TOBACCO (AH WEINBERGER, SECTION EDITOR)

Treatment of Comorbid Tobacco Addiction in Substance Use and Psychiatric Disorders

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Abstract Tobacco addiction is the leading cost of preventable morbidity and mortality in the western world. Substance use (SUD) and psychiatric (PD) disorders are important contributors to the high rates of tobacco addiction, and smokers with these comorbidities demonstrate lower rates of quitting compared with smokers in the general population. This article will review reasons for the high rates of co-occurring SUDs and PDs in people with tobacco addiction, and propose approaches to their assessment and treatment based on the recent literature. The recognition of SUDs and PDs in tobacco smokers is an important goal for all clinicians treating tobacco addiction, and an approach that integrates these treatments leads to optimal treatment outcomes for this important subset of tobacco smokers.

Keywords Tobacco · Nicotine · Psychiatric disorders · Substance use disorders · Comorbidity · Integration · Smoking cessation · Addiction · Drugs of abuse · Mental illness

Introduction

(~20 % in the US population), a high prevalence of cigarette

Despite declines in tobacco use in the general population

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smoking is observed among those with comorbid substance use disorders (SUDs) and psychiatric disorders (PDs) [1, 2]. For PDs and SUDs, tobacco is the most commonly used substance, followed by alcohol, cannabis, stimulants, and other drugs [3, 4]. Importantly, individuals with PDs have greater difficulty quitting smoking than those without PDs [5]. Homeless individuals represent a group particularly at risk, with a tobacco use rate 4 times higher than the US adult population and with frequent coexisting SUDs and PDs [6]. Moreover, tobacco use starts at an early age (11-13 years) and is associated with PDs in youth populations [7•]. Unfortunately, efforts to assist individuals with dual diagnoses reduce or stop tobacco smoking are often unsuccessful. Tobacco use is often overlooked or minimized in clinical settings [1] despite it being a serious public health issue among people with concurrent SUDs and PDs [5]. A recent study showed that individuals with PDs have an average of 12 to 19 year reduction in life expectancy compared with the general population [8•], which has been largely attributed to tobacco-related illnesses [9..]. The goal of this article is to review challenges in the assessment and treatment of tobacco use disorder in people with dual diagnoses as well as recent treatment research advances in this area.

Case Presentation

The case presented below illustrates some of the frequent clinical challenges encountered when treating tobacco dependence in an individual with dual disorders:

Mr. A is a 23-year-old male presenting with an acute psychotic episode, in the context of comorbid use of cannabis, alcohol, cocaine, and tobacco. He has had paranoid delusions and mood swings for weeks and was picked up by police and brought to the local Emergency Department after walking through rush hour traffic. He was committed to a state psychiatric hospital. His symptoms resolved after 2 weeks of



treatment with antipsychotics in addition to alcohol and drug sobriety. He started to contemplate quitting smoking while in the hospital, since his breaks to go out to smoke were limited, but remained ambivalent about long-term tobacco cessation.

Clinical Assessment of Tobacco Use Disorder in Dual Diagnosis Populations

General Assessment of Tobacco Use Disorder

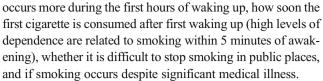
People with co-occurring SUDs and PDs often have a desire to quit smoking [10], but have limited success with cessation [5]. The majority of quit attempts are done unassisted [11], and use of FDA-approved pharmacotherapies (nicotine replacement therapies (NRTs), Bupropion SR, and Varenicline) is limited in this population despite several studies demonstrating efficacy in multiple populations (see Treatment Approaches section).

The first step towards achieving smoking cessation is a comprehensive assessment of tobacco use. Clinicians assess tobacco use by obtaining a detailed profile of past smoking history (age at first use, pattern of use with time, type of tobacco products used) and current smoking habit and context (time to first cigarette, cigarette consumption rate, triggers to use) [1]. Perceived benefits such as psychological, physical, and social benefits of smoking can also be examined to generate a complete addiction profile [12]. Moreover, information about quit attempts (number and duration), the types of treatment previously utilized (if any), previous withdrawal symptoms, triggers of relapse as well as the positive aspects of quitting smoking should be identified.

