription pain medication among a large sample of undergraduate college students. They found that 17.4% of college men and 15.7% of college women reported lifetime illicit pain medication use and that 10.1% of men and 8.7% of women reported illicit use of prescription pain medication in the past year. Nine percent of those students using illicit pain medication in the past year did so on 10 or more occasions. Overall, these findings suggest that college healthcare providers will likely encounter students with opiate-use problems.

Buprenorphine

Buprenorphine is a schedule III partial opioid agonist whose pharmacology was initially studied in the 1970s.⁵ As a partial agonist, it can substitute for other opioids and suppress opiate withdrawal at low doses. At higher doses, it acts as an antagonist similar to naloxone. If buprenorphine is administered to an opiate-dependant patient under the influence of opiates, it can precipitate opiate withdrawal.⁶ One of buprenorphine's advantages is its long duration of action, allowing it to be dosed daily,⁵ and researchers^{7,8} have documented its efficacy in the treatment of opiate dependence. The overdose death rate with buprenorphine is less than with methadone,9 which may be due to its pharmacologic properties that limit the respiratory depressant effect.¹⁰ Because of concerns about potential diversion and abuse, buprenorphine is formulated as a sublingual pill combined in a 4:1 ratio with naloxone.¹¹ Taken sublingually (SL), naloxone is minimally absorbed compared with buprenorphine¹¹; however, addicts who crush and inject the pill will precipitate opiate withdrawal. The prescription drug Suboxone is available in 2 mg and 8 mg strengths containing 0.5 mg and 2 mg naloxone, respectively.¹² Although most insurance plans cover the cost of the medication, the cost to patients paying out-of-pocket is about \$150-\$300 per month, depending on the daily dose prescribed. Although it

Dr DeMaria is with Temple University's Tuttleman Counseling Services in Philadelphia, PA, and **Dr Patkar** is with Duke University Medical Center's Duke Addiction Program in Durham, NC.

Copyright © 2008 Heldref Publications

DeMaria & Patkar

is expensive, many students may pay more on the streets to support their drug habit.

Treatment Options

Prior to 2002, treatment options for addicts had included detoxification using clonidine or methadone or methadone maintenance treatment (MMT).¹³ A number of limitations exist with these treatment options; for one, relapse rates are high after detoxification.¹⁴ In the case of MMT, addicts need to be accepted into an MMT program, go daily to receive their methadone, and meet with their counselor regularly. Although ample data exist on the efficacy of MMT,¹⁵ college students may have difficulty meeting their academic requirements while engaged in treatment. Buprenorphine, unlike methadone, can be prescribed through the college health center by a qualified physician. Counseling also needs to be available to the student taking buprenorphine.

Office-based opioid addiction treatment (OBOT) has become feasible for college students.¹⁶ The Center for Substance Abuse Treatment (CSAT) has published a Treatment Improvement Protocol, *Clinical Guidelines in the Use of Buprenorphine in the Treatment of Opioid Addiction.*¹⁷ These guidelines outline 3 aspects of treatment: initial evaluation, initiation of treatment (induction), and follow-up.

Initial Evaluation

Opiate-dependant students who are potential candidates for buprenorphine/naloxone treatment should receive a careful medical evaluation, including a medical history, physical examination, and laboratory studies. The treating clinician should focus on the specific drugs used and the effect of the addiction on the patient's life. Because of the high rates of polysubstance use,¹⁸ students should be questioned about use of other drugs, including nicotine, caffeine, cocaine and other stimulants, hallucinogens, club drugs, and benzodiazepines. Physicians should consider the potential deleterious effects from both the drugs of abuse and the routes of administration. For injection drug users, questioning and examination for infectious diseases, especially abscesses, cellulitis, human immunodeficiency virus (HIV), hepatitis B, and hepatitis C, are important. Physicians should encourage students to be tested for HIV, given the high risk that drug use and its accompanying lifestyle contribute to the user. The healthcare provider should also obtain a urine drug screen (UDS) to confirm the use of opiates and to screen for use of other drugs. Careful questioning should focus on possible psychiatric comorbidity, given the high rates of dual diagnosis in opiate addicts.¹⁹

During the initial evaluation, physicians should explain treatment options, including the use of buprenorphine/ naloxone. The physicians should review the requirements of the center's treatment program and ensure that the patient signs a treatment contract.

