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Araştırma Makalesi/Research Article

The Effect of Varenicline, Nicotine Replacement, and Acupuncture for Smoking Cessation

Sigarayı Bırakmada Vareniklin, Nikotin Replasmanı ve Akupunkturun Etkisi

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Abstract: Aim: Various methods are used in the treatment of cigarette addiction. The aim of the study is compare the smoking cessation status of patients who applied for smoking cessation treatment and received varenicline treatment, nicotine replacement therapy (NRT), and acupuncture treatment. Methods: In the study, 402 individuals who received varenicline treatment, NRT, and acupuncture treatment for smoking cessation were included. The sociodemographic data of the individuals, the results of the Fagerström nicotine dependence test, and the data on smoking cessation obtained during the 6 months after the treatment were retrospectively scanned from the patient files. Results: Of the 402 individuals included in the study, 60.4% (n=243) were treated with varenicline, 28.1% (n=113) received NRT, and 11.4% (n=46) were treated with Acupuncture. 63.4% (n=255) of all the patients, 71.2% (n=173) of the patients treated with varenicline, 56.6% (n=64) of the patients who received NRT, and 39.1% (n=18) of the patients treated with Acupuncture quit smoking. It was found that the smoking cessation rate was higher in the patients treated with varenicline compared to other treatments (p<0.001), and varenicline was more effective than other treatments in very high addiction (p<0.001). Conclusion: Varenicline treatment, NRT, and acupuncture treatment are all effective methods for smoking cessation. Varenicline treatment is more effective in smoking cessation than other treatments, and this efficiency is higher than other treatments for very high addiction.

Keywords: Smoking cessation, Varenicline, Nicotine replacement therapy, Acupuncture.

Öz: Amaç: Sigara bağımlılığının tedavisinde çeşitli yöntemler kullanılmaktadır. Çalışmanın amacı sigara bırakma tedavisi için başvuran ve vareniklin tedavisi, nikotin replasman tedavisi (NRT) ve akupunktur tedavisi alan hastaların sigarayı bırakma durumlarının karşılaştırılmasıdır. Yöntemler: Çalışmaya vareniklin tedavisi, NRT ve sigarayı bırakma amaçlı akupunktur tedavisi alan 402 kişi dahil edildi. Bireylerin sosyodemografik verileri, Fagerström nikotin bağımlılık testi sonuçları ve tedavi sonrası 6 ay içerisinde sigarayı bırakmaya ilişkin veriler hasta dosyalarından geriye dönük olarak tarandı. Bulgular: Çalışmaya dahil edilen 402 kişinin %60,4'ü (n=243) vareniklin, %28,1'i (n=113) NRT, %11,4'ü (n=46) Akupunktur tedavisi aldı. Tüm hastaların %63,4'ü (n=255), vareniklin tedavisi alan hastaların %71,2'si (n=173), NRT alan hastaların %56,6'sı (n=64), Akupunktur tedavisi gören hastaların %39,1'i (n=18) hastalar sigarayı bıraktı. Vareniklin tedavisi gören hastalarda sigarayı bırakma oranının diğer tedavilere göre daha yüksek olduğu (p<0,001), çok yüksek bağımlılıkta ise vareniklinin diğer tedavilere göre daha etkili olduğu (p<0,001) belirlendi. Sonuç: Vareniklin tedavisi, NRT ve akupunktur tedavisi sigarayı bırakmada etkili yöntemlerdir. Vareniklin tedavisi sigarayı bırakmada diğer tedavilere göre daha etkilidir ve çok yüksek bağımlılık durumlarında bu verim diğer tedavilere göre daha yüksektir.

Anahtar Kelimeler: Sigarayı bırakma, Vareniklin, Nikotin replasman tedavisi, Akupunktur.

Introduction

Smoking addiction is a common public health problem all over the world, and one out of every three people in the world is addicted to tobacco. Most smokers want to quit smoking, but

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their success rate is very low (4-7%) without help (Hurt, Ebbert, Hays and McFadden, 2009). Pharmacological treatments increase the probability of success in smoking cessation. However, most smokers do not use either pharmacotherapy or behavioral counseling in their smoking cessation attempts (Zeng, Chen, Mastey, Zou, Harnett and Patel, 2011). Any treatment modality applied to smokers is beneficial for patients during the smoking cessation process (Raja, Saha, Krishna-Reddy, Mohd, Narang and Sood, 2016). Choosing the most suitable treatment method for the individual will increase the success rate in the treatment of cigarette addiction.

