Dual Diagnosis of Substance Abuse and Schizophrenia: Improving Compliance with Pharmacotherapy

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Abstract

Substance abuse affects approximately half of patients with schizophrenia and can act as a barrier to compliance with antipsychotic medication. Patients may use nicotine, alcohol, cannabis, cocaine or other drugs of abuse in order to overcome symptoms associated with schizophrenia itself or with the side effects of the antipsychotic medications used to treat the underlying illness. The impact of substance abuse for comorbid substance abusers compared with nonabusing schizophrenia patients includes a lower quality of life, increased tardive dyskinesia, increased psychosocial problems, more relationship difficulties, cognitive deficits and even suicide. Patients with a dual diagnosis also tend to have higher relapse rates, higher rates of hospitalization, and by inference, increased healthcare costs. Atypical antipsychotics are recommended for reducing substance abuse in schizophrenia patients and have been shown to be effective in this manner, though no antipsychotic is currently indicated specifically for treating substance abuse in patients with schizophrenia. However, despite the use of atypical antipsychotics in this population, noncompliance remains high and is often associated with rehospitalization or relapse. Long-acting injectable antipsychotic medications increase compliance rates; however, there are limitations to the use of conventional antipsychotic long-acting formulations in this population. Nonpharmacologic interventions such as substance-abuse management skills, training and motivational intervention are also important in reducing substance abuse and increasing compliance with antipsychotic medications. The combination of such nonpharmacologic interventions, along with a long-acting atypical antipsychotic, may be advantageous in treating dually diagnosed patients.

Key Words: Psychotropic, Schizophrenia, Substance Abuse, Dual Diagnosis

Introduction

Patients with psychiatric disorders are at higher risk for substance abuse. Indeed, results from a large United States (U.S.)-based study revealed that those with a psychiatric disorder had an odds ratio of 2.7 and a lifetime prevalence of around 29% for an addictive disorder (1). Furthermore, in patients with schizophrenia, this risk is even higher, with substance abuse affecting approximately 40 to 50% of individuals (Blanchard et al., 2000). In particular, patients with a dual diagnosis of schizophrenia and substance abuse have an increased likelihood of being noncompliant with their antipsychotic therapy, which can result in higher relapse rates, higher cost of medical care and increased distress for the patients as well as their families.

The most frequently misused substances among patients with schizophrenia are alcohol, nicotine, cannabis and psy-

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chostimulants, such as cocaine (2). The onset of substance abuse often occurs before or around the time of onset of schizophrenia. In a study in which 232 patients with first episodes of schizophrenia were interviewed, 62% reported that drug abuse began before the onset of schizophrenia symptoms, and 51% said the same of alcohol abuse. Within this population, 34.6% of drug abuse and 18.2% of alcohol abuse began within the same month as the onset of schizophrenia symptoms. In addition, patients with schizophrenia are twice as likely to have had a history of substance abuse at the time of the first episode of schizophrenia than are healthy subjects (3).

The clinically popular Self-Medication Hypothesis (SMH), which was formulated nearly two decades ago, has proposed that patients use substances in a nonrandom fashion to relieve or change a range of painful affect states (4, 5), including emotional distress (6), or positive or negative symptoms of schizophrenia (2, 4). However, although some studies have reported a consistent and modest support for the SMH for some patients, some substances and some symptoms, there is currently no consensus on the validity of the SMH (5). In fact, Buchanan et al. (1997) observed that patients with negative symptoms are actually less likely to become substance abusers (7). Unique psychosocial or demographic situations such as coexisting personality disorders, homelessness and lower levels of education or professional attainment can present more challenging life circumstances for some patients, which may also result in increased substance abuse (8).

Effective management of schizophrenia requires long-term therapy and is often compromised by poor rates of compliance. This compliance rate is further decreased in patients with schizophrenia who are comorbid substance abusers compared with nonabusers, resulting in this population being particularly at risk for relapse (9). This review investigates the impact of substance abuse on schizophrenia therapy and explores options available to improve compliance.

