

Which form of nicotine replacement therapy is more effective for quitting smoking? A study in Tehran, Islamic Republic of Iran

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أي نمط من أنماط المعالجة باستعاضة النيكوتين أكثر فعالية في الإقلاع عن التدخين؟ دراسة من طهران، جمهورية إيران الإسلامية
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الخلاصة: يمكن للمعالجة باستعاضة النيكوتين أن تضاعف فرص نجاح محاولات المدخنين في الإقلاع عن التدخين. وتهدف هذه الدراسة القائمة على الملاحظة إلى مقارنة معدلات الإقلاع عن التدخين لمختلف تركيبات الاستعاضة عن النيكوتين بين المحالين إلى عيادات الإقلاع عن التدخين في طهران، جمهورية إيران الإسلامية. وقد شارك المُدرِّجون في الدراسة (وعددهم 308) في 4 جلسات للمعالجة السلوكية، واختاروا نمطاً من أنماط الاستعاضة عن النيكوتين (الرقع، أو مضغ العلكة (اللبان)، أو الأقراص، أو كل من الرقعة والعلكة) ليستخدموه، وتم متابعتهم لمدة اثني عشر شهراً. وبعد أربعة أسابيع من الإقلاع عن التدخين، أبلغ 88.2% (246/279) عن امتناعهم عن التدخين. وبلغت معدلات الإبلاغ الذاتي عن الاستمرار في الإقلاع عن التدخين 54.9% بعد 6 أشهر، و 36.2% بعد 12 شهراً من المتابعة. ووجد ترابط يُعْتَدُّ به بين نمط الاستعاضة عن النيكوتين ومعدل الإقلاع. فقد أدَّى استعمال رقع النيكوتين ومضغ العلكة معاً إلى أعلى معدل للإقلاع (95.2%) بعد 4 أسابيع وبعد 12 شهراً من المتابعة (62.5%). وأظهرت الدراسة أن استخدام نمطين من المعالجة بالاستعاضة عن النيكوتين يمكن أن يحسن معدلات الإقلاع عن التدخين لأمد طويل.

ABSTRACT Nicotine replacement therapy can double the chance of success for smokers attempting to quit. This observational study aimed to compare quit rates of different formulations of nicotine replacement among clients referred to a smoking cessation clinic in Tehran, Islamic Republic of Iran. Clients entering the study ($n = 308$) participated in 4 sessions of behavioural therapy, chose a type of nicotine replacement to use (patches, chewing gum, tablets or both patches and gum) and were followed up for 12 months. After 4 weeks of quitting, 88.2% (246/279) reported abstaining from smoking. Self-reported maintenance rates for quitting were 54.9% after 6 months and 36.2% after 12 months follow-up. A significant correlation was found between type of nicotine replacement and quit rate. Use of nicotine patches and chewing gum together had the highest quit rate (95.2%) after 4 weeks and at 12 months follow-up (62.5%). Consuming 2 forms of nicotine replacement in therapy could result in enhanced rates of long-term quitting.

Quelle forme de thérapie de substitution à base de nicotine est plus efficace pour arrêter de fumer ? Une étude à Téhéran (République islamique d'Iran)

RÉSUMÉ La thérapie de substitution à base de nicotine peut doubler les chances de succès des fumeurs qui tentent d'arrêter. La présente étude d'observation visait à comparer les taux d'arrêt pour les différentes formulations des thérapies de substitution à base de nicotine chez des clients orientés vers un établissement de sevrage tabagique à Téhéran (République islamique d'Iran). Les clients sélectionnés dans l'étude ($n = 308$) ont participé à quatre sessions de thérapie comportementale, ont choisi un type de thérapie de substitution à base de nicotine (timbres, chewing-gums, comprimés ou timbres associés aux chewing-gums) et ont été suivis pendant 12 mois. Après 4 semaines de sevrage, 88,2 % (246/279) ont déclaré s'être abstenus de fumer. Les taux autodéclarés de maintien du sevrage étaient de 54,9 % après 6 mois et de 36,2 % après 12 mois de suivi. Une corrélation significative a été retrouvée entre le type de thérapie de substitution à base de nicotine et le taux de sevrage. L'utilisation des timbres de nicotine associés à des chewing-gums avait le taux de réussite le plus élevé (95,2 %) après 4 semaines et à 12 mois de suivi (62,5 %). Le recours à deux formes de thérapie de substitution à base de nicotine pourrait améliorer les taux de sevrage à long terme.

