The Multi-Component Smoking Cessation Support Programme (McSCSP) is effective in patients with severe mental disorder without gender differences

El Programa multicomponente de apoyo para el cese del tabaquismo (McSCSP) es efectivo en pacientes con trastorno mental grave sin diferencias de género

María José Jaén-Moreno*,**, Maria Paz Garcia-Portilla***,****,*****,******,*******, Fernando Sarramea*,*****,********, Teresa Bobes Bascarán***,******,*******,*********, Gonzalo Galvan**********, Eva María Diaz-Mesa**********, Susana Al-Halabi*******,*********, Edorta Elizagarate**********, Pilar Alejandra Saiz Martínez***,****,*****,******,*******, Julio Bobes***,****,*****,******,*******, Leticia Garcia-Alvarez***,****,*****,*******,*********

* Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Córdoba, España
** Departamento de Ciencias Sociosanitarias, Radiología y Medicina Física, Universidad de Córdoba, Córdoba, España
*** Instituto de Investigación Sanitaria del Principado de Asturias (ISPA), Oviedo, Asturias, España
**** Área de Psiquiatría, Universidad de Oviedo, Oviedo, Asturias, España
***** Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Oviedo, Asturias, España
****** Servicio de Salud del Principado de Asturias (SESPA), Oviedo, Asturias, España
******* Instituto de Neurociencias del Principado de Asturias (INEUROPA), Asturias, España
******** Unidad de Gestión Clínica de Salud Mental, Hospital Universitario Reina Sofía, Córdoba, España
********* Área de Personalidad, Evaluación y Tratamiento Psicológico, Universidad de Oviedo, Oviedo, Asturias, España
********** Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Valencia, España
********** Universidad Cooperativa de Colombia, Colombia
********** Universidad Autónoma de Madrid, Madrid, España
********** Unidad de Psicosis Refractarias, Hospital Psiquiátrico de Álava, Vitoria, España

Abstract

High prevalence of smoking in people with severe mental disorders (SMD) contributes to their medical morbidity and reduced life expectancy. Despite the evidence of gender differences in smoking cessation, few studies have tested those differences among people with SMD. This is a non-randomized, open-label, prospective, 9-month follow-up multicentre trial to examine gender differences in the efficacy, safety and tolerability of a Multi-Component Smoking Cessation Support Programme (McSCSP). The results showed that there were no significant differences in short- (males 44.9% vs females 57.7%, *chi-square* = 1.112, *p* = 0.292) or long-term efficacy (week 24: males 40.8%, females 42.3%, *chi-square* = 0.016, *p* = 0.901; week 36: males 36.7%, females 38.5%, *chi-square* = 0.022, *p* = 0.883) between

Resumen

La elevada prevalencia del tabaquismo en personas con trastorno mental grave (TMG) contribuye a su morbilidad médica y reduce su esperanza de vida. A pesar de la existencia de diferencias de género en el cese del tabaquismo, pocos estudios han evaluado esas diferencias en personas con TMG. Este es un ensayo multicéntrico de seguimiento prospectivo, no aleatorio, abierto de 9 meses para examinar las diferencias de género en la eficacia, seguridad y tolerabilidad de un programa multicomponente de apoyo para el cese del tabaquismo (McSCSP). Los resultados mostraron que no hubo diferencias de género significativas en la eficacia a corto (hombres 44,9% vs mujeres 57,7%, chi cuadrado = 1,112, *p* = ,292) ni a largo plazo (semana 24: hombres 40,8%, mujeres 42,0.3%, chi cuadrado = 0.016, *p* = ,901; semana 36: hombres 36,7%, mujeres 38,5%,

