

Role of Nicotine Replacement Therapy in Tobacco Cessation

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Abstract

Tobacco use in smoked as well as smokeless forms is implicated as a scientifically proven, number one cause of oral cancer, leading to a quite significant number of deaths worldwide. The addictive component of tobacco is nicotine which is not a cancer causing agent, but it leads to tobacco dependence & hence patient is exposed to other cancer causing agents contained in tobacco like acetaldehyde, acrylonitrile, 4-aminobiphenyl, arsenic, benzene etc. Dentists being oral health care providers are first to encounter tobacco related changes in patient's mouth. And hence it is a professional as well as moral responsibility of a dentist to help the patients in quitting the habit by spreading awareness among them. Dentist needs to be well aware of different modes of tobacco cessation. Nicotine Replacement Therapy (NRT) is one of these methods. This article highlights the basic role of dentist in lowering the tobacco burden in society by use of Nicotine Replacement Therapy. However the other modes of tobacco cessation like behavioral counselling &

modification, pharmacological modes etc are not discussed in this paper.

Keywords: Nicotine dependence, NRT, Dentist.

1. Introduction

Tobacco has been associated with grave health consequences effecting general as well as oral health. There are scientific evidences that prove that tobacco is most common etiological agent for oral cancer¹. Oral cancer is among top three types of cancers in India². In India oral cancer accounts for about 30% of all cancers³ and more than 5 people in India die every hour everyday because of oral cancer⁴. Tobacco is being used in a smoked as well as smokeless form. The dependence on tobacco has been identified as a life threatening disorder and is proven to have serious health consequences. It has been scientifically proven that the addictive component in tobacco is nicotine⁵. Tobacco use, along with its consequent effects are a major burden on health and financial stability of a nation. It is a social stigma that not only affects the individuals who are using it directly,

through health deterioration & financial constraints, but also the family of the individual at minor scale & whole society at a broader scale. There are chances of 50%, that a lifelong smoker dies prematurely secondary to a complication of smoking.⁶

Tobacco is being used in smoked(cigarette, bidi, hukka etc) & smokeless(Pan, khaini, Naswaar) forms. Smoking-caused disease is a consequence of exposure to toxins in tobacco smoke. Although nicotine plays a minor role, if any, in causing smoking-induced diseases, addiction to nicotine is the proximate cause of these diseases. No matter what the mode of use, it has been associated with addiction, psychological dependence and finally carcinoma⁷. Tobacco contains alkaloid nicotine, and other alkaloids⁸. Commercial tobacco smoke is a mixture of more than 5000 chemicals¹. According to US Department of Health & Human services, few of the known carcinogens of tobacco smoke are; acetaldehyde, acrylonitrile, 4-aminobiphenyl, arsenic, benzene, cadmium, ethylene oxide, heterocyclic amines, 2-Naphthylamine, N-Nitrosodiethylamine, N-Nitrosopiperidine, polonium-210, polycyclic aromatic hydrocarbons etc.⁹

1.1. The Biology Of Nicotine Addiction

Nicotine has been identified as the addictive agent present in tobacco, after a wide research. Nicotine acts on Central nervous system, causing enhancement of mood, directly or indirectly (relief of withdrawal symptoms or augmentation of mental or physical functions).

Tobacco addiction is complex interplay of pharmacology, learned or conditioned factors of individual, genome, and social/environmental factors. Environmental factors like tobacco product design and marketing have also been found to play a role.¹⁰ (Fig. 1).