Varenicline, with its agonist and antagonist functions, reduces the desire to smoke and prevents the emergence of withdrawal symptoms (Argüder et al., 2013). With nicotine replacement therapy (NRT), the majority of the nicotine taken from cigarettes is temporarily externally provided (Stead et al., 2012). Acupuncture causes an increase in dopamine, serotonin, endorphin, norepinephrine, epinephrine, and enkephalin levels in the central nervous system and plasma. Acupuncture application is thought to prevent the psychological symptoms that occur as a result of the deterioration of cigarette taste, the decrease in the desire to smoke, and smoking cessation (Cabioglu, Ergene and Tan, 2007).

This study aims to compare the smoking cessation rates in individuals who received varenicline, NRT, and Acupuncture as a smoking cessation treatment.

Materials and Methods

This non-randomized retrospective experimental study included individuals who applied to a Smoking Cessation outpatient clinic and Traditional and Complementary Medicine outpatient clinic of the Family Medicine Department of a University Hospital between January and October 2019 and who received varenicline, NRT, or Acupuncture for smoking cessation treatment. The following data were retrospectively scanned from the patient files: sociodemographic information about the individuals included in the study, information form to evaluate smoking behavior, Fagerström nicotine dependence test (FTND) results, and the data on smoking cessation at the 6th month after the completion of the treatments. Individuals with missing information in their files were excluded from the study.

The sociodemographic data form included the following information: age, gender, and occupation.

The information form used to evaluate the patients' smoking-related behaviors included the following information: duration of smoking (pack/year); number of smoking cessation attempts; if any, the methods used to quit smoking; whether there is a history of additional disease; symptoms about respiratory system (cough, sputum, reduced effort capacity, shortness

of breath). The control examinations performed six months after the end of the treatment contained some information about the smoking cessation status.

Fagerström Test for Nicotine Dependence was first put forward by Fagerström in 1978 and reconsidered in 1991 by Heatherton et al. Validity and reliability studies of the test in our country were conducted by Uysal, Kadakal, Karşidağ, Bayram, Uysal and Yilmaz (2004). The scale, which is widely used to determine nicotine addiction, consists of six questions (Uysal et al., 2004).

The patients who applied to the smoking cessation clinic were first evaluated, and then varenicline treatment or NRT was started. Varenicline treatment was given for 12 weeks. NRT treatment was given for 2-8 weeks. In this study, ear acupuncture and body acupuncture were applied twice a week for eight weeks for smoking cessation in traditional and complementary medicine polyclinics (Wang et al., 2016).

IBM SPSS software package (v.22.0, IBM) was used in the statistical data analysis. Considering the distribution of data in comparison between groups, student-t test was used for normally distributed values and the Mann-Whitney U test for non-parametric data. Categorical data were compared using the chi-square test. Statistical significance was set at p<0.05.

The local ethics committee approved our study (Approval No: 2020/211, 14/05/2020).

Results

During the study period, 454 patients applied to quit smoking. Of these patients, 52 were excluded from the study because they did not attend follow-up. The study was conducted with the data of 402 people: 243 (60.4%) in the varenicline group, 113 (28.1%) in the NRT group, and 46 (11.4%) in the acupuncture group (Figure 1).

The mean age of the whole group was 39.67±13.04 years, and 34.6% (n=139) of them were female and 65.4% (n=263) were male. In our study, the rate of males was higher among all the patients, including those receiving NRT and varenicline treatment, while the rate of females was higher among those receiving acupuncture treatment.

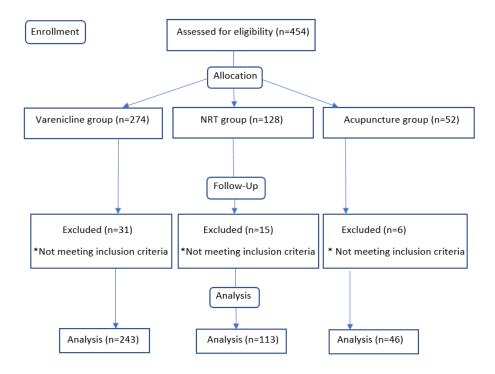


Figure 1. Flow Diagram of The Study

Most of the participants (54.7%) in our study were between the ages of 31 and 50 (p=0.024). Those who were working constituted the significant majority (24.9%) (p<0.001). In the acupuncture group, the rate of non-working individuals (unemployed or housewives) (50.0%) was significantly higher (p<0.001).

