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REVIEW ARTICLE

Pharmacological and Non-pharmacological Interventions for Smoking Cessation

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ABSTRACT

Dentists are in a unique position to advise the tobacco users to quit the habit through various methods and with effective counseling. The present review provides an outline of the different pharmacological and non-pharmacological interventions for cessation of smoking. Smokers who receive assistance – behavioral, pharmacologic, or both – can experience quit rates of around 20% at least 6 months after quitting. Given the nature of tobacco dependence and the associated difficulty in quitting, pharmacotherapy should be advocated, particularly in patients for whom it is not contraindicated and for whom prior unassisted quit attempts have been unsuccessful. For smokers who are dissonant, physicians should use motivational strategies, such as discussing barriers to cessation and their solutions. For smokers who are ready to quit, the physician should show strong support and help to set a cessation date. Physician counseling for smoking cessation is among the most cost-effective clinical interventions.

Keywords: Cessation, Interventions, Non-pharmacological, Pharmacological, Smoking, Tobacco.

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INTRODUCTION

Smoking and use of tobacco increases the disease burden and death, causing serious health, economic, environmental, and social effects.[1] According to the World Health Organization (WHO), the use of tobacco in smoking form is the single largest cause of disease and premature death, claiming one life every 8 seconds and killing one of 10 adults globally, which can be preventable.[2] A survey of WHO in 2011 states that there were 100 million premature deaths due to use of tobacco in 20th century, and if this continues by 21st century the number is expected to increase to 1 billion.[3] In India, the use of tobacco grows at 2 to 3% per annum, and by 2020 it will account for 13% of all deaths in the country.[1]

Smoking and use of tobacco is a global epidemic causing death of more people than HIV/AIDS, malaria and tuberculosis combined. Necessary steps must be taken to prevent this manmade epidemic globally and in the home country. The authors in this review discussed the important steps taken for prevention of smoking, giving more emphasis on pharmacological and non-pharmacological methods of smoking cessation.

PHARMACOLOGICAL METHODS FOR SMOKING CESSATION

"Giving up smoking is the easiest thing in the world. I know because I've done it thousands of times" – Mark Twain.

According to the Clinical Practice Guideline for treating tobacco use and dependence,[4] all smokers trying to quit the tobacco use must be encouraged to use one or more effective pharmacological agents for cessation except in some special circumstances. The following are the pharmacological agents that are used for smoking cessation[5,6] (Table 1).

Table 1: Pharmacological agents used for smoking cessation

First line agents	1 Nicotine replacement therapy: Nicotine gum, transdermal patch, nasal spray, oral inhaler and lozenge
Second line agents	1 Nortriptyline 2 Clonidine
Combination therapy	1 Nicotine replacement therapy and sustained-release Bupropion 2 Nicotine replacement therapy and nortriptyline
Herbal therapies	1 Lobeline, Dianicline
Emerging therapies	1 Anxiolytic agents – buspirone, diazepam 2 Selective serotonin reuptake inhibitors – fluoxetine, paroxetine, sertraline 3 Mecamylamine 4 Rimonabant 5 Varenicline

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First Line Agents

Nicotine Replacement Therapy (NRT)

Nicotine replacement therapy acts on nicotine receptors in the ventral tegmental area of the brain due to which dopamine is released into the nucleus accumbens. The rationale of using NRT for smoking cessation is twofold. First, it reduces the physical withdrawal symptoms associated with nicotine abstinence among dependent smokers. Second, while alleviating the physiologic symptoms of withdrawal, the smoker can focus on the behavioral and psychological aspects of quitting before fully abstaining from nicotine.[7] The different agents used for NRT, their dosages, and availability are described in Table 2.

Second Line Agents

These agents are not approved by Food and Drug Administration (FDA) for smoking cessation and are more prone to adverse effects, so should be used in patients who are unable to use first line agents.