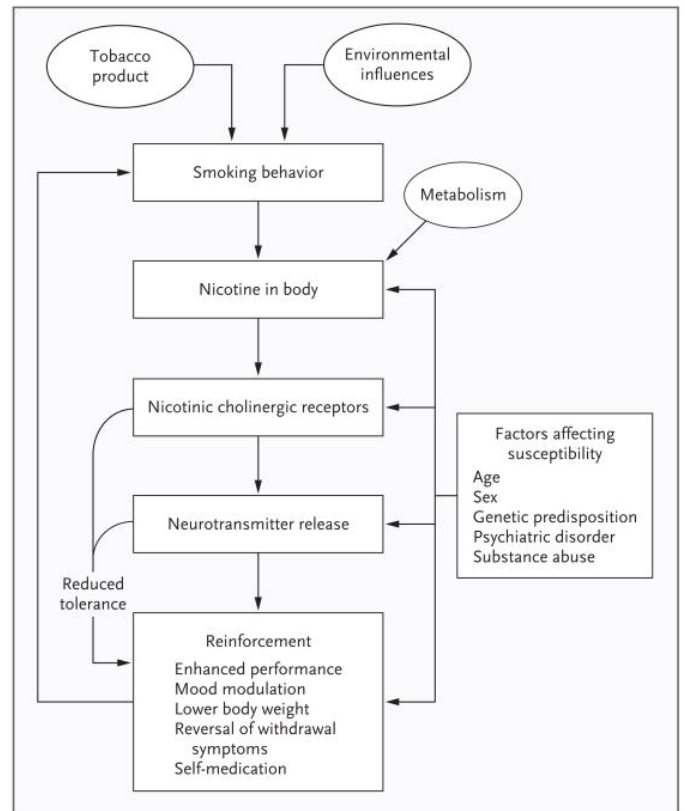


Figure 1: Environmental factors like tobacco product design and marketing have also been found to play a role. Nicotine acts through nicotinic cholinergic receptors located in brain & trigger the release of dopamine and other neurotransmitters. Release of neurotransmitters like dopamine, glutamate, and GABA(Gamma Amino Butyric Acid) are responsible for development of nicotine dependence, and are believed to play a key role in withdrawal also. Addiction to nicotine results when smokers rely on smoking to modulate mood and arousal, for relieving of withdrawal symptoms, or both. Light/occasional smokers are believed to smoke mainly for positive reinforcement in specific situations. A large proportion of current smokers are contributed by people with psychiatric & substance abuse disorders, having an increased susceptibility to addiction. Since past few decades, due to wide research resulting in understanding of the mechanisms of nicotine addiction eventually led to

the development of novel medications (e.g., varenicline) that act on specific nicotinic receptor subtypes.¹¹ Further development is likely to enhance the effectiveness of smoking-cessation pharmacotherapy.¹¹

1.2. Modes of Tobacco Cessation: Broadly classifying, there are two main modes of tobacco cessation. Non-pharmacological (including counselling, behavioral therapy etc) and pharmacological (including Nicotine Replacement Therapy, anti-addiction medications like Bupropion, Varenicline etc). Behavioral modification & counselling is a first & universal step that is indicated for all the patients regardless of the addiction level. In behavioral modification & counselling patient should be motivated & encouraged to step forward to quit. Health, social & financial consequences of tobacco use should be explained to the patient in detail. Moreover patient should be advised to recognize the trigger & provoking factors and to avoid them. Peer pressure has been identified to be the major trigger factor. This paper focuses on role of dentist in tobacco cessation by using Nicotine Replacement Therapy (NRT).

2. Discussion

2.1 Responsibility of a Dentist: Since dentist is the first person who encounters patients with tobacco related habits while history taking or clinical examination and witnesses tobacco related changes. The early diagnosis not only will result in on time treatment and better prognosis of the diseases that have already begun, but also can play a pivotal role in prevention of occurrence of these diseases by timely intervention and helping the individuals in habit cessation. It is responsibility of a dentist to be well aware of his domain in this regard and be concerned about its implementation wherever indicated in his day to day clinical practice. It is need of the hour to consider it as an integral part of patient’s treatment plan as other treatment needs are considered.

2.2 Assessment of Nicotine Dependence Level: After the initial step of behavioral modification & counselling, patients who are ready to quit should be considered for NRT. It has been found that in some patients only NRT proves to be sufficient, however in certain other patients NRT needs to be supplemented by other pharmacological agents. A patient having tobacco related habits whether smoked or smokeless, needs to be assessed for nicotine addiction level prior to administration of NRT. Nicotine dependence differs in light & heavy smokers. The further treatment depends upon the level of addiction, whether mild, moderate or severe. Various scales are being used for this assessment. Most commonly used is FTCD (1978)¹² (Fagerstrom test for cigarette dependence) used in smokers & similar scale for smokeless tobacco users was proposed in 2005¹³.

