Clinical observation

Buprenorphine Replacement Therapy for Adolescents with Opioid Dependence: Early Experience from a Children’s Hospital-Based Outpatient Treatment Program

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Abstract

Opioid use by adolescents is on the rise and replacement therapy is an effective treatment. Methadone replacement has been used safely and effectively with adults, but methadone programs are often unattractive to teenagers. Buprenorphine is a new replacement therapy that has been shown to be as effective as high dose methadone and may be better suited for the treatment of younger patients. We describe the experiences of several adolescent patients who received treatment from an outpatient adolescent substance abuse program that operates within a children’s hospital, with an emphasis on issues of adolescent development. © 2007 Society for Adolescent Medicine. All rights reserved.

Opioid dependence is a growing national problem with an estimated 810,000 opiate-addicted individuals in the United States [1]. Teen use is on the rise; in the late 1990s the use of heroin by American adolescents reached its highest levels since the 1960s [2], and heroin-related emergency department visits among youths aged 12–17 years quadrupled between 1991 and 1996 [3]. According to data from the Monitoring the Future study, use of “narcotics other than heroin” by teenagers has doubled over the last decade, with marked increases in reported use of long-acting oxycodone tablets and hydrocodone/acetaminophen combination tablets [4]. In 2004, the annual prevalence of OxyContin® use by high school seniors was 5.0% [5].

Methadone maintenance improves functioning and decreases heroin use [6], and reduces mortality by two-thirds [7]. The current treatment system is able to engage only a minority of the opioid-addicted population in the United States [8]. Most methadone clinics will only treat individuals with one or more years of dependence, making methadone less accessible to younger users [9], and many clinics do not accept patients under 18 years old.

Buprenorphine is a new synthetic partial opioid agonist that has several advantages over methadone, including lower abuse potential and a stronger safety profile [10]. In contrast to methadone, which is a full agonist, buprenorphine is a partial agonist of the mu-opioid receptor, thus decreasing the ability of patients to use buprenorphine for intoxication and limiting the potential for overdose. Buprenorphine can be formulated as a combination sublingual tablet with the opioid antagonist naloxone. When this combination is taken sublingually as prescribed, the naloxone is not absorbed to any significant extent.
This preparation, however, prevents patients from misusing the medication by injecting it intravenously. Buprenorphine also has higher affinity for the opioid receptor than the full agonists, and as such, provides a block that may diminish patients’ ability to become intoxicated with opiates while receptors are saturated. Because of this higher affinity, buprenorphine treatment must always be started when a patient is in opioid withdrawal (indicating receptor availability) or after withdrawal symptoms have abated. In our clinical program, the first step in buprenorphine induction is to instruct the patient not to use any narcotics for a minimum of 24 hours prior to the scheduled induction appointment. Upon arrival, we confirm that the patient is in withdrawal with a structured tool such as the Clinical Opiate Withdrawal Scale (COWS) [11]. If the patient presents with history of recent narcotic use and a COWS less than five, induction is postponed. For those who will proceed with induction, an initial buprenorphine dose of 2–4 mg is given sublingually and the COWS is repeated in 30–60 minutes. If the COWS score has increased, indicating a precipitous opiate withdrawal, the induction is stopped and the patient is referred for acute stabilization and detoxification. If the COWS has decreased but remains above five, an additional 2-mg tablet is given sublingually and this procedure is repeated until the COWS is five or less, or a maximal dose of 8 mg has been reached. Once patients are stabilized they are discharged home and instructed to take an additional 4 mg of buprenorphine in the evening. Buprenorphine has a half-life of 24–60 hours; most patients are maintained on 8–16 mg daily which can be given in one single dose or divided.

Buprenorphine is as effective in treating opioid dependence as high-dose methadone [8], and can be prescribed by primary care physicians thus providing better access and reducing stigma [1].

A previous trial has demonstrated that short-term (28 day) medication-assisted withdrawal treatment with buprenorphine is more effective than clonidine in adolescent patients [12], but data on buprenorphine maintenance treatment for teens are limited. We describe the experiences of three patients treated in a multidisciplinary outpatient adolescent substance abuse program located at a children’s hospital. All patients underwent a substance abuse evaluation, and medical and psychiatric screens. Buprenorphine treatment was offered after patients agreed to abstain from alcohol and all drugs, participate in appropriate psychological counseling (group or individual as determined by the clinician), cooperate with random drug testing, and allow a parent or guardian to supervise medications.

