

Clonidine As A Drug Of Abuse

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Most clinicians believe that clonidine has minimal abuse potential. Originally introduced as an antihypertensive agent in 1974, clonidine is inexpensive and has well-known and tolerable side effects. In recent years it has been used in a wide variety of clinical situations, including the treatment of opiate dependence and numerous psychiatric disorders in both adults and children.¹ Despite its growth in popularity, however, occasional reports have suggested that clonidine has the potential for abuse in combination with heroin or methadone. We describe here a case of clonidine as a single drug of abuse.

Case Report

A 66-year-old woman came to the emergency department of a southeastern university hospital complaining of severe chest pain and difficulty breathing. She had a 15-year history of severe hypertension requiring multiple therapeutic agents. Clonidine was added to her regimen in 1986, and the dose was gradually increased to 0.3 mg three times a day. Between 1989 and 1992 she was admitted to the hospital seven times for severe chest pain, but on no occasion was infarction confirmed by enzymes. Echocardiograms done in 1986 and 1991 showed progressive worsening of left ventricular function; cardiac catheterizations in 1977, 1986, and 1989 showed normal coronary arteries, and urine catecholamine findings were normal.

Seven days before this admission, she was admitted to the cardiac care unit with chest pain and severe hypertension. Again no evidence of myocardial infarction was found. Believing that abrupt discontinuation of clonidine had been responsible for the severe hypertension and chest pain, her physicians removed the drug from her outpatient regimen. Her discharge medicines

included captopril 50 mg three times a day, furosemide 20 mg every day, atenolol 100 mg twice a day, nifedipine 30 mg three times a day, and isosorbide dinitrate 10 mg three times a day. She did well for 2 days after discharge but then developed substernal chest pain radiating to her left arm accompanied by diaphoresis and some nausea. She was brought to the emergency department for evaluation.

Other past medical problems included a history of pneumonia, multiple urinary tract infections, dyspepsia, and cholecystectomy in 1991. She denied any alcohol or tobacco use or any family or personal history of heart disease or depression. She had been a widow since 1962 and had 4 living children aged 27 to 42 years. She lived with her 42-year-old son; her youngest son, aged 27 years, had a history of drug and alcohol abuse. Another son had died of cancer at the age of 30 years.

Her blood pressure on admission was 210/108 mmHg, and her pulse rate was 85 beats per minute and regular. During a cardiac examination she had normal heart sounds and no murmurs. There was no jugular venous distension or peripheral edema, and she had good peripheral pulses. Her lungs were clear to auscultation. Laboratory studies showed a normal complete blood count, electrolytes, liver profile, and urinalysis. A chest radiograph showed mild cardiomegaly but was otherwise normal. An electrocardiogram showed a regular rate of 80 beats per minute and a left bundle branch block, with no change from previous admissions.

The patient was admitted for cardiac monitoring by telemetry, but her enzymes did not suggest myocardial infarction. We decided to keep her in the hospital to explore the reasons for her frequent hospitalizations and to simplify her drug regimen.

A conference with her children revealed a major concern about clonidine. In response to an initial open-ended question about whether she always took her medicines, the oldest son immediately asked, "What is this clonidine, and what is it doing for her?" He commented that she "ate clonidine like M & Ms"; moreover, clonidine was

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the only medicine she consistently took. Typically, he reported, the patient would finish a month's supply in a few days and then start looking for ways to get more. She would ask neighbors to take her to the pharmacy, because she knew that her son would ask her what happened to her prescription that he had filled a week ago. She saw many physicians in the area to keep her clonidine prescriptions current and to have access to unlimited refills.

The other children confirmed this story. Her daughter described her as "zonked out on clonidine most of the time"; she described incidents in which her mother would go to the local physician and claim that a grandchild had "flushed her pills down the toilet" and that she needed more clonidine. On the rare occasions that she ran out, she would end up in the hospital with chest pain. The family also reported a distant history of alcohol abuse and depression and admission to a psychiatric hospital at that time.

Calls to local physicians' offices and pharmacies corroborated other aspects of the story. We found numerous physicians in three towns who had given her many large prescriptions for clonidine. At least two local pharmacists were also familiar with her excessive clonidine refills; one reported that she had learned the different pharmacists' shifts and would visit at different times to avoid the same pharmacist. When the pharmacists would question her about her excessive refills, she would use the same excuses that she used with the physicians — prescription lost, child flushed it down the toilet, or "left it at the beach." They also reported that her other antihypertensive medicines were refilled only rarely.

Two local pharmacists mailed us records of her clonidine refills during the past year. In a typical month the patient would alternate visits every 4 to 5 days between these two pharmacies, getting 100 of either 0.2-mg or 0.3-mg tablets at each visit. Thus in May 1993, she obtained a total of about 150 mg of clonidine from these pharmacies, which represents about 5 mg/d or more than five times the prescribed dose. This estimate is a minimum because the patient also used other pharmacies around this area; her children could not give us all the names, and not all the pharmacies were able to give us cumulative records easily.