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Introduction

Tobacco use, particularly cigarette smoking, is now a global pandemic [1]. It is becoming increasingly common in Asia, while at the same time quitting rates remain low [2]. Many young smokers think they can quit easily, but find that they are already addicted and develop significant withdrawal symptoms when they attempt to stop smoking [3,4]. Tobacco dependency remains the major preventable cause of early mortality and morbidity in the developed world [5]. It is also a factor that may partly explain the high failure rate of smokers who attempt to maintain long-term abstinence [6,7]. In order to reduce this negative impact on worldwide health, comprehensive tobacco control approaches are needed, including offering effective therapy to aid smoking cessation for current smokers [8]. The Conference of the Parties for the Framework Convention on Tobacco Control recently adopted Article 14, calling on governments to provide cessation assistance to smokers [9] and offering help to quit smoking is one of the 6 components of the World Health Organization's (WHO) MPOWER package [9].

Two recommended quit methods in standard cessation programmes involve either gradual reduction of smoking prior to complete abstinence ("cutting down") or abrupt abstinence from cigarettes ("cold turkey"). Smokers have used these methods of smoking cessation in most cases without nicotine replacement therapy (NRT) or other pharmacological assistance [10]. Optimal treatment for tobacco dependency involves the combination of behavioural therapy and pharmacological treatment [11]. NRT is by far the most thoroughly researched therapy. Tests have shown that, if used correctly, it can double the chance of success, which is good news for those who have found withdrawal very hard

on previous attempts [8,11–13]. The aim of NRT is to at least partially replace the nicotine from cigarettes. This reduces the withdrawal symptoms associated with smoking cessation, helping the smoker to resist the urge to smoke tobacco [14]. There are several forms of NRT available; these include patches, chewing gum, tablets, nasal sprays and inhalators [14]. The present study was conducted to compare quit outcomes for different formulations of NRT among clients attending a smoking cessation clinic in Tehran, Islamic Republic of Iran.

Methods

Study setting and sample

This was an observational study in which the efficacy of 4 formulations of NRT (patches, chewing gum, tablets or both patches and gum) were evaluated in helping smokers to quit. A review was made of the medical records of smokers were referred to the smoking cessation clinic of the Iranian National Research Institute of Tuberculosis and Lung Diseases (NRITLD). This clinic was established in 1998 by the NRITLD at Shahid Beheshti Medical University in association with the municipality of district number 14. Monthly cessation courses are held for women and men separately. These courses comprise 7 sessions each lasting for 2 hours. In these courses the physicians use educational methods, consultations, cognitive-behavioural therapy and pharmacotherapy to help smokers quit smoking. Usually 15–20 smokers participate in each course. All smokers (volunteers) who were referred to the smoking cessation clinic from October 2009 to October 2010 and were followed for 12 months were entered into this study. Of the 310 smokers who were enrolled, initial data were missing for 2, and therefore 308 clients entered the study.

Data collection

Registration and baseline data

At the 1st session, clients were registered and background data were collected using a questionnaire. This included personal and demographic data (age, sex, marital status, level of education and occupation), smoking habits (reasons for smoking, the number of cigarette packs smoked per day during the smoking years) and the Fagerström test which is a standard instrument to evaluate cigarette (nicotine) dependency using items including time, situations and places of smoking as well as number of cigarettes smoked per day [15]. It contains 6 items concerning: how long after waking up the first cigarette is smoked, the most desired cigarette of the day, period of time in the day when most cigarettes are smoked, tendency to smoke during illness and difficulties of smoking in banned or non-smoking areas. We scored the Fagerström questionnaire as 0–4 = mild, 5–7 = moderate and 8–10 = severe dependence. Any person scoring ≥ 7 was chosen as a candidate for NRT. We also asked about the reasons for smoking, the number of cigarette packs smoked per day during the smoking years (pack/year), the number of absences from sessions and the outcome of the course. After they had completed the questionnaire, smokers were physically examined for vital signs, respiratory and cardiac auscultation and expiratory carbon monoxide concentration.

