2017;1(2):5-9.

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Targeting Nicotine Addiction - The Possibility of a Healthier Future

AISHWARYA ARORA[1], AMAR ANAND[2], VARSHA BHATIA[3]

ABSTRACT

Use of tobacco accounts for the highest number of illnesses and deaths around the world. Even though many people are well acquainted with the ill effects of tobacco consumption, they get addicted to its use. This addiction owes to the nicotine dependence in smokers or people consuming tobacco. If allowed for adequate awareness, the counselling becomes the first line of treatment but very few people get convinced to quit this habit and thus agents such as nicotine replacement therapy come into play as a major factor in increasing the number of quit rates. The efficacy may depend on the route of NRT administration which may vary from nicotine gums, lozenges, sublingual tablets, inhalers etc. This review article discusses both the current use and future of NRT.

KEYWORDS: Tobacco, Nicotine gum, Replacement therapy, Transdermal patch, Nicotine safety

INTRODUCTION

Currently tobacco use causes approximately 4.9 million deaths per year. This figure is expected to rise to more than 10 million deaths per year by the year 2030. It is estimated that 1.9 billion people use tobacco products worldwide.[1] Tobacco maybe smoked in a variety of ways such as cigarettes, bidis, cigar, chutta, pipe, hookah, reverse smoking etc. The smokeless forms of tobacco are paan masala, areca nut, manipuri tobacco, khaini, zarda etc. Smoking is one of the primary causes of both morbidity and mortality worldwide. One in every two long term smokers die due to a smoking related illness. For every one death, 30 people are left with some serious illness. On an average, a smoker dies 10 years younger than a non smoker.[2] Figure 1. briefly explains how tobacco addiction occurs.

Smoking not only affects every organ of the body, it has deleterious effects on the oral cavity too. Smokers may be affected by various non communicable forms of diseases such as cancers of the lung, oral cavity, pharynx, oesophagus, cardiac diseases, hypertension etc. The oral effects of smoking are : halitosis, tooth discolouration, increased bone loss within the jaw, increased risk of developing gum disease, increased risk of tooth loss, delayed healing following tooth extraction, periodontal treatment or oral surgery, increased risk of white lesions (e.g. leukoplakia), increased risk of developing oral cancer. Along with smokers, the health of non-smokers is also endangered since passive smokers are exposed to five times more carbon monoxide levels. Smoking may negatively impact the health of people at all stages of life – unborn babies, infants, children, adults and the elderly.

The knowledge of such damaging and harmful health effects associated with tobacco use warrants an immediate need for tobacco control and cessation. Quitting smoking has a considerable impact on health and overall life expectancy of an individual.

With the advent of various non-pharmacological and pharmacological interventions (of which counselling and nicotine replacement therapy are the most common)to aid in smoking cessation, nicotine replacement therapy can be used to assist smokers with their addiction. NRT improves cessation rates by approximately 70%.[3] It is recommended safe to use in high risk group patients including pregnant and breastfeeding women, adolescents and smokers with cardiovascular disease.

What is nicotine replacement therapy?
NRT acts as a powerful intervention aid for smoking cessation. It is a pharmaceutical way which allows consumption of nicotine without the use of tobacco products. The use of NRT increases the abstinence rates by about 50-70%.[4] Any cigarette smoker who is motivated to quit may receive benefits from NRT. NRT must preferably be given in combination with behavioural support – this ensures benefits to patients who are not yet motivated. As opposed to consumption of tobacco in a smokeless or smoke form – NRT products contain relatively less amounts of nicotine and are also devoid of any other chemicals or toxins.

The use of NRT also reduces the nicotine withdrawal symptoms (such as irritability, difficult concentration, disturbed sleep, increased appetite and weight gain etc.)[5] in smokers who refrain from smoking since administration of nicotine causes stimulation of nicotine receptors in the ventral tegmental area of the brain and therefore initiates release of dopamine in the nucleus accumbens. The use of NRT does not entirely eliminate the withdrawal symptoms since none of the available NRT systems completely replace the effects produced by smoking.[6] The NRT products rely on venous absorption and achieve much lower levels over a period of few minutes (for gums, lozenges, sublingual tablets, nasal sprays) and hours (for transdermal patches) whereas the nicotine obtained from consuming tobacco products produces rapid arterial nicotine levels.[7]

Forms of Nicotine Replacement Therapy:

- Nicotine gum
- Nicotine lozenges
- Nicotine sublingual tablet
- Nicotine oral inhaler
- Nicotine nasal spray
- Nicotine transdermal patch

Nicotine gum: It is the first kind of NRT made available to consumers. Nicotine gum is available in two dosages – 2mg and 4mg, without a prescription. The gum must be periodically chewed and is held in mouth for about 30 minutes as opposed to chewing it like an ordinary gum. The 4 mg gum is advised for heavy smokers (>25cigarettes/day). The dosages are gradually tapered down before stopping its use entirely. The use of gum is recommended for 1-3 months at a definite interval schedule.[8] Minor side effects such as gastrointestinal problems and hiccups may be noticed.[9]