Armed with the above facts, we confronted our patient with the possibility of clonidine abuse.

She denied using more clonidine than prescribed and became angry for what she perceived as "labeling" her as an addict. She claimed that she was only taking a medicine prescribed by her physicians and was afraid that she would get chest pain if she did not keep taking her pills.

During the next 4 days, her hypertension treatment regimen was dramatically simplified. The children were warned not to drive her to pharmacies to refill clonidine, and local pharmacies and other community physicians were contacted to make them aware of this patient's abuse of clonidine. She was discharged with prescriptions for captopril 50 mg three times a day and nifedipine 30 mg three times a day; she had excellent blood pressure control and no chest pain on vigorous exertion. One year later some adjustments have been made in the dosages of these two medicines, but the patient has done well. She has had no admissions for chest pain.

Discussion

Addiction is a neurobehavioral syndrome of compulsive seeking and continuing use of a drug despite increasing evidence of adverse effects.² In the *Diagnostic and Statistical Manual of Mental Disorders (Third Edition, Revised)*,³ the term *psychoactive substance abuse disorder* involves both a pattern of pathological use and impairment of physical, social, or occupational functioning caused by the substance. For prescription drugs, abuse can be defined as using a drug for a purpose other than for what it was prescribed or in quantities greater than prescribed.

We believe that our patient had an addiction to clonidine. Her admissions for chest pain and severe hypertension most likely represented clonidine withdrawal, and the overall pattern of excessive use, harm to herself, lying to obtain medication, and a denial of a problem is characteristic of an addiction. She exhibited at least five of the diagnostic criteria for psychoactive substance abuse summarized in Table 1.³

The medical literature has given very little attention to clonidine abuse. In one report 2 ex-heroin abusers who were prescribed methadone and clonidine therapy were later found to be abusers of clonidine,⁴ and another described a patient who used clonidine along with heroin to augment her high. This report also stated that this practice is commonplace on the street.⁵ In

Table 1. Diagnostic Criteria for Psychoactive Substance Dependence.*

At least three of the following must be present:

1. Substance taken in larger amounts or for a longer period than intended
2. Persistent desire or one or more unsuccessful efforts to cut down or control substance use
3. A great deal of time spent in activities necessary to get the substance, taking the substance, or recovering from its effects
4. Frequent intoxication or withdrawal symptoms when expected to fulfil major role obligations at work, school, or home
5. Important social, occupational, or recreational activities given up or reduced because of substance use
6. Continued substance use despite knowledge of having persistent or recurrent social, psychological, or physical problem that is caused or exacerbated by the use of the substance
7. Marked tolerance: need for markedly increased amounts of the substance (i.e., at least 50% increase) to achieve intoxication or desired effect or markedly diminished effect with continued use of the same amount
8. Characteristic withdrawal symptoms
9. Substance often taken to relieve or to avoid symptoms

*Adapted from *DSM III-R* 1987.³

keeping with the relative rarity of reports of abuse with clonidine abuse, the World Health Organization classified the drug as having very low abuse potential⁶ in 1989. Most medical and psychiatric textbooks do not mention the possibility of clonidine abuse.

Our case shows some of the pitfalls of making the diagnosis of clonidine abuse. Patients abusing one substance will frequently have a history of abuse of another substance; our patient denied any such history initially, and we found out about her past problems only through talking with family. A problem specific to clonidine is that physicians and the nurses who refill prescriptions by telephone do not often consider it an abuse-prone drug, which made it much easier for her to continue to get medications. Interestingly, on at least two occasions physicians had been concerned about drug-seeking behavior and had consciously restricted narcotics but not clonidine, and at least 2 pharmacists had noted the pattern of excessive use but did not intervene and notify the physicians. Adding to the diagnostic problem is

that our current health care system makes it relatively easy for a patient to have many physicians and to use many pharmacies, and none knows anything about the other. In this case discovery of the problem was greatly facilitated by her children's observations, as the patient lived with her children and needed to be driven to the pharmacies.

In addition to the difficulty of diagnosis, clonidine abuse can be particularly pernicious because of the substantial withdrawal syndrome associated with clonidine itself, which can dramatically reinforce the use of the drug. Our patient's total drug intake — at least 5 to 6 mg/d — was substantially greater than in the other cases reported in the literature. In routine therapeutic doses, acute withdrawal from clonidine can cause rebound hypertension, as well as nervousness, headache, abdominal pain, tachycardia, and sweating. Given the very large dose our patient was taking regularly, it was not surprising that she felt better when she got her clonidine!

Conclusion

Our case suggests that clonidine carries a definite risk of abuse. Given the large numbers of clonidine prescriptions physicians write, and the relatively small number of reported cases of abuse, the risk is probably relatively low, but physicians should be aware of its potential for abuse both with their own patients and for resale on the street.

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