The initial assessment gives a profile of the type of smoker and helps to develop a personalized treatment plan, which takes into account the presence of psychiatric and substance use disorder comorbidity (Fig. 1). Once the comorbid disorder is stabilized, level of motivation to quit smoking needs to be determined. In cases where motivation is low, then standard motivational interviewing (MI) methods (a nonjudgmental approach to engage smokers in changing addictive behaviors) should be utilized prior to starting evidence-based tobacco treatments.

Scales

Well-established assessment tools such as the Fagerström Test for Nicotine Dependence (FTND; [13]) can be utilized to assess the level of nicotine dependence (with higher scores suggestive of the need for more intensive treatments), and have been shown to be reliable in smokers with schizophrenia [14•]. FTND testing involves asking the smoker 6 questions including number of cigarettes smoked per day, whether the first cigarette of the day is the most satisfying, if smoking



The Tiffany Questionnaire for Smoking Urges (T-QSU) is a 32-item self-reporting tool assessing desire to smoke, positive effects of smoking, anticipation of immediate relief of craving, and intention to smoke [15]. The Minnesota Nicotine Withdrawal Scale is another frequently used tool and assesses withdrawal discomfort by ranking symptoms such as anger, irritability, anxiety, depression, and restlessness [16]. Both these scales can be used to assess the effectiveness of medication or behavioral tobacco treatments during a smoking cessation intervention.

Relationship with Dual Disorders

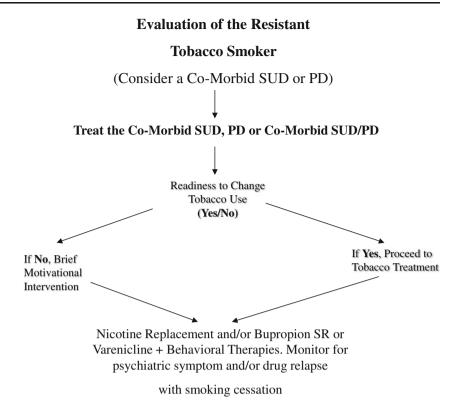
Clinicians should obtain information about other substance use, psychiatric symptoms, treatment and medication, and the relationships between these conditions to provide a comprehensive picture. Some persons with PD will report initiation and maintenance of their tobacco use for the alleviation or reduction of undesirable symptoms. This is consistent with the self-medication hypothesis that proposes that substances are used to reduce distress, feelings of isolation, and dysphoria [17]. However, these symptoms might be secondary to tobacco withdrawal and therefore faultily attributed to the PD. Short-term (<7 days) tobacco abstinence may increase levels of stress, and exacerbate psychiatric symptoms or trigger cravings for other substances. However, cognitive, mood, anxiety and depressive symptoms often improve in the months following biochemically-verified tobacco cessation [18].

Another model to explain this comorbidity is the addiction vulnerability hypothesis, which proposes a common neurobiological substrate for comorbid PD and SUD vulnerability. It suggests that both conditions involve anomalies in the neuronal networks of drug reward and reinforcement. For example, dysregulation of nicotinic acetylcholine receptors (nAChRs) is proposed to explain the shared vulnerability between tobacco dependence and schizophrenia [19]. Since tobacco smoking may remediate the cognitive deficits in schizophrenia [19, 20], this may be further barrier to successful smoking cessation in these patients.

It is also important to note that tobacco cessation decreases P450 1A2 liver enzyme activity. This leads to a reduction in the metabolism of psychotropic medications using this enzyme such as clozapine, olanzapine, and tricyclic antidepressants [21], which may lead to drug toxicity in patients who quit smoking. Therefore, monitoring for psychotropic drug toxicity is important post-cessation.



Fig. 1 Algorithm for assessment and treatment of comorbid tobacco smokers



Organizational Barriers

Misconceptions still exist among clinicians who may minimize risks related to tobacco use compared with mental health issues and other substance abuse risks [22]. Tobacco use disorders have been notoriously neglected when other substances are involved, with an infrequent number of clinicians expressing encouragement of unmotivated smokers to consider cessation [23]. In addition, there is strong evidence that addictions clinicians smoke at a higher rate than the general population [24]. Moreover, staff members who are smokers themselves may contribute to the barriers of tobacco use disorder treatment, as they are less likely to encourage their patients to quit compared with staff who are nonsmokers [25]. Although most staff members feel that tobacco use should be treated, they are less agreeable to implementing smoke-free policies that improve smoking cessation rates [26, 27]. Educating staff members about the positive effects of integrating smoking cessation into mental health and addiction treatment is an important aspect of treating tobacco use disorder.