Methods

This article reviews the literature published between January 1992 and December 2006 that evaluates the impact of dual diagnosis on partial and noncompliance, as identified from literature searches using Medline and EMBASE. The primary search parameters were "partial compliance," "dual diagnosis," "schizophrenia" and "substance abuse." Results presented here are based on original data from published trials, meta-analyses and review papers. Data quality was determined by publication in the peer-reviewed literature and the most relevant information identified.

Results

Prevalence of Dual Diagnosis

The lifetime prevalence of substance abuse (excluding smoking) in patients with schizophrenia has been estimated to be approximately 35 to 55% (10-13). There appears to be little heterogeneity in terms of demographics, social factors, clinical characteristics or resource use between subgroups of patients with different types of substance abuse (14).

Patients with a dual diagnosis may be using one or more of a wide variety of substances. In a survey of patients with serious mental illness and comorbid substance abuse receiving treatment from community mental health teams in the United Kingdom (U.K.), 34% were abusing alcohol alone, 12% cannabis alone, 22% alcohol and cannabis and 25% stimulants (14). Similarly, another survey of patients with psychotic illness, also in the U.K., found that of 33% of patients with a dual diagnosis, 20% were abusing alcohol alone, 5% were abusing drugs alone and 8% were abusing both drugs and alcohol (13). In a large U.S.-based study, rates were found to be higher than those in the U.K.: among patients with a comorbid mental disorder, 37% had an alcohol disorder whereas 53.3% had a drug disorder other than alcohol (1).

Clinical Implications of Dual Diagnosis

Many patients with schizophrenia may abuse substances for "hedonistic" reasons, while others may use them in an attempt to reduce symptoms or distress. Alcohol, in particular, can tend to be used more often than illicit drugs, such as opioids or cannabis (5), though it has also been reported that patients may turn either to alcohol or illicit drugs to alleviate the negative symptoms inadequately treated, or potentially made worse by conventional antipsychotics and the side effect of dysphoria associated with these agents (2). However, although patients may believe that substance abuse ameliorates symptoms of schizophrenia, data suggest that many of these underlying symptoms may, in fact, be worsened (15, 16).

Not only are dual-diagnosis patients, including those who smoke, more likely to experience severe positive symptoms, but they also experience depressive symptoms compared with patients with either a single diagnosis of schizophrenia or a past dual diagnosis. For example, in a study of 447 inpatients with schizophrenia, the dual-diagnosis patients reported a higher frequency of positive symptoms, in particular, more intense hallucinations, and had a higher previous suicide attempt and delinquency rate compared with other schizophrenia patients (10). A cross-sectional survey of 207 outpatients at a continuing care facility also showed that patients with a dual-diagnosis experience more severe positive symptoms; patients with a current dual di-

agnosis had significantly worse Positive and Negative Syndrome Scale (PANSS) positive scores than patients with previous dual diagnosis or a single diagnosis. Furthermore, more patients with a current dual diagnosis were depressed (Hamilton Depression Rating Scale [HAM-D] score ≥12), compared with single-diagnosis patients (69% versus 46%, respectively) (17).

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In addition to experiencing these more severe symptoms, or potentially also as a result, psychosocial problems such as occupational, housing or financial difficulties and crime are endemic in the dual-diagnosis population. In a study of 1,843 patients receiving treatment in U.S. psychiatric practices (including 285 patients with substance-use disorders without schizophrenia; 180 patients with schizophrenia and no substance-use disorder; and 68 dually diagnosed patients), dual diagnosis was associated with a greater risk for four of the six Axis IV psychosocial problems studied compared with either diagnosis alone (18). In addition, use of psychostimulants has been shown to result in an increased frequency of violent episodes compared with schizophrenia patients who use other substances (or no substances) (14).

Patients with schizophrenia who abuse substances (including those who smoke) have been shown to exhibit an increased risk of suicide. Results from a prospective study that followed 980 schizophrenia patients at high risk of suicide for two years after randomization to clozapine or olanzapine demonstrated, via a multivariate analysis, that a history of substance abuse was a significant independent predictor of suicide risk (19).