Fagerstrom Test for Nicotine Dependence

PLEASE TICK (✓) ONE BOX FOR EACH QUESTION		
How soon after waking do you smoke your first cigarette?	Within 5 minutes	<input type="checkbox"/> 3
	5-30 minutes	<input type="checkbox"/> 2
	31-60 minutes	<input type="checkbox"/> 1
Do you find it difficult to refrain from smoking in places where it is forbidden? e.g. Church, Library, etc.	Yes	<input type="checkbox"/> 1
	No	<input type="checkbox"/> 0
Which cigarette would you hate to give up?	The first in the morning	<input type="checkbox"/> 1
	Any other	<input type="checkbox"/> 0
	10 or less	<input type="checkbox"/> 0
How many cigarettes a day do you smoke?	11 – 20	<input type="checkbox"/> 1
	21 – 30	<input type="checkbox"/> 2
	31 or more	<input type="checkbox"/> 3
Do you smoke more frequently in the morning?	Yes	<input type="checkbox"/> 1
	No	<input type="checkbox"/> 0
Do you smoke even if you are sick in bed most of the day?	Yes	<input type="checkbox"/> 1
	No	<input type="checkbox"/> 0
Total Score		
SCORE	1- 2 = low dependence 3-4 = low to mod dependence	5 - 7= moderate dependence 8 + = high dependence

Add up the scores from the questionnaire.

Figure 2: NOTE: Similar scale is available for assessment of nicotine dependence in tobacco chewers. The word ‘smoke’ is substituted by the word ‘chew’.

2.5 Administration of NRT

Depending upon the score of Nicotine dependence (Calculated by Fagerstrom scale), a patient should be given the options available that will aid in tobacco cessation. NRT can be prescribed by dentists. A medically stable patient should be informed about expected withdrawal symptoms like headache, and should be asked

to report back or inform by a phone call. While as in patients having disorders like cardiac, psychiatric, neurological NRT should be prescribed only after physician consultation. Moreover, patient who is on NRT should be asked to completely abstain from smoking. For prescribing any other pharmacological agents, consultation with psychiatrist is required.

In regular smokers who abstain from smoking, NRT leads to reduction in nicotine withdrawal symptoms.¹⁴ it provides a coping mechanism by which patient feels tobacco products are less rewarding. Since none of the available nicotine delivery systems reproduce the rapid and high levels of *arterial nicotine* which is achieved when cigarette smoke is inhaled, so NRT does not completely eliminate the withdrawal symptoms¹⁵. All the available medicinal nicotine products cause *systemic venous absorption unlike the nicotine from smoke* and hence do not achieve rapid systemic arterial levels. It takes only a few seconds for high doses of nicotine from a cigarette to reach the brain; medicinal products achieve lower levels over a period of minutes (for nasal spray or oral products such as gum, inhalator, sublingual tablet, or lozenge) and hours (for transdermal patches).¹⁶

2.5.1 Who Should Recieve NRT?

NRT, in conjunction with behavioral support, should be offered to any regular cigarette smoker prepared to make a quit attempt. NRT is unlikely to help smokers who are not motivated to quit or do not experience or expect to experience nicotine withdrawal symptoms.¹⁷ Any health care professionals can assess these characteristics in the following ways:

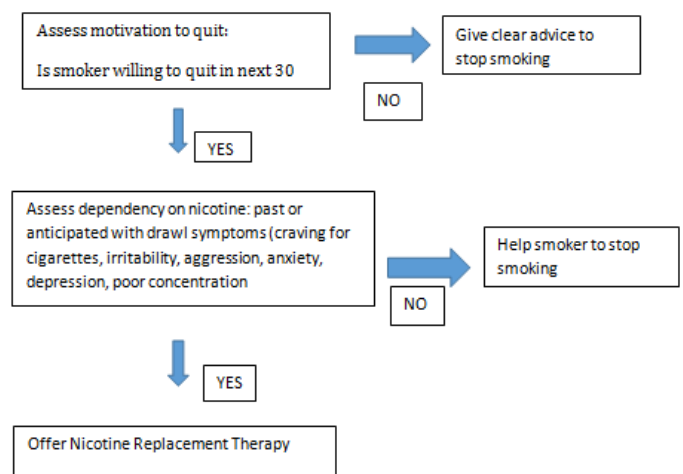


Figure 3: Decision pathway for giving NRT.