### Program Description

According to the Department of Health and Human Services (HHS), patients who meet DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) criteria for opioid dependence for whom buprenorphine may be an appropriate treatment option are those who:

- Are interested in treatment for opioid dependence
- Have no contraindications to buprenorphine treatment
- Can be expected to be reasonably compliant with such treatment
- Understand the benefits and risks of buprenorphine treatment
- Are willing to follow safety precautions for buprenorphine treatment
- Agree to buprenorphine treatment after a review of treatment options [13]

The three patients described in this report were evaluated in a children’s hospital-based substance abuse outpatient program, and were selected for this report because we believe that their age and developmental stage presented unique challenges in their clinical management. In general, adolescents 13–21 years old presenting to the program complete a three-session diagnostic evaluation consisting of a complete drug use history (including an exhaustive list of substances that have been used for intoxication), medical/surgical history, review of systems, school and psychological history, family psychiatric history, physical examination, collateral history from a parent or guardian, and a mental health screening interview. There is an emphasis on behaviors related to drug and drug disorders such as a history of legal problems, school suspensions, gang involvement, fighting, carrying weapons, and selling drugs. Patients that meet DSM-IV criteria for opioid dependence are invited to enter a buprenorphine treatment program if they meet the HHS criteria specified above and, together with a parent or guardian, agree to 1) commit to abstinence from opioids, alcohol and all other illicit substances; 2) participate in a random drug testing program; 3) participate in an individualized program of substance abuse treatment consisting of one or more of the following: individual substance abuse counseling, group substance abuse counseling, family therapy, individual therapy, and/or participation in a 12-step fellowship (e.g., Alcoholics Anonymous); 4) allow parent/guardian to control medication and observe each dose; and 5) permit communication between clinical staff and parent/guardian, physicians, and other therapists. Each patient/guardian pair then signs a contract before the date of induction. Guardians also must agree to monitor the adolescent 24 hours before the scheduled induction to ensure abstinence during this period.

On the day of induction, a clinician briefly interviews both patient and parent to confirm no drug use in the past 24 hours, and to obtain a baseline Clinical Opiate Withdrawal Scale (COWS) score. Patients are given 2 mg buprenorphine sublingually every half hour until the COWS score is less than five, and then are discharged home and told to take 2–4 more mg of buprenorphine at 4 p.m. After completing induction, patients return within 3 to 4 days to check for efficacy and side effects, and then return weekly for dose adjustments. The dose of buprenorphine is increased at each
weekly visit until patient reports cessation (or near cessation) of cravings, a maximal dose of buprenorphine is reached, or side effects (such as nausea, constipation, or sleepiness) develop. Patients then return every 4 weeks for medication checks, at which time a clinician reviews vital signs, reports cravings, side effects or drug use, and a collateral history from a parent. Patients are required to come in for additional appointments if a drug test is positive, dilute or missed.

Case Reports

Patient #1

A 17-year-old male presented for evaluation after an admission to the intensive care unit resulting from an accidental oxycodone overdose. The patient reported using opioids on only one occasion before the overdose, and did not meet criteria for a diagnosis of opioid abuse or dependence. Although not a formal diagnosis, we described his opioid use as “problematic,” indicating that he had a serious consequence as a direct result of use. He did not meet criteria for any psychiatric disorders, and psychiatric evaluation judged him not to be suicidal. We recommended random urine drug testing, and supervised attendance at Narcotics Anonymous meetings. He also attended weekly meetings with a probation officer, which was mandated by court. Eleven drug tests were all negative, and drug testing was then discontinued after 3 months. One month later he returned to the outpatient program after a second accidental oxycodone overdose. At this time the patient met criteria for opioid abuse but not dependence, and again psychiatric evaluation found him without suicidal ideation or intent. Given the history of two life-threatening events, we discussed the risks and benefits of treatment with buprenorphine and offered him a medication trial. On the day of his induction, his COWS score was two and he was started on 2 mg of buprenorphine twice daily. Over the subsequent 3 months he was titrated to 8 mg twice daily; this dose was effective in suppressing cravings and improving overall functioning. Shortly after beginning treatment with buprenorphine the patient reported feeling better and more confident that he would be able to resist drug use if offered, although he reported occasional opioid cravings, which occurred when he was frustrated. Four months into his treatment he complained of opioid cravings associated with breaking up with his girlfriend, and simultaneously running out of medication before his medical appointment. His buprenorphine dose was increased with some improvement. Two months later (approximately 6 months after beginning buprenorphine treatment) he complained of opioid cravings and an episode of isolated opioid use after running out of medications a second time. He was seen by the program psychiatrist (B.L.V.), who again increased his buprenorphine dose and scheduled more frequent physician visits and drug testing. At that time he was also diagnosed with an episode of major depression, but refused a trial of antidepressants. He did receive psychosocial support through individual counseling sessions. He remained on a stable dose of buprenorphine for the next 9 months, during which time he had monthly visits scheduled to monitor vital signs, reports of side effects, and cravings; the patient often missed appointments due to difficulties with transportation and his generally disorganized home life. The patient had no further overdoses, hospital admissions or opioid use. He transitioned to an adult treatment provider on a stable dose of buprenorphine before his 21st birthday.

