

Substance Abuse and Psychosis

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KEYWORDS

- Substance-induced psychosis • Adolescent psychosis • Dual diagnosis
- Cannabis and psychosis

KEY POINTS

- At initial presentation, substance-induced psychosis is almost indistinguishable from a primary psychotic disorder.
- All adolescents presenting with psychotic symptoms and co-occurring substance use should be considered at significant risk of developing a primary psychotic disorder.
- There is a paucity of data on the optimal treatment of patients with a psychotic disorder and co-occurring substance use, because most of these adolescents have been excluded from controlled treatment trials of antipsychotic medications.
- Cannabis use has been identified as a potential risk factor to the development of a primary psychotic illness in at-risk adolescents, and these data suggest that reduction or cessation of cannabis use should be recommended for all adolescents with psychotic symptoms to prevent further deterioration.
- Once psychotic symptoms have been stabilized with antipsychotic medications, developing a therapeutic alliance and ongoing psychoeducation are critical to keep these young people engaged in treatment and abstinent from substance use.

INTRODUCTION

Approximately one-third of people with a primary psychotic disorder experience their first psychotic episode before the age of 19 years. As part of healthy psychological development, adolescence is also a period in which individuals are emotionally separating from their parents. This developmental stage also represents a peak period of time for use and experimentation with alcohol, cannabis, and other illicit substances, which may reflect the influence of culture, media, and peer group in Western societies. Although the ability of illicit substances to induce psychotic symptoms has been well recognized, more recent epidemiologic studies have suggested that cannabis may represent a significant risk factor for the development of a psychotic illness in

Disclosures: Dr Goerke, None; Dr Kumra has received research support from the Minnesota Medical Foundation, the National Alliance for Research on Schizophrenia and Depression, and AstraZeneca.

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Child Adolesc Psychiatric Clin N Am 22 (2013) 643–654

<http://dx.doi.org/10.1016/j.chc.2013.06.001>

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at-risk individuals. In adolescents and young adults with a first episode of psychosis, co-occurring substance use has been reported as many as 74%,¹ and this comorbidity has been associated with less effective treatment responses, decreased medication adherence, and consequently a worsened course of illness.² By extension, these data suggest that identification and treatment of substance abuse are imperative to resolution of psychotic symptoms for adolescents with co-occurring disorders. This article selectively reviews the pertinent literature that provides guidance for clinicians with regard to the most pressing diagnostic and treatment challenges faced in working with this group of adolescents (aged 13–18 years).

The diagnosis of psychotic symptoms in adolescents is difficult, particularly if the adolescent is also abusing chemicals. A case vignette is presented later to highlight the problem of differentiating a substance-induced psychotic disorder (SIPD) from an early stage primary psychotic disorder (PPD) with co-occurring substance use. The vignette also helps to show the multimodal nature of treatment interventions required for this population in terms of psychoeducation, engagement of the patient and family in the treatment process, and use of antipsychotic medications. Recent data suggesting that cannabis may be a causal risk factor in psychotic illness are examined, because these data support clinical recommendations to reduce or cease cannabis use in this population. In addition, treatment strategies that have been found to be effective in adult patients that may be efficacious for youth to abstain from substances after the resolution of psychotic symptoms are presented.

CLINICAL VIGNETTE

Fifteen-year-old A.S. was brought to the emergency room by his parents after expressing concern that the TV was talking to him. Over the last several months, his parents had observed changes in their son's behavior: increasing social isolation, deteriorating school performance, and frequent episodes of being found passed out from alcohol intoxication. He admitted to daily marijuana use and several urine toxicology screens at various emergency department visits confirmed this misuse. At first, his family was turned away from inpatient care because emergency department physicians thought that he did not meet admission criteria because of a lack of behaviors that indicated danger to self or others. The patient started outpatient chemical dependency treatment, but he continued to use both alcohol and marijuana. Over the next several months, his symptoms expanded to include disorganized thought processes, paranoia, anxiety, and eventually refusing to leave his mother's side for several days. He was referred to a university psychiatric clinic where he was observed to have difficulty expressing his thoughts, decreased attention, poor motivation, social isolation, and a further decline in academic functioning. He was then referred for an inpatient evaluation for diagnostic clarification and stabilization of his symptoms. Quetiapine was started to address psychosis and anxiety, which resulted in a rapid cognitive clearing. However, once discharged from the hospital, he refused to take medication. He was insistent that his drug use was the source of his symptoms and that with sobriety all would be well. Weekly visits with his psychiatrist continued. Within 2 weeks, it was noted that he was laughing to himself in class, continuing to have failing grades, and refusing to interact with anyone but his family. He shared with his father his overwhelming fear that something horrible may happen to his family and that, if he took antipsychotic medication, it would not only damage his brain but his family would die. Despite denying all positive symptoms to his psychiatrist, he did express concern over his ongoing difficulty in concentration. With the support of his parents, a low dose of aripiprazole was initiated to help with focus and concentration. He refused to exceed a dose of 5 mg daily. However, thought process, academics, and social engagement with peers all improved. He relapsed on marijuana once, which resulted in a significant worsening of anxiety as noted by the patient. A new level of insight was achieved in that A.S. shared that he could no longer use marijuana because it was detrimental to his mental health. Despite observed improvement by his psychiatrist and family, medication compliance continued to be a daily struggle and, after 4 months, he requested that he be given a trial off medication. His parents agreed that

