

Nicotine Replacement Therapy: An insight

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ABSTRACT

India is the second largest purchaser of tobacco globally and accounts for nearly one million deaths annually, which is one-sixth of the world's tobacco-related deaths. Notably, this figure is expected to grow up to 1.5 million annually by 2020. Now buck up this trend, the Union Ministry of Health and family welfare is promoting Nicotine Replacement Therapy to help people quit smoking as it is thought to be comparatively less dangerous than the tobacco smoking. It is used in various nicotine delivery methods to replace the nicotine obtained from smoking or any other tobacco usage. NRT reduces the withdrawal symptoms and helps to quit smoke cigarettes. So, the main aim of the review is to determine the effectiveness of different forms of Nicotine Replacement Therapy like chewing gums, transdermal patches, nasal sprays, inhalers and tablets in achieving abstinence from cigarettes.

KEYWORDS: Smoking, Tobacco, Nicotine Replacement Therapy

INTRODUCTION

Today tobacco use is a potent risk factor for many human diseases and conditions and it has a major deleterious effect on population health. It can be single preventable cause of death in the world. Although people are fully aware of the health impact but some of the tobacco users wanted to quit the habit but finds difficulty to stop due to the addictiveness of nicotine.¹ The adverse health effects of cigarette smoking are unassailable. In general the health of the tobacco users were reducing and also harm nearly every organ of the body which can induce many serious illness such as cancer, cardiovascular diseases, and pulmonary diseases. Furthermore, tobacco use is also the major cause of various oral diseases and conditions, ranging from mild to life-threatening such as restorations, stained teeth, taste derangement, halitosis, periodontal diseases, poor wound healing, oral precancerous lesions and oral cancers.²

The prevention and control of tobacco use is an emerging issue of global significance, and important association between smoking and oral health provide a unique opportunity for Dentists to involved in tobacco cessation activities. Tobacco cessation is one of the method which helps in improving the life expectancy and reducing the morbidity.²

Several pharmacological interventions are available but most commonly used to stop smoking is Nicotine Replacement Therapy (NRT). It is safe to use to the general population and high nicotine dependent groups including pregnant women, adolescents and the geriatric population.³ There was evidence that NRT helps to stop the craving and is now well accepted and many clinical guidelines recommend as first-line treatment for people seeking pharmacological help to stop smoking.⁴

So, this review aimed at various modes of nicotine replacement therapy methods currently used to treat nicotine dependence.

MODE OF ACTION

- Nicotine acts by stimulation of neural nicotinic acetylcholine receptors in the ventral tegmental area of the brain, which causes dopamine to release in nucleus accumbens and leads to reduction in nicotine withdrawal symptoms in regular smokers who abstain from smoking. NRT may also provide coping mechanism, making tobacco products less productive.
- Blood concentration of nicotine rises quickly during cigarette smoking and highest at the completion of each cigarette. Thus, nicotine absorbed from tobacco smoke can quickly reach various parts of the body.
- The neurotransmitters then cause the elation & relaxation to brain.³

FORMS OF NRT

All the commercially available forms of NRT are effective as part of a strategy to promote tobacco counseling. Several forms have been marketed in India they are as follows-

- Nicotine Patches
- Nicotine Gum
- Nicotine Lozenge
- Nicotine Sublingual Tablets
- Nicotine Oral Inhalers
- Nicotine Nasal Spray
- E- Cigarette

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- High-Dose Nicotine Patches
- Rapid Release Gum
- Combined Patch Plus Acute Forms

Nicotine Patches: Nicotine patches are placed onto the skin from where they release nicotine into the bloodstream at a relatively steady rate. Some patches last for 16 to 24 hours while some remain for complete time.⁵ Patches are available in variety of dosages, which enables the person to use strongest patches for higher-dependent smokers and lower-dependent smokers to use a lower. Patches are discrete, easy to apply and the strength of patch is reduced over time before stopping the release entirely.