As a result of the effects of substance abuse (increased severity of symptoms, increased psychosocial problems and higher risk of suicide), schizophrenia patients may have higher rates of relapse and a higher incidence of hospital admissions. For example, an analysis of 37 patients participating in a twelve-month, dosage-reduction study of fluphenazine showed that patients with a dual diagnosis not only had nearly twice the number of hospitalizations in the two years prior to study entry, but also had four times as many relapses during the year of the study, compared with patients with schizophrenia alone (11). Similarly, results from a retrospective study in patients with schizophrenia reported that dually diagnosed patients had a mean of 2.5 hospital readmissions over two years compared with a mean of 0.5 readmissions for singly diagnosed patients, and that patients who were active substance abusers had significantly higher rates of readmissions due to symptom recurrence, primarily positive symptoms including delusions and hallucinations (20). In another study, which examined the effect of medication compliance and substance abuse on four-year outcomes, noncompliant patients with a dual diagnosis accounted for 57% of all hospital readmissions and averaged 1.5 admissions per patient each year (21).

Missed appointments by patients with a dual diagnosis can also increase hospitalization, as suggested in a review of records from 262 schizophrenia outpatients at a mental health center (22). Interestingly, increases in hospital readmissions for dually diagnosed patients have been shown to correspond with a decrease in the duration of the stay after admission, compared with patients with schizophrenia alone (8). In contrast, a survey of 40 patients found that schizophrenic patients who misused alcohol and drugs were no more likely to have been admitted to a hospital in the previous two years than patients with a single diagnosis of schizophrenia, and the average time spent in the hospital was more than twice as long for patients with a dual diagnosis (13). Nevertheless, the majority of studies suggest that dual diagnosis is associated with an increased risk of hospitalization.

The increased risk of hospitalization and relapse in patients with substance abuse may further increase the financial burden associated with schizophrenia. A comparison of 3,069 patients with a dual diagnosis and 9,538 patients with a single diagnosis of a substance-use disorder reported that dual diagnosis was associated with a significantly increased total cost of care over six years, primarily due to increased utilization of outpatient psychiatric and substance-abuse services (23). Similarly, a one-year study evaluating utilization and cost of institutional (hospital and jail) and outpatient services demonstrated that dually diagnosed patients used institutional services at a significantly higher rate than singly diagnosed patients, or those with only a history of substance abuse (Bartels et al., 1993). In a much larger longitudinal study of 9,813 inpatients and 58,001 outpatients, dually diagnosed outpatients were found to consistently incur higher healthcare costs than psychiatric outpatients with a single diagnosis, probably due to increased need for inpatient and substance-abuse care (24).

To date, the majority of studies that have examined outcomes in patients with dual diagnosis have been based on correlational studies, and longitudinal research is now required to establish whether there are observed differences from childhood in schizophrenia patients who abuse substances versus patients who do not. However, results to date have demonstrated that there are a number of clinical implications of substance use in patients with schizophrenia, which contribute to an increased financial burden of these patients on society and these are reviewed here. These include experiencing more severe positive symptoms, a greater risk of psychosocial problems and an increased risk

of suicide, which can all lead to higher rates of relapse and hospitalization. However, although substance-use disorder in schizophrenia has been associated with a wide range of negative outcomes, it may also, in part, be maintained by the social and recreational functions it serves (25). Indeed, results from a study of 404 patients with schizophrenia spectrum disorders demonstrated that substance users generally had fewer negative symptoms, more social contacts and better social–leisure functioning, although they were more likely to have interpersonal or family problems, as well as a recent hospitalization (25). Likewise, results from a study of 46 dually diagnosed and 43 non-substance-abusing patients with schizophrenia demonstrated that patients with a dual diagnosis expressed higher levels of satisfaction with their quality of life compared with patients with a single diagnosis (26). These factors may present additional barriers to successful treatment of dually diagnosed patients and suggest that effective interventions for dual-diagnosis disorders may be required to address the social factors that maintain substance abuse (25).

