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Nicotine replacement therapy: a treatment angle for oral diagnostician

Abstract

As an oral diagnostician, many of our patients we come across are mostly the potentially malignant disorder cases. Either it might be leukoplakia, nicotina stomatitis, oral submucous fibrosis, tobacco pouch keratosis. In each of this cases where habits are the prime factor for occurrence of the lesions intraorally, the first line of treatment is cessation of the habits. But practically speaking, we don't spend much time about the cessation of the habits. As an oral diagnostician, it is our duty to motivate and educate the patient about the evil effects of the deleterious habits and need to follow up the patient and guide him to quit the habits. This article intends to highlight about one of the methods to stop the deleterious habit of smoking that is nicotine replacement therapy and therewith preventing the transformation of potentially malignant disorders into oral cancer.

Keywords: nicotine replacement therapy, potentially malignant disorders, oral cancer, smoking

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Introduction

Oral cancers have become very common tumors among the people mainly because of the tobacco habits addiction. Epidemiological studies show that the risk of developing oral cancer is five to nine times greater for smokers than for nonsmokers, and this risk may increase to as much as 17 times greater for extremely heavy smokers of 80 or more cigarettes per day.[1] As an oral diagnostician, we come across day to day at least one lesion which is habit associated, it might be either smoking, smokeless tobacoo or gutka or pan chewing. In spite of educating the patients about the ill effects of all this deleterious habits, patient won't quit the habits. So it is important for us find some alternative method to motivate and help the patient to stop habits. Nicotine replacement therapy (NRT) is one of the methods to quit the habit of smoking. This term is heard long time back but still we feel personally, the most of the general dentists are unaware about NRT and its dosing. We have tried to briefly enlighten about the NRT, its mechanism, various modes and its dosages which might guide the general dentists to use NRT regularly in their private practice and thereby prevent the transformation of premalignant lesions into oral carcinoma.

Ingredients of tobacco

Tobacco and its products are extremely toxic. Its smoke has at least 250 chemicals out of 7000, which are harmful and 69 are known carcinogens. Such as Stearic acid, Butane, Methanol, Acetic acid, Hexamine, Methane, Cadmium, Arsenic, Toluene, Ammonia, Carbon monoxide, and finally the main culprit, Nicotine, the addictive product of the tobacco, the role of which cannot be overlooked. Now talking about the smokeless form, 31 carcinogens have been identified till date. Like tobacco-specific nitrosamines, polycyclic aromatic hydrocarbons (PAHs), benzo[*a*]pyrene, urethane, formaldehyde, acetaldehyde, nickel, arsenic and chromium.[2]

Tobacco associated oral lesions

The toxic components of tobacco either as smoke or chewing form, causes damage to the oral mucosa. The free radicals produced from these products penetrate the epithelium and causes damage to the oral structures. The heat generated by the smoking habit also causes damage to these oral structures. These even stimulate the melanocytes. The following Table 1 shows the list of oral lesions associated with tobacco habits.

Table 1 Shows the list of oral lesions associated with tobacco habits

Sl no:	Oral lesion	Habits	Most commom Sites
1	Smoker's melanosis	Smoking	Buccal mucosa + labial mucosa + gingiva
2	Nicotina stomatitis	Smoking	Palate
3	Tobacco pouch keratosis	Smokeless tobacco	Vestibule
4	Leukoplakia	Smoking + smokeless tobacco	Buccal mucosa + labial mucosa
5	Oral submucous fibrosis	smokeless tobacco	Buccal mucosa + labial mucosa + palate + uvula
6	Oral cancer	Smoking + smokeless tobacco	Buccal mucosa+ alveolar mucosa+ tongue

The culprit: nicotine

Nicotine is the main active component of tobacco products leading to its addiction.[3,4] It is the main alkaloid and the principal modulator with psychopharmacological effects.[5] So, if we need to help the patient to quit the tobacco habits, we should have thorough knowledge about the neurochemical and psychopharmacological effects of nicotine.[6]

What is nicotine replacement therapy (NRT)?