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Send correspondence to:
Leticia Garcia-Alvarez. CIBERSAM, Department of Psychiatry, University of Oviedo. C/ Julián Clavería, 33006 Oviedo España. Teléfono: +34 985104227. Fax: +34 985103653
E-mail: lettti@gmail.com

gender, neither controlled by diagnosis or treatment. Regarding safety and tolerability, there was significant increase in abdominal perimeter in males [from 105.98 (SD 13.28) to 108.52 (SD 14.01), t = -3.436, p = 0.002)], but not in females. However, there were no significant gender differences in adverse events (constipation, abnormal/vivid dreams, nausea/vomiting or skin rash/redness around patch site). In conclusion, we have demonstrated that is effective and safe to help either male or female patients with stabilized SMD to quit smoking. However, it might be a tendency in females to respond better to varenicline treatment in the short term. Future research with larger samples is required to more clearly determine whether or not the there are differences, in addition to their reliability and robustness.
Keywords: Gender differences; Smoking cessation; Shizophrenia; Bipolar disorder; Varenicline; Transdermal nicotine patches.

chi cuadrado = 0.022, p = ,883), incluso controlando por diagnóstico o tratamiento. Con respecto a la seguridad y la tolerabilidad, hubo un aumento significativo en el perímetro abdominal en los hombres [de 105,98 (DT 13,28) a 108,52 (DT 14,01), t = -3,436, p = ,002)], pero no en las mujeres. Sin embargo, no hubo diferencias de género significativas en los eventos adversos (estreñimiento, sueños anormales/vívidos, náuseas/vómitos o erupción cutánea/enrojecimiento alrededor de la zona del parche). En conclusión, hemos demostrado que es efectivo y seguro ayudar a los hombres y mujeres con TMG estabilizados a dejar de fumar. Sin embargo, podría haber una tendencia en las mujeres a responder mejor al tratamiento con vareniclina a corto plazo. Se requiere investigación futura con muestras más amplias para determinar con más claridad la existencia de diferencias, además de la fiabilidad y robustez.
Palabas clave: Diferencias de género; Cese del tabaquismo; Esquizofrenia; Trastorno bipolar; Vareniclina; Parches transdérmicos de nicotina.

1. Introduction

In people with severe mental disorders (SMD) and other disorders the smoking estimated prevalence is between 50-80% and 54-68% for schizophrenia and bipolar disorder, respectively (De Hert et al., 2011; Jiménez-Treviño et al., 2019; Rodriguez Muñoz, Carmona Torres, Hidalgo Lopezosa, Cobo Cuenca & Rodríguez Borrego, 2019). In some countries, the smoking rates are similar between men and women with psychotic disorders, in others like Asia females with schizophrenia are less likely to be current smokers than males (Hahn, Rigby & Galletly, 2014; Kim et al., 2013). The multi-component treatment in a clinical settings has demonstrated the importance of the motivation level in the preparation phase (Garcia-Portilla et al., 2016; Sarramea Crespo et al., 2019a; Sarramea et al., 2019b).

Research examining gender differences in smoking cessation outcomes have found some differences between males and females in the general population. Females are less likely to use nicotine replacement therapy (NRT) (Perkins, 2001), tend to have more difficulty quitting (Perkins, 2001; Reid, Pipe, Riley & Sorensen, 2009; Walker et al., 2016) and have poorer smoking-cessation treatment outcomes in large population-based treatment trials (Bjornson et al., 1995; COMMIT, 1995) with Bupropion (Scharf & Shiftman, 2004) or NRT (Davis et al., 1994; Perkins & Scott, 2008; Wetter et al., 1999). However, the unique report in patients with psychosis did not find gender differences in those variables (Filia, Baker, Gurvich, Richmond, Lewin, et al., 2014). Thus, research on this topic is needed in order to determinate which programs could be more effective in each gender.

The aim of this study was to examine gender differences in the efficacy, safety and tolerability of a Multi-Component Smoking Cessation Support Programme (McSCSP) (Garcia-Portilla et al., 2014, 2016) specifically designed for the treatment of patients with SMD under real-world clinical conditions.

2. Methods

2.1. Study design

This is a non-randomized, open-label, prospective, 9-month follow-up, multicenter study, conducted at 3 sites in Spain (Oviedo, Jaén and Vitoria) between March 2011 and June 2013 (see Garcia-Portilla et al., 2014, 2016). The Clinical Research Ethics Committee of Hospital in Oviedo approved the study protocol (Ref. 64/2010).

