

## REVIEW

## Pharmacotherapy in smoking cessation

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### Abstract

**The authors reviewed literature on nicotine replacement therapy and bupropion in smoking cessation. Nicotine replacement therapy increases the quit rate in smoking cessation; however, its efficacy is influenced by numerous factors. Bupropion, particularly combined with nicotine replacement therapy, reaches even higher efficacy. Behavioural therapy as well as individualised approach during the cessation process are beneficial. Beside from this, these agents help to avoid excessive weight gain after quitting. If properly used, they have minimal side effects, and, if not contraindicated, they should be included into standard smoking cessation programs. (Ref. 74.)**  
**Key words: smoking cessation, nicotine replacement therapy, bupropion.**

Smoking ranks among the most important life-style risk factors (25, 57, 59, 69). Beside the measures focused on primary prevention of the habit as such, an important part in decreasing the impact of smoking on health is played also by the secondary prevention aimed on smoking cessation. The task is not an easy one, and it often requires medical assistance. Of importance here, there are some pharmaca alleviating the unpleasant withdrawal symptoms and reducing the possibility of relapses. In some countries, two standardly used groups of pharmaca are currently available: nicotine replacement therapy (NRT) facilitating the nicotine addicts to overcome their withdrawal symptoms after quitting the nicotine intake from cigarette smoking, and the second antidepressant bupropion group with dopaminergic and adrenergic effects. In our country NRT is still rarely used, and bupropion has not yet been registered. The general public and often also physicians are lacking comprehensive information on pharmacotherapy in smoking cessation, which leads to incorrect use of the respective pharmaca, unfavorable experience and the consequent negligence in this field.

Our objective is to present a review of the existing standardized pharmacotherapies assisting smoking cessation, to evaluate the objectively available information on NRT and bupropion, and to provide the relevant recommendation for the use in our country.

### Material and methods

For information retrieval we used the Medline Ovid Database (46) and Cochrane Library (66) and closed it as to 7 February 2001. The following keywords and their combinations were used: “nicotine replacement therapy” + “smoking cessation” and bupropion + “smoking cessation”. Papers were involved that concerned indications, efficacy, side effects, contraindications and risks of

NRT and bupropion in smoking cessation. Left out were the repeating references, editorials, letters to the editor and papers not meeting the mentioned criteria for the review. Eventually 69 references were thus selected.

### Results

#### 1. Nicotine replacement therapy (NRT)

NRT occurs in the following application form: patches for transdermal application, chewing gums (acting through bucal mucosa), nasal spray (acting through nasal mucosa), inhalator (acting through pharyngeal and bronchial mucosa). According to several studies, NRT increases the quit rate 1.5 to 2.0 times, which after one year means a quit rate between 5–30 % (1, 3, 15, 18, 22, 23, 55, 56, 59). This rather wide range is caused by the fact that during cessation also other important factors are acting as well. The treatment reaches the highest successful rate when the group behavioral therapy is used. The efficacy increases also when the physician describes the mode of action and expectations from NRT, and helps the patient with his/her advice (13, 44, 50, 51, 58, 71, 72), while also the degree of addiction is important (8, 41). An important role is played also by respecting the specific needs of the patient and “to tailor” the treatment individually (53). According to the experience from abroad, the over-the-co-

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under sale of NRT is beneficial (9, 45), even in such case the quit-rate decreases. The patient should be recommended to quit smoking completely immediately after NRT has been introduced. The procedure of such decreasing of the risk of nicotine overdosing procedure increases the probability of the lasting effect of the therapy (33, 44). Some authors as the first choice treatment recommend NRT patches (18), however according to other authors patches alone in placebo controlled studies have only a short lasting effect (less than one year) (1, 25, 32, 38). On the other hand, some studies, in which the treated smokers were followed for at least one year, have shown that the NRT inhalator has also a long lasting effect (3, 32). When comparing application forms, inhalators and nasal spray have been shown as most effective (55, 56). Several authors recommend the mutual combination of NRT patches and sprays (1, 55, 62) or patches with inhalator (2). The most promising combination to be that appears of NRT with bupropion (23, 31, 55). In case of youngsters, two studies consider the use of NRT as beneficial mostly in smokers of 10 and more cigarettes per day (52, 60). While another study considers NRT patches in these age groups as ineffective (25). NRT can prevent the weight gain during cessation (7), mostly if combined with bupropion (31).

NRT patches did not show any serious cardiovascular or atherogenic side effects (11, 27, 32, 36, 74). In one study the authors found insulin resistance due to NRT chewing gums (12). Another study has not proved any noxious effects of NRT for the fetus in pregnant women during the cessation course (42). Slight side effects include skin irritation in sites of patches, nose and mouth irritation in chewing gums (26). In chewing gums nausea can occur due to the swelling of salivary glands (34). From the aspect of subjective adverse effects, patches are more suitable than chewing gums (55). After proper use of inhalator no subjective adverse effects were found (22). In 22 mg patches, the occurrence of slight subjective effects was lower compared with 44 mg patches, while the therapeutic effect was almost the same (30). 44 mg patches are recommended only in heavy smokers (6). 4 mg chewing gums in heavy smokers appeared more effective than 2 mg ones (63).

