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TITLE:

Sequential behavioral treatment of smoking and weight control in bipolar disorder

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ABSTRACT

People with severe mental illnesses like schizophrenia and bipolar disorder (BPAD) live significantly shorter lives than people in the general population and most commonly die of cardiovascular disease (CVD). CVD risk behaviors such as smoking are not routinely assessed or assertively treated among people with a severe mental illness. This article provides an illustrative case example of a woman with BPAD who is motivated to quit smoking, despite concerns about weight gain and relapse to depression. It outlines key considerations and describes the patient's experience of participating in a behavioral intervention focussing first on smoking, then diet and physical activity. Clinical challenges encountered during treatment are discussed in the context of relevant literature. These include motivational issues; relapse to depression; medication interactions; weight gain; addressing multiple health behavior change; focussing on a behavioral rather than cognitive approach; collaborating with other health care providers; and gender issues.

Keywords:

Smoking, smoking cessation, bipolar disorder, sequential behavioral treatment, weight gain, physical activity

MAIN TEXT

Patients with severe mental illnesses such as schizophrenia and bipolar disorder (BPAD) have an increased prevalence of metabolic syndrome and its component risk factors for cardiovascular disease (CVD) and diabetes [1, 2]. CVD is the leading cause of death in the mentally ill, with recent studies indicating premature death estimates of 25 years of life lost in this population [3, 4]. People with BPAD are as much at risk of CVD as those diagnosed with schizophrenia [5-10]. The typical CVD risk profile of a person with BPAD is characterized by high rates of cigarette smoking, obesity, metabolic syndrome, diabetes, hypertension and elevated total cholesterol and low levels of high density lipoprotein (HDL) [7-10]. The physical health needs of people with mental illness are often neglected, meaning that behavioral and biomedical risk factors for CVD are not routinely assessed or assertively treated in this population. Although treatment with psychiatric medications is a contributing factor, access to primary health care is often poor and complicated by socioeconomic factors that negatively impact care [11, 12].

Researchers recently have called for specific programs to be implemented for people with BPAD that focus on reducing cigarette smoking, increasing physical activity and improving dietary habits to reduce their risk of CVD and ameliorate the health inequalities they experience [9]. The case below demonstrates one such approach and highlights some of the clinical challenges that may be encountered when working with people with BPAD to quit smoking.

INSERT TABLE 1 ABOUT HERE

Smoking prevalence

Compared to the general population, people with mental illness have significantly increased rates of smoking. Few studies have reported smoking prevalence rates specifically for those

with BPAD. Of those that have, the smoking rates are very similar to those in schizophrenia. A large study (n=2774) conducted in the United States found the prevalence of smoking to be 67% in people with schizoaffective disorder, 66% for BPAD, and 61% for schizophrenia, all of which were much higher than in the general population (24%) [13]. Another found the prevalence of smoking to be 57% for major depression, 66% for BPAD and 74% for schizophrenia, compared to 25% in controls [14]. The prevalence of smoking was higher for those with BPAD (68.8%) than any other psychiatric diagnosis in another large study (n=4411) [15]. In Australia, 16.6% of people in the general community are daily smokers [16], as compared to 51% of people with BPAD [17].

Smoking harms

In addition to significantly contributing to the poor physical health and premature mortality of people with BPAD, smoking adversely affects the clinical presentation, course, treatment response and outcomes in BPAD. A large study in BPAD (n=1904) found that smoking was associated with greater symptom and episode severity; rapid cycling; more lifetime depressive and manic episodes; comorbid psychiatric disorders; being currently symptomatic; greater alcohol and illicit substance use; and a history of suicide attempts [18]. Another study found that smokers with BPAD had significantly poorer outcomes in terms of depression and overall BPAD symptoms; longer hospitalizations; greater substance use and poorer health related quality of life [17]. Smokers with BPAD involved in a clinical trial investigating olanzapine as a treatment for acute mania, had poorer treatment outcomes with greater manic symptoms and overall episode severity [19].