The McSCSP consisted of 2 phases: phase 1, before the active treatment phase, a weekly individual motivational therapy for 4 to 12 weeks; phase 2, a 12-week active treatment phase. During the active treatment phase patients received the medication and an intensive 12-week manualized group therapy on issues relevant for these patients. The choice of the pharmacological treatment for each patient was a shared decision between the clinician and the patient (for more details see Garcia-Portilla et al., 2014).

2.2. Subjects

Subjects were outpatients with a diagnosis of severe mental disorder who were clinically stable and attended their scheduled appointments. During those appointments, their psychiatrics gave them the possibility to take part in a study for smoking cessation.

Inclusion criteria: DSM-IV diagnosis of schizophrenia, schizoaffective or bipolar disorder; currently smoking ≥ 15 cigarettes/day; Fagerström Test for Nicotine Dependence score ≥ 4; breath CO > 9 ppm; 18-65 years; no suicidal ideation; and written informed consent.

Exclusion criteria: PANSS total score >70 (schizophrenia), or HDRS score >14 or YMRS >6 (bipolar disorder); serious suicidal behavior/thoughts in the last 6 months; severe unstable somatic illness; organic brain damage; renal impairment (creatinine ≥1.5 mg/dL); and liver function impairment (twice the normal upper limit).

2.3. Assessments

All subjects were assessed at baseline, during the 12-week active treatment phase, and at weeks 12 and 24 of the post-treatment follow-up phase. They were classified into three categories according the self-reported number of cigarettes smoked per day (CPD): light (CPD ≤ 10), moderate (between 11 and 20), and heavy smokers (>20). For more details about assessment see Garcia-Portilla et al., (2014, 2016).

2.4. Outcome measures and statistical analyses

The week 12 primary outcome measures were gender differences in smoking cessation (previous 7-days self-reported abstinence confirmed by breath CO levels ≤9 ppm) and in the proportion of subjects with at least a 50% reduction in the number of cigarettes per day (CPD) over the last 7 days. Secondary outcome measures were gender differences in safety, including changes in the symptoms of the primary illness and suicide attempts, and tolerability.

The SPSS 17.0 was used and the level of significance was 0.05. All analyses were performed according to an intention-to-treat approach. For dealing with missing data the last observation carried forward (LOCF) method was employed. The chi-square test, Student's t-test, and paired t-test were used to determine statistically significant differences between genders and to test for changes over time between baseline and week 12.

A mixed between-within subject analysis of variance was conducted to assess the impact of the two genders on patient smoking and clinical variables over four time periods (baseline, the 12-week active treatment phase, and at weeks 12 and 24 of the post-treatment follow-up phase).

3. Results

Out of 82 enrolled patients 75 were analyzed [(36 transdermal nicotine patch (TNP), and 39 varenicline; 72% schizophrenia/schizoaffective and 28% bipolar disorder; 65.3% males, 34.7% females (*chi-square*=4.041, *p*=0.044)]. The retention rates in the study were 61.3% (67.3% males, 53.8% females, *chi-square* = 1.323, $p = 0.250$) at week 12, 48% (49.0% males, 46.2% females, *chi-square* = 0.054, $p = 0.816$) at week 24 and 46.6% (46.9% males, 46.2% females, *chi-square* = 0.004, $p = 0.948$) at week 36. There were no statistically significant differences in the retention rates among gender neither among gender and treatments. Baseline descriptive analysis is shown in Table 1.

Efficacy

Figure 1 shows the short- and long-term efficacy for males and females. There were no significant differences in short or long-term efficacy between genders, diagnosis or treatments. Furthermore, the interaction effect between time and gender was not significant for any of the variables (Table 2).

