

Quit smoking

New approaches for an old problem

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Abstract

Tabagism has been recognized as a disease since the 1990s when nicotine dependence was introduced in the group of mental and behavioral disorders due to the use of psychoactive substances. We may characterize smoking as a chronic, recurrent disease characterized by the presence of disagreeable symptoms when interrupted (negative reinforcement) and pleasurable sensations when used (positive reinforcement). The psychoactive action of nicotine appears seven seconds after inhaling cigarette smoke and is explained by changes in cerebral neurotransmitter concentrations induced by nicotine. Nicotine acts on the mesolimbic system, specifically on nicotinic $\alpha 4\beta 2$ acetylcholine receptors and is able to release the up-regulation phenomenon of the receptors, that is, the tolerance effect. There is a need of increasing doses of the drug to obtain the same result which perpetuates and increases tobacco consumption. On the basis of these concepts it was possible to enlarge the therapeutic arsenal for the treatment of tabagism and today the combination of medicaments to treat nicotine abstinence symptoms and to offer the patient training in abilities to cope with situations of risk for relapse, to encourage behavioral changes in order to cancel conditioning effects of the smoking habit and adoption of new habits in daily life which are beneficial to health such as regular practice of physical activity are advocated as a model of treatment of tabagism.

Key words: Tabagism; Approaches for cessation

Introduction

It is not long ago that the treatment of tabagism has become a matter of medical interest. Since the 1980s there were descriptions of the nicotine abstinence syndrome in the Diagnostic and Statistical Manual of Mental Disorders DSM-III-R¹, but only in 1984 in DSM IV² the set of signs and symptoms which characterized what we nowadays know as nicotine abstinence syndrome was reported. After this period the emergence of new medicaments for its treatment was progressive. These facts were determinant for the physicians' change in interest regarding treatment of tabagism.

The present scientific knowledge points to $\alpha 4\beta 2$ nicotine receptors³ preferentially localized in the mesolimbic system as responsible for what was then considered a

habit liable to changes exclusively according to the smoker's disposition. The cerebral effects of nicotine on $\alpha 4\beta 2$ receptors appear on average seven minutes after inhaling cigarette smoke and are explained by changes in the cerebral neurotransmitter concentrations induced by nicotine. Dopamine release in the mesolimbic system is responsible for the behavior of reward or gratification⁴. Increase in norepinephrine concentration modulates the brain's functioning and when there is a decrease in this substance, induced by nicotine withdrawal, immediately symptoms of abstinence are released. All these actions make smoking cessation immensely difficult. The higher the susceptibility of the individual to nicotine dependence, the greater will be the difficulty to get away from it. With the advances in molecular biology, the hereditary aspects of tabagism are

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beginning to be disclosed. Tabagism has been associated with several genetic polymorphisms, independent of environmental factors⁵. Studies in twins⁶ show that there is a concordant behavior regarding tabagism in a significantly higher percent in the monozygotic than in the dizygotic. Some authors quantified this concordance and compared the environmental and individual influence, concluding that the hereditary component could be responsible for 60 to 70% of this character's manifestation⁷. Dopamine receptor, transporter and metabolism genes are being studied, DRD2 polymorphism⁸ being the most related to nicotine dependence. These smokers would be predisposed to depression and nicotine would be used to maintain the emotional balance. Something similar would occur with the genetic polymorphisms linked to serotonin. The polymorphisms involved in nicotine metabolism (CYP2A6)⁹ would determine the rhythm of each smoker, that is, the persons who rapidly metabolize nicotine would need to smoke earlier another cigarette. In smokers with Parkinson's disease¹⁰, attention disorder¹¹, schizophrenia¹² and depression¹³ the difficulty would even be greater, since these patients smoke in order to attenuate the symptoms of these diseases. These psychoactive actions, adequate for the present lifestyle and connected with economic interests, brought forth a worldwide consumption epidemic and transformed smoking into the greatest avoidable risk factor for death¹⁴.

At present tabagism is considered a disease which may require repeated interventions and many attempts to stop smoking. In the following we will present the main orientation for the treatment of tabagism updated by the Clinical Practice Guideline – Treating Tobacco Use and Dependence: 2008 Update U.S. Department of Health and Human Services, Public Health Service. This guideline stimulates the physicians to encourage their patients to stop smoking offering counseling technique and known efficacious and safe medicaments for the treatment of tabagism¹⁵.

The adoption of these technical orientations significantly increase the chance of the patients to definitively stop smoking.