Nicotine lozenges: Patients unwilling to chew gums may be advised help with nicotine lozenges. These lozenges are also available in 2mg and 4mg dosages. Unlike the nicotine gums, the lozenges are not to be chewed – these dissolve in mouth in about 30 minutes. The amount of nicotine absorbed per lozenge is relatively higher than the gum.[8] A 4 mg dosage is usually recommended, although it depends on the cigarette dependency of the smoker. Adverse effects with lozenges are insomnia, cough, headache, heartburn, hiccups.[9] Both gums and lozenges are absorbed slowly through the buccal mucosa and delivered into systemic circulation.[8]

Nicotine sublingual tablet: This tablet must be held under tongue for sublingual absorption. A 2mg tablet has the same level of nicotine as a 2 mg gum. Similar to the lozenge, this tablet does not require to be chewed. The dosage depends on the number of cigarettes smoked by the patient per day. For those smoking <20 cigarettes/day, one tablet/hour is recommended. Anyone smoking >20 cigarettes/day is advised to take two tablets/hour. The patient must never exceed more than 40 tablets in a day. The dosages should be gradually tapered after a period of 12 weeks.[9]

Nicotine oral inhaler: The device consists of a plastic cartridge (containing nicotine) and a mouthpiece. This type of NRT mimics the behavioural aspects of smoking and reduces the physiological symptoms related to withdrawal. Even though it is an inhaler, the nicotine is majorly delivered to the oral cavity and very little to the lungs. The rate of absorption is similar to that of the nicotine gum.[8]

Nicotine nasal spray: In this, nicotine is delivered from a spray which is rapidly absorbed into the bloodstream. There is 10mg/ml of available nicotine in each dispenser. This kind of NRT mimics the rapid levels of nicotine achieved by smoking.[10] The spray is usually available on prescription. A single dose means two sprays - one to each nostril and equals 1 mg. Recommended dose is 1-5 sprays/hour but no more than 40

sprays/day. The nasal spray may however cause nasal and throat irritation, coughing, sneezing and watery eyes.

Despite of the speed by which nicotine is delivered to the brain, the patient compliance with nasal spray is lower when compared to other forms of NRT.[9]

Nicotine transdermal patch: Another accessible method of delivering nicotine using NRT is by using a transdermal patch. These deliver nicotine at a constant rate when applied to skin. Patches are available in a variety of dosages (5-22mg) depending on the need of smoker. It delivers nicotine relatively slowly when compared to other NRT formulations. Some patches may last 16 hours which is to be worn for the time period the patient is awake while others may last 24 hours.[10] The 24 hour patch may disturb sleep, but are effective in reducing the early morning cravings of nicotine. Compared to other forms of NRT, these patches offer a better compliance as it avoids the active use of product throughout the day.[8] The patient may apply the patch once in the morning. However, transdermal patches may cause local skin reactions. To reduce local irritation, the site of application must frequently be changed.[8,11] Other side affects are gastrointestinal problems, headache and dizziness.[9]

Apart from the above mentioned types of NRT, recent more effective advances are:

Rapid release gum: These formulations release nicotine in two phases – increased delivery to enhance relief from craving followed by reduced release of nicotine to avoid overdosing.[8] These gums achieve faster and more efficient relief from cravings compared to the conventional nicotine gums. They also cause a reduced craving intensity for tobacco products. The differences in the efficacy of the nicotine gum and rapid release nicotine gum can be seen as early as during the first three minutes of administration.[12]

High dose nicotine patch: These offer nicotine doses of up to or greater than 42mg and are seen to be more efficacious than 22mg patches. Although these result in higher quit rates, they have not yet been established in medical literature.[8]

Combination therapy: Similar to the synergistic effect seen in various drug interactions, combining a passive nicotine delivery system (transdermal patch) with an active nicotine medication (gum, lozenge, sublingual tablet)improves the efficacy of NRT. The passive system achieves constant concentration of nicotine – which helps relieve cravings and withdrawal symptoms whereas the faster acting preparations offer immediate relief. Using a combination therapy has been seen to increase quit rates by 34-54% compared to using a patch alone.[8]

The combination therapy of NRT and bupropion (a potent drug for smoking cessation) also exhibits superior results compared to using either agent alone.[13]

Nicotine vaccine: Use of vaccines is currently employed to treat various disorders – among these vaccines many are still under investigation. One of such vaccinations is for the treatment of nicotine dependence. The nicotine vaccine is one of the latest approaches which aims at eliminating nicotine dependence. This works on the principle of antigen-antibody reaction. Upon smoking a cigarette, nicotine quickly passes into the bloodstream to enter the brain within seconds, where it causes release of dopamine to exert its effects similar to those caused by tobacco consumption.[7]

With introduction of nicotine vaccines, the immune system is prompted to produce antibodies against nicotine which bind to nicotine and thus prevent it from entering the brain due to the change in size of the nicotine molecule. This will therefore prevent the release of dopamine which is known to cause addiction in a smoker – thus breaking the vicious cycle of nicotine addiction.[14]

Following vaccination, there is an irreversible effect on immune system for 6-12 months. This is an advantage over the existing cessation therapies as it may improve patient compliance to NRT.[7]

Is nicotine safe?