Table 1. *Patient demographic and baseline clinical and smoking characteristics for the total sample and for male and female patients separately.*

	Total sample n= 75	Males n= 49	Females n= 26	Statistical test, *p*
Mean age (sd)	45.3 (9.0)	44.1 (9.7)	47.8 (7.2)	2.957[d], 0.090
Civil status [n (%)]				17.635[e], <0.0001
Never married	47 (62.7)	39 (79.6)	8 (30.8)	
Married or living as married	16 (21.3)	5 (10.2)	11 (42.3)	
Widowed or separated/divorced	12 (16.0)	5 (10.2)	7 (26.9)	
Educational level [n (%)]				2.500[e], 0.287
Primary school	32 (42.7)	18 (36.7)	14 (53.8)	
Secondary school	32 (42.7)	24 (49.0)	8 (30.8)	
University	11 (14.7)	7 (14.3)	4 (15.4)	
Work status [n (%)]				6.043[e], 0.110
Working (full / part-time)	7 (9.3)	5 (10.2)	2 (7.7)	
Disabled (temporary / permanent)	33 (44.0)	26 (53.1)	7 (26.9)	
Illness benefit	19 (25.3)	9 (18.4)	10 (38.5)	
Other[a]	16 (21.3)	9 (18.4)	7 (26.9)	

Table 1 (cont.). *Patient demographic and baseline clinical and smoking characteristics for the total sample and for male and female patients separately.*

	Total sample n= 75	Males n= 49	Females n= 26	Statistical test, *p*
Diagnosis [n (%)]				4.041[e], 0.044
Schizophrenia	54 (72.0)	39 (79.6)	15 (57.7)	
Bipolar	21 (28.0)	10 (20.4)	11 (42.3)	
Length of illness, months [Mean (sd)]	209.2 (125.4)	201.8 (127.1)	223.2 (123.5)	0.004[d], 0.950
First episode, yes [n (%)]	10 (13.5)	5 (10.4)	5 (19.2)	1.121[e], 0.290
Comorbid SUD [n (%)]	10 (13.3)	7 (14.3)	3 (11.5)	0.111[e], 0.739
Suicidal attempts				
Yes [n (%)]	29 (38.7)	15 (30.6)	14 (53.8)	3.867[e], 0.049
Mean number (sd)	2.8 (1.8)	2.6 (1.2)	2.9 (2.3)	3.992[d], 0.056
CGI-S [Mean (sd)]	3.5 (1.0)	3.6 (1.0)	3.5 (1.0)	0.022[d], 0.884
PANSS[b] [Mean (sd)]				
Positive	11.4 (3.8)	11.5 (3.8)	11.1 (4.0)	0.020[d], 0.887
Negative	14.9 (5.6)	15.1 (5.0)	14.4 (7.1)	0.920[d], 0.342
General psychopathology	27.2 (8.2)	26.3 (5.9)	29.5 (12.4)	2.326[d], 0.133
Total	52.2 (11.4)	52.9 (11.1)	50.3 (12.4)	0.146[d], 0.704
HDRS[c] [Mean (sd)]	5.1 (4.0)	5.6 (4.3)	4.6 (3.8)	0.322[d], 0.577
YMRS[c] [Mean (sd)]	2.9 (2.5)	1.9 (2.7)	3.7 (2.1)	1.095[d], 0.308
Self-reported CPD [Mean (sd)]	30.1 (11.8)	31.4 (12.7)	27.7 (9.8)	2.111[d], 0.150
Smoking status				0.687[e], 0.407
Moderate (self-reported CPD 11-20)	27 (36.0)	16 (32.7)	11 (42.3)	
Heavy (self-reported CPD >20)	48 (64.0)	33 (67.3)	15 (57.7)	
Breath CO levels	27.3 (18.3)	30.0 (20.6)	22.1 (11.4)	4.636[d], 0.035
FTND score	6.3 (2.6)	6.1 (2.7)	6.7 (2.4)	0.484[d], 0.489
G-NSBQ score	17.8 (6.9)	17.6 (7.3)	18.2 (6.0)	0.405[d], 0.526
Treatment				0.517[e], 0.472
TNP	36 (48.0)	25 (51.0)	11 (42.3)	
Varenicline	39 (52.0)	24 (49.0)	15 (57.7)	

Note. CGI-S: Clinical Global Impression - Severity; CO: carbon monoxide; CPD: cigarettes per day; FTND: Fagerström Test for Nicotine Dependence; GN-SBQ: Glover-Nilsson Smoking Behavioral Questionnaire; HDRS: Hamilton Depression Rating Scale; PANSS: Positive and Negative Syndrome Scale; sd: standard deviation; SUD: substance use disorder; TNP: transdermal nicotine patch; YMRS: Young Mania Rating Scale.
[a] Other includes: unemployed, housewife, student and retired.
[b] Data for PANSS are from patients with schizophrenia (n= 54).
[c] Data for HDRS and YMRS are from patients with bipolar disorder (n= 21).
[d] Student's t-test.
[e] Chi-square test.

