Substance misuse in patients with schizophrenia: a primary care guide

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ABSTRACT

- Smoking presents a substantial health and economic burden to people with schizophrenia.
- Comorbid use of other substances is common, under-recognised, and associated with a number of serious adverse consequences, such as psychotic relapse and poorer social outcomes.
- All patients with schizophrenia need to be screened for substance misuse.
- Effective interventions involve integrated, modified pharmacological and psychosocial strategies.

MJA 2003; 178: S71–S75

THE VAST MAJORITY of people with schizophrenia misuse substances, but this comorbidity is frequently under-recognised and poorly addressed. Between 60% and 90% of people with schizophrenia smoke cigarettes,[1] which has a substantial impact on the morbidity and mortality of this population.[2] In addition, between 40% and 60% misuse other substances,[3] related in part to the general increase in availability and accessibility of drugs, and the change from institutional care of the severely mentally ill to their management in the community, often in locations with high drug availability.[4] In Australia, the most frequently misused psychoactive substances are alcohol, cannabis and amphetamine,[5] and less commonly opioids, hallucinogens, inhalants (eg, petrol, glue and paint) and anticholinergics.

People with schizophrenia and concurrent psychoactive substance misuse present unique challenges to those involved in their care, but often the disjunction between psychiatric services and specialist drug and alcohol services results in these patients being rejected or shuttled between services. This failure of cooperation and coordination between specialist services lays a greater responsibility for the care of these patients onto GPs, despite the fact that many feel under-resourced and inadequately trained to meet the complex needs of people with schizophrenia.

GPs may play a variety of roles in managing this comorbid group. They may be the sole clinician, or provide shared care with mental health or addiction services. This may involve monitoring the physical wellbeing of patients in psychiatric services, or the mental health needs of patients linked only with drug and alcohol services. Both these roles require close collaboration and communication between all treatment providers. For patients with complex needs or severe symptoms, it is important to seek specialist advice early. However, cigarette smoking is rarely addressed in either setting for this population, and the GP is in a key position to motivate patients for change.

Diagnostic issues

Understanding the basis of psychotic symptoms in the substance-using individual often presents the clinician with a difficult diagnostic challenge. Of most value is the temporal association between using psychoactive substances and the onset and resolution of psychotic symptoms. Guidelines exist to help differentiate between a primary psychotic disorder and a substance-induced disorder (Box 1). However, in cases of chronic and unremitting substance misuse, with gradual onset of psychotic symptoms and marked functional decline, diagnosis may be extremely difficult. In such situations, treatment should be initiated regardless, with the diagnosis deferred until a perspective over time can be gained.

Reasons for substance misuse

A number of hypotheses exist on the relationship between substance misuse and established schizophrenia, and reasons why such psychotic patients may use substances. One hypothesis is that both the choice and use of substances is a method of "self-medication", to treat adverse states induced by either the schizophrenia or its treatment.[8] These may include primary positive symptoms (eg, hallucinations and delusions) and primary negative symptoms (eg, amotivation, anhedonia) of schizophrenia, negative symptoms secondary to neuroleptic treatment, depressive mood states, and neuroleptic-induced extrapyramidal movement disorders. (For definitions of "positive" and "negative" symptoms, see Lambert and Castle, *page S57*[9].) Despite the intrinsic appeal of this hypothesis, there is conflicting evidence, and it seems that factors associated with substance use in people with schizophrenia are similar to those in the general community (ie, availability, cost, peer-group use and acceptance, facilitation of social interaction, intoxication and relaxation).[4,10] Nevertheless, exploring individual reasons for substance misuse may uncover symptoms that are readily alleviated by pharmacological strategies, such as

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optimising antipsychotic treatment or initiating antidepressant medication.

