

## Practical approach to tobacco cessation: A review

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Received – 07 August 2020

Initial Review – 18 August 2020

Accepted – 04 September 2020

### ABSTRACT

Tobacco use is one of the most important causes of preventable death and disability worldwide. Quitting the habit of tobacco consumption has substantial benefits. Although, nicotine gum was the only Food and Drug Administration approved pharmacotherapy until 1991, however, today, a variety of therapies are available for tobacco cessation. It becomes important that the health care professionals are familiar with the spectrum of therapies so that they can address the needs of tobacco users effectively. Health care professionals can contribute to the health of the community by motivating the tobacco users to quit and assisting them in the process of tobacco cessation. This review discusses the pharmacological and nonpharmacological therapies that have been used for the treatment of tobacco dependence.

**Key words:** Behavioral therapy, counseling, nicotine replacement therapy, tobacco cessation

Nicotiana, the generic name of tobacco plant is derived from the name of the French ambassador, Jean Nicot, who introduced tobacco into the French court in 1560. Tobacco was brought to India in the late 16th and early 17th century [1]. Since then tobacco consumption has continued to rise in India. It has been estimated that there are 1.1 billion smokers worldwide, most live in developing countries (84%) and 182 million (16.6%) of them live in India [2]. The US Surgeon General's Report 2004 reports that smoking harms almost every organ of the body causing many diseases and reducing the health of the smokers in general. Globally, tobacco is responsible for the death of 1 in 10 adults with 2.41 million deaths in developing countries and 2.43 million deaths in developed countries [3]. Because of the morbidity and mortality associated with tobacco use and the substantial benefits of cessation, it is vital that all the

clinicians make a concerted effort to motivate tobacco users to cease their use of tobacco and to assist in their cessation process. The present review discusses the pharmacological and nonpharmacological tobacco cessation methods which will effectively assist a person trying to get rid of this deadly habit of tobacco consumption.

### TOBACCO CESSATION METHODS

The Clinical Practice Guideline on treating tobacco use and dependence published by the Public Health Service offers the following recommendations (5A's) to intervene with tobacco users willing to quit. The 5A's is a model that presents the five major steps in providing a brief intervention in the primary care setting. These steps are: (1) ask the patient if he or she uses tobacco, (2) advise him

or her to quit, (3) assess willingness to make a quit attempt, (4) assist those who are willing to make a quit attempt, and (5) arrange for follow-up contact to prevent relapse. These strategies are designed to be brief, requiring 3 minutes or less of direct clinician time. Office systems that institutionalize tobacco-use assessment and intervention will foster the adoption of these strategies. First-line pharmacotherapies have been found to be safe and effective, therefore should be considered first as part of tobacco dependence treatment except in cases of contraindications [4]. On the other hand, second-line medications although show evidence of efficacy for treating tobacco dependence however are associated with potential side effects, therefore are not approved by FDA for tobacco dependence treatment [5].

## FIRST LINE PHARMACOTHERAPY

### Nicotine Replacement Therapy (NRT)

Nicotine replacement therapy is the use of various forms of nicotine delivery methods intended to replace nicotine obtained from smoking or other tobacco usage and way of getting nicotine into the bloodstream without smoking [6]. There are 6 types of nicotine replacement products in the market.

**1. Nicotine transdermal patches:** Nicotine patches are applied to the skin and deliver nicotine through the skin at a relatively steady rate. Patches are applied each morning on a rotational basis to a variety of non-hairy skin sites [7, 8]. During initial treatment period, patient should receive a dose same as or slightly more than the number of cigarettes smoked per day for 4 weeks. Following which, the dose can be stepped down by 7-14 mg every 2 weeks. The advantage of this therapy is good patient's compliance, while the adverse effect is skin irritation at the patch site [9].

**2. Nicotine nasal spray:** The nicotine nasal spray was approved by the FDA in 1997 [10]. Each spray contains 0.5 mg of nicotine with a dose of 1 spray in each nostril (total =1 mg). Patients are instructed to spray it against the lower nasal mucosa and not to sniff it up into the upper nasal passages. The treatment is started with 1 or 2 doses per hour, which may be increased up to a maximum of 40 doses per day. The most common adverse effects are cough, nasal and eye irritation which usually subside after the first week [11].