NRT is replacing the harmful nicotine with the 'clean' or therapeutic nicotine. The 'clean' or 'therapeutic' nicotine is referred to as nicotine that is not associated with the harmful constituents found in tobacco smoke. So this NRT targets the patient in two aspects, firstly it helps in de-addiction, secondly the emotional aspects associated with it.[7]

Mechanism of action

NRT is assumed to help in release of neurochemical, dopamine from the nucleus accumbens, by stimulating the nicotinic receptors present in the ventral tegmental area of the brain. Not only it is effective centrally but its peripheral action also helps in reduction in nicotine withdrawal symptoms in regular smokers who abstain from smoking.[8]

It will not help to completely stop the habits, but helps to reduce to certain extent mainly because of the compromised nicotine delivery system. That means, none of the different delivery systems cannot reach high levels of nicotine in the arteries which is easily achieved during cigarette smoking. For medicinal products such as nasal spray or gum, inhalator, sublingual tablet, or lozenge achieve lower levels over a period of minutes and for transdermal patches, it's in hours.

Different forms of NRT:

The different NRT products have been summarized in Table 2 with the dose, its uses, adverse effects and the precautions. Various available forms includes: gum, transdermal patch, nasal spray, oral inhaler, and tablet.[9]

Table 2 Different formulations of NRT.[6,9,13,14]

NRT formulations	Available doses	Cautions / warning	Uses	Adverse events	Availability
Transdermal patches	5 mg, 10 mg, 15 mg doses worn over 16 hours 7 mg, 14 mg, 21 mg doses worn over 24 hours	For smokers with insomnia and other sleep-related adverse events, the patches should be removed before bedtime.	One daily on clean, unbroken skin; remove before bed (16 h patch) or next morning (24 h); new patch, fresh site	Local skin reaction Insomnia	US FDA (OTC), MHRA (OTC)
Chewing gum	2 mg and 4 mg doses	Temporomandibular joint disease Caution with dentures Do not eat or drink 15 min before or during use	Chew gum until taste is strong, then rest gum between gum and cheek; chew again when taste has faded. Try not to swallow excessively.	Mouth soreness, Hiccups, Dyspepsia and Jaw ache	US FDA (OTC) MHRA (OTC)
Sublingual tablet	2 mg dose	Nicotine dependence, insomnia	Rest under tongue until dissolved	Mouth soreness	MHRA (Rx)
Lozenge	1mg, 2 mg and 4 mg doses	Do not eat or drink 15 minutes before or during use One lozenge at a time Limit 20 in 24 hours	Allow to dissolve in mouth (about 20–30 minutes), moving from side-to-side from time-to-time. Try not to swallow excessively. Do not chew or swallow whole	Nausea/ Heartburn	US FDA (OTC) MHRA (OTC)
Nicotine inhalation Cartridge plus mouthpiece	Cartridge containing 10mg	May irritate mouth/throat at first	Spray into the mouth, avoiding the lips. Do not inhale while spraying. Use when cigarettes would usually be smoked or if cravings emerge. Do not swallow for a few seconds after spraying	Local irritation of mouth and throat	US FDA (Rx) MHRA (Rx)
Nicotine metered nasal spray	0.5mg dose/spray	Not for patients with asthma May cause dependence	Take shallow puffs approximately every 2 seconds or alternatively take four puffs every minute. Continue for up to 30 minutes.	Nasal irritation	US FDA (Rx) MHRA (Rx)