Treatment Approaches

Integrated vs Sequential Treatment

Recent studies suggest that tobacco use disorders share common genetic, environmental, and psychosocial risk factors with SUDs and PDs. For example, tobacco and cannabis share common environmental factors and smoking cues that may contribute to sustained use [28]. Alcohol and tobacco use increase the cravings for one another suggesting underlying biological and physiological mechanisms that have been extensively studied [29]. These links demonstrate the importance of integrating tobacco use in the treatment plan of dual-disordered smokers.

Different approaches have been developed to address dual disorders. The best evidence is in favor of integrated treatment compared with sequential or parallel treatment [30••]. In this model, each disorder is conceived as primary but interrelated to the other disorders and is therefore considered in the treatment plan. Effective treatment of individuals with dualdisorders requires the integration of tailored psychiatric and substance misuse treatment, while being sensitive to motivation fluctuation. One example of an effective integrated approach is the Behavioral Treatment for Substance Abuse in severe and persistent mental illness (BTSAS). This is a 6month biweekly group treatment program that includes motivational interviewing, urine analysis contingency, structured goal setting, social skills, and drug refusal skills, education about reasons for substance use, and the dangers of addiction while having a concurrent PD, including the use of relapseprevention training [31].

While well-defined components for efficient dualdisordered treatment are emerging, tobacco use management for this population is less studied. Stopping alcohol or drug



misuse will generally improve mental health condition, and treating mental illness can decrease substance use. However, the benefit of smoking cessation is often less obvious in the short-term, particularly when the person experiences craving and withdrawal symptoms when attempting to quit. Mental health providers' prioritization of other substances and view of tobacco smoking as a coping strategy for psychopathology likely contribute to dismissing tobacco use. Efforts should be maintained by the clinical team to integrate tobacco dependence in the comprehensive care. Monitoring tobacco stages of change and providing appropriate management strategies are ways to help people considering tobacco cessation.

Individualized integrated treatment plans can give rise to different strategies of treatment including simultaneous and sequential tobacco cessation. Moreover, changing substance use pattern often implies lifestyle changes. Therefore, it might be easier for some patients to stop all substances at the same time. However, empirically-validated treatments tailored for co-occurring use are lacking [28]. When an individual decides to stop all substances at once, the clinical team should support the person in this direction and provide the necessary tools to succeed. However, if the person fails, emphasis should be placed on the learning experience and the intensity of the challenge, while proposing new approaches for future quit attempts. One can then suggest to the patient to start by quitting the substance that is associated with the most short-term harm before attempting another tobacco cessation trial.

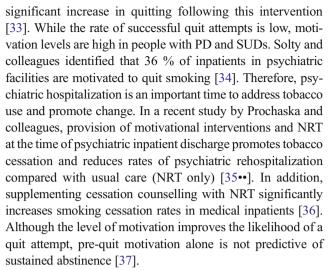
Other patients prefer to quit 1 substance at a time. In this case, it may be beneficial to quit the most detrimental substance first. For example, in the case of Mr. A, quitting cocaine and cannabis, drugs that are associated with acute psychiatric and tobacco relapse, may facilitate tobacco cessation. In this case, the clinician should support the person's choice to maximize success, build alliance, and provide empowerment. Collaborative care is the cornerstone of such success [32].

Some organizations have addiction and tobacco cessation programs, which are distinct from mental health programs. In these settings, collaboration is of great importance as studies have demonstrated that professionals or mental health providers often view the situation differently from ones suffering from addiction or mental health disorders. Maintaining good communication between agencies offers opportunities for capacity building across programs and consequently the occasion for more comprehensive treatment plan.

Components of Treatment

Building and Maintaining Motivation

Assessing motivation and readiness is as important as the description of substance use. A recent review of motivational interviewing (MI) for smoking cessation showed a modest but



When a smoker is in the precontemplation or contemplation stages of change, offering MI can engage smokers who are unmotivated to consider quitting [32] (Fig. 1). Psychoeducation helps people gain a better understanding of the relationship between tobacco use, PDs and SUDs and provides additional resources to consider change. In addition, behavioral interventions like social skills building groups and cognitive behavioral therapy are usually beneficial for the preparation, action and maintenance stages of change [31].