Alternative hypotheses for the high rates of comorbidity include the possibility of a common underlying neurobiological vulnerability toward both disorders, or traits (eg, antisocial personality) that increase the likelihood of comorbid disorders independently.[8]

Consequences of use

People with schizophrenia have a mortality rate three times higher than people in the general population, with most of this excess attributable to cigarette smoking.[2] Typically, these patients are heavily nicotine dependent and inhale more deeply.[11] Smoking also places a heavy financial burden on individuals, who spend a sizeable proportion of their income on cigarettes.[11] Importantly, the majority of patients admit smoking is a problem, and about half want to quit.[11] However, although effective treatments exist,[1,12] the prevailing view of most clinicians is that treatment of this group is futile, and interventions are not routinely offered to this population.[11]

Misuse of other substances has a significant impact on both the course of illness and the outcome of treatment (Box 2), and patients do poorly in standard treatment settings.[14] On a positive note, comorbid patients may have a better prognosis than non-using patients if they cease using,[8] owing to their generally higher level of premorbid functioning. Further, even limited, brief interventions have been shown to improve outcomes for previously refractory patients.[14]

Management

The key principles of assessment and treatment are summarised in Box 3. Developing a collaborative therapeutic alliance is essential for a successful outcome, and requires the clinician to adopt an empathic, non-judgemental approach. This may be especially difficult when working with patients with schizophrenia given their poor interpersonal skills, and the engagement phase may be protracted. Screening for substance misuse is an important first step, although patients with schizophrenia often deny and minimise their substance use.[13,14] It is therefore useful to monitor progress using urine testing and/or breath analysis for alcohol. These patients are often unusually sensitive to the effects of psychoactive substances, experiencing adverse effects with dosages that produce no difficulties in people without schizophrenia.[14,15]

"Dual diagnosed" patients (ie, those with combined diagnoses of schizophrenia and substance misuse) commonly evoke powerful, unpleasant feelings in health professionals.[16] Clinicians may feel unskilled to handle, and overwhelmed by, the multitude of presenting problems, and unclear which issue to tackle first. Moreover, practitioners are often pessimistic regarding outcomes and believe that intensive time and effort will produce minimal gains. Hence, it is not uncommon for the clinician to want to avoid involvement with these patients. However, appropriate interventions have been shown to be beneficial,[14] and clinicians should remain optimistic with realistic expectations.

For comorbid patients, the most appropriate management combines effective pharmacological treatment of the psychotic illness with modified psychosocial strategies to reduce substance misuse.[14] As improved medication compliance increases the effectiveness of psychosocial interventions,[14] the initial goal is to effectively treat patients' psychotic symptoms and ensure minimal side effects. Ideally, the mental state of patients with established substance dependence should be relatively stable before attempting detoxification in a community setting. Chaotic patients with frank

1: Guidelines to assist in differentiating between a primary psychotic and a substance-induced disorder

Substance-induced psychotic symptoms can result from intoxication, chronic use or withdrawal:[6]

- Intoxication with cannabis can induce a transient, self-limiting psychotic disorder characterised by hallucinations and agitation;
- Prolonged heavy use of psychostimulants (eg, amphetamine, methylenedioxymethamphetamine [MDMA]) can produce a psychotic picture similar to schizophrenia;
- Hallucinogen-induced psychosis is usually transient, but may persist if use is sustained;
- Heavy alcohol use has been associated with alcoholic hallucinosis and morbid jealousy;
- Psychotic symptoms can also occur during withdrawal (eg, delirium tremens) and delirious states.

*A non-substance-induced psychotic disorder should be considered when:**

- Psychosis precedes the onset of substance use;
- Psychosis persists for longer than one month after acute withdrawal or severe intoxication;
- Psychotic symptoms are not consistent with the substance used;
- There is a history of psychotic symptoms during periods (> one month) of abstinence;
- There is a personal or family history of a non-substance-induced psychotic disorder.

*Adapted from Woody et al[7]

2: Possible consequences of psychoactive substance misuse in patients with schizophrenia[4,13]

- Increased psychotic symptoms;
- Reduced treatment compliance;
- High relapse rates;
- Frequent use of healthcare services and increased rates of hospitalisation;
- Increased rates of tardive dyskinesia;
- HIV infection;
- Early mortality;
- Suicide;
- Housing instability and homelessness;
- Violent behaviour;
- Criminal behaviour and incarceration;
- Increased family conflict;
- Increased healthcare costs.

psychosis, intractable substance misuse and non-compliance are difficult to manage in the community, and require referral to mental health services for inpatient detoxification and stabilisation of their psychotic illness. Standard community-based detoxification units can be used with more stable patients, but patients may still relapse in the sometimes confrontational environment of these units. Thus, these patients require a tailored detoxification regimen incorporating slower withdrawal and close monitoring of their mental state.