Intervention

At the 2nd session, which took place 1 week after registration, clients were clinically evaluated and asked about any medical or psychological problems they suffered. At this session, the treatment plan was adjusted as needed and behavioural therapy and the strategy for changing smoking habits was discussed. In this study, we combined the "cold turkey" method of cessation with pharmacological treatment (NRT)

plus cognitive behavioural therapy to increase the likelihood of cigarette cessation. Instructions were given to improve the clients' readiness to quit smoking through education about changing the routine smoking habits for each person. The clients were requested to set a firm quit date for the next session.

The 3rd session was scheduled 1 week later. This was the quit date and the day of starting NRT and completing behavioural therapy. Participants could select their preferred NRT method considering the cost of each and following counselling guidance. The types of NRT and the instructions for correct use as well as the price of each method were discussed and clients received advice about which form of NRT might be most suitable. However, the final choice of NRT was left to the client. The recommended duration of use of NRT was at least 6 weeks. The NRT options used in this study included patches, chewing gum and tablets. Clients also had the option of combining patches and gum. Patch usage had 3 steps: 52.5, 35, 17.5 mg/cm² patches were used for 2 weeks each with daily replacement. Nicotine gum was of 2 types: 2 mg and 4 mg were prescribed to be used as needed with a maximum of 12 pieces per day as needed. Nicotine tablets also were prescribed as needed with a daily maximum of 8 tablets.

Follow up

At the 4th session, 4 weeks after the quit date, clients were contacted at the clinic to ask them if they had given up smoking, and also to evaluate withdrawal symptoms, quit-related problems, relapses and potentially dangerous situations threatening continued abstinence. Follow-up assessments were then performed by telephone 6 months and 12 months after the quit date.

Research ethics

All clients selected their preferred quit methods and were informed that they could exit the study whenever they wished. Registration forms and charts were safeguarded by researchers in order to maintain confidentiality.

Outcome measures

We defined successful quitting as the absence of any smoking, even a single cigarette, at 1-year follow-up. Intermediate abstinence outcomes were assessed at each session following the quit date and at 6 and 12 months.

Analysis of data

Demographic data as well as the results of questionnaires and follow up contacts were entered and analysed using SPSS, version 16. Chi-squared tests were performed and when required the Fisher exact test was used to evaluate the correlation between 2 variables. In addition, logistic regression was performed

to find the odds ratio for efficacy of each NRT method when the chi-squared of the cross-tables was significant ($P < 0.05$).

Results

Background data

A total of 308 individuals were recruited to in the study and used at least 1 form of NRT. These included 211 males (68.5%) and 97 females (31.5%). The mean age was 42.4 (standard deviation 13.4) years (median age 41, range 19–80 years). Fagerström scores were distributed as follows: 89 (28.9%) mild, 111 (36.0%) moderate, and 108 (35.1%) severe. Although the difference was not statistically significant, more male clients reported severe dependency than did females (38% versus 25%), whereas more female participants reported moderate dependence (44% versus 31%) ($P = 0.128$).

Table 1 shows the choice of type of NRT by sex, age, level of dependency and outcome at follow-up. Of those entering the study, 31 (1.10%) selected nicotine patches, while 161 (52.3%) chose nicotine gum, 29 (9.4%) chose nicotine tablets and 87 (28.3%) preferred 2 types of NRT simultaneously. There was no significant relationship between the NRT forms selected by the clients as a function of nicotine dependence scores ($P = 0.88$).

Table 1 Baseline demographic variables and Fagerström scores for nicotine dependence for clients at entry to the study by type of nicotine replacement therapy NRT selected

Type of nicotine replacement therapy	Total entering study	Male		Female		Age years		Fagerström score	
	No.	No.	%	No.	%	Mean	SD	Mean	SD
All methods	308	211	68.5	97	31.5	42.4	13.4	5.8	2.1
Gum	161	114	70.8	47	29.2	42.1	14.6	5.6	2.5
Patches	31	20	64.5	11	35.5	41.9	8.9	5.8	3.1
Tablets	29	21	72.4	8	27.6	43.2	10.1	5.7	2.6
Patches + gum	87	56	64.4	31	35.6	46.1	12.8	6.0	2.8
P-value			0.66				0.30 ^a		0.88 ^a

^aAnalysis of variance.

