



## Nicotine replacement therapy: A review

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### Abstract

Nicotine replacement therapy (NRT) involves using different types nicotine delivery methods which replace the effects of nicotine obtained from smoking. NRT helps people who are willing to quit the habit. They crave straight into the bloodstream without producing the harmful effects produced by the chemicals present in the smoking forms. It aims to decrease the withdrawal symptoms associated with smoking. This article narrates various dosage forms of NRT.

### Introduction

Smoking is a most common habit found in population. Nicotine is a main ingredient found in tobacco. Nicotine is a plant alkaloid derived from plant belonging to the family Solanaceae. Cessation of smoking habit improves quality of life, reducing the rate of morbidity, and also treatment expenditure of possible advanced diseases caused by smoking habit. Various modalities are used for cessation of smoking starting from the counseling of the person. Nicotine replacement therapy (NRT) is the most commonly used formulation of nicotine to stop the habit of smoking. It includes various forms of nicotine delivery methods meant to replace the nicotine obtained from smoking or other forms of tobacco usage and helps the patient to deal with the sequence of withdrawal symptoms.<sup>[1]</sup>

Nicotine causes addiction in most of the smokers. Most of the patients who are willing to quit the habit suffer from withdrawal symptoms. NRT is the method of choice for such persons. Various nicotine dosage formulations are available as chewable gum, oral and nasal sprays, inhalers, patches, and sublingual tablets.

### NRT Products

#### Nicotine gum

Nicotine polacrilex (nicotine gum) was the first commercially available NRT product. It delivers nicotine transmucosally. Nicotine

gum is chewed intermittently and retained in the mouth for approximately 30 min for the release of nicotine. It is available in both 2 mg and 4 mg dosages. More success rate of withdrawal was achieved with 4 mg chewable gum. The number of doses per day is reduced gradually after a few weeks or months until it is no longer required. Patients should avoid acidic beverages (e.g., soda, coffee, and beer) as they tend to interfere with buccal absorption of nicotine.<sup>[2]</sup>

Nicotine gum is usually recommended for 6–12 weeks, with the maximum being 6 months.

After 2–3 months, the chewing time is reduced, or the gum is cut into smaller pieces, or the nicotine gum is alternated with sugar-free gum and gradually chewing is stopped completely. The disadvantage of nicotine gum is that some people do not like the taste or always feel like having something in their mouth.<sup>[3]</sup>

#### Rapid-release gum

Rapid-release gum provides nicotine faster with an increased delivery to fulfill rapid craving relief and also it avoids overdosing of nicotine.

When rapid-release gum was compared with the conventional nicotine gum, fast-release gum proved rapid and more complete relief of craving.<sup>[4]</sup>

#### Nicotine patches

Nicotine patches applied directly over the skin. There is a relatively steady rate of nicotine delivery through the skin.<sup>[5]</sup>

Nicotine patches are commercially available in various dosages. Dosage can be prescribed to the patient depending on the intensity of smoking dependence. These ranges in dosages will allow the person to reduce their intake of nicotine gradually over a period of several weeks or longer, and enables adjustment of their bodies to lesser nicotine levels and finally to a nicotine-free state.<sup>[6]</sup>

Nicotine patch is simple to use. The patient can place the nicotine patch over the skin once in the morning, rather than using throughout the day.<sup>[7]</sup> There is a slow release of nicotine when compared to other acute NRT products. Plasma concentration of nicotine gets elevated during the day with patch use than with acute NRT use. Dose can range from 5 to 22 mg of nicotine over a 24 h period, resulting in plasma levels similar levels seen in heavy smokers.

Reported side effects are local skin irritation.<sup>[8]</sup> To avoid skin irritation, the site of application of patch has to be changed daily. Insomnia has also been reported with 24 h patches.

### Nicotine oral inhaler

Nicotine inhaler consists of a mouthpiece and a plastic cartridge containing nicotine was designed to satisfy behavioral aspects of smoking, while delivering nicotine to minimize physiological withdrawal symptoms caused by tobacco cessation.<sup>[9]</sup> Nicotine inhalers deliver nicotine into the oral cavity (36%) and esophagus and stomach (36%). Very minimal quantity of nicotine is delivered to the lungs (4%). Absorption of nicotine occurs mainly through oral mucosa, and the rate of absorption is same as that of nicotine gum. Each inhaler cartridge contains 10 mg nicotine, of which up to 4 mg can be delivered and 2 mg can be absorbed following frequent "puffing."<sup>[10]</sup>

### Nicotine lozenges

Nicotine lozenges are available in 2 mg and 4 mg formulations. Lozenges dissolve in the oral cavity in about 30 min. It slowly delivers nicotine which gets absorbed through the oral mucosa and finally into the systemic circulation. The lozenge provides an alternative to the nicotine gum for persons who require intermittent and controllable nicotine dosing, but who do not find gum chewing acceptable. The amount of nicotine absorbed per lozenge appears to be somewhat higher than that delivered by gum.<sup>[11]</sup>

### Nicotine nasal/oral spray

There is a more rapid delivery of nicotine is seen with nicotine oral/nasal sprays when compared to other products. It is available as a multidose bottle with a pump which is fitted to a nozzle which delivers 0.5 mg of nicotine per 50  $\mu$ L single spray. Each dose consists of two sprays, one to each nostril.

Method of usage involves starting dose with 1–2 sprays/doses per hour, which can be increased up to a maximum of 40 doses/day. One dose of nasal spray per hour (1 mg nicotine) for 10 h produces average plasma concentrations of 8 ng/ml.<sup>[12]</sup>

### Combined therapy

People with intolerable withdrawal symptoms can opt for combined therapy. Commonly used combination is an NRT patch with nicotine gum or a nasal spray, which is taken every now and then to compensate the level of nicotine for a sudden craving. These combinations provide a small but significant raise in success rate of the NRT, when in comparison with a single dosage form.<sup>[13]</sup>

### Discussion

Nicotine is an addictive drug recognized worldwide. Quitting the habit can be difficult to the person and is usually associated with withdrawal symptoms.<sup>[14]</sup> Researches have found that the rate quitting the habit of smoking is doubled using NRT. However, success rate of quitting remains low.

Most of the NRT users stop the therapy without completing the course prescribed by clinician. This could be due to lack of information regarding the concerns about safety, cost, and lack of confidence. Patients assume that the treatment is no longer necessary once the cravings and withdrawal are controlled by the therapy. Hence, patients should be explained the scientific effects of therapy and duration of the therapy accurately before starting the therapy.<sup>[15]</sup>

Fewer side effects encountered in NRT include headaches, nausea, gastrointestinal disturbances, and sleep apnea.<sup>[16]</sup> Nicotine may not be advised in pregnancy, cardiovascular disease patients, and children/adolescents due to safety concerns.<sup>[17]</sup>

### Conclusion

Adverse effects of NRT are minimal. Choice of NRT depends on the persons need, tolerability, and cost considerations. Clinicians should inform the patients regarding the benefits and possible side effects before starting a therapy.

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