Initiation of Treatment (Induction)

Buprenorphine/naloxone should be initiated in the office where the clinician can observe the patient's response to the initial dose (2–8 mg). Most patients note a decrease in their opiate withdrawal symptoms within 30-60 minutes. If the patient continues experiencing withdrawal symptoms after 1 hour, the healthcare worker can administer a second sublingual dose. Once opiate withdrawal symptoms are relieved, the patient may leave the office with instruction for dosing at home the next day. The induction dose is usually 8-12 mg. Over the next few days, the physicians may adjust the dose to ensure that opiate withdrawal symptoms are suppressed for the full 24-hour period. The clinician should aim for a stabilization dose of 12-24 mg/d, although lower doses may be adequate for some students, especially those with shorter addiction histories or less severe opiate habits. Clinicians should see patients at least weekly until symptoms are alleviated and they are stabilized. Physicians can use telephone contact to ensure smooth induction. Once stabilized, sessions can be extended to biweekly or monthly.

Follow-Up

During follow-up visits, the clinician should focus on drug use, cravings, suppression of opiate withdrawal symptoms for a full 24 hours, and potential buprenorphine/naloxone side effects, including excess sedation or constipation. Stabilized patients are typically seen monthly, at which time a UDS is performed. The physician can prescribe a 1-month supply of buprenorphine/naloxone with refills to cover a student over breaks and vacations. Physicians should encourage individual and group counseling and participation in 12-step programs because pharmacotherapy alone is rarely sufficient.²⁰ An understanding of the local 12-step programs can be useful to direct patients to meetings of young people where they would potentially feel most comfortable.

The clinician must eventually decide whether to gradually taper the dose of buprenorphine/naloxone (eg, detoxify) or maintain a patient on buprenorphine/naloxone. This decision does not need to be made quickly, given the impact that addictive disease typically has on a person's life. Helping a patient achieve stability and develop tools to prevent relapse is important. For young adults with a short addiction history, the CSAT guidelines recommend an initial attempt at medically supervised withdrawal.¹⁷ For patients with a longer history of addiction or multiple failed treatment attempts, maintenance is advisable. In the case of patients who want to taper their dose of buprenorphine/naloxone, a gradual reduction of not more than 4 mg/wk is advisable. In the event of drug cravings or relapse to drug use, the physician should halt tapering and return the patient to a stabilizing dose. The CSAT guidelines¹⁷ recommend that clinicians offer naltrexone to patients who successfully taper off buprenorphine/naloxone to help ensure their sobriety. Naltrexone is a pure opiate antagonist that does not produce specific effects itself but rather helps prevent a relapse by blocking the euphoriant effect of ingested opiates.²⁰

Case Report

Joe was a 23-year-old single, male, senior English major who reported injuring his back in a boating accident while on vacation 1 year prior to his presentation. He was treated with oxycodone, which he continued to use after returning home. He said his initial therapeutic use turned into recreational use because of its euphoriant properties. He began to buy OxyContin on the street and reported daily oral use of 60-80 mg. Aside from controlled use of alcohol about once a week, he denied the current abuse of alcohol or marijuana. He reported using his girlfriend's Adderall to help him study and denied intravenous drug use. He denied significant past medical history. At initial evaluation, the first author (P. DeMaria), who was the attending physician, obtained informed consent, and the patient signed a treatment contract. On the day of initiation, his pupils were dilated, he was yawning, and he had piloerection. His UDS was positive for opiates and benzodiazepines (which he denied using). P. DeMaria administered 8 mg SL buprenorphine/ naloxone. Within 1 hour, he reported significant improvement in opiate withdrawal symptoms without evidence of sedation. P. DeMaria prescribed him a 1-week supply of buprenorphine/naloxone and instructed him to take an additional 4 mg SL later in the day if opiate withdrawal symptoms recurred. He was to take 8 mg the next day.

He was initially seen weekly for evaluation and counseling and continued on an 8-mg SL dose. All subsequent UDSs were free of illicit drugs. Because of the patient's strong family history for addictive disease, counseling focused on addiction education. He said he used his girlfriend's Adderall to help him with concentration and focus, a problem he had dating back to early childhood. This raised a concern about his having attention deficit/hyperactivity disorder (ADHD). P. DeMaria referred him for testing that confirmed a diagnosis of ADHD, and he was prescribed 5 mg mixed amphetamine salts daily. Six months after initiation of buprenorphine/naloxone, the patient remained free of illicit drug use. He continued to do well academically and graduated with honors. He was able to taper his buprenorphine/naloxone dose to 4/1 mg.

Summary

Buprenorphine/naloxone offers many advantages in opiate dependence treatment in the college health setting. Its relative ease of induction, safety, and efficacy allows for outpatient use, thereby permitting patients to continue their academic and personal commitments while addressing their addiction. With few changes, many college health centers could expand their services to include the use of buprenorphine/naloxone.