2.5.2 Different Forms of Nicotine Replacement Therapy

Nicotine Transdermal patches: Nicotine replacement patches are transdermal patches which deliver nicotine at a steady & constant rate through skin. It is a slow mode of delivery system preferably for patients who have low addiction levels & low frequency of cravings. Nicotine patches are available in different doses which gradually deliver nicotine through days or weeks which results in gradual adjustment of body to nicotine withdrawal.¹⁸ It can deliver from 5mg to 22mg over a period of 24 hours. Main advantage is patient compliance.¹⁹ Most common disadvantage being skin reactions. To avoid this, site of placement of patch should be changed.²⁰ Sleep disturbances have also been reported in some patients. Faster delivery transdermal patches are under research.

Acute Dosing Nicotine Delivery Products

These products provide nicotine at a higher plasma concentration in short period of time. These dose products have an important advantage that timing and dose can be titrated by the user himself. So a person with higher nicotine tolerance or higher frequency of cravings, can increase the dose accordingly. Similarly, a person experiencing the adverse effects can reduce the dose. In

this regard, NRT acts as “rescue medication” for patients having strong cravings. Acute dosing nicotine products include gum, lozenge, sub-lingual tablet, oral inhaler, and nasal spray.

Nicotine Gum: First introduced NRT formulation & over the counter available, in 2 or 4 mg(per piece) formulations. Should not be chewed as regular gum, but to be chewed until the taste is strong, then it is rested between gum and teeth and chewed again once the taste fades. Upto 20 gums in a day are found to be safe. Absorption occurs through oral mucous membrane.

Nicotine Inhaler: Available in dose of 10mg per cartridge, to be inhaled when required. Inhalation of nicotine in vaporized form leading to absorption into blood stream by mucous membranes in the mouth and larynx.

Sub-lingual Tablet: 2-4mg per tablet formulations, to be kept in floor of mouth until dissolved. It has an advantage of faster absorption through sub-lingual route.

Nicotine Lozenge: 1,2 or 4mg formulations, to be kept between gum and cheek until dissolved. After dissolution, the nicotine is absorbed through oral mucous membrane. It is recommended for patients with high cravings.

Nasal spray: 10mg per ml, 0.5mg per spray. To be used as one spray each nostril as per required. It has been found to double the chances of quit. At-least 16 sprays(8 in each nostril) daily should be taken to a maximum of 40 sprays, if the patient is smoking 20 cigarettes per day or smokes within half an hour after waking up. Nicotine nasal spray is costlier than other formulations and is available only with prescription²⁰.

2.5.3 Adverse Effects of NRT:

Cardiovascular: Common adverse effect associated with NRT is palpitations & chest pain, although it is not associated with increased mortality or chances of

Myocardial Infarction(MI). NRT should be cautiously advised in patients with cardiovascular disease. NRT in cardiovascular disease patients should be administered only after the consent of physician.²¹ Patients should be warned of these risks and counseled to desist smoking and arrange intensive behavioral support.

It is found that patients using NRT who continue to smoke, high serum concentrations may stimulate the sympathetic nervous system, so increasing blood pressure, stroke volume and cardiac output. NRT has been found to be a risk factor in patients with atrial fibrillation.²²

Oral: Mouth soreness and ulcerations are associated with orally administered NRT. It is due to the success of cessation rather than NRT because mouth ulcers occur in about 40% of all individuals achieving tobacco abstinence regardless of cessation intervention. Such patients may need treatment discontinuation hence it is important to give alternate options to assist patients unable to continue oral administered NRT due to mouth ulcers like increasing the nicotine patch dose, use of nicotine spray, or an alternative form of smoking cessation pharmacotherapy such as bupropion or varenicline.²³

Psychological: Common but less severe adverse effect is insomnia. Suicidal ideation, is major concern in some patients initiating smoking cessation.²⁴ NRT aggravates the symptoms of insomnia, depression & other mental disorders. Clinicians to remain vigilant about NRT-related sleep disturbance among patients with a history of psychiatric illness. Headache is also noted.