Tobacco Cessation Strategies for Co-Occurring Addictions

Interventions for tobacco addiction are widely studied in the general population of tobacco smokers. The latest Cochrane review confirmed that NRT, bupropion, and varenicline are effective aids to smoking cessation [38]. Further, combining the transdermal nicotine patch (TNP), (which provides low levels of nicotine to reduce withdrawal symptoms) with an acute dosing form (eg, nicotine nasal spray, gum, or inhaler) may be superior when compared with the use of a single form. Interestingly, abrupt cessation or reducing cigarettes smoked before quit day give similar results [38]. Nonetheless, due to stringent exclusion criteria in most nicotine dependence studies, there is a scarcity of literature on interventions in persons with other substance use and PDs.

The following section presents a review of tobacco treatment in co-occurring SUDs; see the review by Mackowick et al. [1] for a review of tobacco treatment in specific psychiatric disorders. The 2 substances most frequently used alongside tobacco are cannabis and alcohol. Polysubstance use disorders are associated with a lower likelihood of smoking cessation, but this observation has not been well-studied in terms of treatment development, posing more challenges for clinicians developing treatment plans for these smokers.



Tobacco and Alcohol Use Disorders

A recent study has shown that alcohol use at pre-treatment of nicotine dependence decreases the likelihood of tobacco abstinence [39]. As introduced earlier, a debate, in both the literature and clinical setting, exists on whether treatment of nicotine dependence should occur simultaneously or sequentially in alcohol-dependent patients [40]. Few studies have been conducted to compare the 2 modes of treatment [41, 42]. A significant concern is whether concurrent tobacco cessation increases the risk of alcohol relapse. Some studies have produced conflicting results and methodological differences have been cited as a confounding factor [40]. Nieva and colleagues [43] recently tested this hypothesis on a group of 92 patients in a randomized controlled trial to investigate the effect of tobacco cessation treatment on alcohol consumption. The study participants were randomly assigned to 2 groups and received either simultaneous treatment of alcohol and tobacco dependence, or delayed tobacco cessation treatment after 6 months. They observed no significant difference in alcohol abstinence rates during the first 6 months for both groups; showing simultaneous treatment has minimal to no effect on alcohol abuse relapse. However, Kalman and colleagues found that short-term (<12 months) alcohol abstinence was associated with more difficulty in achieving smoking cessation compared with longer-term abstinence (>12 months) [42]. Finally, Carmody and colleagues found that intensive tobacco treatment with NRT and behavioral interventions led to higher smoking cessation rates compared with usual care, and did not increase the risk of alcohol relapse [44]. Such studies emphasize the importance of aggressive tobacco interventions in alcoholic smokers.

The role of specific smoking cessation medications for alcoholic smokers needs further study. Karam-Hage and colleagues [45] conducted a double-blind pilot study on alcohol and nicotine dependent patients admitted to an outpatient alcohol treatment program (N=11). The participants were randomized to bupropion SR or placebo with follow-up for 8 weeks. Although more patients achieved abstinence on bupropion SR versus placebo, the results were not statistically significant; however, the small number of participants limited power to detect group differences. Subsequently, Kalman and colleagues conducted a double-blind placebo-controlled study on smokers with recent abstinence from alcohol (N=148). The study compared transdermal nicotine patch (TNP) plus bupropion with TNP plus placebo. Although there were group differences, they were not found to be statistically significant [46].

Recent studies have also highlighted the role of varenicline, the nicotinic partial agonist, for smoking cessation in the alcohol-dependent population. Hays and colleagues conducted an open-label pilot study on smokers with 6 months or more of recovery from alcohol dependence (N=32). After the

12-week course, 28 % had achieved smoking abstinence [47]. Moreover, varenicline has been associated with reduced alcohol cravings in human laboratory studies, making it a potential treatment in this population. [48, 49]. However, double-blind placebo-controlled trials are required in this population to further establish safety and efficacy for smoking cessation in alcoholic smokers.