Smoking treatment

A range of approaches have been implemented to assist people with severe mental illness to quit smoking, including pharmacotherapy (e.g. nicotine replacement therapy (NRT), bupropion and varenicline) and psychological approaches (e.g. counselling, education, motivational interviewing (MI), cognitive-behavioral therapy (CBT) and contingency management). A combination approach, adding psychosocial interventions to an appropriate smoking cessation pharmacotherapy over a sustained period works best in helping people with severe mental illness to quit smoking [20]. Three reviews of smoking cessation interventions for people with severe mental illness reported that this population are able to quit or reduce smoking, and that standard approaches to smoking cessation have comparable success with the general population and people with severe mental illness [21-23].

To our knowledge, there have been no published studies to date that evaluate smoking cessation interventions solely in people with BPAD. In one of the largest smoking cessation intervention studies among people with severe mental illness, 298 participants were randomly assigned to treatment as usual or an individually administered smoking intervention that included NRT + CBT + MI [24]. Significantly more people who attended all treatment sessions had quit smoking at each follow-up point compared to those assigned to the control condition (e.g. total abstinence at 12 month follow-up = 19% vs 7%). While this study did not analyze outcomes according to diagnosis, 9.1% of the sample comprised people with BPAD. Similarly, in the first study to implement and evaluate a multi-component CVD risk factor intervention targeting smoking, diet and physical activity in people with psychosis, 13.9% of the sample had BPAD [25]. In a current study, in which Ms A was enrolled as a participant, 30.2% of the sample have a diagnosis of BPAD [26]. Early smoking results for the total sample are promising, with participants significantly reducing their daily cigarette

intake at the first assessment point (15 weeks). While the current evidence is limited, it seems likely that people with BPAD can quit smoking.

Pharmacological interventions for smoking cessation in BPAD require some additional considerations. Combination NRT seems the most suitable first-line option for people with BPAD. Combination NRT is indicated for heavy smokers with high levels of nicotine dependence and involves combining one medication that allows for passive nicotine delivery (i.e. transdermal nicotine patch) with another that allows ad lib nicotine delivery to manage cravings (e.g. nicotine gum, lozenges or inhaler) [27, 28]. The use of combination NRT has been recommended for people with severe mental illness to effectively manage their higher levels of nicotine dependence [25, 29-34], and is effective for smoking reduction and cessation in people with BPAD [25, 26]. The dose and mode of NRT needs to be modified according to individual nicotine withdrawal symptoms, and a combination of patch and titratable ad lib forms of NRT (e.g. lozenges, gum) up to 42mg/day has been recommended for people with severe mental illness [31,32]. Bupropion, an antidepressant, should be used with caution in people with BPAD due to the propensity for precipitating a manic episode [33]. Although varenicline may offer another plausible alternative smoking cessation pharmacotherapy for use in BPAD, thus far no trials have been reported in samples with BPAD.

Clinical challenges in smoking cessation treatment in BPAD

Motivation

People with a severe mental illness are as motivated to quit smoking as the general population [35] and motivation to quit smoking waxes and wanes throughout ongoing treatment for smoking cessation. Although people with severe mental illness do recognize

the serious consequences of smoking, and want to quit mainly for health reasons [36, 37], they commonly lack confidence in their ability to successfully quit [37]. Smoking cessation interventions for people with severe mental illness, such as BPAD, thus need to target motivational and self-efficacy issues [38]. Several studies have found MI to be an effective and feasible treatment option for tackling comorbid substance use (mainly cannabis and alcohol) among people with psychosis [39-42] and smoking cessation in people with psychosis [24, 25]. MI techniques [43] involving the discussion of the positive and less positive aspects of smoking and smoking cessation should be employed as required during the course of intervention.