The newer atypical antipsychotics (eg, olanzapine, risperidone, quetiapine, amisulpride)[9] are recommended first-line agents for this population in view of their efficacy, tolerability and reduced risk of extrapyramidal symptoms. There are, however, associated side effects, such as postural hypotension, sedation, and corrected QT (QTc) prolongation, which may be more problematic in a substance-using population. Although there are limited published data on the effect of clozapine in dual-diagnosed patients, it has been reported to reduce substance misuse in psychotic patients when switched from typical antipsychotics.[15] In addition, compared with typical antipsychotics, clozapine and other atypical agents enhance smoking cessation rates when used in combination with nicotine-replacement therapy.[1] Patients who are non-compliant or chaotic may benefit from a switch to the longer-acting depot antipsychotics. Daily pick-up of antipsychotics from a local pharmacy, especially if combined with appropriate substance-misuse medications, may also be a useful approach.

There is little published research on the use of medications to treat substance misuse in schizophrenia, but most appear to be safe and effective in combination with antipsychotics.[15] Naltrexone and acamprosate, both effective treatments for alcohol dependence, may also be useful in the comorbid patient. However, disulfiram at high doses (1000 mg) has been associated with psychotic symptoms in people without schizophrenia,[15] and should be used with caution in dual-diagnosed patients. Nicotine replacement therapies and bupropion have both been successfully and safely used in patients with schizophrenia.[1,11,12,17] Although bupropion is contraindicated in patients with a history of seizures or mania, it has rarely been reported to exacerbate psychotic symptoms in schizophrenia.[17]

Medications with misuse potential (eg, benzodiazepines, anticholinergics) should be prescribed only for brief periods. There should be a clear indication for their use (eg, alcohol withdrawal), and their continued prescription should be frequently reassessed. Comorbid patients stabilised on methadone should have their dose reduced gradually, as rapid withdrawal may precipitate a psychotic relapse in some individuals. Although acute nicotine withdrawal has not been clearly linked to an increase in psychotic symptoms, tapered nicotine replacement therapy is better tolerated.[11]

Smoking induces hepatic metabolism of psychotropic drugs through the cytochrome P450 system. Thus, increased antipsychotic dosages are often required to control psychotic symptoms in patients who smoke.[17] In view of this, patients should be monitored closely for the emergence of dose-dependent side effects or toxicity

3: Principles of management of patients with schizophrenia and comorbid substance misuse

Assessment

- Screen all patients with psychosis for substance misuse and other psychiatric disorders (eg, social phobia);
- Determine severity of use and associated risk-taking behaviours (eg, injecting practices, "unsafe sex");
- Exclude organic illness or physical complications of substance misuse;
- Seek collateral history — families or close supports should be involved where possible.

Treatment

- First engage patient, adopting a non-judgemental attitude;
- Educate patient:
  - ➤ Give general advice about harmful effects of substance misuse;
  - ➤ Advise about safe and responsible levels of substance use (eg, National Health and Medical Research Council guidelines for safe alcohol use);
  - ➤ Make individual links between substance misuse and patient's problems (eg, cannabis use and worsening paranoia);
  - ➤ Inform patient about safer practices (eg, using clean needles, not injecting alone, practising "safe sex");
- Treat psychotic illness and monitor patient for potential side effects;
- Help patient establish advantages and disadvantages of current use, and motivate patient for change (see Box 5);
- Evaluate need for concurrent substance-use medications (eg, methadone, acamprosate, nicotine-replacement therapy);
- Refer patient to relevant clinical and community services, as appropriate;
- Devise relapse prevention strategies that address both psychosis and substance misuse;
- Identify triggers for relapse (eg, meeting other drug users, being paid, family conflict) and explore alternative coping strategies (see Box 4).