SD = standard deviation.

Abstinence rates

After 4 weeks of quitting 29 clients had left the study and the quit rate of those remaining in the study was 246/279 (88.2%). After 6 and 12 months a further 66 clients had relapsed. At 6 months follow-up 135/246 (54.9%) clients who had quit after 4 weeks reported maintaining abstinence and at 12 months 89/246 (36.2%) reported that they were still abstaining.

The outcomes after 4 weeks and the other 2 follow-up contacts are summarized by sex and age group in Table 3. A statistically significant correlation was detected between sex and quit rate only at the first evaluation at 4 weeks ($P = 0.048$). Women tended to be less successful than men at 6 months follow-up in the younger age groups while slightly more successful than men after 12 months at the older age groups but these differences were not significant.

Abstinence rate by type of therapy

Using the chi-squared test a significant correlation was found between the formulation of NRT and quit rate at all evaluation stages. After 4 weeks clients using both patches and gum had the highest quit rate of all the methods; 95.2% of those who started on this therapy reported quitting (Table 2) ($P = 0.028$). At 6 months follow-up those using nicotine patches had the highest abstinence rate (91.7%) ($P <$

0.001). At the end of the programme (at 12 months follow-up), however, use of patches and gum together had the best outcome with 62.5% maintaining quitting versus only 16.7% for those using patches ($P < 0.001$) (Table 2).

Discussion

Implementing smoking cessation methods is an essential issue in tobacco control programmes. The recent adoption of article 14 of the WHO Framework Convention on Tobacco Control called for dissemination of effective treatment by all parties to this treaty (of which Islamic Republic of Iran is one) [14]. Unfortunately, however, only a few countries have effectively implemented and disseminated smoking cessation services. Often these services are not available or are unaffordable for most tobacco users [8]. Most of those who have quit have done so without formal assistance. However, success rates for interventions that include either counselling or medication are substantially higher than for unaided quit attempts.

It may be especially important to offer cessation services to highly dependent smokers who have not been able to quit on their own, as well as to individuals at especially high risk or with already existing smoking-related disease. Smoking cessation services can be widely

provided at low prices, especially when counselling is conducted by trained lay providers [1]. Currently, however, medications are often priced far too high for tobacco users in low- and middle-income countries and substantially less costly medication options may be needed. Commitment to quitting may be greater if individuals are required to pay part of the cost of treatment [11]. Smoking cessation treatment has been demonstrated to be highly effective when compared with other commonly accepted medical interventions and prevention services [8,11–13]. The efficacy of counselling and medications including nicotine replacement therapy in smoking cessation is well-established [13,16].

The aim of the current study was to evaluate a specialized smoking cessation service which included several options for NRT. The results of our study showed that nicotine chewing gum was the preferred method among smokers given a choice of gum, patches, tablets or a combination. A total of 52.3% used gum alone and most of those who chose combination medications used the gum as well. Low price and easy access undoubtedly influenced this preference for gum. Nicotine patches have been suggested to be more suitable for those that smoke steadily throughout the day, while gum allows flexibility for those who smoke primarily in response to cravings or stress [13].

Table 2 Smoking abstinence rates by type of nicotine replacement therapy for clients at each stage of the study by type of nicotine replacement therapy (NRT) selected

Type of NRT	Total remaining in study No.	Quit smoking after 4 weeks		Maintained quitting:			
		No.	% ^a	After 6 months		After 12 months	
				No.	% ^b	No.	% ^b
All methods	279	246	88.2	135	54.9	89	36.2
Gum	143	120	84.0	55	45.8	31	25.8
Patches	27	24	88.8	22	91.7	4	16.7
Tablets	25	22	88.0	4	18.2	4	18.2
Patches + gum	84	80	95.2	54	67.5	50	62.5
<i>P</i> -value			0.028		< 0.001		< 0.001

^aPercentage of those entering this phase of the study; ^bPercentage of those who had quit after 4 weeks.