Risk of relapse to depression

While available evidence from studies in schizophrenia and schizoaffective disorder do not suggest a deterioration in mental state during smoking cessation [21, 24, 25, 44], evidence suggests that smokers with a previous history of depression may experience a recurrence of depression during smoking cessation [45]. This is more likely for those depressed at baseline and those who experience protracted nicotine withdrawal symptoms. Nicotine withdrawal symptoms can act as stressors for people experiencing mental illness, in turn triggering or exacerbating other mental illness symptoms [38]. Ideally, people with BPAD embarking on a smoking cessation attempt should be stable in terms of their mood. Before and during any smoking cessation attempt, mood symptoms need to be closely and regularly monitored in people with BPAD. Any depressive symptoms that may emerge during a smoking cessation attempt must be addressed immediately, as these can have a detrimental impact on motivation to quit. Additionally, an assertive approach to managing nicotine withdrawal symptoms in people with BPAD is crucial. Ms A experienced a depressive relapse during her smoking cessation attempt and this impacted on her motivation to quit and the amount she smoked.

Prompt and effective management of these symptoms by her treating team enabled Ms A to recover and continue with her quit attempt.

Smoking and medication

Smoking reduction or cessation can alter the doses of some psychiatric medications. Toxic products released during tobacco consumption, not nicotine, increase the metabolism of some psychiatric medications in the liver by inducing the cytochrome P450 (CYP) enzyme system, primarily CYP1A2 [46]. As smoking reduces, this metabolism will slow, subsequently increasing the doses of some medications in the body, possibly resulting in the emergence or exacerbation of medication side-effects. Alternatively, patients may experience an increased therapeutic benefit upon smoking reduction or cessation with increased doses of medication available in their system. Psychiatric medications frequently used in the treatment of BPAD that are affected by changes in smoking and liver metabolism include olanzapine, chlorpromazine, fluvoxamine, mirtazapine and diazepam. It is important to advise patients of these potential interactions at the outset of smoking cessation treatment, to regularly monitor possible changes to medication side-effects and to adjust dosage of medications as required.

Risk of weight gain: need for multi-component intervention

People with severe mental illnesses are at significant risk of obesity due to the illness itself and partly as a consequence of their psychiatric treatment [47-49]. Medications commonly used to treat the symptoms of BPAD such as mood stabilizers (e.g. lithium, sodium valproate), atypical antipsychotics (olanzapine and risperidone) and some antidepressants (e.g. paroxetine and mirtazapine) have been associated with significant weight gain [50]. Like smoking, obesity has been associated with poorer clinical presentation and outcomes in

BPAD [51, 52]. It thus seems sensible to offer interventions that target a number of CVD risk factors in people with BPAD.

Evidence indicates that changing multiple health behaviors is feasible [53]. A recent meta-analysis of randomized controlled trials (RCTs) was conducted comparing combined smoking treatment and behavioral weight control to smoking treatment alone for smokers in the general population [54]. Results indicated that combined smoking cessation and weight control treatment, compared to smoking cessation treatment alone, enhanced tobacco abstinence and also reduced post-cessation weight gain significantly in the short-term. Specifically, the best results for weight gain associated with smoking cessation in female smokers were achieved by offering a sequential approach, whereby smoking cessation was addressed *before* initiating weight control treatment [55].

We developed, implemented and evaluated a multi-component intervention targeting smoking, diet and physical activity in overweight smokers with psychosis [25], finding this to be both feasible and effective in decreasing CVD risk scores, smoking and weight. We have since commenced a larger and longer duration multi-component study in people with severe mental illness, again sequentially targeting smoking, diet and physical activity [26, 56]. The first session employs MI to examine the person's unhealthy behaviors and goals for change are set. Smoking is specifically addressed first, with the intervention for physical activity starting in week 4, and diet in week 7. Ms A benefited from our sequential, multi-component intervention. Although she gained 2.7kg in the first 15 weeks, she weighed 1.2kg less than she weighed before treatment after 18 months. Weight gain with smoking cessation has been clearly documented [57], and the amount gained usually varies between 3-6kg, with women being more likely to gain more. In this context, Ms A's initial weight gain was comparatively

small. Weight gain can seriously undermine a successful quit attempt, particularly in female smokers [58]. Interventions designed to minimize weight gain may increase the appeal of smoking cessation treatments, especially for female smokers. Smoking interventions for people with BPAD will benefit from being multi-component and sequential, firstly addressing smoking and then targeting issues around weight, diet and exercise.

