Introduction

Weight gain (WG) and its subsequent negative health effects (e.g., diabetes, hypertension) is one of the most detrimental widespread consequences of quitting (Bush et al., 2016; Chen et al., 2021; Chio et al., 2020; Hu et al., 2018; Kos, 2020; Sung et al., 2016), and one of the main reported barriers to smoking cessation (Germeroth & Levine, 2018; Tuovinen et al., 2015; Veldheer et al., 2014). Additionally, post-cessation WG has been related to long-term tobacco relapse (Borrelli et al., 2001; Copeland et al., 2006; Salk et al., 2019), although the results are not consistent, since some studies have pointed out the absence of this relationship (see e.g., Killen et al., 1990; Perkins, 1994).

Research indicates that between 36.7% and 84% of people who quit smoking gain weight, whereas between 4%-38.9% maintain their baseline weight, and 11.4%-28.6% lose weight (Aubin et al., 2012; Bush et al., 2014; Jeremias-Martins & Chatkin, 2019; Kmetova et al., 2014; Pisinger et al., 2017). Overall, WG in abstinent individuals at one-year post-cessation, ranges from 1.67-4.86 kg in pharmacological treatments (Aubin et al., 2012; Taniguchi et al., 2014), and between 3.29 and 3.88 kg in psychological interventions (Spring et al., 2009; Tan et al., 2018). Among general population, the majority of WG appears to occur within the first six months after smoking cessation (Tan et al., 2018; Yang et al., 2013), and after a year WG stabilizes (Aubin et al., 2012; Køster-Rasmussen et al., 2015; Robertson et al., 2014).

The underlying mechanism of post-cessation WG is unclear (see e.g., Chao et al., 2019). Studies prompt that a decrease in the basal metabolic rates, an imbalance in caloric intake due to the nicotine withdrawal, an increase in appetite, or eating behavior changes, stand out as feasible explanations (Filozof & Pinilla, 2004; Gottfredson & Sokol, 2019; Jo et al., 2002; Mineur, 2011; Stojakovic et al., 2017).

Smokers with elevated depressive symptoms report greater tendency to smoke cigarettes to control appetite and weight than smokers without that condition (Larsen et al., 2009; Rosemblum et al., 2020; Weinberger et al., 2011). One recent study also indicated that smokers with high levels of depressive symptoms and weight concerns are especially vulnerable to long-term smoking relapse (Salk et al., 2019). However, to our knowledge, no study has examined the post-cessation WG among smokers with depression and its effects on abstinence rates. It is important to evaluate if depressed smokers show greater risk than average for post-cessation WG and relapse, and explore individual differences in order to develop personalized comprehensive smoking cessation interventions targeting at post-cessation weight, especially for smokers with depression.

Amid this background, this study aims were three-fold: 1) to describe WG at posttreatment and follow-ups among smokers with depression who achieved smoking abstinence at the end of treatment; 2) to examine which baseline characteristics were associated with post-cessation WG; and 3) to analyze whether WG impact on tobacco relapse at six-month follow-up.

Methods

Participants

This secondary analysis is based on a randomized controlled trial of smoking cessation treatment in smokers with depression (Clinical Trials.gov Identifier: NCT03163056). The sample was comprised of 180 smokers with depression recruited through advertisements in the local media and flyers posters in the community. Individuals were enrolled in a smoking cessation treatment at the Addictive Behaviors Clinic of the University of Oviedo (Spain). All participants provided written informed

consent, and the study protocol was approval from the research ethics committee of the local community (nº 124/15). The current study sample consisted of 125 participants who achieved tobacco abstinence at posttreatment.

The inclusion criteria were smoking at least 10 cigarettes per day during the last year, meeting the criteria for nicotine dependence according to the DSM-IV-TR (American Psychiatric Association, 2000), and having a score equal to or higher than 14 on the Beck Depression Inventory (BDI-II; Beck et al., 1996). Participants were excluded if they met diagnostic criteria for severe mental disorder other than major depressive disorder (i.e., bipolar disorder or psychotic disorder) or for substance use disorders (except for nicotine dependence), and if they were receiving either psychological or pharmacological treatment for smoking cessation at the study onset.

Participants' characteristics at baseline assessment are displayed in Table 1, including sociodemographic data, smoking-related variables, health-related variables, and body weight.

Measures

At baseline, all participants completed an ad-hoc questionnaire in which sociodemographic data (e.g., age, sex), smoking-related characteristics, health-related variables, standard drinks (10 grams of pure alcohol) of alcohol weekly, and body weight, were collected.

Smoking-related characteristics

Participants self-reported the number of cigarettes smoked per day, years of regular use, and previous quit attempts. Furthermore, two biochemical measures of tobacco consumption were collected: carbon monoxide (CO) and urine cotinine.

The Fagerström Test for Cigarette Dependence (FTCD; Fagerström, 2012; Heatherton et al., 1991) was used to evaluate nicotine dependence, whose levels correspond to very low (0-2), low (3-4) medium (5), high (6-7), and very high (8-10) nicotine dependence (Fagerstrom & Kozlowski, 1990). The urge to smoke was measured with Questionnaire of Smoking Urges - Brief (QSU; Tiffany & Drobes, 1991) where higher scores indicate a higher urge to smoke.