Several studies emphasize the cost-effectiveness of NRT in smoking cessation (4, 5, 14, 15, 23, 29, 35, 61, 65, 68).

## 2. Bupropion

The mechanism of effect of bupropion in smoking cessation is not yet fully known. However, its effect does not differ in the group of smokers under cessation course with depressions in their history, from smokers with no depression in their history. This finding implies that the positive effect of bupropion in smoking cessation is not due its antidepressant effect, but rather to the increasing dopamine level which is decreased in smokers (24). From short term aspect, bupropion helps to reduce the withdrawal symptoms during cessation (53, 54). The use of bupropion alone increases the quit rate after one year by 10 to 30%, which is twice higher than placebo (21, 28, 30, 48, 64). Direct correlation between the dose and quit rate has been found, where the best results have been achieved in patients on 300 mg bupropion per day (19, 28). Also in another randomized study comparing the effect of 100, 150 and 300 mg bupropion/day with placebo a significantly higher quit rate has been found in higher doses (19). According to one already mentioned randomized controlled trial, the mutually

potentiating effect of NRT patches with bupropion has been found (31, 43, 48). A beneficial effect of bupropion has also been revealed in coincidence with excess weight gain during cessation, which was higher in combination with NRT (31).

In current recommendations, bupropion with sustained effect should be used by each smoker unless contraindications are present. Its application in the course of treatment should start about a week prior to complete quitting commonly first three days by one 150 mg bupropion/day and the dose should be increased on the third day to 300 mg/day (two 150 mg doses). The treatment should continue at least seven weeks (13, 23, 35, 49, 67, 74).

Clinically relevant side effects of bupropion are very rare. The described adverse effects include convulsions, tremor, urticaria, edemas, anxiety, insomnia, tachycardia, nausea, dyspnoea, arthralgia, myalgia, hypoglycaemia, sight disorders etc. (10). In bupropion with sustained effect used during smoking cessation courses no serious side effects were observed. The most frequently reported side effects were insomnia, mouth dryness, nausea (24), incidentally headache (31). Depression occurred very rarely during the treatment (47).

Bupropion is contraindicated in patients disposed to convulsions or those with convulsions in their history, in eating disorders (mental anorexia, bulimia) (10, 13). Precautions are necessary in diabetes mellitus (10). Similarly as in NRT, some studies emphasize cost-effectiveness of bupropion in smoking cessation (13, 17, 20, 40).

## Discussion

Several evidences exist on the efficacy of the mentioned pharmacology, and their use should be come an integral part of standard procedures in the secondary prevention of smoking also in our country. Unfortunately, there is still lack of evidence which could unambiguously lead to preferential use of one application form of NRT to another. Therefore the existing guidelines and recommendations (15, 23, 29, 35, 51, 62, 70, 71, 74) comply in the point that the choice should be based on individual needs of the patient. The patches enable a precise and continuous dosage of nicotine while its application is very simple. Chewing gums on the other hand provide tactile perception and enable the patient to control nicotine intake according to the speed of chewing, which however, requires a certain level of experience. Sprays and inhalators enable rapid releasing of nicotine, which is welcomed mostly in the moments of irresistible craving for cigarettes. Beside this, the manipulation with them alone could replace to a certain degree the rite of lighting a cigarette.

The described results originate mostly from countries of Western Europe and USA with some different social-economic, behavioral, psychological and cultural conditions distinct from ours (16). This can bring about different understanding of side effects, different motivation in smoking cessation and thus different compliance. Even the application of the results of studies following the cost-benefit of these means is difficult in our conditions. The lack of our own experience is mostly important in bupropion which has not yet been registered in our country. However, if its future use should be effective we find it necessary to get the medical as well as the lay public ready for it. One of the reasons why the use of NRT has not met with sufficient acceptance in Slovakia, was also the lack of information among the public and insufficient knowledge of health providers. Therefore in order to respond to the mentioned questions

and to prepare the guidelines, as well as to attract attention of health insurance companies, it is necessary to obtain objective scientific information taking our conditions into account.

### Recommendation for practice

Smoking should be comprehended as a disease that often requires medical treatment.

If not contraindicated, certain form of pharmacotherapy is indicated in each patient entering the smoking cessation cure.

The use of pharmacotherapy in some population groups requires cautious considerations depending on individual conditions (e.g. pregnant women, adolescents, smokers of less than 10 cig./day). In such cases, great importance resides mainly on the primary prevention (13, 37, 39, 52, 73, 74).

In smoking cessation, the decisive value is assigned to the physicians approach and his/her assistance (43, 57). A mere advice from the physician not to smoke, increases the likelihood of successful quit rate in the patient by about 10 % (48).

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