Individual or group counseling, in the presence of the counselor, or by telephone is necessary for the treatment of tabagism and efficacy is proportional to the intensity with which they are performed. Counsels should involve handling and solution of problem techniques and training of abilities.

Social support, such as backing by family, work colleagues, friends is part of the treatment and increases the chance of success of the intervention. To stop smoking is contagious. A study by Nicholas Christakis¹⁶ observing a subpopulation of 12067 individuals of Framingham ob-

served a grouping behavior among the ex-smokers. When a consort stops smoking he reduces the chance of the other to continue to smoke by 67%. Among friends the reduction is 36%. In small enterprises the reduction is 34%.

Drugs for the treatment of the nicotine abstinence syndrome

There are 7 medicaments (5 nicotinic and 2 non nicotinic) that when utilized significantly increase tobacco abstinence rates as compared to therapy with placebo. In Table 1 the expected efficacy rates are shown for each of these products.

- Nicotine gum.
- Nicotine inhalation.
- Nicotine pastilles.
- Nasal nicotine spray.
- Nicotine adhesives.
- Bupropion SR.
- Varenicline.

Pharmacologic treatment should only be started if the patient is willing to stop smoking, if not, he/she should be motivated to change behavior in view of the perspective to continue to smoke. Among the suggested techniques by the North-American guideline are: evaluation of gains and losses; fear of failure should be minimized by the possibility of success; presence of abstinence symptoms should not be feared since their intensity will be reduced through the use of drugs.

The choice of the pharmacologic treatment should consider some aspects such as: history of previous use of

Table 1. Efficacy of the medicaments for the treatment of tabagism (monotherapy).

Medication	Odds ratio	Abstinence rate at 6 months
Nicotine gum or pastille	2.2 (1.5–3.2)	26.1(19.7–33.6)
Nicotine inhalation	2.1 (1.5–2.9)	24.8(19.1–31.6)
Nasal nicotine spray	2.3 (1.7–3.0)	26.7(21.5–32.7)
Nicotine adhesives	1.9 (1.7–2.2)	23.4 (21.3–25.8)
Bupropion	2.0 (1.8–2.2)	24.2 (22.2–26.4)
Varenicline	3.1 (2.5–3.8)	33.2 (28.9–37.8)

Table 2. Efficacy of associated medicaments for the treatment of tabagism.

Medication	Odds ratio	Abstinence rate at 6 months
Adhesives + nicotine gum	3.6 (2.5–5.2)	36.5 (28.6–45.3)
Adhesives + bupropion	2.5 (1.9–3.4)	28.9 (23.5–35.1)
Adhesives + inhalation	2.2 (1.3–3.6)	25.8 (17.4–36.5)

