

Nicotine replacement therapy across the globe

Dr KK Aggarwal, 29 November 2018

<https://www.emedinexus.com/post/8808>

Nicotine replacement therapy (NRT) is used to relieve nicotine withdrawal symptoms by providing nicotine without the use of tobacco, while the smoker breaks the behavior of cigarette smoking. NRT is effective for smoking cessation. Many smokers worry that they will become dependent on NRT, but nicotine dependence rarely occurs, especially with the long-acting patch (USPSTF 2015). Smokers may also worry that nicotine causes cancer, which it does not.

NRT is safe to use in patients with known stable cardiovascular disease. While there is limited information regarding its use after acute coronary syndrome, it is generally used to reduce nicotine withdrawal symptoms in the hospital when needed. In randomized trials, individual NRT products were found to be superior to placebo, increasing quit rates up to twofold (1). One randomized trial among the NRT patch, gum, inhaler, and nasal spray found no difference in efficacy (2).

Single-agent NRT is less effective than combining the long-acting patch with a short-acting form such as gum, lozenge, or inhaler.

In a meta-analysis of nine randomized trials, use of a nicotine patch combined with a short-acting NRT product (gum, spray, or inhaler) was more effective than a single type of NRT (3). For smokers wishing to use NRT it is recommended to combine long- and short-acting NRT as initial therapy.

Differences in the bioavailability of nicotine replacement products provide a rationale for combining NRT products to increase efficacy for smoking cessation (4).

Each agent produces a lower blood nicotine level than does smoking one pack of cigarettes daily. In addition, smokers have experience titrating their nicotine intake to avoid both nicotine withdrawal and nicotine overdose, as they have done this titration throughout their years as cigarette smokers.

In general, NRT use is recommended for two to three months after smoking cessation, though NRT use for as long as a smoker is at high risk for relapse is acceptable because NRT is much safer than continuing to smoke. Some smokers may need to use the products indefinitely. NRT products can also be used while the smoker is still smoking.

Nicotine transdermal patch (long-acting): provides the most continuous nicotine delivery among all NRT products and is the simplest NRT to use. The patch has a long-acting, slow-onset pattern of nicotine delivery (5) but requires several hours to reach peak levels. The patch is available over the counter and by prescription in the United States. Dosing is determined by the number of cigarettes smoked daily when the patch is started: >10 cigarettes per day and weight >45 kg – Start with the highest dose nicotine patch (21 mg/day) for six weeks, followed by 14 mg/day for two weeks, and finish with 7 mg/day for two weeks; ≤10 cigarettes per day or weight < 45 kg – Start with the medium dose nicotine patch (14 mg/day) for six weeks, followed by 7 mg/day for two weeks.

Short-acting nicotine replacement therapy: (lozenge, gum, inhaler, or nasal spray) can be used as a single agent or can be added to daily nicotine patch therapy to help control cravings and withdrawal symptoms. However, short-acting forms require repeated use throughout the day, lead to more variable nicotine levels than the patch, and require more instructions for correct use. The nicotine patch, lozenge, and gum are available in the United States without a prescription; nasal spray and oral inhaler require a prescription. A nicotine mouth spray and sublingual tablet are available in some countries, though not in the United States.

Nicotine gum: Chewing the gum releases nicotine to be absorbed through the oral mucosa, resulting in peak blood nicotine levels 20 minutes after starting to chew. Nicotine gum is available in several flavors that most users find preferable to the original flavor. For those who smoke ≥ 25 cigarettes per day – 4 mg dose of gum is recommended; for those who smoke < 25 cigarettes per day – 2 mg dose of gum is recommended; chew at least one piece of gum every one to two hours while awake and also whenever there is an urge to smoke; up to 24 pieces of gum per day for six weeks. Gradually reduce use over a second six weeks, for a total duration of three months.

Nicotine lozenge is a commonly used short-acting NRT product, with pharmacokinetics similar to nicotine gum. Lozenges are easier to use correctly than nicotine gum and are also available in different flavors. Smokers who smoke within 30 minutes of awakening: 4 mg dose recommended; Smokers who wait more than 30 minutes after awakening to smoke: 2 mg dose recommended. Use up to one lozenge every 1 or 2 hours for six weeks. The maximum dose is five lozenges every 6 hours or 20 lozenges per day. Gradually reduce number of lozenges used per day over a second six weeks.

Nicotine inhalers consist of a mouthpiece and a plastic, nicotine-containing cartridge. The inhaler addresses not only physical dependence but also the behavioral and sensory aspects of smoking (having a cigarette between ones fingers and inhaling from the cigarette). When the smoker inhales through the device, nicotine vapor (not smoke) is released, deposited primarily in the oropharynx, and absorbed through the oral mucosa. Nicotine vapor does not reach the lungs to an appreciable extent. The ad lib use of the nicotine inhaler produces plasma nicotine levels that are roughly one-third of those that occur with cigarette smoking. The pharmacokinetics of the inhaler resemble those of nicotine gum. Use 6 to 16 cartridges per day for the first 6 to 12 weeks and gradually reduce dose over the next 6 to 12 weeks

Nicotine nasal spray results in peak nicotine levels 10 minutes after nasal spray use, which is a more rapid rise in plasma nicotine concentration than that produced by agents absorbed via the oral mucosa (gum, inhaler, or lozenge) (6). Dose is 1 or 2 sprays per hour. Use for about three months. The maximum dose is 10 sprays per hour, not to exceed 80 total sprays per day

Nicotine mouth spray: 1 mg nicotine is delivered per spray; use 1 or 2 sprays when cravings occur, up to four sprays per hour.

Nicotine sublingual tablet: One 2 mg tablet to dissolve sublingually (typically over 30 minutes) every one to two hours. Patients who are heavily nicotine-addicted can use two tablets sublingually (4 mg total) for each dose (7).

ENDS: Electronic nicotine delivery systems are a new entry in the market.

References

1. Cunningham JA, Kushnir V, Selby P, et al. Effect of mailing nicotine patches on tobacco cessation among adult smokers: a randomized clinical trial. *JAMA Intern Med.* 2016;176(2):184-90.
2. Hajek P, West R, Foulds J, et al. Randomized comparative trial of nicotine polacrilex, a transdermal patch, nasal spray, and an inhaler. *Arch Intern Med.* 1999;159(17):2033-8.
3. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev.* 2013 May 31;(5):CD009329.
4. Rigotti NA. Clinical practice. Treatment of tobacco use and dependence. *N Engl J Med.* 2002;346(7):506-12.
5. Hartmann-Boyce J, Aveyard P. Drugs for smoking cessation. *BMJ.* 2016;352:i571.
6. Hughes JR, Goldstein MG, Hurt RD, et al. Recent advances in the pharmacotherapy of smoking. *JAMA.* 1999;281(1):72-6.
7. Glover ED, Glover PN, Franzon M, et al. A comparison of a nicotine sublingual tablet and placebo for smoking cessation. *Nicotine Tob Res.* 2002;4(4):441-50.