Perspectives

Prescription Opioid Abuse and Potential Role of Office-Based Opioid Maintenance Treatment in Integrating Medical and Substance Abuse Care

Patrick G. O'Connor, MD, MPH, reviewed issues in identifying, managing, and preventing prescription opioid abuse and discussed the potential benefits of office-based opioid maintenance therapy at the 4th Annual HIV Clinical Conference for Ryan White Care Act Title III and IV clinicians, sponsored by the International AIDS Society–USA and funded by the HIV / AIDS Bureau of the US Health Resources and Services Administration. The conference was held in San Diego in June, 2001.

Prescription Opioid Abuse

Case Presentation

Dr O'Connor began his presentation with a case illustrating potential prescription opioid abuse. A 27-year-old woman with HIV infection is added to a physician's schedule as an urgent visit. The patient states that she was in a car accident 5 days ago and has acute back pain. She is traveling by air later today and wants "Percocet" for her pain. Physical examination is unremarkable. The patient has been seen before for chronic and acute back pain and has been receiving oxycodone for both. She does not see her primary care physician regularly. There is a vague reference to "drug abuse" on her chart. While the physician is trying to contact the patient's regular physician, the patient and clinic assistant begin arguing in the hallway; the patient has been going from room to room "looking for the doctor and her prescription." The physician and patient begin arguing, and the patient leaves the clinic untreated.

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Considerations in Addressing Potential Abuse

For patients diagnosed with chronic nonmalignant pain, there are a number of clinical criteria for effective treatment. The primary goals of treatment are to relieve pain and to reduce functional impairment that may accompany chronic pain. Development of a feasible treatment plan should include consideration of use of both nonpharmacologic and pharmacologic modalities, with the aim of providing a stable, effective regimen. In general, effective management of pain requiring opioid treatment includes careful consideration of whether short-acting or long-acting opioids are indicated. Long-acting agents are considered to be more suitable in patients with chronic pain, since they provide steady pain relief for a prolonged period. In addition, effective pain control requires a feasible patient-physician interaction, with the relationship remaining stable over time and regular follow-up being conducted.

The course to be adopted in managing a patient who is receiving opioid treatment for chronic nonmalignant pain and who may be a prescription opioid abuser depends on the evaluation of evidence for the presence of pain that requires such treatment and the evidence for prescription drug abuse. Diagnosis of chronic pain depends on consideration of both subjective evidence derived from patient history and objective evidence supporting presence of a chronic pain condition. With regard to subjective evidence, it is important to consider whether the patient history is consistent with a specific diagnosis of chronic pain and whether severity is sufficient to warrant opioid treatment, as well as to evaluate the patient's responses to prior nonpharmacologic treatment, nonopioid medication, and opioid medication. Objective evidence of a chronic pain condition is derived from physical examination, diagnostic tests, and evaluation by specialists.

The prevalence of prescription drug abuse in patients with chronic nonmalignant pain is rather poorly understood, with most of the little data available coming from studies in pain management centers. One 1992 meta-analysis of 24 studies indicated that 3% to 19% of patients had comorbid substance abuse disorders (Fishbain et al, *Clin J Pain*, 1992). A Seattle Veterans Affairs study indicated that 28% of a relatively small sample of patients (n=76) treated with opioids met the criteria for prescription drug abuse (Chabal et al, *Clin J Pain*, 1997).

> Estimates of prevalence of prescription drug abuse in patients with chronic nonmalignant pain range from 3% to 28%

However, the prevalence of such abuse among primary care populations of chronic pain patients or HIV disease patients has remained relatively undefined. A recent study by Dr O'Connor and colleagues from Yale University found that history of substance abuse/dependence was high among outpatients in primary care who received opioid treatment for chronic nonmalig-

nant pain (Reid et al, J *Gen Intern Med*, 1999). The most common pain diagnoses were low back pain (35%), degenerative joint disease (15%), injury-related pain (12%), and diabetic neuropathy (9%). The most commonly used opioid was the short-acting agent oxycodone (usually Percocet), which was being taken by 39% of patients. Given the current dictum that long-acting agents are more suitable for treatment of chronic pain, this finding suggests that many patients were being suboptimally managed. The lifetime prevalence of alcohol abuse/dependence was 39% and that of drug abuse/dependence was 28%. Lifetime prevalences of psychiatric diagnoses, including depression (47%) and anxiety (19%) were also high.