4: Selected psychosocial interventions for addiction, specially modified for patients with schizophrenia

- Explore reasons for substance misuse, including relationship to psychiatric symptoms, antipsychotic treatment and feelings of social isolation;
- Address patient's motives and degree of commitment towards treatment of both their psychotic illness and their substance misuse;
- Adopt concrete problem-solving approach with patient, where appropriate;
- Set tasks that are simple and readily achievable (eg, keeping a diary of substance use or psychotic symptoms; regularly taking medication; keeping appointments);
- Focus on specific skills to deal with high-risk situations, and consider use of role play (eg, learning how to say "no" to a dealer or drug-using friends);
- Suggest alternatives to substance use for coping with stressful situations (eg, exercise, contacting a support person);
- Treat comorbid anxiety with behavioural techniques (eg, breathing exercises, progressive muscular relaxation);
- Remain supportive and emphasise any gains made;
- Recommend group support (eg, refer patient to SANE SmokeFree program (<http://www.sane.org/ourworksmoking.html>);
- Encourage participation in alternative activities and contact with non-substance-using peer group (discuss available resources with local community health centre or mental health service);
- Adopt a long-term perspective, with ongoing intervention.

5: Motivational enhancement techniques

Motivational interviewing[18] is a useful therapeutic approach, based on a model conceptualising stages through which behavioural change occurs. It emphasises the role of both ambivalence and relapse within the process of change.[19] Thus, it is normal for patients to cycle several times through the various stages before making long-lasting changes.

This therapeutic approach aims to match appropriate treatment options with the patient's motivational level, based on the patient's current stage within the cycle (see below).

Stage	Intervention
Precontemplation	Educate patient about substance misuse and allow patient to examine problems with current behaviour
Contemplation	Explore pros and cons of change; acknowledge patient's ambivalence and resistance to change
Preparation	Help patient to determine most appropriate strategies for change
Action	Assist patient to instigate planned changes
Maintenance	Encourage new skills and rehearse relapse-prevention strategies
Relapse	Support patient and assist in renewing process of change

following prolonged periods of cigarette reduction or abstinence.

Psychosocial interventions for addiction need to be modified for people with schizophrenia (Box 4) in view of the cognitive deficits and poor self-belief of these patients.[15] Techniques to enhance motivation remain an important component of treatment.[15] Enhancing motivation reduces substance use and can be applied by the GP as a brief, ongoing intervention (Box 5). Relapse prevention,[20] based on a cognitive behavioural approach, helps patients to identify triggers to relapse, both to psychosis and substance misuse (eg, social stressors), and to develop alternative strategies when confronted with high-risk situations. "Lapses" should be expected and seen as opportunities to modify and develop patient coping strategies rather than viewed as failures. At these times, patients often feel demoralised, and it is important to remind them of their previous successes in treatment.

Twelve-step peer-support groups (eg, Alcoholics Anonymous or Narcotics Anonymous) and smoking-cessation groups, which are invaluable in traditional addiction settings, are often not appropriate for patients with psychosis, who may feel stigmatised and misunderstood. In response, programs in the United States have been modified to support this population,[14] but few such programs exist in Australia. There are, however, publicly available smoking-cessation programs, such as Quitline, which offer specialised packages incorporating telephone advice and supporting materials for people with mental illness. In addition, smoking-reduction management guidelines for GPs, and associated resources, are available from the SANE Australia website (www.sane.org).

Families can play an important role in supporting and monitoring treatment, and should be included in the management plan, with the patient's consent. However, carers themselves often require additional support, and should be advised about local support networks (eg, Al-Anon, SANE).

Conclusion

Given the excess morbidity and mortality associated with cigarette smoking, helping patients with schizophrenia to reduce and stop smoking should be a key goal for clinicians. In addition, patients with comorbid psychoactive substance misuse need an integrated treatment program that addresses both disorders. Such programs, incorporating assertive outreach with intensive case management, boast better engagement and retention of patients and improved treatment outcomes.[14] Currently, few such programs exist in Australia, but, encouragingly, in response to the identified need, a number of innovative approaches have been introduced that await further evaluation. Given the high prevalence of comorbidity in people with schizophrenia, primary and secondary prevention strategies for substance misuse are urgently required. Even with adequately resourced, targeted interventions, the GP remains a key treatment provider for this population.

Competing interests

SS has received honoraria from Eli Lilly and AstraZeneca. DIL has received conference support from Pfizer, Eli Lilly and AstraZeneca.

Acknowledgement

Dr Lubman is supported by the Norma Licht Trust.

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