Gastrointestinal: GI effects like nausea and vomiting have been reported. Hiccoughs are most common.

Dermatological: Skin reactions have been associated with use of nicotine trans-dermal patch in majority of patients.²⁵

2.5.4 Safety of NRT

Myths are common among people regarding safety of NRT. Since it is scientifically proven that nicotine is not the carcinogen, it acts as addictive agent, administration of nicotine in any form helps to manage the cravings. However, it is important to understand that NRT alone can not work and it will not stop the cravings of smoking.

2.6 NRT in Pregnancy

Smoking during and after pregnancy poses a serious risk to the health of both mother and baby. Nicotine crosses placenta and gets accumulated in amniotic fluid. NRT may also have adverse effects on placental function and fetal development, but although the magnitude of these pure nicotine effects in humans is uncertain. Obtaining nicotine from cigarette smoke is far more harmful than through the NRT.²⁶ Even though safety of NRT in pregnancy is controversial, research shows that majority of women are ready to quit in pregnancy and more than 40% of them actually quit. Behavioral counselling is most effective method to encourage the tobacco cessation in pregnant women. According to WHO, 2013; recommendation on NRT use during pregnancy cannot be made.²⁷

2.7 NRT in Young Smokers

Most adult smokers establish their smoking habit in young age. Even in adolescence, many smokers are addicted to nicotine and would like to stop smoking. Several NRT products are licensed for use in smokers aged under 18, on medical advice. Recent National Institute for Clinical Excellence guidance on NRT suggests that smokers under 18 who want to quit using NRT should discuss this with a relevant health-care professional. It is reasonable to use NRT in adolescent smokers who are motivated to quit and show evidence of nicotine dependence, until any contradiction arises.²⁸

2.8 Nicotine Vaccine: A novel therapeutic agent to treat the nicotine dependence. Since nicotine is a small molecule and acts as an incomplete antigen, it is linked to a carrier protein to stimulate necessary immune response. It can be achieved by either passive or active immunization. Various pharmacological companies have formulated nicotine vaccines, but none have been proved effective by clinical trials as far now, and research is in second phase of clinical trial²⁹.

2.9 Nicotine Preloading: It is based on the concept of use of NRT prior to quitting smoking. In this approach NRT is given for several weeks before actual quitting which results in habituation with use of NRT hence helpful after quitting, attenuation of desire to smoke due to nicotinic receptor saturation and also reduces satisfaction from smoking. Research shows that use of transdermal patches for few weeks before quitting gives better results³⁰.

2.10 Pharmacotherapy With Non-Nicotinic Agents : (Overview)

Bupropion: It was developed as an antidepressant, currently available as first non-nicotine based drug for smoking cessation. It primarily acts through the inhibition of dopamine re-uptake into neuronal synaptic vesicles. Although bupropion is a safe and cost effective smoking cessation agent, NRT remains the dominant pharmacotherapy to aid smoking cessation.³⁰ Bupropion is licensed for smoking cessation in both the UK and US and is recommended as a first line agent for smoking cessation.³¹

Varenicline: It maintains a moderate level of dopamine release, which reduces cravings and withdrawal symptoms during abstinence. It also blocks the reinforcing effects of nicotine obtained from smoke in case of relapse.³²

Apart from these two commonly used drugs, other drugs like Fluoxetine, Nortriptyline, Clonidine are also being used in selected individuals. For managing the withdrawal

symptoms, anxiolytics like alprazolam has also prescribed in some patients.³²

3. Conclusion

Tobacco burden is alarmingly at rise along with its various consequences. It is a global issue. Dentists being oral health care providers are mostly the first to recognize tobacco related oral changes. They are professionally authorized and have a responsibility to spread awareness among masses about the adverse effects related to this habit. Apart from spreading awareness, they should be well acquainted with the knowledge of different pharmacological & non pharmacological means of assisting the addicted individuals in quitting the habit. Nicotine Replacement Therapy being one of the important modes and has been found to be effective. Moreover, the individuals, who, during the course of quit attempt claim to have stopped the tobacco use should be tested for the authenticity of their effort & response as well as for the further management. For this assessment cotinine level estimation & carbonmonoxide test are widely used tests, the description of which is beyond the scope of this manuscript.

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