Compliance with Therapy

As schizophrenia is a lifelong illness, it requires long-term, uninterrupted treatment to optimize outcomes. The low rate of therapy compliance already associated with schizophrenia can be further compromised when patients are also active substance abusers. Intoxication may impair judgment, reduce motivation to pursue long-term goals and lead to a devaluation of the protection offered by antipsychotic medications, resulting in increased hospital readmissions and significantly more severe symptoms (21, 27).

In general, outpatients with schizophrenia who form strong alliances with their therapists seem to be more likely to comply with prescribed medications than patients who form weaker alliances (29). This is also the case amongst those with substance abuse. Indeed, results from a six-month, longitudinal study demonstrated that subjects who abused substances had no outpatient contact and were noncompliant with medication (28). Furthermore, Brief Psychiatric Rating Scale scores for patients with schizophrenia, who were noncompliant with their medication, were increased by approximately 30% for substance abusers in contrast with nonabusers (9). A cross-sectional survey of 207 schizophrenia outpatients also showed that 27.6% of patients with a dual diagnosis were noncompliant, compared with 4.5% of patients with a single diagnosis of schizophrenia (17). Similarly, a study of patients discharged after inpatient treatment for schizophrenia reported that those patients who were noncompliant with antipsychotic medication three months after discharge (19.2%) were more likely to have a history of substance abuse or dependence in the previous six months (28).

As expected, there is also a clear trend for dually diagnosed patients, especially those who are noncompliant, being readmitted to hospitals more frequently. Results from a prospective study demonstrated that patients with a single diagnosis of schizophrenia, who were compliant with their medication, had a median time to hospital readmission of 37 months, compared with ten months for those who had a single diagnosis and were noncompliant. For patients with a dual diagnosis, the median time to readmission was ten months in patients who were compliant with their medications, compared with five months for those who were noncompliant. Over the four-year period, noncompliant patients with a dual diagnosis accounted for 57% of all hospital readmissions (21).

Not only are dual-diagnosis patients, including those who smoke, more likely to experience severe positive symptoms, but they also experience depressive symptoms compared with patients with either a single diagnosis of schizophrenia or a past dual diagnosis.

The medications used to treat schizophrenia are associated with a number of side effects that can also result in partial or noncompliance, regardless of comorbid substance abuse. In particular, conventional antipsychotics are associated with side effects that compromise tolerability. For example, extrapyramidal side effects (EPS), including akathisia, dystonia and parkinsonism, are frequently encountered (29) and have been associated with high rates of noncompliance (30); tardive dyskinesia is also common (29). Although atypical antipsychotics are less likely to cause EPS than high-potency conventional agents (29), their advantage over low-potency conventional antipsychotics in terms of EPS is less clear, since the latter have not been the mainstay of treatment in most industrialized countries, and some of these agents such as perazine have been insufficiently examined in randomized studies (31). In addition, metabolic side effects in patients treated with atypical antipsychotic agents is increasingly receiving more attention in the literature, with recent evidence suggesting that some atypical antipsychotics may increase risk factors for diabetes and cardiovascular disease, including weight gain and adverse effects on glucose and lipid metabolism (32-34). Of these, weight gain is the side effect most likely to interfere with compliance with atypical antipsychotics. According to the American Diabetic Association/American Psychiatric Association (ADA/APA) consensus study, clozapine and olanzapine are associated with a particularly high risk of weight gain, although there is also an increased risk in patients receiving risperidone, or

quetiapine, albeit to a lesser degree. In contrast, the atypical antipsychotics ziprasidone and aripiprazole are associated with a relatively low risk of weight gain (35).

In addition to these general barriers to compliance, patients with a dual diagnosis face further obstacles. Results from a retrospective analysis of 1,027 patients with schizophrenia reported that a history of substance abuse was strongly correlated to a diagnosis of tardive dyskinesia in patients receiving conventional antipsychotics (36), which again may increase the risk of noncompliance. Likewise, a study of 284 psychiatric patients with chronic substance abuse found that 16% of patients had tardive dyskinesia, with higher rates occurring among users of alcohol alone (25.4%) or in combination with cannabis (26.7%) (37). The strong association between alcohol abuse and tardive dyskinesias has also been demonstrated in other studies (38), and it has been suggested that alcohol may be used by patients with akathisia to alleviate agitation and dysphoria (39).