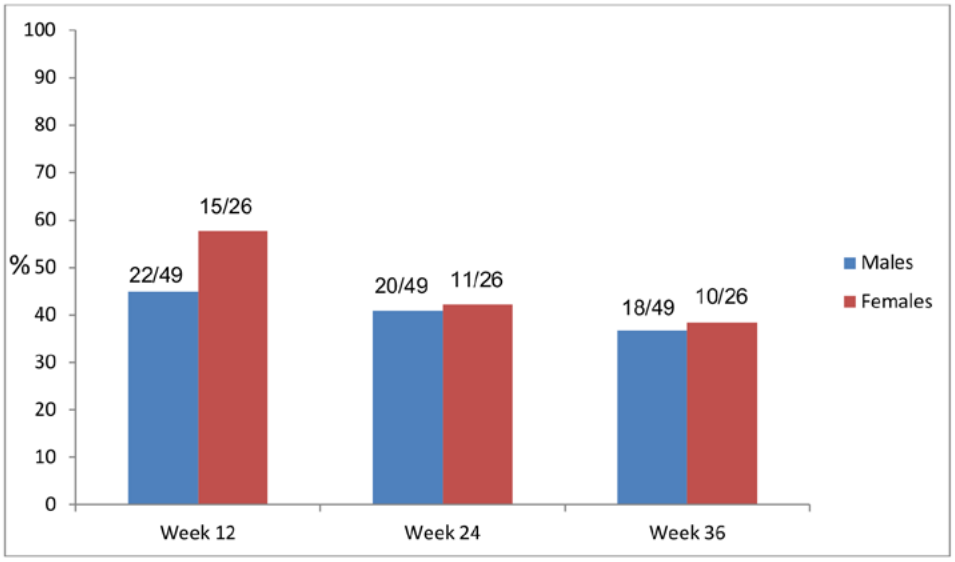

Figure 1. Short- and Long-term efficacy[a] for males and females.

Note. There were no statistically significant differences in efficacy rates between males and females at any time period.
[a] Patient's self-report of previous 7-day abstinence confirmed by breath CO levels ≤ 9 ppm.

Table 2. *Smoking characteristics for males and females across four time periods.*

	Males				Females			
	Baseline	**W12**	**W24**	**W36**	**Baseline**	**W12**	**W24**	**W36**
[mean (sd)]								
CPD	31.4 (12.7)	6.8 (8.7)	9.6 (10.5)	9.1 (9.0)	27.7 (9.8)	7.9 (12.3)	10.4 (12.2)	10.3 (12.4)
Breath CO level	30.0 (20.6)	12.4 (14.6)	13.6 (14.7)	14.4 (15.6)	22.1 (11.4)	9.2 (12.6)	11.9 (13.2)	12.2 (12.0)
FTND scores	6.1 (2.7)	2.6 (3.1)	2.8 (3.1)	3.2 (3.0)	6.7 (2.4)	2.2 (3.1)	2.9 (3.5)	3.2 (3.4)
GN-SBQ scores	17.6 (7.3)	9.0 (8.9)	9.2 (9.1)	9.7 (9.8)	18.2 (6.0)	7.5 (7.7)	9.4 (8.8)	10.2 (7.8)
Smoking[a] [n (%)]								
Abstinent		24 (49.0)	21 (42.9)	18 (38.8)		16 (61.5)	12 (46.2)	12 (46.2)
Mild		10 (20.4)	6 (12.2)	10 (20.4)		2 (7.7)	3 (11.5)	4 (15.4)
Moderate	16 (32.7)	12 (24.5)	16 (32.7)	17 (34.7)	11 (42.3)	4 (15.4)	7 (26.9)	5 (19.2)
Heavy	33 (67.3)	3 (6.1)	6 (12.2)	3 (6.1)	15 (57.7)	4 (15.4)	4 (15.4)	5 (19.2)

Table 2 (cont.).