Behavioral interventions for smoking cessation

Evidence strongly supports the use of both counselling and pharmacotherapy for smoking cessation [21, 24, 25, 34, 59]. Furthermore, as people with severe mental illness may experience cognitive and/or other difficulties, behavioral interventions may be a preferred approach in smoking cessation treatment, as was the case for Ms A. Behavioral interventions targeted at the high risk situations for smoking are warranted e.g. first thing in the morning; drinking coffee/alcohol; socialising with other smokers; stress/depression; and boredom.

Unique additional high risk situations exist for smokers with severe mental illness like BPAD, e.g. smokers increase their consumption of cigarettes during manic episodes [19] and smoking behavior is reinforced in the psychiatric treating system [60]. Given the decreased opportunity or availability of alternate activities to smoking; absence of well-developed alternative coping strategies for stress and other emotions; and associated motivation and cognitive difficulties seen in severe mental illness, smokers with BPAD will require additional support in identifying and implementing suitable behavioral interventions for smoking cessation. This may include assisting patients to problem solve in order to formulate methods to change patterns of behavior associated with smoking, as well as determining suitable distraction techniques. Role playing these strategies with patients is helpful.

Close collaboration with health care providers

Given that smoking cessation efforts in people with severe mental illness need to address issues related to mental state, medication, weight, physical health, and daily functioning, mustering support and expertise from all available health care providers is worthwhile.

Establishing contact with other health care providers involved in the patient's treatment at the outset is a good practice, as is providing regular feedback regarding their patient's smoking cessation efforts. Harmonious working relationships between health care providers can contribute towards the success of smoking cessation treatment. A united and consistent message regarding smoking cessation from all health care providers to patients is necessary. This was a key factor that contributed to Ms A's successful quit attempt. The provision of relevant education to health care providers may neutralize unhelpful staff attitudes such as people with mental illness don't want to and can't quit smoking; the patient's psychiatric condition will deteriorate if they don't smoke; patients need to smoke due to their mental illness symptoms; and smoking is the only coping strategy people with mental illness have [60, 61].

Gender differences

The risks of several of the most serious smoking related illnesses appear to be higher in women than men who smoke [58]. Additionally, smoking poses unique health risks for women (e.g. obstetric and perinatal complications, breast and cervical cancer). All smokers with BPAD should be offered smoking cessation treatment, but efforts aimed at females may be particularly worthwhile in reducing the overall morbidity, mortality and health care costs associated with smoking in BPAD.

There have been no published studies examining gender differences in smoking variables specifically among people with BPAD. In the general population, women are more likely to smoke to suppress their appetite and cope with the stresses of daily life, and be more concerned about weight gain during a quit attempt than men [62]. We found that women with severe mental illness reported being more likely to smoke to prevent weight gain, and had significantly more reasons for quitting than men [63]. Smoking cessation approaches for people with BPAD need to be gender sensitive, addressing weight issues for women, and strengthening reasons for quitting for males via MI.

Summary

The prevalence of smoking and its associated harms are significant problems among people with BPAD, and contribute to increased medical comorbidity and mortality. While there is a wealth of scientific evidence to justify and guide smoking cessation treatment in BPAD, clinical practice has still to catch up. All smokers with BPAD should routinely be offered smoking interventions. Optimal smoking cessation treatment in BPAD involves the combination of appropriate pharmacotherapy with an extended duration psychosocial intervention. Specific attention needs to be directed to issues of motivation, risk of relapse to depression and medication. Interventions need to be gender sensitive, addressing weight gain after smoking cessation, and a close collaboration with other health care providers needs to be established. Smoking cessation attempts should not be abandoned in the event of a smoking relapse or with mental health symptoms provided the patient wishes to continue.