Although it might be expected that substance abuse could impair cognitive function in patients with schizophrenia, there is a substantial body of evidence to suggest that cognitive function is as good in patients with a dual diagnosis as it is in those with a single diagnosis of schizophrenia (26, 40-42). This observation may reflect higher socioeconomic status and cognitive function prior to disease onset (43). However, there is some evidence to suggest that cocaine users have impaired ability to learn and recall verbal information, compared with patients with a single diagnosis of either schizophrenia or cocaine use (44), which, therefore, may be expected to increase the risk of noncompliance.

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It has been shown that patients' insights and attitudes to schizophrenia (especially their belief that medication is helpful, stated willingness to take medications and a generally optimistic outlook) are also associated with levels of compliance (45). A study of patients with schizophrenia revealed that when analyzing both singly diagnosed and dually diagnosed patients, there was no difference between the level of insight and compliance with antipsychotic medication. However, when substance abusers were removed from the analysis, insight was found to be related to compliance, suggesting that substance abuse prevents patients from complying with their medication whatever their level of insight (46). Therefore, the likelihood of insight leading to high levels of compliance with therapy may be reduced by concomitant substance abuse (47).

In summary, comorbid substance abuse is associated with poor compliance with treatment regimens in patients with schizophrenia. The most common treatment-related issue that may affect compliance is primarily related to the tolerability of an antipsychotic agent. A strong therapeutic alliance also appears to be an accurate predictor of compliance. However, current research suggests that the relationship between insight and cognition and compliance in schizophrenia patients who are substance abusers may not be straightforward.

Improving Compliance

Strategies to improve compliance should address both patient behavior and the selection and optimization of medication. Behavioral interventions may help to improve compliance by addressing patient-related factors and by optimizing the choice of medication. Use of pharmacologic methods that simplify medication use, such as long-acting agents, can also improve compliance, although further research is required to substantiate this (48).

There is a substantial body of evidence that psychosocial interventions such as social skills training, cognitive therapy, vocational rehabilitation and family psychoeducational interventions, combined with medication, are associated with significant improvements in symptom control, self-esteem, satisfaction with life and treatment compliance and a reduction in the risk of relapse compared with medication alone (49-55). In particular, a novel treatment for persons who have both schizophrenia and substance abuse was evaluated by incorporating cognitive-behavioral drug relapse prevention strategies into a skills training method originally developed to teach social and independent living skills to patients with schizophrenia. Results demonstrated that participants learned substance-abuse management skills, and that their drug use decreased. Improvements were also noted in medication adherence, psychiatric symptoms and quality of life (56). Motivational interviewing can also be used to improve attendance rates for therapy. Indeed, a study of 121 psychiatric inpatients, 77% of whom had a dual diagnosis, showed that attendance at the first outpatient appointment was significantly higher, but still quite low, among patients who received motivational interviewing, compared with standard treatment alone (21% in the total group and 16% in the dual-diagnosis group) (57). In addition, results from a comprehensive review of 36 studies on the effectiveness of integrated treatment for dually diagnosed patients demonstrated that certain methods of delivering care, such as case management and assertive community treatment, provided encouraging evidence of the program's potential to engage dually diagnosed patients in services and to help them reduce substance abuse and attain remission (58).

Most treatment guidelines and expert consensus reports favor the use of atypical antipsychotic drugs as the first-line approach to the pharmacologic management of schizophrenia (59-62). Recent guidelines also support the first-line use of atypical antipsychotic drugs in patients with a dual diagnosis (63). However, it is important to note that these guidelines were not based on controlled research, did not take into account the newly acquired information regarding the diabetogenic potential of some currently available atypical agents and preceded the results of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study. Results from the CATIE trial demonstrated that 74% of 1,493 patients with schizophrenia discontinued treatment with one of four atypical oral antipsychotics or the conventional oral antipsychotic perphenazine over an eighteen-month period (64), suggesting that suboptimal efficacy and tolerability remains a challenge with atypical antipsychotic agents.