	Statistical test		
	Interaction effect (Time*Gender) Wilks Lambda, *F, p*	**Main effect for Time Wilks Lambda, *F, p***	**Main effect for Gender *F, p***
[mean (sd)]			
CPD	0.970, (3,71) 0.741, 0.531	0.298, (3,71) 55.683, <0.0005	0.005, 0.942
Breath CO level	0.936, (3,68) 0.882, 0.455	0.586, (3,68) 16.037, <0.0005	1.349, 0.249
FTND scores	0.959, (3,71) 1.015, 0.391	0.436, (3,71) 30.646, <0.0005	0.011, 0.917
GN-SBQ scores	0.949, (3,69) 1.238, 0.303	0.434, (3,69) 30.047, <0.0005	0.000, 0.985

	Between gender Chi square, *p*	**Within gender Chi square, *p***	
		Males	**Females**
Smoking[a] [n (%)]			
Abstinent	Base: 0.687, 0.407		
Mild	W12: 4.440, 0.218	Base-W12: 59.571, <0.0005	Base-W12: 27.635, <0.0005
Moderate	W24: 0.356, 0.949	W12-24: 2.771, 0.428	W12-24: 1.590, 0.662
Heavy	W36: 4.574, 0.206	W24-36: 2.251, 0.522	W24-36: 0.587, 0.899

Note. CO: carbon monoxide; CPD: cigarettes per day; FTND: Fagerström Test for Nictoine Dependence; GN-SBQ: Glover-Nilsson Smoking Behavioral Questionnaire; TNP: transdermal nicotine patches; sd: standard deviation; W: week.
[a] Smoking self-reported status: Abstinent: self-reported CPD 0, Mild: self-reported CPD 1-10, Moderate: self-reported CPD 11-20, Heavy: self-reported CPD >20.
[b] F is presented as: (Hypothesis df, Error df) F value.

Safety and tolerability

During the 12-week active treatment no patients made suicide attempts or required hospitalization (Table 3). There was significant increase in abdominal perimeter in males [from 105.98 (SD 13.28) to 108.52 (SD 14.01), t=-3.436, p=0.002)], but not in females.

There were no significant gender differences in adverse events. The most common were constipation (14.3 males, 26.9% females), abnormal/vivid dreams (18.4 males, 15.4% females), nausea/vomiting (10.2 males, 26.9% females) and skin rash/redness around patch site (14.3 males, 15.4% females).

Variables related to cessation

At week 12, success in tobacco smoking cessation in males was associated with: lower proportion of suicide history (p= 0.020) and lower psychopathology severity (p = 0.020) and psychological nicotine dependence (p = 0.011) at baseline. In females, it was associated with being married or living as married (p= 0.047).

4. Discussion

The present study is the first to examine gender differences in the efficacy, safety and tolerability of the McSCSP specifically designed for the treatment of patients with SMD under real-world clinical conditions. It has demonstrated the effectiveness in males and females. There were not differences between groups in the cessation rates at any time point, neither controlled by diagnosis or treatment.

There were no significant gender differences on a range of smoking related variables at baseline. As in previous