Identification/Diagnosis of Prescription Opioid Abuse

Identification of potential opioid abuse in pain patients is difficult, since many "drug-seeking" behaviors are also exhibited by patients who wish only to achieve relief from pain. Nevertheless, such behaviors may prompt suspicion of drug abuse; these include over-reporting of symptoms, reporting of multiple somatic complaints or vague symptom complexes, insistence on specific medication or "brand name only" (which may also occur in cases in which the drug is being sold on the street), arguments about pharmacology, assertion of high tolerance to medication, veiled threats, flattery followed by prescription requests, and demands for polypharmacy. Statements that may indicate abuse include:

- "I spilled the bottle"
- "I lost the prescription"
- "_____ is the only drug that works"
- "I'm allergic to everything but _____"
- "I washed the prescription in the laundry"
- "Someone stole my medication"
- "Only the brand name works for me"
- "I needed to use more this month"

Diagnosis of prescription drug abuse in patients with nonmalignant chronic pain is not straightforward. The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for diagnosing substance abuse are difficult to apply to this patient population, since some of the characteristics figuring in diagnosis—eg, tolerance and dependence—may be expected in patients receiving long-term opioid treatment. Specific diagnostic criteria for prescription drug abuse in this population, proposed by Chabal and colleagues (*Clin J Pain*, 1997), are shown in Table 1.

Several physician actions are in order for patients found to be abusing prescription drugs. The appropriate indications for the drug at issue should be reviewed with the patient, and the patient should be educated about the potential dangers of the drug. It should be clearly stated why the drug is not indicated in the patient's case. Concern over and evidence for drug abuse or dependence should be discussed. Alternative drug treatment or referral should be recommended, with the physician emphasizing that he or she is not refusing to treat the patient but is instead focusing on another form of treatment. Finally, it is imperative that the patient be referred for substance abuse treatment, irrespective of whether it is believed that the patient will act on the referral.

Minimizing Potential for Abuse

Physicians may contribute to prescription drug abuse by relying on outdated drug information, being poorly educated on the effects of mood-altering drugs, remaining unfamiliar with principles of pain management, and by avoiding confrontation of patients for whom there is evidence of abuse. Actions that physicians can take to minimize potential for prescription drug abuse (Table 2) include documenting the rationale for treatment, establishing goals for treatment, identifying how long the drug at issue will be prescribed, and maintaining a flow chart of prescribed controlled substances. Patients should be continually monitored for effectiveness of therapy, evidence of tolerance or dependence, and evidence of abuse. Use of a controlled prescription drug "contract" may be highly advantageous.

Strategies for minimizing abuse include controlled prescription drug "contracts" between physicians and patients

Dr O'Connor and colleagues currently are conducting a clinical trial of the effect of such contracts on treatment efficacy and frequency of substance abuse in chronic pain patients. Experience in the study thus far suggests that such contracts should acknowledge physician responsibility for good patient care and emphasize patient responsibility for the medication. In addition, they should stipulate that the patient will not request medications from any other provider, only 1 pharmacy will be used for prescription filling, refills will be made on time and at regular appointments, and continuation of medication relies on adherence to the contract. According to Dr

Table **1.** Diagnostic Criteria for Prescription Drug Abuse in Patients with Chronic Nonmalignant Pain

Three or more criteria are required for diagnosis:

- Overwhelming focus on opioid issues that persists beyond 3 visits
- Early refills (3 or more) or escalating drug use in absence of clinical change
- Numerous phone calls or visits to staff requesting more opioids
- Pattern of "lost," "spilled," or "stolen" medication
- Supplemental sources of opioids: multiple providers, emergency departments, illegal sources

Adapted with permission from Chabal et al, *Clin J Pain,* 1997.

O'Connor, despite early fears regarding patient acceptance of contracts, most patients receiving opioids have responded well to the contracts in the study and have cited benefits in terms of security and regularity in the provision of medication.

Quality of care and minimization of abuse potential also are enhanced by use of a team approach to management of chronic pain patients. In addition to the patient and primary care physician, the team should include psychiatry personnel to assist in management of long-term treatment with controlled substances. Other important components of the team include qualified pain management specialists and such other professionals as social workers, counselors, and drug treatment program staff, as needed and as available, as well as the patient's family.