Nortriptyline

It is a tricyclic antidepressant. In general, the dose is started at 25 mg/day and is gradually increased over 2 weeks to a target dosage of 75 to 100 mg/day. As it causes sedation, daily dosage should be taken at bedtime. The adverse effects with nortriptyline therapy are sedation, dry mouth, blurred vision, urinary retention, lightheadedness, tremor, and constipation.[10]

Clonidine

Centrally acting alpha-2 adrenergic agonist reduces sympathetic outflow from the central nervous system. The dosage for smoking cessation is 0.15 to 0.75 mg/day orally and 0.1 to 0.3 mg/day transdermally. Initially,

Table 2: Various pharmacological agents used in NRT[8,9]

	Nicotine gum	*Nicotine lozenge*	*Nicotine transdermal patch*		*Nicotine nasal spray*	*Nicotine oral inhaler*
Product	Nicorette[a], 2, 4 mg	Commit[a], 2, 4 mg	Nicotrol patch[b] 5, 10, 15 mg (16 hours)	Nicoderm CQ[a], 7, 14, 21 mg (24 hour)	Nicotrol NS[b] matered spray (0.5 mg nicotine in 50 ml aqueous nicotine solution)	Nicotrol[b], 10 mg cartridge delivers 4 mg inhaled nicotine vapor
Precautions	Pregnancy, lactation, respiratory conditions for nasal spray and inhaler					
Dosing	(1) For patients smoking 25 or more cigarettes/d: 4 mg	(1) For patients who smoke their first cigarette ≤ 30 minutes after waking: 4 mg	(a) More than 10 cigarettes/d:	(a) More than 10 cigarettes/d:	(1) Initial recommended dose: One to two doses/hour (one dose = one spray in each nostril), increasing as needed for symptom relief	(1) Six to 16 cartridges daily (approximately one cartridge every 1–2 hours)
	(2) For patients smoking fewer than 25 cigarettes/d: 2 mg	2 For patients who smoke their first cigarette > 30 minutes after waking: 2 mg	(i) 15 mg/day × 6 weeks	(i) 21 mg/day × 6 weeks	(2) Recommended duration of therapy: 3–6 months	(2) Each cartridge delivers 4 mg of nicotine over 80–100 inhalations (approximately 20 minutes of active puffing).
	(a) Weeks 1–6: One piece every 1–2 hours	(a) Weeks 1 through 6: One lozenge every 1–2 hours	(ii) 10 mg/day × 2 weeks	(ii) 14 mg/day × 2 weeks		(3) Recommended duration of therapy is up to 6 months (taper dosage during final 3 months of treatment)
	(b) Weeks 7–9: One piece every 2–4 hours	(b) Weeks 7 through 9: One lozenge every 2–4 hours	(iii) 5 mg/day × 2 weeks	(iii) 7 mg/day × 2 weeks		
	(c) Weeks 10–12: One piece every 4–8 hours	(c) Weeks 10 through 12: One lozenge every 4–8 hours	(b) Who smoke 10 cigarettes/d or fewer: Not recommended	(b) Who smoke 10 cigarettes/d or fewer: (i) 14 mg/day × 6 weeks (ii) 7 mg/day × 2 weeks		
Adverse effects	Common adverse effects associated with all NRT agents are mouth soreness, hiccups, dyspepsia, hypersalivation, and jaw ache, headache, flatulence, insomnia, nasal/throat irritation (hot, peppery, or burning sensation), rhinitis, tearing, sneezing.					

[a]Marketed by GlaxoSmithKline; [b]Marketed by Pfizer

the therapy is started with 0.1 mg orally twice daily or 0.1 mg/day transdermally and is increased by 0.10 mg/day each week as tolerated. The duration of therapy differed in various clinical trials, ranging from 3 to 10 weeks. The adverse effects include dry mouth, drowsiness, dizziness, sedation, and constipation.[11]

COMBINATION THERAPY

It uses long-acting formulation (patch) in combination with short-acting formulation (e.g., gum, oral inhaler, lozenge, nasal spray). The long-acting formulation prevents the onset of withdrawal symptoms. Short-acting formulation is helpful to control withdrawal symptoms that occurred during potential relapse conditions (e.g., after meals, when stressed, or when around other smokers).[12]

Nicotine replacement therapy and sustained-release bupropion and NRT and nortriptyline are the two combinations mostly used in therapy. Till now research and clinical studies are going for the establishment of standard dosages and time period for therapy.

EMERGING THERAPIES

New compounds that have demonstrated encouraging preliminary results include rimonabant and varenicline.