The Advantage of nicotine patches is that compliance is simple and the patient can easily place the patch onto the skin in the morning, rather than actively using a product throughout the day. Disadvantage is that sometimes steady amount of nicotine is delivered and causes skin irritation beneath the patch in some individuals.³

Nicotine Gum: Nicotine gums are available in 2 doses, i.e. 2 mg and 4 mg. 12-15 pieces of gums are taken per day to start with about one per hour. Smokers those who are more dependent are advised to take 4 mg dose rather than 2 mg.⁵ After few weeks or months, the number of doses per day is gradually reduced until it is no longer required. Nicotine gum is not chewed like ordinary confectionary gum, but it is chewed slowly in the mouth until the taste is strong and then placed in the vestibule to allow absorption of nicotine into the bloodstream. Acidic beverages (like coffee, soda, beer) should be avoided, as they are shown to interfere with buccal absorption of nicotine; therefore, patients must avoid acidic beverages for about 15 minutes before and after chewing gum use.

The Disadvantage of nicotine gums is that some individuals did not like the taste or always feels like something having in their mouth.

Nicotine Lozenge: Nicotine Lozenges are available in doses of 2 mg and 4 mg. Doses and instructions for use are almost similar to as nicotine gum. The main difference is that lozenges are not chewed; but it dissolves into the mouth approximately for 30 minutes with some variation among different individuals.⁷ Lozenges are dissolved slowly under the tongue (as they are not swallowed) and then delivered into the systemic circulation. It is provided for individuals who need intermittent and controllable nicotine dosing, and finds difficulty from nicotine gums as they are not acceptable by some individuals. The amount of nicotine absorbed per lozenge is somewhat higher than by nicotine gums.

The advantage of Nicotine Lozenge is that they are easy to use and taste is acceptable.

Nicotine Sub-Lingual Tablet: Nicotine sub-lingual tablet dose is similar to as nicotine lozenge i.e. 2 mg. It is placed under the tongue and the nicotine is absorbed sublingually. The recommended dose for highly

dependent individuals is 16 to 24 tablets daily (i.e. 2 mg tablets maximum 30 tablets throughout the day) whereas for low dependency 8-12 tablets daily were used.⁶ Like the lozenge, the tablet also has the advantage of not requiring chewing. It is recommended for at least 8-12 weeks and after that the number of tablets used is reduced gradually.

Nicotine Oral Inhaler: Nicotine oral inhaler consists of mouthpiece and plastic cartridge which contains nicotine. When patient puff on the mouthpiece, the cartridge releases nicotine to help relieve from craving and satisfy behavioural aspects of smoking. The use of inhaler is to take shallow puff for every 2 minutes or 4 deep puffs every minute and continue this for at least 20 minutes. Each inhaler cartridge dosage contains 10 mg nicotine, out of which approximately 4 mg is delivered and 2 mg is absorbed following frequent "puffing". Use 6-12 cartridges per day for about 12 weeks, this depends on how many cigarettes per day were consumed. The major of nicotine is delivered into oral cavity (36%) and (36%) in the oesophagus and stomach. Moreover, only 4% is delivered to the lungs. As absorption is primarily through the oral mucosa, the rate of absorption is similar to that of nicotine gum.

The inhaler is contraindicated in patients with recent heart attack or stroke, pregnant and breast-feeding women, irregular palpitations and uncontrolled angina.

Nicotine Nasal Spray: One dose of nicotine nasal spray per hour (1 mg nicotine) for 10 hours produces average plasma concentration of 8ng/ml. It is rapidly absorbed into the blood stream from the nose. It was designed to deliver doses of nicotine more rapidly. The nasal spray is available in a multi-dose bottle with a pump mechanism fitted to a nozzle that delivers 0.5 mg of nicotine per 50- μ L squirt. Each dose consists of two squirts, one to each nostril.

Disadvantages of Nicotine nasal spray are nose and throat irritation, coughing and watering eyes.

