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Quetiapine Misuse and Abuse: Is it an Atypical Paradigm of Drug Seeking Behavior?

Sean Kim,[1] Gayoung Lee,[2] Eric Kim,[3] Hyejin Jung,[4] and Jongwha Chang[5]

[1]Institute of Pharmaceutical Outcomes and Policy, University of Kentucky, Lexington, Kentucky, USA
[2]Wolfe Harry Feinstone Department of Molecular Microbiology and Immunology, Johns Hopkins University, Baltimore, USA
[3]Department of Biology, University of Alabama, Birmingham, Alabama, USA
[4]Department of Social Work, University of Texas, El Paso, Texas, USA
[5]Department of Pharmacy Practice, University of Texas, El Paso, Texas, USA
Address for correspondence: Prof. Jongwha Chang, E-mail: jchang@utep.edu

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Abstract

Recent case reports in medical literatures suggest that more and more second-generation atypical antipsychotics (AAs) have been prescribed for off-label use; quetiapine (Brand name: Seroquel®) showed increase in its trend for off-label use. Little is known about the reasons behind this trend, although historical sedative and hypnotic prescription patterns suggest that despite relatively superior safety profiles of quetiapine (especially for movement disorders), it may be used for treating substance abuse disorder. In addition, recent studies have shown a strong potential for misuse and abuse (MUA) of quetiapine beyond Food and Drug Administration-approved indications. This includes drug-seeking behaviors, such as feigning symptoms, motivated by quetiapine and use of quetiapine in conjunction with alcohol. Quetiapine appears to be the most documented AA with street values bartered illicitly on the street. A recent report from the Drug Abuse Warning Network has shown a high prevalence of quetiapine-related emergency department visits involving MUA. Several other case studies have found that quetiapine causes seeking behaviors observed in substance use disorder. In fact, the majority of quetiapine MUA involved patients diagnosed with substance use disorder. In the absence of a definitive mechanism of action of quetiapine's reinforcing properties, it is imperative to gather robust evidence to support or refute increasing off-label use of AAs.

Key Words: *Abuse*, *atypical antipsychotics*, *misuse*, *Quetiapine*

Introduction

Atypical antipsychotics (AAs), also known as second-generation antipsychotics, are a group of antipsychotic medications used to treat serious mental illness such as bipolar disorder, schizophrenia, and anxiety disorder.[1] Currently, there are 11 commonly prescribed AA medications approved by the Food and Drug Administration (FDA): aripiprazole, asenapine, clozapine, iloperidone, lurasidone, olanzapine, olanzapine/fluoxetine, paliperidone, quetiapine, risperidone, and ziprasidone.[1] Since the introduction of the first AA drug, clozapine, in the 1970s, the advent of AAs has provided new treatment options for patients with serious psychiatric conditions.[2,3,4] AAs are often considered safer than typical antipsychotics, they are associated with a decreased risk of neuroleptic malignant syndrome and extrapyramidal symptoms such as tardive dyskinesia (a movement disorder), tremor, and dystonia (muscle spasm and contractions).[1,5]

Recently, increasing off-label use of AAs outside FDA-approved indications has been evident.[1] In 2013, the Drug Utilization Sub-committee of Australian Department of Health showed evidence of antipsychotic use among people aged 20–59 for the treatment of conditions other than schizophrenia or bipolar disorder.[6] In the same year, the National Prescribing Service identified issues with off-label use of antipsychotics as means of behavior control in people with dementia in residential aged-care and other specialized-care facilities.[7]

A series of case reports of AA abuse was reported in literature more than a decade ago,[8,9] and several studies documented quetiapine as the most commonly abused AA.[10,11,12,13] Although off-label prescribing in psychiatry is a common practice, changing trends in AA off-label use and the associated risks need to be scrutinized due to a potential correlation between previous substance abuse history (i.e., schizophrenia or bipolar disorder) and likelihood of misusing and abusing AAs.[14,15] Use of AAs in patients with substance abuse has been noted where drug-seeking behaviors were observed in correctional facility settings.[10] Quetiapine abuse may be more prevalent among prisoners since commonly abused drugs are not readily available due to limited pharmaceutical formulary.[10]