Although vigilance regarding drug abuse is warranted in chronic pain patients, physicians prescribing opioids need to be aware of the potential for "auto-lobotomy," whereby suspicion of rampant abuse leads to failure to provide good care. Underprescribing opioids can be as much of a problem as overprescribing them. Patients with substance abuse disorders can have pain-related diagnoses and syndromes just as do patients without such disorders. For physicians managing HIV-infected patients, it should be recognized that such patients may be at increased risk for pain. It also needs to be remembered that due to tolerance, patients on methadone maintenance can require higher doses of opioids that are indicated for pain treatment. The need to remain sensitive to the concerns of individual patients in treatment is also illustrated by frequent expression of fear of readdiction by patients with prior substance abuse problems who require opioids for pain treatment. These patients may require specific support during the course of their pain treatment.

Dr O'Connor noted that after leaving the clinic, the patient described in the case above went to the emergency room and received oxycodone. Eventually, she returned to the clinic and was placed on a controlled drug contract. She failed to comply with the contract on numerous occasions, "losing" prescriptions and running out of medication too soon. The local pharmacy called the physician regarding the patient's use of altered prescriptions and multiple providers. After much discussion with the patient, she finally accepted referral to methadone maintenance. Although her course has been rocky, the patient currently is doing reasonably well in both medical and substance abuse treatment.

Office-Based Opioid Maintenance Treatment

Case Presentation

In a second case presentation, Dr O'Connor described a scenario in which office-based opioid maintenance treatment may be an effective therapeutic approach. A 45-year-old woman presents with the complaint "I want my life back." The woman has a medical history of HIV disease, hepatitis C virus infection, hypothyroidism, type 2 diabetes mellitus, opioid dependence, and depression. Of the medications that have been prescribed for her, she is taking only insulin for her diabetes and levothyroxine for hypothyroidism. The patient is married with 2 children, aged 13 and 17 years, and works as a retail clerk. Her substance abuse history includes heroin by injection since age 18 (4 "bags" per day); she has undergone treatment by pharmacologic withdrawal, opioid antagonist treatment (naltrexone), and opioid agonist treatment (methadone), but currently resists drug abuse treatment because of the stigma associated with treatment programs. She has not found a physician to address both her medical problems, including HIV disease, and substance abuse problems.

Rationale for Office-Based Opioid Maintenance Treatment

Recent legislation appears to be clearing the way for office-based opioid maintenance treatment, which could be of considerable utility for patients like the woman in this case. The Narcotic Addict Treatment Act of 1974 established the groundwork for the very strict rules and regulations that govern methadone maintenance programs and serve to isolate such treatment from mainstream medicine. In 2000, the US Food and Drug Administration and the Center for Substance Abuse Treatment released regulations that, when adopted, will allow for exemptions for office-based methadone maintenance care and permit transfer of stable patients to care in physicians' offices.

The Congressional Drug Addiction Treatment Act of 2000 now permits qual-

Table **2.** Actions to Minimize Prescription Opioid Abuse

Document treatment rationale and plan and period of time drug will be prescribed in patient chart

- Maintain a flow chart of prescribed controlled substances, recording number of pills and number of refills
- Evaluate patient for continued use of the drug:
  - Is there a documented cause for patient's symptom(s)?
  - Is there evidence of tolerance (eg, escalating dose) or dependence?
  - Is the therapy effective—eg, does it allow patient to function at higher level?

Establish policies for prescribing controlled substances

- Use controlled substance contracts
- Do not leave prescriptions in unsecured areas
- Do not refill prescriptions for patients you do not know unless you have access to their medical records
- Do not write controlled prescriptions initiated by another physician; establish with the patient and other provider that there will be just 1 physician responsible for renewing the prescriptions
- Practice good prescription "hygiene": write prescriptions clearly and spell out all numbers

ifying office-based physicians to use approved schedule III, IV, and V controlled substances for treatment of opioid dependence. The US Department of Health and Human Services has proposed additional exemptions for office-based care, but has emphasized that more data on this issue need to be collected.