Table 3 Smoking abstinence rates of clients at each stage of the study by age and sex

Age/sex	Total remaining in study	Quit smoking after 4 weeks		Maintained quitting:			
		No.	% ^a	After 6 months	% ^b	After 12 months	% ^b
				No.		No.	
19-31 years							
Male	47	42	89.4	21	50.0	8	19.0
Female	19	17	89.5	2	11.8	0	0.0
32-40 years							
Male	49	45	91.8	29	64.4	15	33.3
Female	11	9	81.8	1	11.1	1	11.1
41-52 years							
Male	41	39	95.1	21	53.8	14	35.9
Female	41	30	73.2	23	76.7	15	50.0
> 52 years							
Male	51	45	88.2	23	51.1	21	46.7
Female	20	19	95	15	78.9	15	78.9
All ages							
Male	188	171	91	94	55.0	58	33.9
Female	91	75	82.4	41	54.7	31	41.3

^aPercentage of those entering this phase of the study;^bPercentage of those who had quit after 4 weeks.

At the end of treatment the self-reported abstinence rate was 88.2% and after 6 and 12 months follow-ups maintenance of quitting was 54.9% and 36.2% respectively. These figures compare quite favourably to the results of other studies [8,11–13]. The results also indicated that the quit rate among women (at the end of treatment after the 4th session) was significantly lower than for men, especially for those who were younger, while the abstinence rate for women at 12 months follow-up was slightly higher than that for men, especially for those who were older. Differences in abstinence rates as a function of age were not statistically significant, however.

The results suggested better long-term abstinence at 12 months follow-up for those who used 2 forms of nicotine replacement. However, although quit rates were better for combination NRT at 4 weeks, at 6 months follow-up there was a significant trend for higher abstinence rates among those who selected nicotine patches. The results of this study suggest that using 2 forms of NRT could lead to higher success rates based

on 1-month and 12-month outcomes (however, this advantage for 2 forms of NRT was not evident at 6 months). The abstinence rates for combined NRT were quite encouraging, with a self-reported quit rate of 95.2% after 4 weeks and a still very impressive 62.5% after 12 months. It appears plausible that use of combined NRT was effective in reducing withdrawal symptoms and that this reduction contributed to long-term abstinence.

The current study had some major limitations, including the fact that participants self-selected NRT or a combination. In addition, abstinence outcomes were based on self-reporting. However, we assumed that the pressure to falsely report abstinence was not likely to differ as a function of NRT type.

Although no significant correlation between participants' sex and success rate was detected, women were slightly less successful than men at 6 months follow-up while slightly more successful than men after 12 months. Women may be less nicotine-dependent than men and there tends to be less acceptance

of smoking for women than men in Iranian society. Tobacco use is far more prevalent among men than among women in the Islamic Republic of Iran [9]. Men may also come into greater contact with other men who smoke, thus making quitting more challenging. Future work is needed to assess the relative effectiveness of different forms and combinations of NRT in a randomized study design. Our data in this study confirm what is already known regarding the use and acceptability of treatment including NRT for those referred to tobacco quitting programmes. These results are quite encouraging, as are the 12-month abstinence rates for those who selected 2 forms of therapy.

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Treatment of tobacco dependence

Treatment of tobacco dependence should be an integral part of any comprehensive tobacco control programme as indicated in the WHO FCTC. Article 14 of the WHO FCTC addresses the issue of tobacco dependence treatment. It obligates Parties to this Convention to endeavour to: a) design and implement effective programmes aimed at promoting the cessation of tobacco use, in such locations as educational institutions, health care facilities, workplaces and sporting environments; b) include diagnosis and treatment of tobacco dependence and counselling services on cessation of tobacco use in national health and education programmes, plans and strategies, with the participation of health workers, community workers and social workers as appropriate; c) establish in health care facilities and rehabilitation centres programmes for diagnosing, counselling, preventing and treating tobacco dependence; and d) collaborate with other Parties to facilitate accessibility and affordability for treatment of tobacco dependence including pharmaceutical products pursuant to Article 22 [3].

Source: *Integration of tobacco cessation efforts into primary health care in the Eastern Mediterranean Region* (WHO-EM/TFI/077/E).