he was looking better and so supported the discontinuation of medication against medical advice. Within 1 week, he was found heavily intoxicated with alcohol and returned to chemical dependency treatment. At continued monthly visits to his psychiatrist, his improvement in thought process and resolution of anxiety persisted, despite the discontinuation of his low-dose second-generation antipsychotic. Both the patient and his parents agreed to continue to follow with the psychiatrist, but did not want to resume antipsychotic medications at that time.

INITIAL EVALUATION

Adolescents are often concerned about confidentiality so separate interviews for the individual and family are optimal. The substances most commonly used by adolescents with schizophrenia are alcohol and cannabis. A detailed history and physical with a subsequent diagnosis is traditionally the primary goal at initial contact with an adolescent presenting to medical services. Based on this diagnosis, a treatment course is recommended. As illustrated in the vignette, the initial clinical presentation of SIPD and a PPD with co-occurring substance use is often indistinguishable. Clinicians rely on the definition of SIPD as stated in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (**Box 1**).

However, these criteria oversimplify the complexity of differentiating these diagnoses. Cannabis in particular has the potential to induce psychotic symptoms acutely and may play a causal role in primary psychotic illnesses. Therefore, it is possible for a young person to meet criteria for an SIPD and also be at high risk of developing a PPD over time.

Several studies have focused on differentiating a SIPD from a PPD with co-occurring substance use at initial presentation. The Psychiatric Research Interview for DSM-IV Substance and Mental Disorders (PRISM-IV) has proved reliable at this task. The length and the intensive training required to administer this structured

Box 1 DSM-IV Text Revision criteria for SIPD

- a. Prominent hallucinations or delusions. Note: do not include hallucinations if the person has insight that they are substance induced.
- b. There is evidence from the history, physical examination, or laboratory findings of either (1) or (2):
 1. The symptoms in criterion A developed during or within a month of substance intoxication or withdrawal
 2. Medication use is causally related to the disturbance
- c. The disturbance is not better accounted for by a psychotic disorder that is not substance induced. Evidence that the symptoms are better accounted for by a psychotic disorder that is not substance induced might include the following: the symptoms precede the onset of the substance use (or medication use); the symptoms persist for a substantial period of time (eg, about a month) after the cessation of acute withdrawal or severe intoxication, or are substantially in excess of what would be expected given the type or amount of the substance used or the duration of use; or there is other evidence that suggests the existence of an independent non-SIPD (eg, a history of recurrent non-substance-related episodes).
- d. The disturbance does not occur exclusively during the course of delirium.

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interview hinder its usefulness in everyday practice; however, specific clinical markers with the potential to differentiate between these diagnoses were identified. For example, using the PRISM-IV, cannabis dependence, a history of trauma, and the absence of a family history of psychosis correctly identified 78.7% of patients with SIPD in a sample of young people experiencing their first episode of psychosis with concurrent substance use.³ However, the consensus among longitudinal studies is that these initial diagnoses are not stable. A large number of those diagnosed with an SIPD, followed over time, eventually meet criteria for a PPD. A 3-year longitudinal study found that, out of a total of 238 patients, 44.5% of those diagnosed with cannabis-induced psychotic symptoms later developed a schizophrenia-spectrum disorder. This proportion increased with length of follow-up. Male gender and young age related to increased risk of conversion to a PPD. Compared with patients without a history of cannabis-induced psychosis, they developed schizophrenia at a significantly younger age. This effect was most marked for paranoid schizophrenia.⁴⁻⁷