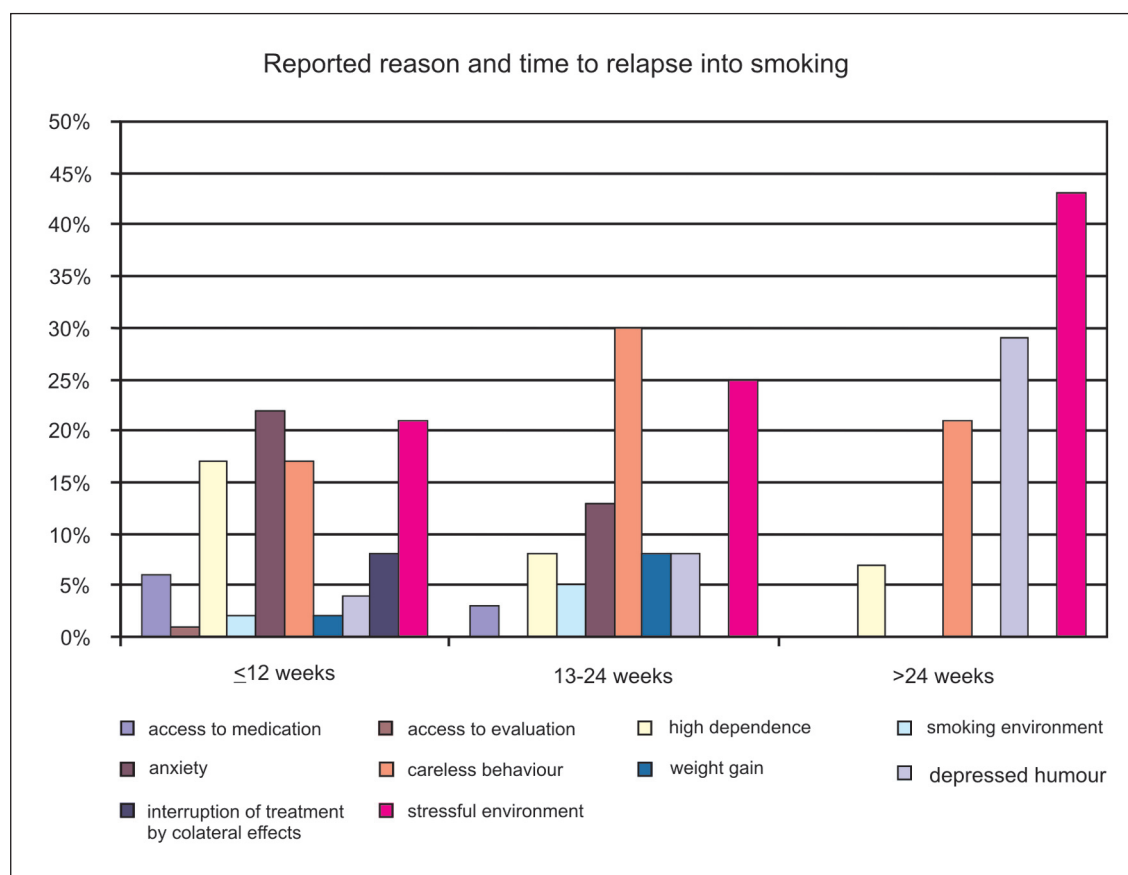


Figure 1. Causes of relapse in the first 12 hours, between the 13th to the 24th week and after 24 weeks of abstinence.

any of these products, obtained results, specific contraindication regarding one of these substances and gender. In women the results with nicotine replacement are not as good as those obtained in men and for this reason prescription of bupropion or varenicline should be preferred. This present recommendation of the choice of drug according to gender had already been adopted by the Outpatient Clinic of the Heart Institute of the University of São Paulo Medical School since 2002 based on two local studies with nicotine replacement and with the use of bupropion where significant differences between smoking cessation rates according to gender were observed^{17,18}.

Comparison between drugs has already been made by randomized clinical studies. Varenicline has a higher efficacy than bupropion^{19,20} and nicotine adhesives²¹.

The North-American guideline also recommends the possibility of combination of drugs with the purpose to reduce abstinence symptoms in those patients who are already in use of any of the drugs for the treatment of tabagism. Some associations have already been tested and are shown in Table 2. Although varenicline has not been studied in association with bupropion, its concomitant use

seems safe. On the other hand, there are reports that the use of varenicline with nicotine replacement reinforces the emergence of digestive side effects such as nausea and vomiting. Efficacy of the association also was not studied.

Treatment of tabagism should include a phase of drug use with a suggested minimum of 12 weeks followed by a follow-up phase. In the former a visit in the presence of a counselor is suggested. In the follow-up phase consultation can also be by telephone or e-mail.

The Outpatient Clinic of Treatment of Tabagism of the Heart Institute, University of São Paulo, evaluated 465 smoker patients submitted to tabagism treatment²² in the period from 2002 to 2004, 264 being women (57%) and 201 men (43%), mean age 49.39 (± 10.82 years) and mean consumption of 23.12 cigarettes/day (± 10.74). They were cared for individually and pharmacotherapy with nicotine adhesive, bupropion and nicotine gum was used. Success rate was 39% at the end of the 52nd week of follow-up. The main cause for reduction in the success rate was relapse which occurred mainly in the first 12 weeks of treatment. Among the evaluated patients, 218 (46.8%) relapsed, 109 (67%) in the first 12 weeks, 39 (24%) in

the 12th to the 24th week and 14 (9%) after the 24th week; of these 162 (74%) were able to identify the cause of relapse. Anxiety, carelessness (voluntary cigarette use during abstinence) and high stress level were the main reasons for the relapse in the first 12 weeks, between the 12th and 24th week and after the 24th week, respectively. The wish to smoke and anxiety decrease with time while depressed state and high stress level become more relevant as cause of relapse (Figure 1). Orientation for the patient to avoid acting on impulse and to attentively observe alterations in mood and special attention to cope with situations which involve intense emotional stress are fundamental in order to act effectively in relapse prevention.

The hope is that the medical class becomes more and more interested and feels more confident to treat tabagism, adopting adequate techniques and drugs. Finally, to treat tabagism is the medical attitude with the best cost-efficacy ratio in health²³.

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