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TABLES

Table 1: Case study of a woman with bipolar disorder who wanted to give up smoking but was concerned about weight gain and relapse to depression

Ms A was a 63 year old woman, with a diagnosis of Bipolar Affective Disorder (BPAD). Her current condition was stable. Her medication included a mood stabilizer (sodium valproate), an antidepressant (fluvoxamine) and simvastatin for hypercholesterolemia. Ms A saw a psychiatrist monthly and a community mental health service case manager fortnightly. She smoked 25 cigarettes a day, and had made 3 serious quit attempts in 48 years of smoking, the longest lasting two weeks. Relapses to smoking were precipitated by stress and lowered mood. Ms A had not previously used pharmacotherapy for smoking cessation. Although she was motivated to quit smoking, she was preoccupied with the possibility of gaining weight, and experiencing a relapse to depression. She was overweight, and her diet lacked fruit/vegetables. Ms A was sedentary and wanted to increase her level of physical activity.

Ms A participated in a multi-component CVD risk reduction intervention over a 38 week period that provided an intensive psychosocial intervention together with combination nicotine replacement therapy (NRT). In Session 1, motivational interviewing techniques examined Ms A's unhealthy behaviors and goals for change were set. The intervention then sequentially targeted smoking (from week 1), physical activity (from week 4) and diet (from week 7). Ms A made her first quit attempt two weeks into treatment. She used one 21mg nicotine patch daily and tried one 2mg nicotine lozenge but disliked the taste. Within a week of commencing the 21mg patches, she began experiencing nightmares and sleep disturbance, and reported feeling mildly depressed, with initial insomnia, amotivation and anhedonia. Ms A smoked ½-1 cigarette per day for the next 4 weeks. She was encouraged to persist with the lozenges, and used up to 5 per day. She persisted with the patches, and the sleep disturbance

and vivid dreams dissipated. After 6½ weeks Ms A had ceased smoking. Ms A resisted working within a cognitive therapeutic framework and the focus was placed on behavioral strategies such as avoiding coffee first thing in the morning; not smoking inside her home; distraction activities (e.g. knitting, crosswords, cards) and using sugar-free mints. Seven weeks into treatment Ms A reported the depression had worsened and she was increasingly anxious and irritable. She was less reactive, had difficulty concentrating and was slowed in her speech and movements. She described feelings of worthlessness and hopelessness, but did not express any suicidal ideation. Increased support options were arranged and Ms A saw her case manager and psychiatrist more frequently during this time. Her valproate levels were checked and found to be sub-therapeutic, and medication adjustments were made. Ms A remained abstinent from cigarettes during this time, and the moderate depression resolved by week 14. However from weeks 22-34, she experienced mild depression. During week 22 Ms A had two cigarettes on two separate days. This smoking relapse coincided with a return of the depressive symptoms. She struggled over the next month, smoking 1-4 cigarettes per day. However, by week 30 she had stopped smoking, and remained abstinent from cigarettes at the final therapy session at week 38.

Following Session 1, Ms A self-initiated some healthy behaviors based on her existing knowledge of healthy eating. After Session 1, she started eating breakfast. By week 3, Ms A was eating 2 pieces of fruit a day and cooking a main meal for dinner. She struggled to maintain these positive changes to her diet between weeks 7-12 when her depressive symptoms were at their most severe. By week 26, Ms A was again eating fresh fruit/vegetables regularly and having 3 balanced meals a day. She gained 2.7kg over the first 15 weeks. One year following commencement of treatment, Ms A's weight remained constant, and by 18 months she was 1.2kg lighter than her starting weight.

At the commencement of the program, Ms A was walking only short distances. From weeks 4-14, she was inactive due to the depression. By week 18 Ms A commenced a walking program. She started by walking 20 minutes a day 4 times a week, and increased this to 40 minutes a day 6 times a week by the end of the intervention.