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Clozapine is the most widely studied atypical antipsychotic in patients with a dual diagnosis. Clozapine has been shown to increase both abstinence from alcohol and the likelihood of remission from alcohol abuse for at least six months, although it should be noted that these results are based solely on correlational data. In a post hoc analysis, alcohol-abusing patients with schizophrenia or schizoaffective disorder who received clozapine consumed alcohol an average of 12.5 days over a six-month period versus 54.1 days for patients not receiving clozapine therapy (65). Similarly, results from a retrospective survey of dual-diagnosis patients demonstrated that 85% of patients receiving clozapine reduced their substance use compared with levels at the time of treatment initiation. For patients who had continued using clozapine, the reduction in substance abuse was highly correlated with improvements in global clinical symptoms (66). With cocaine-abuse patients, however, precaution should be employed when administering clozapine. In a small study examining the effect of clozapine on cocaine abuse, clozapine pretreatment diminished the effect of cocaine, based on subjective responses, in a dose-dependent manner. However, despite the reduced effect, peak serum levels of cocaine were significantly increased, leading to a near-syncopal episode in one subject (67).

Other atypical agents may also be associated with improvements in substance abuse in patients with a dual diagnosis. A small observational study showed that patients receiving atypical antipsychotics were less likely to abuse substances, primarily alcohol, than patients receiving conventional agents (68). A six-week, open-label pilot study demonstrated that risperidone is associated with significant reductions in craving and relapse in patients with cocaine dependency, and that these patients had greatly reduced negative and global symptoms (69). Finally, a small, prospective, open-label, twelve-month study evaluating the efficacy of olanzapine showed that this agent improved substance-abuse remission in 30% of patients (70).

In general, the atypical antipsychotic agents have been associated with higher rates of compliance than conventional agents. For example, an analysis of medical and pharmacy claims data reported compliance rates of 87% for ziprasidone, 78% for risperidone and 80% for olanzapine over a twelve-month period (71). In addition, an analysis of outcomes in 1,996 patients with schizophrenia enrolled in two clinical trials showed that the atypical antipsychotic olanzapine was superior to the conventional agent haloperidol in terms of rates of study discontinuation, relapse and noncompliance, while there were no differences between olanzapine and risperidone (72). The association between improved compliance and the use of atypical agents may be due, at least in part, to their improved side-effect profiles, as atypical antipsychotics have been associated with a lower risk of EPS and tardive dyskinesia than conventional agents.

The use of long-acting injectable agents may help to improve compliance in patients with a dual diagnosis. Such agents are considered more convenient than oral treatments due to the decreasing responsibility of patients to take their medication and allowing the differentiation of partial compliance from lack of efficacy of the agent (48). In addition, these agents allow for more effective monitoring of compliance since patients must see their clinician for treatment. In the event that a treatment appointment is missed, the clinical team will know immediately and can initiate contact with the patient before symptoms recur. Regular contact with a clinician can also provide the opportunity for greater psychosocial support, such as psychoeducation or social skills training (73). Although long-acting agents are unable to prevent relapse completely, with a systematic meta-review demonstrating that some 20 to 25% of patients relapse despite receiving long-acting agents, results from a meta-analysis of six double-blind studies in 520 outpatients reported relapse rates to be significantly reduced among patients treated with long-acting conventional agents (30.0%) versus oral conventional agents (47.1%) (74). In addition, results from a prospective cohort study of 2,230 consecutive adults with schizophrenia or schizoaffective disorder reported that the use of long-acting perphenazine was associated with a substantially lower risk of rehospitalization or discontinuation (for any reason) of therapy than the majority of the ten most commonly used oral antipsychotic agents (75). A number of other conventional antipsychotics (such as flu-

phenazine and haloperidol) can also be delivered as depot injections and have been shown to be associated with high rates of compliance (96% of patients attended scheduled appointments) (76). Nonetheless, conventional antipsychotics delivered via this route are associated with a higher risk of EPS and tardive dyskinesia than atypical antipsychotics and the lack of a long-acting atypical injectable agent has presented an obstacle toward improving compliance in schizophrenia.