A potential explanation for this high rate of conversion is that youth presenting for medical care of psychotic symptoms are in the early stages of the disease process. A well-defined period of decline with attenuated psychotic symptoms, often referred to as the prodromal period, can be identified in most patients presenting with a first episode of psychotic illness. Identification of those young people still in prodrome, deemed at ultrahigh risk to develop a psychotic illness, is now a top priority. A focus on this early stage of the illness has the potential to prevent cognitive decline and intervene while that patient maintains some insight into the symptoms. Often intervention in this earlier stage is better received by the adolescent and the treatment process has the potential to be more collaborative. Those presenting with attenuated psychotic symptoms are likely to present with co-occurring substance use given the average age of onset for both disorders. Therefore, a young person presenting in the prodrome or early stages of a psychotic illness with co-occurring substance use could be mistaken for SIPD.⁵

Given the high level of diagnostic instability, specifically the rate of conversion from an SIPD to a PPD with co-occurring substance use, differentiating between the two diagnoses may be arbitrary from a treatment perspective. Instead, recognizing that these individuals with early psychotic symptoms are on a spectrum at a substantially increased risk of developing PPD provides the framework necessary for an effective treatment plan.

TREATMENT CONSIDERATIONS

The treatment of adolescents is different from that of adult patients in that the families are typically more involved in the treatment process. It is common for parents to be scared and to be in shock and denial about the diagnosis. Adolescents frequently do not want to cooperate with the assessment or treatment process, regardless of diagnosis. With the lack of insight experienced in a psychotic illness, engaging them in treatment can be particularly challenging.

As in the case vignette, the treatment of dually diagnosed patients with mental illness and substance use disorders is often fragmented. It is common for mental health and substance use services to be provided separately. Practitioners may refer youth using substances to chemical dependency treatment programs. However, these programs are often not as helpful to the recovery process of those who are still actively psychotic. Staff and programming tend to be highly focused on chemical dependency with the mental illness as a secondary focus. This approach is helpful for other mental health diagnoses but is not suitable for actively psychotic youth. They

may not be cognitively ready for the rigorous requirements of groups and their delusional state may make them vulnerable to peers. Paranoia and confusion may necessitate a locked unit. A multidisciplinary integrated approach that provides special attention to mental health concerns is optimal to promote retention in the treatment process.^{8,9}

Some practitioners are reluctant to refer young people for psychiatric services because of fear of stigma or what they deem may be unnecessary antipsychotic medications because of the belief that substance-induced psychosis resolves spontaneously with cessation of the illicit substance. In our experience, there is a subgroup of adolescents who present with psychotic symptoms that persist beyond the period of intoxication and that result in a decline in adaptive function, dangerousness to self or others, and/or other types of deleterious consequences. In this context, antipsychotic medications may facilitate the treatment process by alleviating impairments in reality testing, reducing anxiety, promoting sleep, and stabilizing mood. Stabilization of psychotic symptoms may have other long-term benefits in terms of reducing the likelihood of future episodes of substance use and preventing the deterioration associated with untreated psychosis. In adults, substance use in combination with psychotic illness correlates with more frequent hospitalizations, suicide attempts, relapse of psychotic symptoms, homelessness, health problems, legal problems, violent behavior, and residential instability.¹⁰⁻¹²

Programs giving equal attention to substance use and mental health symptoms are preferable. Intervention should be multimodal and include individual and family therapy, medication, and referral to formal treatment programs for longer-term chemical dependency treatment. Some adolescents significantly decrease or discontinue substance use after their first episode of psychosis without specific substance abuse treatment. The experience of psychosis, education about the relationship of symptoms to use, treatment of psychosis, and interruption of social interactions are all postulated to contribute to discontinuation.¹³⁻¹⁵ Integral to reduction of substance use is the treatment of psychotic symptoms. Youth engaged in a comprehensive mental health program with a primary focus on addressing psychotic symptoms display the lowest levels of chemical use with improved clinical outcomes.¹ Few patients begin using substances following entry into treatment.^{1,16-20} However, in some instances, formal chemical dependency treatment may be helpful, particularly if the adolescent has little insight or motivation. In these programs, education by adult staff on the risks of use may be better received than that given by parents. Second, peers can hold adolescents accountable and peer accountability becomes the criterion for peer acceptance.