Health-related variables

Depressive symptomatology was measured with BDI-II (Beck et al., 1996), whose scores represent minimal (0-13), mild (14-19), moderate (20-28) and severe depression (>29). The Spielberger State-Trait Anxiety Inventory (STAI; Spielberger et al., 1970) was used to evaluate anxious symptoms, where scores are transformed in T scores, whose mean is 50, and standard deviation 10. In addition, blood pressure and pulse were assessed using a calibrated blood pressure monitor.

Weight measures

All participants were weighed in personal clothing without shoes both at baseline, posttreatment, and at one-, two-, three-, and six-month follow-up. The same calibrated digital scale was used to measure patients' weight in kilograms.

Smoking abstinence measures

Participants were categorized as nonsmokers when self-reported smoking abstinence (not even a puff) for the past 24 hours at end-of-treatment and for the last seven days at the follow-ups. Also, they had to present a breath CO level of ≤ 4 parts per million (ppm) and urine cotinine samples of ≤ 80 nanograms per milliliter (ng/ml), following prior recommendations (Benowitz et al., 2020; Karelitz et al., 2021). Breath CO and urine cotinine were respectively measured through piCO Smokerlyzer (Bedfont

Scientific Ltd, Rochester, UK) and the BS-120 analyzer (Shenzhen Mindray Bio-medical Electronics Co. Ltd., Shenzhen, China).

Intervention

Treatment conditions have been previously described elsewhere (González-Roz et al., 2019; Secades-Villa et al., 2019). On the whole, participants were randomly assigned to one of three conditions: 1) Cognitive-behavioral therapy (CBT), 2) CBT + behavioral activation (BA), or 3) CBT + BA + contingency management (CM). Treatment consisted of eight weeks of group-based therapy, maximum four people. Participants had to attend the clinic twice a week, for the therapy session and a mid-week session, whose aim was to collect biochemical samples (i.e., CO and urine cotinine). Smoking cessation was achieved through a weekly reduction of nicotine intake by 30%, thereby, participants had to attain tobacco abstinence 48-hour prior the fifth session.

Data analysis

Descriptive and frequency statistics were conducted to calculate WG at posttreatment and follow-ups. T-tests were used to examine statistical differences in WG among abstinent and relapse participants.

In order to analyze which characteristics were associated with WG at posttreatment, Pearson's correlations were calculated between baseline variables (i.e., sociodemographic, body weight, smoking-, and health-related variables) and WG at posttreatment. Subsequently, multiple linear regression by stepwise procedure was performed to examine which baseline variables predicted WG at posttreatment.

A hierarchical logistic regression was carried out to analyze whether the increase of weight at posttreatment, one-, two-, three- and six-month follow-up predicted six-

month relapse. Additionally, sex, baseline weight, and depressive symptoms measured through BDI-II were introduced as covariates. All statistical analyses were conducted using the SPSS package (V.20, Inc., Chicago, IL).

Results

Weight gain

Table 2 shows the descriptive and frequency statistics of WG at posttreatment and each follow-up based on the smoking status. Abstinent participants increased their body weight 1.85 kg at posttreatment and 3.55 kg at six-month follow-up. At the end of treatment, 40.9% of abstinent participants increased more than two kg their baseline body weight. At one-, two-, three- and six-month follow-ups, the percentage of abstinent individuals who gained at least two kg were 57.8%, 56.6%, 64.0% and 68.9%, respectively. Finally, participants who gained more than 10 kg after quitting smoking were 1.1% at the 1-month follow-up, 2.6% at 2 months, 3.8% at 3 months, and 3.4% at 6 months.

Baseline predictors of weight gain

Greater WG at posttreatment was significantly associated with a higher number of daily cigarettes smoked (r_{xy} = .187, p = .041), greater nicotine dependence (r_{xy} = .256, p = .005), lower age of initiation of tobacco use (r_{xy} = -.191, p = .036), and a higher diastolic pressure at baseline (r_{xy} = .191, p = .040) (see supplementary material).

The multiple linear regression model to predict WG was statistically significant (R^2 = .193, F = 8.495, p < .001). Results prompted that greater nicotine dependence (β = .372, p = .001) and higher diastolic pressure (β = .252, p = .021) were the only variables that significantly predicted WG at posttreatment.

Relationship between weight gain and smoking relapse

The logistic regression model tested the relationship between the WG at posttreatment and follow-ups, and smoking relapse at six months (see Table 3). The model indicated that exclusively a higher WG at posttreatment increased the likelihood of smoking relapse at six-month follow-up [B = .303, OR = 1.354 (95% CI = 1.006, 1.822), p = .046]. The rest of WGs at follow-ups did not predict subsequent smoking relapse (all p values ≥ .271).