NOTE

For comments and further information, address correspondence to Dr Peter A. DeMaria, Jr, Tuttleman Counseling Services, 1810 Liacouras Walk, 5th Fl. (66-09), Philadelphia, PA 19122, USA (e-mail: pdemaria@temple.edu).

REFERENCES

1. Drug Addiction Treatment Act, 42 USC §3502a (2000).

2. Southern Illinois University CORE Institute. Core Survey Web site. http://www.siuc.edu/~coreinst. Accessed March 3, 2005.

3. Overall teen drug use continues gradual decline, but use of inhalants rises [online press release]. Ann Arbor, MI: University of Michigan News and Information Services; December 21, 2004. http://www.monitoringthefuture.org. Accessed February 28, 2005.

4. McCabe SE, Teter CJ, Boyd CJ. Illicit use of prescription pain medication amongst college students. *Drug Alcohol Depend*. 2005;77:37–47.

5. Jasinski DR, Pevnick JS, Griffith JD. Human pharmacology and abuse potential of the analgesic buprenorphine. *Arch Gen Psych.* 1978;35:501–516.

6. Johnson RE, Strain EC, Amass L. Buprenorphine: how to use it right. *Drug Alcohol Depend*. 2004;70:S59–S77.

7. Johnson RE, Chutuape MA, Strain EC, et al. A comparison of levomethadyl acetate, buprenorphine, and methadone for opioid dependence. *N Engl J Med.* 2000;343:1290–1297.

8. Ling W, Charuvastra C, Collins JF, et al. Buprenorphine maintenance treatment of opiate dependence: a multicenter randomized clinical trial. *Addiction*. 1998;93:475–486.

9. Auriacombe M. Deaths attributable to methadone vs buprenorphine in France. *JAMA*. 2001;284:45.

10. Walsh SL, Eissenberg T. The clinical pharmacology of buprenorphine: extrapolating from the laboratory to the clinic. *Drug Alcohol Depend*. 2004;70:S13–S27.

11. Mendelson J, Jones RT. Clinical and pharmacological evaluation of buprenorphine and naloxone combinations: why the 4:1 ratio for treatment? *Drug Alcohol Depend*. 2003;70:S29–S37.

12. Reckitt Benckiser Pharmaceuticals, Inc. Prescribing information for Suboxone/Subutex. In: *Physicians' Desk Reference*. Montvale, NJ: Thomson PDR; 2006:2719–2723.

13. Knapp CM, Ciraulo DA, Jaffe J. Opiates: clinical aspects. In: Lowinson JH, Ruiz P, Millman RB, Langrod JG, eds. *Sub-stance Abuse: A Comprehensive Textbook*. 4th ed. Philadelphia, PA: Lippincott, Williams & Wilkins; 2005:185–192.

14. Collins ED, Kleber HD. Opioids: detoxification. In: Galanter M, Kleber HD, eds. *The American Psychiatric Publishing Textbook of Substance Abuse Treatment*. 3rd ed. Washington, DC: American Psychiatric Publishing: 2004:265–289.

15. Gerstein DR. Outcome research: drug abuse. In: Galanter M, Kleber HD, eds. *The American Psychiatric Publishing Textbook of Substance Abuse Treatment*. 3rd ed. Washington, DC: American Psychiatric Publishing; 2004:137–157.

16. Fiellin DA, Rosenheck RA, Kosten TR. Office-based treatments for opiate dependence: reaching new patient populations. *Am J Psych.* 2001;158:1200–1204.

17. Center for Substance Abuse Treatment. *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction.* Treatment Improvement Protocol (TIP) Series #40. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2004. DHHS Publication No. (SMA) 04-3939. http://buprenorphine.samhsa.gov/Bup%20guidelines.pdf. Accessed November 29, 2007.

18. Mohler-Kuo M, Lee JE, Wechsler H. Trends in marijuana and other illicit drug use among college students: results from 4 Harvard School of Public Health college alcohol study surveys: 1993–2001. *J Am Coll Health*. 2003;52:17–24.

19. Brooner RK, King VL, Kidorf M, et al. Psychiatric and substance use comorbidity among treatment-seeking opioid abusers. *Arch Gen Psych.* 1997;54:71.

20. Fiellin DA, Kleber H, Trumble-Hejduk JG, et al. Consensus statement on office-based treatment of opioid dependence using buprenorphine. *J Subst Abuse Treat*. 2004:27;153–159.

21. O'Brien CP, Kampman KM. Opioids, antagonists and partial agonists. In: Galanter M, Kleber HD, eds. *The American Psychiatric Publishing Textbook of Substance Abuse Treatment*. 3rd ed. Washington, DC: American Psychiatric Publishing; 2004:305– 319. Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.