22.4% of the whole group had a history of comorbidity, with cardiovascular diseases (CVD) having the highest incidence (38.9%). As for the symptoms related to the respiratory system, 60.4% of the whole group had no symptoms. Cough was the most common symptom (37.7%).

The FTND mean score of the whole study group was 7.17 ± 2.1 . When the treatment groups were compared in terms of their FTND mean scores, it was found that the acupuncture group had a significantly higher score than the other groups (p=0.005). When the addiction levels were examined according to FTND scores, it was found that 49.8% of the whole group was highly dependent, and there was no significant difference between the treatment groups (p=0.128).

Table 1: The Demographical Characteristics and Smoking Habits of Participants

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No 147 (36.6) 70 (28.8) 49 (43.4) 28 (60.9)		255 (63.4)	173 (71.2)	64 (56.6)	18 (39.1)	$0.000\mathrm{a}$
T 1 (0)		, ,		, ,	, ,	
	Total, n (%)	402 (100)	243 (60.4)	113 (28.1)	46 (11.4)	0.000 a

^aChi square test, ^bANOVA test; n, number; SD, Standard Deviation; NRT, Nicotine Replacement Therapy; CA, Cigarette amount; PQT, Previous quitting trial; PUM, Previously used method; FTND, Fagerström Test for Nicotine Dependence; ADH, Additional disease history; CVD, Cardio vascular disease; DEC, Decrease in effort capacity.

The average smoking amount of the whole group was 20.4 ± 12.1 packs/year, and the rate of the individuals who smoked between 11 and 20 packs/year (35.8%) was significantly higher (p<0.001). When the treatment groups were compared in terms of cigarette packs/year, it was found that the rate of those smoking ≤ 10 packs/year was lower in the acupuncture group (8.7%) than in the other groups (p<0.001). It was found that 50.0% of the whole group had never attempted to quit smoking before. When the treatment groups were compared, the rate of those who did not try to quit smoking before was significantly higher in the acupuncture group (87.0%) than in the other groups (p<0.001). In the individuals who tried to quit smoking before, the rate (45.0%) of those who did not receive any support was higher than the rates of those who received pharmacological (NRT 3.7%, bupropion 0.2%) or psychosocial (0.7%) support (p<0.001).

The rate of smoking cessation at the follow-up six months later was 63.4%, and the rate of quitting smoking was significantly higher in the patients who received varenicline treatment (71.2%) compared to the NRT and acupuncture groups (p<0.001) (Table 1).

When those who quit smoking and those who were not able to quit smoking were compared at the follow-up six months later, the rate of those who quit smoking was 63.4%, which was significantly higher than the rate of those who could not (p<0.001). No significant difference existed between the groups in terms of gender, age, occupation, history of the additional disease, presence of respiratory symptoms, FTND score, amount of cigarettes smoked (packs/year), history of smoking cessation, and methods used in previous quitting attempts. However, a significant difference was observed in the treatment methods used. Accordingly, the rate of quitting smoking was significantly higher in those who received varenicline treatment than those who received NRT and acupuncture treatment (p<0.001) (Table 2).

When the smoking cessation rates of the treatment groups were compared in terms of the addiction levels determined by FTND, it was found that there was no statistically significant difference between those with very low, low, moderate, and high levels of addiction. However, among the very highly addicted patients, the rate of quitting smoking was significantly higher in those who received varenicline treatment than those who received NRT and acupuncture treatment (p<0.001) (Table 3).