Table 3. *Safety in males and females.*

	Males		
	Baseline Mean (sd)	**Week-12 Mean (sd)**	**Paired *t* test, *p***
PANSS			
- PANSS-Positive	11.5 (3.8)	10.7 (3.9)	2.252, 0.030
- PANSS-Negative	15.1 (5.0)	14.5 (5.5)	1.812, 0.078
- PANSS-General Psychopathology	26.3 (5.9)	24.2 (6.0)	2.840, 0.007
- PANSS-Total	52.9 (11.1)	49.5 (11.4)	3.099, 0.004
HDRS	5.6 (4.3)	4.9 (5.7)	0.381, 0.712
YMRS	1.9 (2.7)	2.0 (4.6)	-0.086, 0.933
CGI-S	3.6 (1.0)	3.5 (1.0)	0.206, 0.837
Weight (kg)	89.2 (18.5)	90.7 (18.7)	-3.371, 0.002
BMI (kg/m^2)	30.3 (5.8)	30.9 (5.8)	-4.126, <0.0005
Heart rate (bpm)	81.8 (15.6)	82.3 (17.8)	0.297, 0.768
Blood pressure			
- Diastolic (mmHg)	75.0 (12.6)	76.8 (11.0)	-1.255, 0.216
- Systolic (mmHg)	116.0 (17.9)	121.0 (19.5)	-1.638, 0.109
Creatinine (mg/dL)	0.9 (0.1)	0.9 (0.1)	1.807, 0.077
Urea (mg/dL)	29.2 (7.9)	29.8 (8.0)	-0.813, 0.420
Glomerular filtration rate mL/min per 1.73 m^2	100.9 (18.7)	101.4 (18.9)	-0.329, 0.744
AST (U/L)	21.6 (9.1)	22.4 (8.7)	-1.155, 0.254
ALT(U/L)	28.5 (17.0)	32.6 (21.1)	-1.933, 0.059
GGT(U/L)	42.2 (30.6)	43.4 (30.0)	-0.678, 0.501
Total bilirubin (mg/dL)	0.5 (0.2)	0.4 (0.2)	1.033, 0.308
ALP (U/L)	71.3 (21.0)	70.3 (20.9)	0.990, 0.327
Cholesterol (mg/dL)	207.2 (43.9)	198.3 (44.5)	2.281, 0.027
HDL-cholesterol (mg/dL)	40.5 (10.7)	41.4 (11.1)	-1.300, 0.200
LDL-cholesterol (mg/dL)	134.3 (41.9)	120.8 (40.9)	2.823, 0.009
Triglycerides (mg/dL)	202.6 (142.5)	224.4 (158.8)	-1.357, 0.184

Table 3 (cont.).

	Females		
	Baseline Mean (sd)	**Week-12 Mean (sd)**	**Paired *t* test, *p***
PANSS			
- PANSS-Positive	11.1 (4.0)	8.9 (2.2)	2.219, 0.044
- PANSS-Negative	14.4 (7.1)	15.0 (7.6)	-0.402, 0.694
- PANSS-General Psychopathology	29.5 (12.4)	24.3 (7.0)	1.549, 0.144
- PANSS-Total	50.3 (12.4)	48.2 (13.1)	0.477, 0.641
HDRS	5.0 (3.8)	4.8 (4.8)	0.210, 0.838
YMRS	4.1 (1.9)	2.7 (3.9)	1.288, 0.230
CGI-S	3.5 (1.0)	3.3 (1.0)	1.309, 0.203
Weight (kg)	79.4 (14.2)	81.9 (14.1)	-3.375, 0.003
BMI (kg/m^2)	31.5 (5.7)	32.6 (5.8)	-3.594, 0.002
Heart rate (bpm)	85.6 (16.4)	81.3 (15.6)	1.456, 0.160
Blood pressure			
- Diastolic (mmHg)	75.8 (9.2)	77.2 (9.5)	-0.811, 0.426
- Systolic (mmHg)	115.4 (14.2)	116.4 (11.5)	-0.279, 0.783
Creatinine (mg/dL)	0.7 (0.1)*	0.7 (0.1)*	-2.119, 0.045
Urea (mg/dL)	34.6 (9.9)	33.7 (10.4)	0.571, 0.574
Glomerular filtration rate mL/min per 1.73 m^2	98.2 (23.3)	92.4 (17.1)	2.191, 0.043
AST (U/L)	17.5 (5.6)	19.3 (8.4)	-1.187, 0.248
ALT(U/L)	19.8 (8.2)	22.3 (15.4)	-0.738, 0.468
GGT(U/L)	31.0 (18.6)	31.4 (18.9)	-0.387, 0.702
Total bilirubin (mg/dL)	0.4 (0.2)**	0.4 (0.2)**	-2.127, 0.045
ALP (U/L)	76.2 (19.9)	73.8 (18.7)	1.470, 0.155
Cholesterol (mg/dL)	206.4 (39.2)	209.7 (36.9)	-0.944, 0.355
HDL-cholesterol (mg/dL)	51.8 (10.8)	52.6 (10.5)	-0.796, 0.434
LDL-cholesterol (mg/dL)	132.4 (29.7)	129.4 (31.3)	0.522, 0.610
Triglycerides (mg/dL)	134.8 (109.8)	148.3 (104.0)	-1.522, 0.149