At present, specific guidelines regarding the use of antipsychotics in this patient population are lacking. To date, all of the clinical trials supporting the use of second-generation antipsychotic medications in adolescents with schizophrenia have excluded subjects actively using substances. In adult patients with schizophrenia, clozapine has been found to be the most effective medication in reducing cannabis and alcohol use. Because of the potential adverse effects of clozapine in youth, this is a second-line intervention reserved for treatment-refractory patients. The paucity of data regarding adolescents with schizophrenia and comorbid substance misuse makes it unclear whether any of the second-generation antipsychotic medications influence substance misuse or reduce drug cravings. To date, there have been no trials of anticraving agents (eg, naltrexone, topiramate) in these adolescents. Given that these youth are in their first episode of psychosis, lower doses of antipsychotic medications may be required to achieve remission of psychotic symptoms than what is typically recommended for adults with chronic schizophrenia. Frequent psychiatric appointments are essential,

not only to build a therapeutic alliance but also to closely monitor side effects. Young people are more susceptible to side effects and tend to be resistant to taking medication in general. A collaborative effort by a mental health provider to reduce these side effects is likely to result in improved adherence. Recent studies have identified a high rate of relapse to psychotic symptoms after discontinuation of antipsychotic medications in those adequately treated for a first psychotic episode. However, if able to maintain sobriety and a quick resolution of psychotic symptoms is experienced, a brief period of antipsychotic medications may be enough. A high level of vigilance for the return of symptoms remains essential, including involvement of the patient's family, educators, and significant others who are often the first to observe reemergence of symptoms. Cannabis use is regarded as benign by most adolescents. Encouraging reduction and cessation of this substance in particular can be challenging. However, understanding of the role cannabis plays in psychotic illness is evolving.

CANNABIS

The role of cannabis in psychotic illness has been controversial. Experts have debated whether those who are psychosis prone are more likely to use cannabis or whether cannabis use independent of other risk factors can cause or precipitate psychotic symptoms.

Lifetime prevalence of cannabis use in grade 12 students in the United States was 49% in 2007.²¹ In 2008, more than 15% of 12th graders reported using cannabis daily for at least a month.²² This finding is particularly concerning given the increased risk of developing psychotic symptoms with increased frequency and dose used.^{23–26} For example, transition to daily cannabis abuse in particular has been linked with an increased risk of psychotic symptoms up to 5 times that of nonusers.^{23–31} Patients often report the onset of psychosis after the initiation of cannabis use and can recall that their first psychotic symptoms occurred while intoxicated.^{31–33} This relationship indicates a causal role as opposed to use for self-medication.

Despite up to 15% of those who use the substance experiencing psychotic symptoms, only a minority go on to develop permanent impairments that include PPDs,³⁴ indicating that cannabis use alone is not sufficient to cause psychotic illness. Instead, it is likely that, in combination with predisposing risk factors (genetic vulnerability, environmental factors, obstetric insults, and social adversities), cannabis is an additive risk factor in those with increased vulnerability.^{33,35,36} In those predisposed, cannabis use is associated with an earlier age of onset for a first episode of psychosis.^{37–49} The higher rate of onset of schizophrenia in early cannabis users may reflect an interaction with the catechol O-methyltransferase (COMT) genotype.⁵⁰ In adults with schizophrenia, cannabis use was associated with greater brain volume loss over a 5-year period.⁵¹

Proposed theories focus on the role of the endocannabinoid system in the developing adolescent brain. The role of the endocannabinoids in the development of the infant brain has been shown. Of importance in adolescence, neurodevelopment continues to occur with the prefrontal cortex. During this critical time period (age 15–17 years), synaptic development and pruning, receptor distribution, volumetric growth, myelination, and programming of neurotrophic levels are particularly active.^{52–55}

During this same time period, CB1 receptors have been found to increase greatly in the frontal cortex,⁵⁶ leading to the theory that the endocannabinoid system is integral to adolescent neurodevelopment as well.⁵⁷ Therefore, it is proposed that adolescence represents a critical time period in which the toxic effects of environmental factors, such as cannabis, have the potential to alter neurodevelopment. The prefrontal cortex has been implicated as a core region involved in PPDs. Overpruning of neuronal

connections and decreased density of dendritic spines have been implicated in psychosis. Whether by direct toxic effects on neurons or through social deprivation essential to gaining life skills, heavy cannabis use in this critical time period poses a significant increased risk of developing a PPD that has not been observed in those who start using later in life.⁵⁸

Practitioners must be vigilant in screening for cannabis use. Use of cannabis during adolescence is common and increasing in prevalence. With this increased use, it can be assumed that there will be an increase in the number of adolescents experiencing psychotic symptoms. Once identified as being at high risk, acutely stabilized, and educated on the likely contribution of cannabis to the symptoms, long-term engagement in treatment is essential to prevent relapse and potential future episodes.