Table 2: Parameters That Considered to Effect Quitting Success

Variables	All Patients	Quit sm	oking	p
		Yes	No	
Gender, n (%)				0.364a
Female	139 (36.4)	84 (60.4)	55 (39.6)	
Male	263 (65.4)	171 (65.0)	92 (35.0)	
Age Groups (year)	$39.6 \pm 13.0 (18-72)$	39.1 ± 12.7	40.6 ± 13.5	0.274^{b}
Mean ± SD (min-max)	37.0 ± 13.0 (10 72)	37.1 = 12.7	40.0 ± 15.5	0.728 a
(30, n (%)	102 (25.4)	67 (65.7)	35 (34.3)	0.720
31-50, n (%)	220 (54.7)	140 (63.6)	80 (36.4)	
	80 (19.9)	48 (60.0)		
251, n (%) Occupation, n (%)	80 (19.9)	46 (00.0)	32 (40.0)	0.294 a
Not working	84 (20.9)	53 (63.1)	27 (36.9)	0.274
Retired	47 (11.7)	25 (53.2)	22 (46.8)	
Vorker	100 (24.9)	63 (63.0)	37 (37.0)	
Officer	88 (21.9)	63 (71.6)	25 (28.4)	
Student	48 (11.9)	27 (56.3)	21 (43.8)	
	35 (8.7)	24 (68.6)		
self-employment	33 (0.1)	24 (00.0)	11 (31.4)	0.7400
ADH, n (%)	212 (77.6)	201 (64.4)	111 (25.6)	0.542 a
Vo	312 (77.6)	201 (64.4)	111 (35.6)	
Chronic lung disease	7 (1.7)	5 (71.4)	2 (28.6)	
Diabetes mellitus	11 (2.7)	9 (81.8)	2 (18.2)	
CVD	35 (8.7)	20 (57.1)	15 (42.9)	
Psychiatric illness	12 (3.0)	6 (50.0)	6 (50.0)	
Other	25 (6.2)	14 (56.0)	11 (44.0)	
System query, n (%)	242 (62.1)	150 / 50 00	00 (27.0)	0.137 a
No	243 (60.4)	153 (63.0)	90 (37.0)	
Sputum	44 (10.9)	33 (75.0)	11 (25.0)	
DEC	34 (8.5)	23 (67.6)	11 (32.4)	
Shortness of breath	21 (5.2)	15 (71.4)	6 (28.6)	
Cough	60 (14.9)	31 (51.7)	29 (48.3)	
TND (mean ± SS)	7.17 ± 2.1	7.07 ± 2.0	7.34 ± 2.2	0.227 b
Very little, n (%)	15 (3.7)	10 (3.9)	5 (3.4)	0.568 a
Little, n (%)	31 (7.7)	17 (6.7)	14 (9.5)	
Medium, n (%)	38 (9.5)	26 (10.2)	12 (8.2)	
High, n (%)	118 (29.4)	80 (31.4)	38 (25.9)	
Very high, n (%)	200 (49.8)	122 (47.8)	78 (53.1)	
CA (pack / year)	$20.4 \pm 12.1(1-60)$	19.7 ± 11.6	21.6 ± 13.0	0.129 b
nean ± SD (min-max)				0.060 a
≤10, n (%)	102 (25.4)	62 (60.8)	40 (39.2)	
1-20, n (%)	144 (35.8)	103 (71.5)	41 (28.5)	
21-30, n (%)	96 (23.8)	58 (60.8)	38 (39.6)	
231, n (%)	60 (14.9)	32 (53.3)	28 (46.7)	
PUM, n (%)	(/	- (200)	- ()	0.861 a
No support,	181 (45.0)	113 (62.4)	68 (37.6)	3.001
VRT	15 (3.7)	11 (73.3)	4 (26.7)	
Psychosocial support	3 (0.7)	2 (66.7)	1 (33.3)	
Supropion	1 (0.2)	1 (100)	0	
Not tried	202 (50.2)	128 (63.4)	74 (33.3)	
PQT, n (%)	202 (30.2)	120 (05.7)	17 (33.3)	0.975 a
Vot tired	201 (50.0)	127 (63.2)	74 (36.8)	0.713
			, ,	
time	127 (31.6)	82 (64.6)	45 (35.4)	
time	46 (11.4)	28 (60.9)	18 (39.1)	
3	28 (7.0)	18 (64.3)	10 (35.7)	0.000.0
Treatment, n (%)	242 (60.4)	172 (71.2)	70 (20 0)	0.000 a
Varenicline	243 (60.4)	173 (71.2)	70 (28.8)	
NRT	113 (28.1)	64 (56.6)	49 (43.9)	
Acupuncture	46 (11.4)	18 (39.1)	28 (60.9)	*
Total, n (%)	402 (100)	255 (63.4)	147 (36.6)	0.000

^aChi square test, ^bIndependent sample t test (in evaluation of mean values); n, number; SD, Standard Deviation; NRT, Nicotine Replacement Therapy; CA, Cigarette amount; PQT, Previous quitting trial; PUM, Previously used method; FTND, Fagerström Test for Nicotine Dependence; ADH, Additional disease history; CVD, Cardio vascular disease; DEC, Decrease in effort capacity.