Misuse and abuse (MUA) of pharmaceuticals is associated with medications that produce euphoria or other desirable effects such as relaxation or alertness.[16] Therefore, AAs are not generally considered drugs of abuse. However, AAs are being used to either enhance the effects of illicit substances such as cocaine and marijuana or counter their adverse effects.[17]

Quetiapine in the Treatment of Substance Abuse

AAs are commonly prescribed to aid in treating withdrawal symptoms from abused substances (i.e., alcohol, cocaine, benzodiazepines, or opioids) while increasing abstinence. However, this treatment showed inconsistent evidence with varying degrees of success.[18,19,20,21,22] Quetiapine decreased psychiatric symptoms such as sleeplessness and anxiety for alcoholic patients with comorbid conditions such as bipolar disorder or schizoaffective disorder when patients were provided with 300–800 mg/day for 16 weeks following detoxification treatment.[14] One possible speculation is that quetiapine alleviated mood symptoms and anxiety associated with withdrawal symptoms.

It is interesting to note that when patients do not have comorbid psychiatric conditions, AAs used to treat substance abuse did not show any significant benefit versus placebo.[1] One possible explanation is that high comorbidity rate is thought to originate from the common biological roots of schizophrenia and bipolar disorders. Dopamine sensitivity in schizophrenic patients was found to make them more susceptible to the rewarding effect of the substance.[14]

Quetiapine Off-Label Use

The use of AAs in clinical practice has extended beyond FDA-approved indications and off-label uses; there have been signs that corroborate the emergence of quetiapine as the most commonly abused AA.[23] These signs include existence of street names and values in the black market, diversion in prisons and other institutionalized settings, users seeking drug by feigning symptoms, and reports of intravenous or intranasal use of the drug.[16] Some street names include “Susie-Q,” “baby-heroin,” and “squirrel,” when used in conjunction with other drugs of abuse, combinations are referred to as Maq-ball (quetiapine + marijuana) or Q-ball (quetiapine + cocaine or heroin).[10,13,24,25] Numerous early reports and case studies focused on illicit use in incarcerated populations, which are at high risk of quetiapine MUA.[11,12,13] In most cases, MUA of AAs are shown to be associated with forensic settings such as incarceration, court-ordered hospitalization, or other oversight by the legal system. Numerous case reports and several systematic studies have shown that quetiapine MUA is not confined to penal populations; it also occurs in other settings such as psychiatric inpatients, outpatients, and patients attending drug treatment clinics.[14,25,26]

Although the magnitude of AA MUA is unclear, this emerging trend has gained recognition. Patients often misuse AAs in an attempt to self-medicate and ameliorate unpleasant symptoms of withdrawal. Substance abusers may take AAs to counteract the effects of the addicted agent. In addition, polydrug users who were prescribed numerous psychoactive drugs are associated with illegally obtaining quetiapine in combination with other drugs.[27,28,29]

Quetiapine Abuse and Adverse Health Outcomes

Quetiapine abuse is most frequently related to its sedative and anxiolytic characteristics.[10] It is proposed that the motivation for quetiapine MUA is "self-medication" for symptoms of anxiety and sleep withdrawal rather than euphoric effects.[14] Nationally representative data presented by a recent study of emergency department (ED) visits involving MUA of quetiapine further highlight this emerging trend. The Drug Abuse Warning Network (DAWN) has contributed evidence stating MUA of quetiapine is warranted.[16] The study found that high frequency of quetiapine-related ED visits involving MUA occurs among the noninstitutionalized general population, suggesting the need for evaluating potential MUA of quetiapine by patients.[16]