Patient #2

A 19-year-old male, residential college student presented for assistance in discontinuing heroin use. He had an eight-month history of opioid use, beginning with intra-nasal use of oxycodone and progressing to intra-nasal use of heroin. At the time of his initial evaluation, he met diagnostic criteria for opioid dependence, without any other active substance use disorders. He came to treatment on his own and did not want his parents notified. After an assessment, including a screening for family violence in which he was judged to be low risk, we offered him a medication trial on the condition that he complied with all programmatic requirements, including supervision by a parent or guardian. Alternatively, we offered to refer him to another buprenorphine provider. The patient opted to continue his care at our program and presented to the clinic with his father on a subsequent visit. With the patient present, a physician explained the patient’s diagnosis, treatment recommendations, and the structure of the buprenorphine program. The family agreed to participate. On the day of his induction his initial COWS was nine; he received a total of 4 mg of buprenorphine and was discharged home with a COWS score of two and instructed to take 4 mg of buprenorphine at 4 p.m. Shortly after his induction he reported complete remission of withdrawal symptoms and abatement in cravings. His parents continued to report general lack of energy and interest in activities. Over the subsequent 6 months his dose was titrated to 8 mg buprenorphine each morning and 16 mg each evening to manage cravings. During his initial assessment the patient was noted to have considerable difficulty with anxiety. After 2 months of treatment with buprenorphine and abstinence from all illicit substance use, psychiatric assessment found him to have generalized anxiety disorder and depressive disorder. Pharmacotherapy was initiated with sertraline; although this was helpful it did not lead to remission. Another medication trial with fluoxetine similarly was not sufficient. His treatment was complicated by his resistance to participating in individual psychotherapy, although he did complete a 12-week weekly substance abuse group program. Nonetheless, he was treated for 1 year without further drug use. He was transferred to an adult
provider, including individual psychotherapy, on a stable regimen of buprenorphine, by his 21st birthday.

**Patient #3**

A 17-year-old female presented for evaluation and treatment of opioid dependence. History revealed that she met diagnostic criteria for opioid, alcohol, and nicotine dependence, marijuana, sedative (benzodiazepine), and cocaine abuse. She had some symptoms of depression, but did not meet criteria for a mood disorder. She was interested in discontinuing opioids, but did not want to stop using other drugs. Several days after completing an assessment she agreed to the terms of the buprenorphine program, including cessation of all alcohol and illicit drug use. On the day of her induction her initial COWS score was 12; she received a total of 6 mg of buprenorphine and was discharged with a COWS score of four and instructed to take 4 more mg of buprenorphine at 4 p.m. She continued to report mild cravings and anhedonia. Her dose of buprenorphine was increased to 8 mg twice daily over the subsequent 2 months, which relieved cravings, though anhedonia persisted.

The patient continued to use alcohol and marijuana regularly. She agreed to re-establish weekly individual counseling with program staff, but no change in behavior occurred. Her overall functioning had not improved as evidenced by her running away from home and not attending school. After 3 months of treatment she relapsed to opioid use. Ultimately, she returned home and to the clinic, and was re-admitted to the buprenorphine program. During her second induction her initial COWS score was 17; her buprenorphine induction dose was 12 mg each morning and 6 mg each evening. Her dose was titrated to 16 mg twice daily over the next month. Once again she continued to use alcohol and marijuana despite her treatment contract and counseling sessions. The clinic psychiatrist evaluated her and diagnosed a personality disorder, but did not recommend additional medications. The patient again relapsed to opioid use and left home a second time, and, once again returned a few weeks later seeking buprenorphine treatment. The treating clinician decided she needed more intensive support and referred her to a residential treatment program.

**Discussion**

Although residential treatment and detoxification may be viable options for some adolescent patients, our early experience demonstrates that many adolescents with opioid dependence can benefit from buprenorphine therapy. At the time of this writing, we have treated more than 30 patients with buprenorphine and, of those, about half have achieved improved functioning in multiple domains. Physicians who prescribe buprenorphine to adolescent patients should be aware of the challenges, such as early diagnosis in patients without a long substance use history and overall lack of life experience for young patients as well as the opportunities, such as the possibility of early treatment before the development of medical and psychological sequelae, and the availability of parents or guardians who can help increase structure in the environment for treating younger patients.

The three patients discussed in this case report were selected because we believe they each presented management challenges that are unique or more prominent in adolescents. Patient #1 did not meet criteria for opioid dependence, but was offered a trial of buprenorphine because of two previous life-threatening opioid overdoses; the second near-fatal overdose occurred after a trial of conservative treatment that included monitoring with drug testing and support from Narcotics Anonymous. Even after a second hospital admission, the patient did not meet DSM-IV criteria for opioid dependence. Given two life-threatening events, the excellent safety profile of buprenorphine and the absence of long-term complications, the clinical team decided to offer buprenorphine as an addition to the treatment plan with good result. We believe that this patient may have presented for treatment very early in the course of his opioid disorder, before meeting full diagnostic criteria for opioid dependence and, given that addictive disorders often begin during adolescence, other adolescents may present similarly early in the course of the disorder.