**3. Nicotine gum:** The first NRT approved by the US FDA in 1984 was a transmucosal product, nicotine gum

containing 2-mg nicotine, intended for absorption through the mucosal lining of the oral cavity. The 4-mg form was approved later in 1992 [11]. Smokers who use less than 25 cigarettes per day are instructed to use the 2 mg dose and those who smoke more are instructed to use the 4-mg gum [7]. The patients should be instructed to chew the gum a few times until they feel a mild tingling or peppery taste indicating nicotine release, then park the gum between the cheek and gums for several minutes before resuming chewing. Repeated cycles of "chew and park" will allow gradual nicotine absorption and should be continued for approximately 30 minutes per piece of gum. The most common adverse effects are jaw soreness, nausea, indigestion and mild burning sensation in the mouth and throat [9].

**4. Nicotine lozenge:** Like nicotine gum, the nicotine lozenge delivers nicotine through oral mucosa. It is available in 2 and 4 mg since 2002 and the most recent NRT to receive approval in United States for smoking cessation [7]. For patients who smoke the first cigarette within 30 minutes after waking, 4-mg strength is indicated and if the first cigarette is smoked after 30 minutes of waking, 2-mg dose is prescribed. The lozenge should be placed between the cheek and gum and not chewed or swallowed whole. The most common adverse effects are headache, diarrhea, heartburn, hiccups and nausea [9].

**5. Sublingual tablet:** The product is designed to be held under the tongue. Patients who smoke less than 20 cigarettes per day are instructed to use one tablet per hour, whereas those who smoke 20 or more cigarettes per day must use 2 tablets every hour, not exceeding 40 tablets per day. It is recommended to use sublingual tablet for 12 weeks, following which tapering of the dose is advised [7].

**6. Vapor Inhaler:** The nicotine inhaler delivers vaporized nicotine to the oral mucosa where it is absorbed. The inhaler consists of a mouth piece and plastic cartridge containing nicotine. When the inhaler is puffed, nicotine is drawn through the mouth piece into the mouth. Each inhaler cartridge contains 10 mg nicotine, of which 4 mg can be delivered and 2 mg is absorbed. The recommended duration of treatment is 3 months, after which patients may be weaned by gradual reduction of the daily dose over the following 6-12 weeks [7].

### Bupropion

Bupropion is the first non-nicotine-containing agent to be approved by the FDA for smoking cessation, is a monocyclic antidepressant that inhibits the reuptake of

dopamine and norepinephrine [10]. Patients are instructed to begin taking bupropion 1 week before their quit-smoking date, at an initial dose of 150 mg per day for 3 days followed by 150 mg twice daily for approximately 6-12 weeks. Long-term treatment with bupropion sustained release may reduce or delay relapse to smoking [9]. It also can be stopped abruptly and can be used in combination with NRT and with varenicline. The most common adverse effects are dry mouth and insomnia. Seizure disorders, history of anorexia and bulimia and uncontrolled hypertension are the contraindications for bupropion therapy [12, 13].

## SECOND LINE PHARMACOTHERAPY

**Varenicline:** Varenicline is a partial agonist of a nicotinic receptor which is associated with addictive effects, was approved by the FDA in May 2006 for smoking cessation [7]. The recommended dosing for the first week of treatment is 0.5 mg once daily for 3 days followed by twice daily for next 4 days; the dosage is then “ramped up” to 1 mg twice daily for 11 weeks. Patients should plan to quit on day 8 of therapy. The most common adverse effect is nausea and drowsiness and serious adverse effects include, suicidal thoughts, aggressive and erratic behavior [9].

**Nortriptyline:** Nortriptyline is a tricyclic antidepressant that predominantly act to block reuptake of norepinephrine which suppress the nicotine withdrawal symptoms [7]. Previous studies reported that nortriptyline led to an increased cessation rate compared to placebo and transdermal patches. Most common side effects include, tachycardia, blurred vision, urinary retention, dry mouth, constipation, weight gain or loss [14-16].

**Clonidine:** Clonidine is used primarily as an antihypertensive medication and has not been approved by the FDA as a smoking cessation medication [5]. It reduces anxiety, tensions and irritability thus showing promise as a smoking cessation aid. One study showed that of clonidine had twice the rate of abstinence than with placebo. The Cochrane review of six clinical trials showed evidence of efficacy, but its usefulness is limited by appreciable sedation and postural hypotension [17].

### Other non-nicotine pharmacological agents

- Mecamylamine is a ganglion-blocking agent used previously has shown contradictory results [5, 18].