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Table Continued

NRT formulations	Available doses	Cautions / warning	Uses	Adverse events	Availability
Electronic cigarette		May cause dependence	E-Cigarette vapor is drawn very slowly into mouth, then held there for a second or two. Then, it can be inhaled if desired. The vapor is then expelled through the mouth or nose.	Mouth and airway irritation, chest pain, and palpitation [15,16]	Untill now, it is not approved by any agency
High dose nicotine patches[17]	≥42 mg daily	Irritation at the patch application site. Sleep disturbances	One daily on clean, unbroken skin; remove before bed	Headache, cardiovascular events, asthenia, dyspepsia, myalgia, and vomiting	Untill now, it is not approved by any agency
Combined Patch + acute forms (nicotine gum, spray, lozenge, & inhaler)[18,19]	Transdermal nicotine doses of 7, 14, and 21 mg + dosage of any one acute form	Nicotine dependence, insomnia	Both patch and acute nicotine forms should be used parallel.	Mouth and airway irritation, Nausea and vomiting	US FDA

*US FDA: U S Food and Drug Administration; MHRA: Medicines and Healthcare products Regulatory

Rx, Prescription; OTC, Over the counter

How soon after waking do you smoke your first cigarette?

a. Less than 5 minutes (3 points)

b. 5 to 30 minutes (2 points)

c. 31 to 60 minutes (1 point)

d. More than 60 minutes (no points)

How many cigarettes do you smoke each day?

a. More than 30 cigarettes (3 points)

b. 21 to 30 cigarettes (2 points)

c. 11 to 20 cigarettes (1 point)

d. 1 to 10 cigarettes (no points)

Score	Nicotine dependence
5 or 6	Heavy
3 or 4	Moderate
2	Low

Acute dosing is reached using gum, nasal spray, oral inhalers and tablets which helps in general craving relief with immediate release of nicotine whereas the transdermal patch acts slowly with sustained release.[10,11] Different formulations have different levels of efficacy with different rates of nicotine absorption. But the psychiatric counseling has an additive effect along with this formulations (Table 3).[12]

Table 3 Guide for the selection of NRT product.[7,20,21,22]

Product	Dosage Heavy - moderate	Dosage Moderate – low
Gum	4mg (after the first 2 weeks you may prefer to use the 2mg gum)	- 2mg - Use 1 piece per hour or 10-15 pieces per day
Patch	21mg/24 hour patch or 25mg/16 hour patch	- 14mg/24 hour path - Use 1 patch daily
Nicotine mouth spray	Maximum of 4 sprays an hour/ 64 sprays a day	One or two sprays under the tongue or onto the inner cheek to relieve cravings

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Table Continued

Product	Dosage Heavy - moderate	Dosage Moderate – low
Lozenge	- 4mg lozenge - 4mg & 2mg lozenges (9-15 per day) - 1.5mg lozenge (9-20 per day)	2mg lozenge or 1.5mg lozenge
Inhalation	- 1 cartridge when you have urge to smoke or every 2-4 hours - For best results use 3-6 cartridge for a day	
Combination therapy	- 25mg/16 hour patch in combination with 2g gum or lozenge - 21mg/24 hour patch in combination with 2mg gum or 2mg or 1.5mg lozenge - Patch in combination with any intermittent form of NRT	

Side effects of the NRT

The symptoms of nicotine overdose includes nausea, salivation, abdominal pain, sweating, headache, and diarrhea, dizziness, delayed wound healing and weakness.[25] At very high doses, it depresses neuronal activity whereas at low doses, it stimulates.[23,24] It acute lethal dose of nicotine in 40–60 mg[25] and it can lead to death at 500mg or more dosages, due to generalized blockade of respiration.[23] But, at the prescribed dosages of NRT, there was no evidence of any life threatening problems.[25,26]

Little caution is required while prescribing these NRT's in medically compromised patients like acute cardiovascular disease, pregnancy, or breast feeding. NRT is safe in stable cardiac disease, but caution is needed in unstable.[8] It has been studied that the adverse effects of NRT during pregnancy has substantially lower risk compared to that of smoking.[27]

Conclusion

NRT is one of the best options as a treatment for all habit associated lesions in the oral cavity. Most of the lesions respond well by cessation of the habits. And NRT helps the patient to quit the habit. As an oral diagnostician, we have to motivate and educate the patient about the use of NRT. This article briefly describes the dosages, forms and side-effects of NRT.

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Conflic of interest

No conflict of interest declared.

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