TREATMENT ENGAGEMENT

Substance use is often cited as one of the strongest predictors of disengagement of treatment in specialized early psychosis programs.^{59–62} Adolescents are particularly challenging to engage in treatment of any illness. Psychosis often presents with a low level of insight, making encouragement to take medications challenging. Antipsychotic medications have side effects, the most common being weight gain, fatigue, and sexual side effects, all of which negatively affect the social structure that is of utmost importance to adolescents. Adolescents with psychotic disorders frequently have neuropsychological deficits in attention and executive function. These deficits make psychoeducation and attendance of appointments particularly challenging. The social isolation that ensues with psychosis may alienate that person from those who would have been most helpful in managing day-to-day life.

First-episode programs have shown improved adherence and clinical outcomes, compared with treatment as usual. These programs focus on the lowest effective dose of medications, early engagement of family and caregivers, psychoeducation, group and individual psychotherapy, intensive case management services, and frequent interaction with mental health providers. Motivational interviewing and cognitive behavior therapy are emphasized to foster the therapeutic relationship and encourage participation. These programs have been shown to reduce substance use in patients with psychotic illness.^{48,63}

Disengagement in treatment often results in relapse to substance use, which in turn leads to relapse of psychotic symptoms.⁶⁴ Even after patients are stabilized on antipsychotic medications, ongoing substance use can result in relapse of symptoms. Subsequent psychotic episodes not only tend to worsen in severity and duration, but may result in resistance to antipsychotic medications.

Early engagement of youth through showing genuine interest in their interests and opinions, including their opinion on what may be causing their symptoms, is imperative. Attention to their concerns (academic, social, and legal) shows desire to help them and to improve cohesiveness.⁶⁵

Treatment recommendations for the combined treatment of psychosis and substance use include, first and foremost, treatment of the psychotic symptoms. A significant proportion of those who experience their first episode of psychosis stop using illicit substances with antipsychotic treatment and psychoeducation. Both of these treatment modalities require excellent engagement in a treatment plan to have efficacy.

SUMMARY

The diagnosis of adolescents with psychotic symptoms and co-occurring substance use disorders is a complex and dynamic process that must take developmental issues

into account. Early interventions for adolescents presenting with psychotic symptoms are essential. In both SIPD and PPD, better premorbid adjustment, shorter duration of untreated psychosis, better insight into psychosis, and lower severity of symptoms predict 12-month remission rates.⁶⁶ Therefore, timely identification and referral to mental health services are imperative to prevent adaptive decline and to improve overall functional outcomes.

Given the significant overlap in presenting symptoms between SIPD and first-episode PPD with a co-occurring substance use, long-term observation of these youth by a mental health provider experienced in psychosis is required. A premature diagnosis of SIPD has the potential to provide false comfort to patients and families, making engagement in further treatment more difficult. This future delay in treatment could result in subsequent, more severe psychotic episodes that are more difficult to treat. First-episode psychosis programs that provide intensive case management, along with psychiatric, psychological, and peer support, have proved most effective to reduce chemical use and prevent additional psychotic episodes.⁶⁷

The subject of cannabis use remains controversial in our society. A few states recently passed laws making the use of marijuana legal. With the ever-increasing availability of cannabis products in society, education on the risks of use is imperative. Recreational use of cannabis in those who are sensitive to the psychosis-inducing effects of the substance could result in a severe and persistent mental illness in at-risk adolescents. Cannabis use is a highly modifiable risk factor to prevent the onset of PPDs in our society. Youth have reported that the most common reason for abstaining or quitting cannabis use was their concern for psychological and physical damage.⁶⁸ It is the obligation of practitioners to educate their patients, families, and communities about the risks associated with cannabis use.

Key to the prediction of clinical outcome for youth experiencing psychotic symptoms is a trusting relationship with their primary mental health provider and the education of those family members closest to them. Both of these factors require an extended relationship with patients and their families. Engagement in treatment through building a therapeutic alliance and psychoeducation should be the top priority in treating youth presenting with psychosis and substance use.

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