- Fluoxetine has been used as an tobacco cessation agent, however, no significant improvement in smoking cessation rates have been reported [19].
- Moclobemide is a monoamine oxidase (MAO) inhibitor and has shown increased cessation rate in heavy smokers. Cigarette smoke has MAO inhibitory properties and smokers have low MAO activity. However, the role of MAO inhibitor in smoking cessation needs to be evaluated [11].
- Nicobrevin is a formulation containing menthyl valerate, quinine, camphor and eucalyptus oil. A placebo-controlled double blinded trial carried out with this product has shown it to be superior to placebo in quitting smoking [12].
- Methoxsalen has inhibitory effect on the enzyme cytochrome P450 2A6 which is responsible for the metabolism of nicotine in the body. Inhibition of this enzyme reduces metabolism of nicotine and thus prolongs its therapeutic action. One odd trial has been reported to increase nicotine level in plasma. However, further investigations to study the toxicity and safety of the drug for the same needs to be carried out [8].
- Glucose tablets have shown to increase one month abstinence rates significantly in a placebo-controlled study. The low cost of glucose tablets can make it a useful adjunct in smoking cessation treatment [19].
- Rimonabant is a selective cannabinoid receptor antagonist, has shown good results in the treatment of obesity and smoking cessation. The most common side effects were nausea and upper respiratory tract infections [8,19].
- Herbal cigarettes (tobacco-free/ nicotinefree cigarettes) were cigarettes developed in 2000 which contains a mixture of different herbs and/or other plant material. Although, Asian herbal tobacco cigarettes claim to reduce harm, but no published literature is available to verify or investigate unidentified toxicities [20].
- Electronic cigarettes contain a battery and an electronic device that produces a warm vapour or ‘mist’ containing nicotine, and does not produce smoke. Although they are less harmful than tobacco smoking, yet are more dangerous than medicinal nicotine inhalers. According to FDA analysis, e-cigarettes contain carcinogens [21]. Therefore, in September 2008, the WHO issued a release proclaiming that it does not consider the electronic cigarette to be legitimate smoking cessation aid [22].

- Nicotine vaccine induces antibodies against the nicotine molecule, prevents the drug from reaching neural receptors and produce similar effects associated with smoking. By eliminating the nicotine that reaches the brain, there is reduction in the efficacy of tobacco smoking, eventually leading to extinction of the behavior. Although nicotine vaccines could be theoretically used in adolescents to prevent initiation of tobacco use, the risks, benefits and ethical implications of nicotine vaccine will undoubtedly require much more thorough evaluation before such application could be recommended [23]. Phase I studies of nicotine vaccines carried out till date, suggest that these vaccines are safe, well-tolerated and immunogenic [8].

### NON-PHARMACOLOGICAL METHODS

**Counseling:** Counseling about smoking cessation can be delivered effectively in person or by telephone. Providing a brief period of counseling (3 minutes or less) by trained counselors is more effective than simply advising the patient to quit. It doubles the rate of tobacco cessation as compared with no intervention [5, 24].

**Hypnosis:** The patient is put into a deeply relaxed state where he is open to suggestions that motivate to quit smoking and increase negative feelings towards cigarettes. There is insufficient evidence to recommend hypnotherapy as a specific treatment for smoking cessation [25].

**Acupuncture:** Acupuncture is used with an aim of reducing the withdrawal symptoms by triggering the release of endorphins. The evidence suggests that acupuncture for smoking cessation may, in the short term, be more effective than no treatment [26].

**Behavioral Therapy:** Behavioral therapy programs consist of self-help, individual counseling/therapy or group behavior therapy. Self-help materials include written leaflets and manuals, audio/video tapes and computer programs. Potentially, they can reach many more people than interventions delivered by therapists [18]. Although self help materials are helpful, group programs have shown better cessation rates than self-help and individual counseling [27].

### CONCLUSION

Although, tobacco use is associated with significant morbidity and mortality, cessation of the habit has substantial benefits. Hence, physicians should routinely identify patients' smoking status and willingness to quit,

advise and assist in the process. The choice of pharmacotherapy depends on patients' preferences and past experiences. A general approach is to start with a single agent and subsequently add a second agent if the patient experiences withdrawal symptoms, cravings, or difficulty maintaining abstinence. The physicians' awareness of the benefits and limitations of the available medications is of utmost importance which not only benefits the patient but also the society.

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**How to cite this article:** Mittal S, Jain Vibha, Duvvuru LS, et al. Practical approach to tobacco cessation: A review *J Orofac Res*. 2020; 14 September. Epub ahead of print.

*Funding: None; Conflict of Interest: None Stated.*