Younger patients who present for treatment of drug dependence often have a shorter history of drug use than treatment-seeking adults. Treatment early in the course of the disorder presents the opportunity to prevent co-morbidities associated with drug use, including acute and chronic medical conditions, and psychiatric and social complications. However, buprenorphine is an expensive medication that may be required long term. It requires significant supervision and monitoring and has the potential to cause irritating side effects such as appetite and sleep disturbances. Treating physicians should carefully evaluate potential patients and consider alternative therapies.

Adolescents are not yet fully independent and have rules imposed upon them by parents or guardians. As healthy adolescents mature into adulthood, the relationship between parent and child is renegotiated gradually, and ultimately the young person achieves independence. Parents or guardians, however, can continue to provide structure for adolescents with drug and alcohol problems, and clinicians can take advantage of this natural situation to help support young patients in their efforts at recovery. Patient #2 was 19 years old at presentation, legally of age to consent for treatment. However, he was not yet fully independent, as his parents were supporting him through college and continued to play a major role in his life. The patient initially preferred for his parents not to be involved in his treatment for fear of their embarrassment or disapproval upon revealing his diagnosis. Although referral to an adult provider was offered, the patient chose to involve parents and remain in an adolescent program. He was relieved that his parents were
supportive and willing to be involved in treatment. The parents remained an active part of the patient’s treatment while in an adolescent program. A requirement for parental participation in treatment may be controversial, and although implementation can be complicated, laws protect the right of minors to seek treatment without parental notification [14] as a means of eliminating treatment barriers for adolescents and young adults. However, as with adults who benefit from family support as part of substance abuse treatment [15], we believe that active parental participation helps improve compliance, prevent diversion of medication, and detect early relapse. Such family participation may be even more important in the treatment of adolescents, because parents may have more authority over even adult children than other family members. This case demonstrates that such a requirement can be implemented with good result and without creating a treatment barrier.

In preparation for independence, adolescents typically over-represent their abilities to themselves and to the world [16]. Parents may experience this phenomenon as the young person believing s/he is immortal, and a natural consequence is increased risk taking [17]. As with adults who are addicted to substances, many adolescents believe they can “control” drug use on their own, even when their history provides evidence to the contrary. This may be a stronger inclination in adolescents and young adults who, as compared with adults, have relatively shorter drug histories, fewer negative consequences, and may have been sheltered from consequences of drug use by parents. It is thus not surprising that many adolescents present to our buprenorphine program committed to discontinuing opioids while intending to continue using other drugs. At the same time, adolescents with less drug use experience, and less capacity for abstract thinking, may have more difficulty implementing and maintaining risk reduction strategies. In our clinical experience, many adolescents have reported that risk reduction is not a practical strategy, as they view risky events (such as driving while intoxicated) inevitable once they have used drugs on a given occasion. Traditional abstinence-based programs have had mixed success with heroin-dependent adults [18], but newer promising approaches combine the nonconfrontational aspects of harm-reduction models with the goal of working toward abstinence [19]. Similarly, our program uses nonconfrontational techniques such as motivational interviewing [20] to help adolescents work toward abstinence. In our experience, patients who make a complete life style change and discontinue all drug use are most successful. Our patients are required to sign an abstinence contract to enter treatment. Patient #3 did sign an abstinence contract, but due to her significant substance use disorder she was not yet ready to work toward abstinence, and did not fully engage in counseling. After a second opioid relapse more intensive therapy was recommended. We believe that the treatment we provided helped to prepare her for the major lifestyle change (abstinence from all drugs) by allowing her to experience the consequences (opioid relapse) of her action (continued marijuana and alcohol use) in a monitored setting. In addition, her participation in treatment helped to establish a therapeutic alliance that made her more likely to accept a referral.

Conclusion

The cases presented here demonstrate that substance use can be life-threatening, particularly for inexperienced users, even when the diagnostic nomenclature may not suggest such high risk. Parental involvement may provide enough structure to eliminate the need for intensive programs, even for older adolescents. Finally, adolescents who commit to abstinence may have fewer relapses; adolescents who are not ready to discontinue other drugs may benefit from more intensive programs, although allowing young patients the opportunity to experience the consequences of continued drug use in a monitored situation may be a necessary step in accepting the need for such change.

This report provides early evidence that buprenorphine replacement treatment in an outpatient setting may be a viable treatment option for adolescent patients. Future controlled trials should be directed at comparing the efficacy of buprenorphine replacement therapy with other treatment modalities, such as detoxification and long-term residential programs.

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