The development of a long-acting injection formulation of the atypical agent, risperidone, provides a new option for the treatment of schizophrenia (77). This long-acting formulation is based on the use of risperidone microspheres, in which the drug is encapsulated in a biodegradable polymer matrix of glycolic acid–lactate, rendering it suitable for intramuscular injection. The aqueous nature of long-acting risperidone results in reduced pain, induration and inflammation at the site of injection in comparison with the conventional injectable antipsychotics, which are suspended in an oil-based solution for injection (78). Long-acting risperidone has been shown to be effective and well tolerated in a number of large-scale clinical trials of patients with schizophrenia (79-82). Patients can also be switched effectively to long-acting risperidone from other oral and long-acting antipsychotic agents when appropriate strategies are used. Furthermore, significant improvements have been reported in patients considered clinically stable on other antipsychotic agents who were switched to long-acting risperidone (83-86). In addition, it has been suggested that long-acting risperidone can reduce rates of relapse, as it has been shown to reduce incidences of hospitalization (87). Overall, results from pivotal trials have reported continuation rates with long-acting risperidone of 51 to 92% (81, 82, 88-92). Furthermore, across the pivotal studies, withdrawals due to insufficient response (1.2–22%), adverse events (1–15%) and lack of compliance (1.3–3%) with long-acting risperidone were low.

Patients with schizophrenia who are believed to be partially compliant, therefore, may be considered appropriate for treatment with long-acting injectable agents to promote compliance and, consequently, improve long-term outcomes (93). Indeed, results from a recent randomized, controlled, open, six-month, follow-up study in 115 subjects with schizophrenia and substance-use disorders demonstrated that long-acting risperidone is more effective than zuclopenthixol-depot in improving substance abuse and schizophrenia symptoms in subjects with dual diagnosis. In this study, long-acting risperidone patients presented fewer positive urine tests (8.67 compared with 10.36, p=0.005). There were significant differences in the Negative and General Psychopathology PANSS subscales at the end of the study, with the percentage of subjects with a PANSS score 20% lower than at baseline higher in the long-acting risperidone-treated group (89% compared with 50%, p<0.0001). Patients treated with long-acting risperidone also attended a significantly larger number of Substance Abuse Management program sessions than those of the zuclopenthixol-depot group. Overall, 92.9% of those in the long-acting risperidone group were classified as good compliers (94).

Thus, cognitive-behavioral interventions, as well as long-acting atypical antipsychotic treatment, should be considered as an approach to improving compliance in patients with a dual diagnosis.

Thus, cognitive–behavioral interventions, as well as long-acting atypical antipsychotic treatment, should be considered as an approach to improving compliance in patients with a dual diagnosis. The recent development of The Substance Use Event Survey for Severe Mental Illness (SUESS) has the potential to provide valuable information regarding dual-diagnosis patients. The SUESS assesses clinical issues, appears to be understood and accepted by dual-diagnosis patients and has demonstrated encouraging preliminary reliability and validity (95). This new clinical measure could be used to monitor the treatment and status of dual-diagnosis patients, providing insight into medication compliance and, thereby, advancing long-term prognoses.

Conclusions

Successful management of schizophrenia requires long-term medication compliance, which is frequently difficult to achieve, especially in those with schizophrenia who are also abusing substances. As discussed, this is a sizable proportion of patients with schizophrenia, with estimates ranging from 40 to 50%. Long-acting injectable antipsychotics, especially atypicals, offer advantages in compliance that should be considered in this population.

Conventional antipsychotics are associated with side effects that can complicate the management of patients with a dual diagnosis and present additional barriers to compliance, although injectable formulations of these agents can increase compliance rates. Atypical antipsychotics, in contrast, are associated with an improved side-effect profile and have been shown to improve compliance compared with conventional agents. By combining the advantages of an atypical antipsychotic with a long-acting injectable formulation, use of an agent such as long-acting risperidone might be particularly advantageous in patients at high risk of noncompliance or partial compliance, including those with a dual diagnosis of schizophrenia and substance abuse.

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