Discussion

In our study, it was found that 63% of cigarette addicts quit smoking at the end of the 6th month. The quit rate was significantly higher in the varenicline group (71.2%) than in the NRT (56.6%) and acupuncture groups (39.1%). No significant difference was found between those who quit smoking and those who did not in terms of gender, age, occupation, history of additional disease, presence of symptoms related to the respiratory system, amount of cigarettes used (packs/year), history of smoking cessation, and the methods used in the previous quit attempts. While most of the similar studies (Demir et al., 2004; Gonzales et al., 2006; Argüder et al., 2013; Yaşar, Kurt, Talay and Kargı, 2014) reported no difference between genders in terms of smoking cessation, some of them reported that men were more successful in smoking cessation (Gourlay, Forbes, Marriner, Pethica and McNeil, 1994). The previous studies examining the effect of age also found different results, and the majority of them reported that success in quitting smoking was directly proportional to age (Gourlay et al., 1994; Argüder et al., 2013; Ucar et al., 2014; Chen and Wu, 2015).

Table 3: Comparison of Cessation Rates According to FTND Scores of Varenicline, NRT and Acupuncture Group

FTND	Smoking	Varenicline	NRT	Acupuncture	Total	p
	cessation	n (%)	n (%)	n (%)	n (%)	
Very little	Yes	7 (77.8)	3 (50.0)	0	10 (66.7)	
	No	2 (22.2)	3 (50.0)	0	5 (33.3)	
	Total	9 (100)	6 (100)	0	15 (100)	0.264^{a}
Little	Yes	14 (63.6)	3 (37.5)	0	17 (54.8)	
	No	8 (36.4)	5 (62.5)	1 (100)	14 (45.2)	
	Total	22 (100)	8 (100)	1 (100)	31 (100)	0.238^{a}
Middle	Yes	18 (66.7)	7 (70.0)	1 (100)	26 (68.4)	
	No	9 (33.3)	3 (30.0)	0	12 (31.6)	
	Total	27 (100)	10 (100)	1 (100)	38 (100)	0.774^{a}
High	Yes	50 (67.6)	20 (74.1)	10 (58.8)	80 (67.8)	
	No	24 (32.4)	7 (25.9)	7 (41.7)	38 (32.2)	
	Total	74 (100)	27 (100)	17 (100)	118 (100)	0.572^{a}
Very high	Yes	84 (75.7)	31 (50.0)	7 (25.9)	124 (62)	
•	No	27 (24.3)	31 (50.0)	20 (74.1)	76 (38)	
	Total	111 (100)	62 (100)	27 (100)	200 (100)	0.000^{a}
Total	Yes	173 (71.2)	64 (56.6)	18 (39.1)	255 (63.4)	
	No	70 (28.8)	49 (43.4)	28 (60.9)	147 (36.6)	
	Total	243 (100)	113 (100)	46 (100)	402 (100)	0.000^{a}

^aChi square test; n, number; NRT, Nicotine Replacement Therapy; FTND, Fagerström Test for Nicotine Dependence.

Dependence on smoking has two types: physical and psychological. Physical dependence is the physiological desire for the presence of a substance due to an adaptation to the substance used. Psychological addiction, on the other hand, is a person's addiction to that substance to satisfy their needs due to their emotional structure or personality structure (Üzer, 2018). When

the FTND scores of our study group were examined, it was found that 49.8% of them were highly dependent, and the average amount of smoking was 20.4±12.1 packs/year. The smoking cessation rate among the very highly addicted patients was significantly higher in those who received varenicline treatment than those who received NRT and Acupuncture. Today, NRT is the most widely used and preferred treatment among the nicotine-containing and non-nicotine-containing pharmacological treatments recommended by the World Health Organization (WHO) and included in all smoking cessation guidelines. It has been reported that the rate of quitting smoking for one year with NRT varies between 15 and 25%. In a meta-analysis of 53 studies involving 17,703 cases in which various forms of NRT were used, it was shown that NRT doubled the rate of quitting smoking in the long term (6-12 months) (Er et al., 2002).

