Abuse of second-generation antipsychotics: What prescribers need to know

Gregory T. Bogart, PharmD, and Carol A. Ott, PharmD, BCPP

Mr. Z, age 27, seeks treatment for substance abuse at a mental health clinic. He has a 7-year substance use history and his last urine drug screen 1 month ago was positive for marijuana, opiates, and benzodiazepines. Mr. Z reveals that he purchases prescription drugs on the street, including hydrocodone, diazepam, and quetiapine. He states that when he takes a 100-mg dose of quetiapine, he feels happy, relaxed, and "drunk without the mind-numbing effects that you get with alcohol." Mr. Z often takes quetiapine while smoking marijuana. He sleeps well with this and does not experience a hangover effect.

Although clinicians always are vigilant about patients' misuse of psychoactive substances, recent case reports have described abuse of antipsychotics, particularly second-generation antipsychotics (SGAs). A PubMed and PsycINFO literature search revealed several case reports of quetiapine abuse (***Table, page 78***)[1-6] and 2 case reports of olanzapine misuse.

Quetiapine

Methods of quetiapine misuse include ingesting pills, inhaling crushed tablets, and injecting a solution of dissolved tablets.[1-7] In case studies, patients report abusing quetiapine for its sedative, anxiolytic, and calming effects.[1,2,4-7] One patient reported snorting crushed quetiapine tablets combined with cocaine for "hallucinogenic" effects.[3] Street names for quetiapine include "quell," "Susie-Q," and "baby heroin," and "Q-ball" refers to a combination of cocaine and quetiapine.[8] Quetiapine tablets have a street value of $3 to $8 for doses ranging from 25 mg to 100 mg.[9] Although outpatient misuse of quetiapine is common, abuse in correctional settings also is becoming more frequent.[10] Residents of jails and prisons misuse quetiapine for reasons similar to those cited by outpatients: sedation, relief of anxiety, and hallucinogenic effects or "getting high."[1,2,10] Clinicians must differentiate inmates who have legitimate psychiatric symptoms that require antipsychotic treatment from those who are malingering to obtain the drug. Efforts to treat inmates for substance use disorders may be thwarted by the easy availability of drugs in correctional settings.[10]

Practice Points

- Antipsychotics have been **abused and misused** by inpatients and outpatients.
- Most published **case reports of antipsychotic abuse involve quetiapine**, although some describe misuse of other agents, including olanzapine.
- **Serotonin, histamine, and α-adrenergic neurotransmitter systems** may play a role in second-generation antipsychotics' abuse potential.
- Although individuals have misused quetiapine and olanzapine, evidence indicates that **these drugs may be effective for treating substance use disorders.**

continued

Dr. Bogart is a Second-Year Psychiatric Pharmacy Resident and Dr. Ott is a Clinical Assistant Professor of Pharmacy Practice, Purdue University College of Pharmacy, Indianapolis, IN.

Vicki L. Ellingrod, PharmD, BCPP, FCCP
Series Editor

Table

Case reports of quetiapine abuse

Reference	Patient	Setting	Description of abuse
Hussain et al, 2005[1]	Woman, age 34, with history of polysubstance abuse, depression, and borderline personality traits	Prison	Crushed tablets dissolved in water and injected intravenously
Morin, 2007[2]	Woman, age 28, with history of schizoaffective disorder, polysubstance abuse, and personality disorder not otherwise specified	Hospital	Tablets crushed with aspirin and inhaled intranasally
Waters et al, 2007[3]	Man, age 33, with history of polysubstance abuse	Outpatient	Crushed tablets dissolved in water and injected intravenously
Reeves et al, 2007[4]	Man, age 49, with history of alcohol dependence and benzodiazepine abuse	Outpatient	Misuse without psychiatric symptoms or a diagnosed psychiatric disorder
	Man, age 23, with history of benzodiazepine dependence	Outpatient	Misuse without psychiatric symptoms or a diagnosed psychiatric disorder
	Man, age 39, with history of bipolar disorder	Outpatient	Oral use in doses more than the prescribed amount
Murphy et al, 2008[5]	Man, age 29, with unclear history of schizophrenia	Psychiatric walk-in clinic	Malingering psychiatric symptoms to obtain an oral dose and overnight stay
Fischer et al, 2009[6]	Man, age 53, with history of depressive symptoms	Court-mandated outpatient clinic	Malingering psychiatric symptoms to obtain higher oral doses

Clinical Point

Quetiapine's rapid dissociation from the dopamine receptor has been theorized to contribute to the drug's abuse potential

Other SGAs

The incidence of misuse of olanzapine and other SGAs is more difficult to ascertain. Only 2 case reports describe olanzapine abuse, both in outpatient settings. One describes a patient treated for depression with psychosis who was using increasingly higher doses of olanzapine to obtain euphoric effects.[11] Switching to aripiprazole effectively treated her illness and addressed her olanzapine misuse.

In the other case, a patient with bipolar disorder was able to obtain olanzapine, 40 mg/d, by complaining of worsened manic symptoms.[12] He described the experience of misusing olanzapine as getting a "buzz," feeling "very relaxed," and blunting the negative jitteriness he felt when he used cocaine.[12] This patient stated that he had observed others abusing olanzapine, both orally and intravenously.