Discussion

The current study analyzed post-cessation WG in smokers with depression who successfully achieved tobacco abstinence in a psychological treatment, and its association with long-term tobacco relapse. The highlighted results were: 1) The average of wight gain among abstinent participants was 1.85 kg at post-treatment, and 3.55 kg at six-month follow-up, 2) greater baseline nicotine dependence and higher diastolic pressure predicted an increased WG at post-treatment, and 3) greater WG at post-treatment increased the likelihood of smoking relapse at six-month follow-up.

Those participants who were abstinent at six-month follow-up gained an average of 3.55 kg, compared to 1.49 kg in smokers. Although the evidence indicates that population with depressive symptomatology gains more weight after quitting (Salk et al., 2019), these findings indicated that WG is slightly less than the WG in previous studies with smokers from the general population (Aubin et al., 2012; Spring et al., 2009). The nicotine fading implemented for smoking cessation, as well as the incorporation of basic information relative to post-cessation WG and its approach, could be accounting for this finding.

It is also noteworthy that, in line with previous findings (see e.g., Aubin et al., 2012; Bush et al., 2014; Jeremias-Martins & Chatkin, 2019; Kmetova et al., 2014; Pisinger et al., 2017), between 12.1% - 20.8% of the participants maintained or decreased their baseline weight throughout all follow-ups. This suggests that smoking cessation is not inexorably followed by WG.

According to previous studies, higher rates of nicotine dependence at baseline (Killi et al., 2019; Kmetova et al., 2014; Komiyama et al., 2013; Prod'hom et al., 2013), and baseline diastolic pressure predicted WG at post-treatment. Incorporating a prolonged gradual cessation of nicotine intake than this study does, by a 20% weekly instead of 30% for instance, could reduce withdrawal symptomatology, and therefore post-cessation WG (Baha & Le Faou, 2014; Lindson et al., 2019). Otherwise, it is well known that high diastolic pressure entails hypertension risk and coronary disease (Franklin et al., 2001; Hasegawa et al., 2019), which are considerably prevalent in obese population (DeMarco et al., 2014; Julius et al., 2000). In the absence of having assessed the participants' height, and thus the body mass index (BMI), the association found between diastolic pressure and WG could indicate that individuals with a higher BMI at baseline had greater post-cessation WG (see e. g. Lycett et al., 2011).

Post-cessation WG increased the likelihood of smoking relapse at six-month follow-up. This relationship has been evidenced in general population (Borrelli et al., 2001), women with depression (Salk et al., 2019), and among weight-concerned individuals (Clark et al., 2006; Salk et al., 2019; Tuovinen et al., 2018). This could be explained by the use of tobacco as a method of weight regulation, that is, to suppress appetite, and reduce their body weight and consequently their body dissatisfaction (Burr et al., 2020; Chao et al., 2019; Lopez Khoury et al., 2009; Seoane-Collazo et al., 2020; White et al., 2007). Tobacco abstinence, and therefore the post-cessation WG, brings

about a withdrawal syndrome characterized by changes in appetite, eating behavior changes (e. g. emotional, restrained and external eating) and a high emotional response (e. g. sadness, anxiety, anger), which causes individuals with distress intolerance to use tobacco again (Brown et al., 2005; Rosen et al., 2019). Addressing post cessation WG could have a meaningful impact on both smoking cessation rates (Leeman et al., 2006) and weight management (Bush et al., 2012; White et al., 2019), and therefore, it could prevent long-term tobacco relapse.

Incorporating weight management strategies stands out as a requirement in smoking cessation treatments (Aubin et al., 2012; Aveyard et al., 2012; Lycett et al., 2020). It may be particularly useful the implementation of nutrition education (Gottfredson & Sokol, 2019), exercise (Jain et al., 2020; Marcus et al., 1999; Prochaska et al., 2008), mindfulness or distress tolerance training for food craving (Kragel et al., 2019) and post-cessation emotional eating (Bloom et al., 2020; Burr et al., 2020), Therefore, it seems that addressing WG concerns, exercise, diet and disordered eating are key components of weight management interventions. Finally, contingency management in which both smoking cessation and weight maintenance are reinforced seem promising (Bloom et al., 2019).

This study should be interpreted in light of several limitations. First, the sample consisted mainly of women, so further research should examine post-cessation WG in a population with depression balanced by sex. Second, post-cessation weight concerns diet, disordered eating, and exercise patterns were not evaluated, which have been widely related to impact on WG and tobacco relapse (see e.g., Tuovinen et al., 2018; Veldheer et al., 2014). Third, depressive disorder has not been assessed by diagnostic scales (e.g., Hamilton Depression Rating Scale; HDRS), and depression subtypes, which have been related to differential appetite and body weight profiles, were not

identified (Silva et al., 2019). However, the BDI-II is a valid and reliable clinical tool for depression screening, psychometrically supported and widely used in community settings. Finally, participants' height was not registered, so BMI could not be calculated and, consequently, individuals with overweight or obesity were not identified (Okorodudu et al., 2010).

Despite these limitations, our study revealed that a high rate of abstinent participants gained weight and that post-cessation WG increased the likelihood of smoking relapse at six-month follow-up. Weight control strategies should be part of any comprehensive approach to nicotine addiction treatment to decrease the prevalence of smoking among individuals with depression.

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