In the meta-analysis conducted by Fiore, Smith, Jorenby and Baker (1994) and including 17 studies, the six-month success rates were found to be 22% with NRT and 9% with placebo. In his study, Demir et al. (2004) reported that the one-year success rate was 33.6% in the NRT group, while it was 10.9% in the untreated group (Demir et al., 2004). In our study, it was found that 56.6% of the patients who received NRT at the end of the 6th month quit smoking, and this rate is quite high. These people applied to the smoking cessation clinic and had the intention to quit, and some motivational interviews were done with the patients in addition to NRT. Lindson, Chepkin, Ye, Fanshawe, Bullen and Hartmann-Boyce (2019) reported in a meta-analysis that there was high-quality evidence that NRT increased the quit rates in six months or longer in the adults motivated to quit. These results show us that NRT is effective in smoking cessation and this effect can be increased by motivational interviews (Lindson et al., 2019).

In our study, smoking cessation rates were found to be higher in the varenicline group compared to NRT and acupuncture groups. Gonzales et al. (2006) found that varenicline was more efficacious than placebo at all time points. In their study, Aubin et al. (2008) compared varenicline and NRT and found that the rate of abstinence from smoking was higher, and the levels of craving, withdrawal symptoms, and smoking satisfaction were lower at the end of the treatment with varenicline than with the transdermal NRT (Aubin et al., 2008). In the study by Garrison and Dugan (2009), varenicline was found to be more effective than other treatments for smoking cessation. A meta-analysis by Cahill, Stevens, Perera and Lancaster (2013) showed that methods such as NRT, bupropion, and varenicline increased the chance of quitting compared to placebo, and varenicline was more effective than both NRT and bupropion. In the meta-analysis carried out by Wu, Sun, He and Zeng (2015), NRT and varenicline were found to be effective in smoking cessation in individuals who did not intend to quit, but this effect

was not observed in behavioral support and bupropion. None of the individuals in our study group were using bupropion, so we could not make a comparison related to bupropion. However, the rate of quitting smoking with varenicline was found to be 71.2%, and this result was considerably higher than the results of similar studies (Argüder et al., 2013). This may be because the patients received motivational interviewing along with the treatment.

Acupuncture is a traditional Chinese therapy (White, Rampes and Ernst, 2002). In our study, 39.1% of the individuals who preferred Acupuncture for smoking cessation quit smoking. In their research including a meta-analysis of 6 studies (823 patients), Tahiri, Mottillo, Joseph, Pilote and Eisenberg (2012) reported that Acupuncture was an effective method for smoking cessation. Clavel-Chapelon, Paoletti and Benhamou (1997) found that smoking cessation rates after 4 years of treatment with Acupuncture and nicotine gum were quite similar. In their study, He, Berg and Høstmark (1997) reported that 31% of the individuals quit smoking after an acupuncture treatment applied to the points used to prevent smoking; however, nobody quit smoking in the control group in which the acupuncture treatment was applied to the issues that were thought to not affect quitting smoking, so choosing the right treatment points could affect the success in acupuncture (He et al., 1997). In the study by Wu, Chen, Liu, Lin and Hwang (2007), Acupuncture was found to cause a significant decrease in thenicotine withdrawal symptom score. In their study, Bier, Wilson, Studt and Shakleton (2002) reported that while the smoking cessation rate was 10% in the acupuncture application alone, it increased to 40% when it was applied along with education. We think that the reason why the smoking cessation rates were low in our study was because the acupuncture group smoked more packs/year and had a higher level of addiction, and the number of patients who could not quit smoking despite having tried any method before was high. Still, our rates were high compared to other studies.

Our study is limited in that it is a single-center and retrospective study. There is a need for multicenter and prospective studies involving more individuals in the future. The strength of our study lies in that it compares the frequently used smoking cessation treatment methods, that is, varenicline treatment, NRT, and Acupuncture.

Conclusion

Our study shows that varenicline treatment, NRT, and Acupuncture are effective methods in smoking cessation, varenicline treatment is more effective than NRT and Acupuncture, varenicline is more effective in highly dependent individuals, and Acupuncture is much less effective than the other methods. Acupuncture may be considered in individuals for whom

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pharmacological treatment is contraindicated. Future studies should be carried out with larger samples and more extended follow-up periods in order to evaluate the long-term results of varenicline, NRT, or Acupuncture in smoking cessation.

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