Note. ALP: alkaline phosphatase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; CGI-S: Clinical Global Impression - Severity; GGT: gamma glutamyl transferase; HDL: High-density lipoprotein; HDRS: Hamilton Depression Rating Scale; LDL: low-density lipoprotein; PANSS: Positive and Negative Syndrome Scale; sd: standard deviation; YMRS: Young Mania Rating Scale. *Baseline 0.7096 (0.11767); Week-12 0.7308 (0.10480); ** 0.3565 (0.17629); 0.3700 (0.18918).

studies we found fewer gender differences in smokers with SMD compared to those in the general population (Filia et al., 2014). People with SMD (males and females) have higher rates of smoking (Kumari & Postma, 2005) and nicotine dependence than smokers in the general population, they smoke more cigarettes per day and have higher FTND scores (Gurpegui et al., 2005), so this may make smokers with severe disorders a more homogenous group (Filia et al., 2014).

As in scarce previous studies in patients with mental illness (Filia et al., 2014), there are no gender differences in the cessation rates which is different from the general population where females have more difficulty quitting and poorer smoking-cessation treatment outcomes (McKee, O'Malley, Salovey, Krishnan-Sarin & Mazure, 2005; Perkins & Scott, 2008; Reid et al., 2009; Smith, Bessette, Weinberger, Sheffer & McKee, 2016). However, in spite of this lack of significant differences, the cessation rate at 12-week looks higher in females. At 24-week and 36-week the cessation rate looks the same. These results are of interest since it looks like males who achieve short-term abstinence keep it while a high percentage of women return smoking after abstinence (15.4% vs 4.1%).

There were not psychopathological exacerbations, neither suicide attempts or hospitalizations. Moreover, males improved more than females, decreassing PANSS positive, general psychopathology and total scores, while females just improved in positive symptomatology. According previous studies (Ostacher et al., 2006), there is an association between smoking and greater severity of the mental disorder, so maybe the smoking cessation of those patients could contribute to this improvement. Other studies find that higher PANSS total scores are less frequent in mildly dependent smokers (Aguilar, Gurpegui, Diaz & De Leon, 2005).

Smoking cessation is frequently associated with weight gain (Aubin, Farley, Lycett, Lahmek & Aveyard, 2012). In agreement with this, we found that both, males and females, experienced significant increases in weight (around 4 kg) and BMI and, males, in abdominal perimeter as well. As in previous studies (Filia, Baker, Gurvich, Richmond & Kulkarni, 2014), there were no gender differences regarding weight increased.

In this study, the variables related to successful tobacco smoking cessation at week-12 in males were the lack suicide history and lower psychological nicotine dependence and psychopathology severity (CGI-S) at baseline. In females the variable related to successful tobacco smoking cessation was civil status, specifically be married or living as married. Among males and females with mental illness, baseline expired CO level and a greater number of visits to the program have been shown as predictive of smoking cessation while among males, having a history of alcohol, heroin and other opioids, and marijuana use were predictive of unsuccessful smoking cessation (Okoli et al., 2011). The knowledge about the factors related with the successful tobacco smoking cessation may be important in the design of future smoking cessation programs for individuals with SMD.

Our results should be interpreted in light of a series of methodological limitations. First, the relatively small sample size in each group, which can be related with the absence of more gender differences. For this reason, we did not divide each gender group by diagnosis, in spite the significant differences. Secondly, this study was conducted with a sample of smokers with psychosis and bipolar disorders, so they are not a homogeneous group.

In conclusion, we have demonstrated that is effective and safe to help patients either males or females with stabilized SMD to quit tobacco. Future research with larger samples is required in order to more clearly determine if there are or not differences and the reliability and robustness of them.

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