Electronic Nicotine Delivery Systems (Ends) or Electronic Cigarettes: E-cigarettes are one of the newest nicotine delivery methods. There is much controversy and speculation about their effectiveness. An Electronic Cigarette also known as e-cig, shisha pen or personal vaporizer is a device that produces a vapour that resembles the look and feel of smoking. The vapour usually contains flavouring, some nicotine and a base liquid. The liquid usually contains propylene glycol, glycerol, water, nicotine and a variety of flavors that people can choose.³

By using this device, nicotine is delivered to the upper and lower respiratory tract without any combustion involved. Nicotine varies widely among products, ranging between 0 and 34 mg/ml. E-cigarettes are preferred as an alternative way for nicotine delivery among many smokers because of their realistic look, feel and taste compared to conventional cigarettes.

High-Dose Nicotine Patches: The high dose of nicotine patches is available in 22-mg which only replace approximately half of baseline serum nicotine and cotinine levels in smokers.

Therefore, higher transdermal nicotine doses of about ≥42 mg were evaluated. The efficacy of the patch is numerically higher abstinence rate that was achieved with high-dose transdermal NRT.³

Rapid Release Gum: A rapid-release gum developed to provide biphasic nicotine delivery, starting with increase amount of nicotine to promote rapid relief from craving and then levelling off to avoid overdosing.

The rapid-release gum achieved faster and more complete craving relief, differentiating itself from current nicotine.³

Combined Patch Plus Acute Forms: It is especially used in the individuals with bad withdrawal symptoms. To improve the efficacy of NRT, combination of one medication for passive nicotine delivery (e.g. transdermal patch) with another medication that permits delivery of nicotine and sudden relief from craving (e.g. gum, nasal spray and inhaler). Combined nicotine patch with an oral form of nicotine have shown to increase quit rates by 34-54% compared to nicotine patch alone.⁸

Several forms of Nicotine Replacement Therapy have been marketed (Table 1) which are effective as part of a strategy to promote smoking cessation.

ADVANTAGES OF NRT

- Nicotine Replacement therapy is easy to use and non-carcinogenic.
- NRT does not contain the harmful chemicals which were found in cigarettes and tobacco smoke, such as the chemicals known to cause cancer.
- NRT does not cause irritability.
- NRT reduces the craving for tobacco use.
- It doesn't stained teeth.
- It is cheaper and can easily be used by every individual.
- No tar was present.

CONCLUSION

Today, various forms of Nicotine Replacement Therapy have been used to help people stop smoking. Several nicotine medications are available in different forms, doses and flavors and their use has been recommended for all tobacco consumers who don't have medical problems. Evidence suggests that commercially available forms of NRT (like transdermal patches, nicotine gums, nasal spray, inhalers, sublingual tablets/lozenges and E-cigarettes) increase their chances of successfully stopping smoking. NRTs increase the rate of quitting by 50% to 70%. Beholding the potential capacity of NRT, it's essential for the professionals to become familiar with all

Nicotine products	Available Doses	Cautions/ Warnings	Uses	Adverse events	Availability
NICOTINE 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	Temporo-mandibular joint disease. Care for dentures users. 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)
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 20–30minutes), moving from side-to-side from time-to-time. Try not to swallow excessively. Do not chew or swallow	Nausea/ Heartburn	US FDA (OTC) MHRA (OTC)
SUBLINGUAL TABLET	2 mg dose	Nicotine dependence, insomnia	Rest under tongue until dissolved	Mouth soreness	MHRA (Rx)
NICOTINE ORAL INHALER	Cartridge containing 10 mg	Might irritate in mouth/ throat.	Spray in 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 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)
HIGH DOSE NICOTINE PATCHES	≥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,	Not approved by any agency
COMBINED PATCH + ACUTE FORMS (NICOTINE GUM, SPRAY, LOZENGE, & INHALER)	Transdermal nicotine doses of 7, 14, and 21 mg +dosage of any one acute form	Nicotine dependence and Insomnia	Both patch and acute nicotine forms should be used parallel.	Mouth and airway irritation, Nausea and Vomiting.	US FDA

Table 1: Nicotine replacement therapy formulations^{1,4,5,7} *US FDA: U S Food and Drug Administration; MHRA: Medicines and Healthcare products Regulatory, Rx: Prescription, OTC: Over the counter

forms of NRT which able to address the questions and needs of tobacco users who appear to be increasingly interested in tobacco cessation.

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