Although the literature lacks reports on the risks of antipsychotic abuse, numerous Web sites purport to sell these drugs without a prescription and some describe the experience of illicit use of drugs such as haloperidol, risperidone, quetiapine, and olanzapine and ways to "enhance" the experience by combining drugs.[13] Reported experiences with risperidone tend to be negative, citing extrapyramidal side effects and feeling "numb," whereas olanzapine and quetiapine users describe feeling "drunk without the bad effects of alcohol" and "really happy, calm." These sites also describe hallucinogenic effects of these agents.[13]

Mechanism of action

The neuropharmacologic reasons for antipsychotics' abuse potential are difficult to quantify. Quetiapine and olanzapine have been used to treat cocaine and alcohol abuse, and work perhaps by decreasing the dopamine reward system response to substance use.[14,15] Quetiapine's rapid dissociation from the dopamine receptor has been theorized to contribute to the drug's abuse potential, possibly through relatively lower potency and decreased residence time

at the dopamine receptor.[14-16] This mechanism also contributes to quetiapine's lower risk of extrapyramidal side effects, which make the drug easier to tolerate.

Although dopamine is a factor in substance abuse and treatment of psychotic disorders, other neuropharmacologic mechanisms must be considered. SGAs are theorized to cause dopamine release in the frontal cortex through effects as 5-HT1A agonists and 5-HT2A antagonists.[16] Antagonism of α-adrenergic and histaminic receptors may account for these agents' anxiolytic and sedative properties.[8]

Misuse of anticholinergic agents has been reported for >50 years.[17] Psychiatric patients have been reported to increase use of anticholinergics for their movement side effects as well as hallucinogenic effects.[18]

Treatment

Regardless of the substance that patients abuse, the treatment goals are the same: to reduce use and achieve recovery. If a patient with psychosis is abusing an SGA, consider switching to an antipsychotic with less abuse potential. Another option is to limit the supply of the abused drug by prescribing smaller quantities or increase the frequency of follow-up visits to ensure compliant use.

References

1. Hussain MZ, Waheed W, Hussain S. Intravenous quetiapine abuse. Am J Psychiatry. 2005;162:1755-1756.
2. Morin AK. Possible intranasal quetiapine misuse. Am J Health Syst Pharm. 2007;64:723-725.
3. Waters BM, Joshi KG. Intravenous quetiapine-cocaine use ("Q-ball"). Am J Psychiatry. 2007;164:1.
4. Reeves RR, Brister JC. Additional evidence of the abuse potential of quetiapine. S Med J. 2007;100:834-836.
5. Murphy D, Bailey K, Stone M, et al. Addictive potential of quetiapine. Am J Psychiatry. 2008;165:7.
6. Fischer BA, Boggs DL. The role of antihistaminic effects in the misuse of quetiapine: a case report and review of the literature. Neurosci Biobehav Rev. 2009;34:555-558.
7. Pierre JM, Shnayder I, Wirshing DA, et al. Intranasal quetiapine abuse. Am J Psychiatry. 2004;161(9):1718.
8. Sansone RA, Sansone LA. Is seroquel developing an illicit reputation for misuse/abuse? Psychiatry (Edgemont). 2010;7(1):13-16.
9. Tarasoff G, Osti K. Black-market value of antipsychotics, antidepressants, and hypnotics in Las Vegas, Nevada. Am J Psychiatry. 2007;164:350.
10. Keltner NL, Vance DE. Biological perspectives: incarcerated care and quetiapine abuse. Perspect Psychiatr Care. 2008;44(3):202-206.
11. Lai CH. Olanzapine abuse was relieved after switching to aripiprazole in a patient with psychotic depression. Prog Neuropsychopharmacol Biol Psychiatry. 2010;34(7):1363-1364.
12. Reeves RR. Abuse of olanzapine by substance abusers. J Psychoactive Drugs. 2007;39(3):297-299.
13. The Vaults of Erowid. Available at: http://www.erowid.org/pharms/pharms.shtml. Accessed April 1, 2011.
14. Hanley NJ, Kenna GA. Quetiapine: treatment for substance abuse and drug of abuse. Am J Health Syst Pharm. 2008;65:611-618.
15. Tcheremissine OV. Is quetiapine a drug of abuse? Reexamining the issue of addiction. Expert Opin Drug Saf. 2008;7:739-748.
16. Kuroki T, Nagao N, Nakahara T. Neuropharmacology of second-generation antipsychotic drugs: a validity of the serotonin-dopamine hypothesis. Prog Brain Res. 2008;172:199-212.
17. Smith JM. Abuse of the antiparkinson drugs: a review of the literature. J Clin Psychiatry. 1980;41(10):351-354.
18. Land W, Pinsky D, Salzman C. Abuse and misuse of anticholinergic medications. Hosp Community Psychiatry. 1991;42:580-581.

Related Resources

- Substance Abuse and Mental Health Services Administration. www.samhsa.gov.
- Galanter M, Kelber HD. The American Psychiatric Publishing textbook of substance abuse treatment. Arlington, VA: American Psychiatric Publishing, Inc; 2008.

Drug Brand Names

Aripiprazole • Abilify
Diazepam • Valium
Haloperidol • Haldol
Hydrocodone/acetaminophen • Vicodin
Olanzapine • Zyprexa
Quetiapine • Seroquel
Risperidone • Risperdal

Disclosure

The authors report no financial relationships with any company whose products are mentioned in this article or with manufacturers of competing products.

Clinical Point

If a patient is abusing an SGA, consider switching to an antipsychotic with less abuse potential or limiting supply of the drug