There is a growing concern within the medical community in regard to the potential harm from prescribing quetiapine for its off-label use as well as dependence potential. In addition, there have been a number of international high-profile court cases in the media regarding quetiapine-related death involving either drug-drug interactions or overdose.[6,30] Little is known about the reasons for off-label prescribing, but a historical perspective of sedative and hypnotic prescribing trends may explain this escalating use. The transition from barbiturates from early to mid-20th century (1920–1950s) to benzodiazepines in the 1960s were mainly due to safety concerns.[24,31] Benzodiazepines use became more prevalent, but there have been increasing safety concerns over benzodiazepines, in particular alprazolam.[32] It is interesting to note that patients whose symptoms with insomnia may be able to benefit from sedating characteristic of second-generation antipsychotics. More importantly, long-term use of both benzodiazepines and barbiturates has shown dependence with withdrawal symptoms, tolerance, and drug-seeking behavior despite a maladaptive pattern of substance abuse.[33] Quetiapine, on the other hand, poses very low dystonia and extrapyramidal side effects. Hence, it is predicted that this seemingly safer profile is what makes quetiapine a more attractive treatment option than other antipsychotics. However, some known side effects such as metabolic disturbances such as weight gain, diabetes, and dyslipidemia are prominent in second-generation AAs.[34,35] Clozapine and olanzapine carry significantly higher risk than other AAs, whereas aripiprazole, lurasidone, and ziprasidone are associated with the lowest risk of metabolic disturbances.[36,37,38,39,40,41]

Discussion: Public Health Implication

From a public health perspective, how does MUA of AAs pose a public health challenge? When AAs are used for recreational/self-medication purposes without medical supervision, there are negative health consequences as MUA poses health risks as well as ED visits.[16] According to Mattson *et al*., ED visits involving MUA of quetiapine accounted for 52% of visits due to any antipsychotics. In addition, the greatest contributor to ED visits was quetiapine where 62% of visits were due to second-generation AAs.[33] These findings suggest the need for heightened vigilance on potential MUA of quetiapine as well as other AAs. In addition to personal health risks, quetiapine MUA may pose negative public health implications. Providing AAs to malingering individuals in forensic settings affects mental health budgets as well as our available public health resources. Injudicious prescription of quetiapine is a rising problem as health-care providers need to have tighter regulations and clinical guidelines to follow. There is a need to consider quetiapine as a potential candidate to be classified as a scheduled controlled substance if there are robust research findings in the future.[27,42]

Tarasoff and Ostisuggest that there is evidence for quetiapine being commonly diverted from prescribed users for its cash street value.[29] Hence, clinicians need to be especially concerned about MUA when prescribing quetiapine to patients with comorbid mental health conditions for self-treating substance MUA as well as quetiapine's potential for abuse. Clinicians should be aware of the fact that patients who are looking out for quetiapine should pay close attention to potential substance abuse and dependence. This emerging public health problem merits continued surveillance and awareness on the part of prescribers and the public health community of the potential for misuse of AAs.[16]

Conclusion

Quetiapine MUA is increasing due to the fact that clinicians are prescribing fewer benzodiazepines,

barbiturates, and stimulant drugs because of their addictive characteristics.[14] Quetiapine has its unique motivation for anxiolytic and sedative effects without dependence. However, several case studies have found that quetiapine causes seeking behaviors observed in substance use disorder in the absence of definitive mechanism of action of quetiapine's reinforcing properties. Therefore, it is imperative to gather robust evidence to support or refute increasing off-label use of AAs as well as dependence.

Authors' Contribution

Sean Kim was responsible for idea and draft writing for the manuscript. Gayoung Lee was responsible for literature search as well as draft writing for the manuscript. Eric Kim was responsible for formatting and editing the overall manuscript. Hyejin Jung was responsible for writing public health implication section. Jongwha Chang was responsible for the overall supervision of the editing, manuscript writing, as well as all the support for literature search and providing resources.

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