Tobacco and Cannabis Use Disorders

The rate of smoking in adult cannabis users ranges from 41 %–94 %. In a recent study of people with bipolar disorder, cannabis use disorder was 6 times the general population rate and the cannabis users had a 2-fold higher rate of nicotine dependence (67.5 % vs 32.7 %) as well as a more severe course of illness compared with noncannabis users [50].

Concurrent use of tobacco and cannabis is increasingly common. Multiple mechanisms have been hypothesized as explanations for the strong relationship between the two substances [28]. One such hypothesis, the "gateway" hypothesis (which suggests that use of certain drugs like alcohol, tobacco leads to subsequent use of illicit drugs such as cannabis, cocaine, and heroin), has been criticized as cannabis initiation does not always following the onset of tobacco (and alcohol) use; in fact, a common liability or addiction vulnerability model appears to be a better explanation for this comorbidity of tobacco and cannabis use [51]. Despite the high comorbid use, studies in this population are is relatively sparse and minimal data exists on interventions for both substances. One pilot study suggested the safety and efficacy of combined transdermal nicotine and cognitive-behavioral therapy (CBT) for the treatment of comorbid tobacco and cannabis use disorders [52].

Tobacco and Cocaine Use Disorders

Rates of tobacco use are reported to be >80 % in cocaine use disorders [53]. The search for potential pharmacotherapies that target both cocaine and tobacco use disorders is important as most cocaine users concurrently smoke cigarettes. Studies conducted on Rhesus monkeys showed that nicotine increases the reinforcing effects of cocaine [54]. A recent study investigated the effectiveness of buspirone in reducing the selfadministration of intravenous nicotine, cocaine and their combinations in a small sample of trained Rhesus monkeys. Results showed a significant dose dependent effect of buspirone in decreasing cocaine and nicotine self-administration, with a decrease of 85 % at the highest dose in the study (0.56 mg/kg/ h) [55]. Interestingly, a double-blind placebo-controlled trial of varenicline for cocaine and tobacco dependence treatment in methadone-maintained participants (N=31) showed no effect on cocaine use but a reduction in the number of cigarettes smoked per day [56]. These preliminary results are



promising, and further human trials in cocaine addicted tobacco smokers are warranted.

Tobacco and Opioid Use Disorders

It has been reported that rates of smoking use in opioid use disorders exceed 80 % [53]. Many studies suggest the utility of NRTs, bupropion SR, and varenicline combined with behavioral interventions as safe and effective for smoking cessation in individuals with opioid use disorders [57–59]. However, cessation rates in opioid dependent smokers are very low (0 %–11 %) [60], and more effective treatments based on an increased understanding of tobacco-opioid agonist maintenance interactions are warranted.

Conclusions and Recommendations

The neurobiological correlates of tobacco and comorbid SUDs and PDs may increase our understanding of the relationships between disorders. They also strongly suggest that we must approach these comorbid disorders with an integrated treatment model. The literature suggests that current treatments for tobacco dependence can be useful in dual diagnosis populations (eg, NRTs, bupropion SR, and varenicline in schizophrenia, bipolar disorder, alcohol, opioid, and cocaine addictions) although success rates are typically lower than in the general population. Psychosocial adjunct treatment appears key to develop long-term strategies of abstinence. There is a need for further evaluation of existing treatments in naturalistic studies of persons with tobacco use disorders in the context of dual disorders. Other strategies to decrease tobacco use include changes at the health care delivery policy level. Providing tobacco treatment free of charge raises awareness of the benefits of and promotes smoking cessation [38]. In addition, routine screening for tobacco use and tobacco-free policies can contribute to successful tobacco treatment efforts in people with comorbid SUDs and PDs [6, 26].

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Compliance with Ethics Guidelines

Conflict of Interest Clairélaine Ouellet-Plamondon declares that she has no conflict of interest. Nourhan S. Mohamed declares that he has no conflict of interest. Maryam Sharif-Razi declares that she has no conflict of interest. Emily Simpkin declares that she has no conflict of interest. Tony P. George reports that in the past 12 months he has been a consultant to Pfizer on smoking cessation medications, has received grant support

for multi-center and investigator-initiated studies from Pfizer, and has been a member of a data monitoring committee (DMC) for Novartis.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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