Rimonabant

It antagonizes cannbinoid-1 receptors selectively in central nervous system. The various clinical effects of rimonabant are decrease in appetite, weight loss, increased HDL cholesterol, decrease in triglycerides, smoking cessation, improved glycemic control from favorable insulin action via higher dinopectin. It also improves abstinence among smokers.[13]

Random clinical trials worldwide showed that those who had been on rimonabant 20 mg and were abstinent at 10 weeks were randomized to continue on 20 mg/day, use 5 mg/day, or use placebo. Those who had been abstinent on 5 mg/day were randomized to continue on 5 mg/day or use placebo.[14]

The major adverse effects are nasopharyngitis, upper respiratory tract infection, headache, nausea, dizziness, back pain, influenza, and diarrhea.[14]

Varenicline

It was approved in 2006 for cessation of smoking by FDA. It is a selective alpha-4-beta-2 nicotinic acetylcholine receptor partial agonist.[14] Preliminary data from a phase II clinical trial indicate that in patients randomly assigned to placebo, varenicline (0.5 mg) twice daily, or varenicline (1.0 mg) twice daily, the pooled abstinence rates at weeks 9 through 12 were 12.4, 45.1, and 50.6% respectively. The adverse effects observed in more than 10% of patients taking varenicline included nausea, insomnia, headache, and abnormal dreams.[15]

NON-PHARMACOLOGICAL METHODS OF SMOKING CESSATION

The first smoking cessation guideline was developed in 1996 and was updated in 2000 by the US Public Health Service (USPHS).[16] These guidelines are based on evidence-based approach for cessation of smoking. They formulated "Five As" approach (Table 3) that consists of steps or questions for addressing when to screen and treat patients for tobacco use and cessation.[4]

The limitation of "Five As" approach is it may not be helpful for the patients who are not motivated for smoking cessation. For the smokers who want motivation to quit smoking "Five Rs" (Table 4) practitioner application is useful.[4,17] A successful motivational intervention requires a practitioner who acknowledges patient-specific concerns and previous successful lifestyle changes.[18]

Enabling the Smoker to succeed

The most efficient method for a smoker to successfully quit the habit is combination of pharmacotherapy

Table 3: The 5 As for facilitating smoking cessation[4]

Ask about tobacco use	Identify and document tobacco use status for every patient at every visit
Advise to quit	In a clear, strong, and personalized manner urge every tobacco user to quit
Assess willingness to make a cessation attempt	Is the tobacco user willing to make a cessation attempt at this time?
Assist in cessation attempt	For the patient willing to make a cessation attempt, use counseling and pharmacotherapy to help him or her quit
Arrange follow-up	Schedule follow-up contact, preferably within the first week after the cessation date

Table 4: The 5 Rs to enhance motivation to quit smoking[4,17]

Relevance	Identify motivational factors that are relevant for the patient: Risk of heart disease, cancer, social situation, second-hand smoke, personal barriers to cessation and prior quit attempts.
Risks	Ask the patient about negative health effects of smoking
Rewards	Ask the patient about potential benefits of smoking cessation
Roadblocks	Ask the patient to identify barriers that will make a quit attempt difficult. Provide patient with information on how these barriers can be addressed.
Repetition	Repeat motivational intervention with each patient encounter.

with non-pharmacological interventions (i.e., advice and behavioral support). Using both the methods in combination multiplied the success rate than when used alone.[19] Psychosocial intervention for quitting the smoking is advice to intensive group or individual counseling. Self-help manuals should be distributed to individuals in large numbers who had the desire and who are highly motivated and confident to quit the smoking, and this intervention has the efficacy rate of 5%. Counseling that is delivered in person and interactive telephone counseling are more effective than simply providing educational or self-help materials.[20]

Complementary and Alternative Therapies

Other interventional therapies like hypnosis, acupuncture, diet aids, and low-level laser therapy have been suggested for smoking cessation. There are no evidences and clinical studies that improved the quit rates with these therapies. On individual basis these interventions may boost the confidence of the individual toward smoking cessation.[21]

CONCLUSION

Many randomized clinical trials and various studies showed that when using both pharmacological and non-pharmacological interventions had a great success in smoking cessation. Besides these interventions, other measures like increase of tax on tobacco products, implementation of strict laws on use of tobacco by the governments, health awareness programs among public, incorporating the different topics of tobacco cessation as a syllabus to both medical and dental graduates, conducting various Continuing Dental Education programs, workshops, etc. are very important for the millions of individuals to quit the habit.

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