Adverse effects caused due to NRT, if any, are considered minor and much safer than continuing

the use of cigarettes.

Nicotine when delivered from NRT is absorbed slowly and reaches lower peak blood levels as opposed to the sudden high levels achieved by smoking.[5] Administration of nicotine using NRT also prevents exposure to other toxins found in cigarette. However no medication is devoid of adverse effects and the use of NRT is no exception.[7] The adverse effects (other than those caused due to nicotine poisoning) are minimal and harmless when compared to the deleterious effects of smoking. As mentioned above, the adverse effects due to NRT which vary with the type of delivery system are skin irritation, throat irritation, disturbed sleep, nausea, hiccups etc. The risk of nicotine poisoning is very rare. The acute lethal dose of nicotine is within the range of 40-60 mg. This can only occur with inappropriate use of NRT – use of more than one form of NRT, use of dosages higher than recommended or continuing smoking while receiving NRT therapy.[11]

CONCLUSION

Currently there are more myths about NRT and only little is known about its efficacy. The clinicians and public health centres must spread awareness about the effectiveness of NRT. Due to lack of information and improper availability of NRT, not many people are familiar with this therapy. The major belt (living in rural areas of India) that is exposed to tobacco products is not aware about the ill effects of smoking or the benefits of quitting.

To avail utmost advantage of NRT, government initiatives should be taken at national level in the form of both free of cost availability of NRT to people below poverty line and its awareness at dental camps.

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Cite this article as:
Arora A, Anand A, Bhatia V. Targeting Nicotine Addiction - The Possibility of a Healthier Future. Int Healthcare Res J 2017;1(2):5-9.

Source of support: Nil, **Conflict of interest:** None declared

AUTHOR AFFILIATIONS:
1. Intern
2. PG Student, Department of Prosthodontics
3. Intern
BRS Dental College and Hospital, Sultanpur, Panchkula, Haryana, India

Corresponding Author:
Aishwarya Arora
Intern
BRS Dental College and Hospital
Sultanpur, Panchkula, Haryana, India
Pin Code- 134118
+91 9465033091
aroraaishwarya.94@gmail.com

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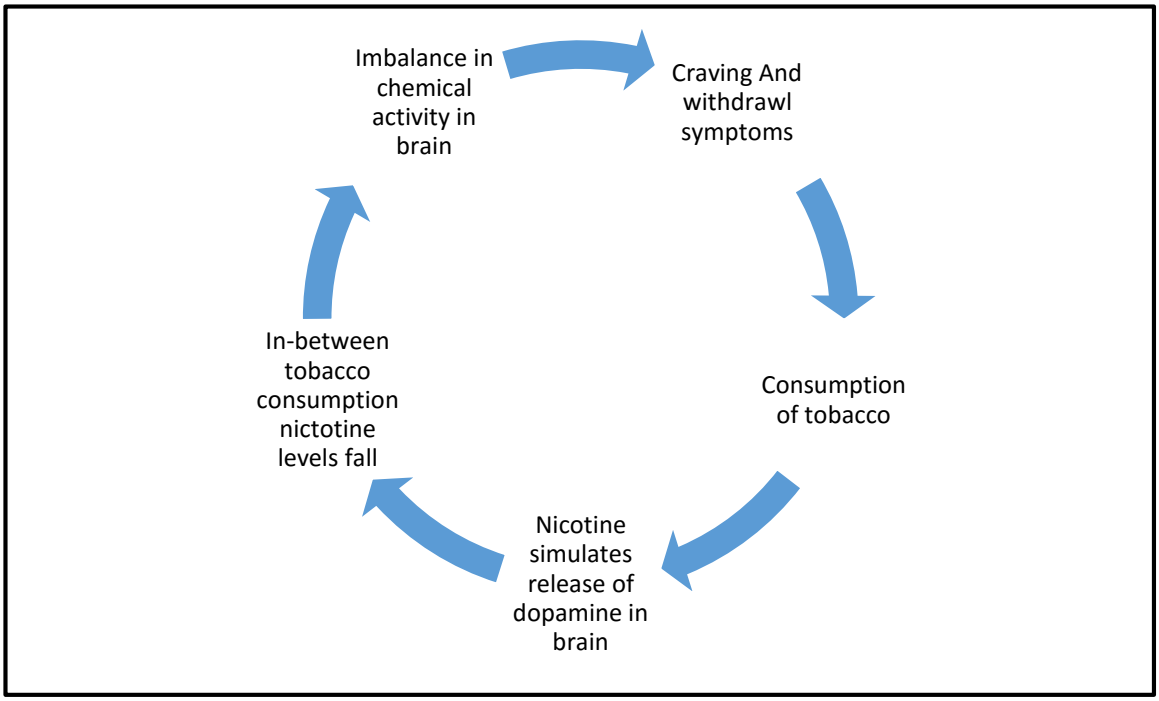

Figure 1. Short cycle explaining addiction to tobacco