There is considerable rationale for office-based opioid maintenance treatment. It would increase access to treatment, an important issue since approximately 80% of opioid-dependent individuals are not in treatment, and it would improve coordination of medical, psychiatric, and substance abuse care. Movement of such treatment into the medical mainstream would weaken the distinction between opioid dependence and other chronic diseases and allow for recognition and reinforcement of patients' treatment successes within their medical care setting. It has also been suggested that treatment in the office setting would permit a beneficial limiting of contact between the patient and other patients who are still using drugs. Data supporting the feasibility of office-based opioid treatment come from uncontrolled studies (Novick et al, JAMA, 1988; Novick et al, J *Gen Intern Med*, 1994; Schwartz et al, *Am J Addict*, 1999) and a small number of randomized clinical trials showing that properly conducted office-based treatment is effective in stabilized patients transferred from methadone maintenance clinics (Senay et al, J *Addict Dis*, 1993), or in those who are entering maintenance treatment (O'Connor et al, *Am J Med*, 1998).

There is at least preliminary evidence that physicians will accept a role in office-based opioid maintenance treatment. Dr O'Connor and colleagues in the Connecticut Medical Maintenance Project (JAMA, in press) recently completed a study of patients who had received treatment at a narcotic treatment program for more than 1 year and had no evidence of illicit substance use for 1 year, no medical or psychiatric contraindication to leaving the program, and no dependence on cocaine or alcohol. The patients were randomized to continued care in the program or to office-based methadone maintenance. Treatment retention rates were approximately 80% in both the office setting and narcotic treatment program setting and rates of illicit drug use were equivalent at the 2 treatment sites. The measure of patient satisfaction with office-based treatment was higher than that for the maintenance program. Assessment of provider satisfaction indicated that physicians in the office-based maintenance arm were just as satisfied with providing treatment as were program treatment providers, with satisfaction with patient relationships even being somewhat greater among the office-based physicians.

Data indicate that office-based opioid maintenance treatment can be effective in patients transferred from methadone clinics or who are entering treatment

Dr O'Connor and colleagues currently are performing a study assessing the feasibility and efficacy of initiating opioid maintenance treatment in primary care. In this study, patients are receiving the agent buprenorphine and are allocated a minimum level or high level of psychosocial counseling. Buprenorphine, which is not yet approved for use in the United States, may prove to be quite suitable for use in office-based treatment. This agent is a partial mu-agonist that is associated with less risk of respiratory depression and a lower level of physical dependence than other opioids. It can be administered 3 times a week and is available in a combination tablet form with naloxone that is intended to decrease abuse potential (eg, the tablet cannot be broken up to be used for injection of the opioid). Buprenorphine has been shown to be as effective as methadone and LAAM (levomethadyl) in treatment of opioid dependence in randomized trials (eg, Johnson et al, N *Engl J Med*, 2000).

Dr O'Connor noted that the patient in the second case has succeeded in "getting her life back." She entered office-based methadone maintenance treatment, was abstinent after 1 month, and has had excellent long-term success in treatment. She has been reengaged in primary care for her other conditions. She initiated antiretroviral therapy for HIV disease and has shown excellent compliance with treatment. She underwent evaluation for hepatitis C virus infection at a liver clinic and currently is being closely monitored for infection status. Her blood glucose control has improved with institution of twice-daily insulin treatment. She is doing well on levothyroxine treatment for hypothyroidism and has initiated selective serotonin reuptake inhibitor therapy and counseling for treatment of depression.

Pharmacologic treatment is very successful in decreasing illicit opioid use and associated medical and social complications. There is accumulating evidence that office-based opioid maintenance treatment is feasible and associated with high patient and physician satisfaction. Office-based care may improve access to and coordination of care of patients who require medical and substance abuse treatment and management, a factor that may be particularly beneficial for many patients with HIV disease.

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Suggested Reading

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Coming in December: Update on Drug Resistance Mutations in HIV-1

Members of the International AIDS Society–USA Resistance Mutations Project, a subgroup of the Resistance Testing Guidelines Panel, are currently updating their listing of antiretroviral drug resistance mutations to reflect new data from recent scientific conferences. Updated mutations figures will be published in the December, 2001, issue of *Topics in HIV Medicine* and posted on the International AIDS Society–USA Web site (www.iasusa.org). More information about the Resistance Mutations Project and the current version of the mutations figures are available at www.iasusa.org.