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A review on innovations in Pharmacotherapy for tobacco addiction

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Abstract

The World Health Organization (WHO) provides that India will have the fastest rate of rise in deaths attributable to tobacco in the first two decades of the twenty first century. There are strong evidences that smoking behavior is related to social factors. Taste and smell also influence the inclination to smoke where exciting sensory organs in the lips, mouth and throat provide sensations of touch, taste and irritation. It has been suggested that high negative mood variability is a risk factor for future smoking escalation and that its mood stabilizing effects may reinforce and maintain daily cigarette use among youths. Cigarette smoking is the largest modifiable risk factor and reason for male and female infertility and several other disorders (like: for pregnancy, respiratory disorder, diabetes, tuberculosis, coronary heart disease and during substance abuse treatment). Epidemiological status in India an estimated 65% of all men and 33% of all women use some form of tobacco. Tobacco consumption continues to grow in India at 2-3% per annum, and by 2020. It is predicted that it will account for 13% of all deaths in India. Interventions to aid smoking cessation are among the most important treatments such as nicotine replacement therapy and non nicotine replacement therapy like antidepressants drugs that can be offered to smokers to improve their current and future health and reduce the risk of premature death. Recent treatment with new technologies like use of electronic cigarettes, devices that deliver a nicotine-containing vapor, has increased rapidly across the country and globally. The proliferation of smart phones used in novel ways to promote smoking cessation. New possibilities for using mobile phones as tools for health promotion Smart phones are being used in novel ways to promote smoking cessation. The approach to smoking cessation and adherence to the U.S. public health service's 2008 clinical practice guidelines for treating tobacco use and Dependence. It is recommended that current apps be revised and future apps be developed around evidence-based practices for smoking cessation.

Key words: Pharmacotherapy, Smoking, Addiction

Introduction

Tobacco, which is the foremost cause of preventable death in the world today, and India, which is the second largest country in the world, with a billion plus population. This article is also an examination of the methods and tools available to reduce prevent and control tobacco use. The World Health Organization (WHO), which provides these estimates, also predicts that India will have the fastest rate of rise in deaths attributable to tobacco in the first two decades of the twenty first century. Many of these deaths will occur in the productive years of adult life, as a consequence of an addiction acquired in youth. The most widely prevalent and most studied form of tobacco use globally is cigarette smoking. India share of the global burden of tobacco-induced disease and death is substantial.

The major smoking problem in India is beedi smoking, and a large part of the overall tobacco problem is the oral use of smokeless tobacco products.¹ Smoking is a major cause of ill-health and premature death among women in many countries and this is increasing rapidly. Even in countries where smoking is still low among women, many women's lives are already negatively affected by smoking, for example through their husbands' spending scarce resources on cigarettes, their constant exposure to second-hand smoke. While religious and cultural attitudes, often combined with low economic status, have kept female smoking levels low in many countries, history shows that unless strong, comprehensive tobacco control policies are implemented, female smoking prevalence will increase. The tobacco industry has identified women as a key target group around the world. Countries with newly opened markets, such as China and Eastern Europe, or which have no restrictions on tobacco promotion, are

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particularly vulnerable to mass targeting by the tobacco industry.²

Tobacco products are popular as a dentifrice in different parts of India and children also use such dentifrices. Among female smokeless tobacco users, the dominating form is tobacco toothpowder (41.3%). Among men it was khaini (57.1%) followed by tobacco tooth powder (8.8%). Many companies take advantage of this misconception and exploiting the addictive nature of nicotine by packaging and positioning their products as dental care products without explicitly stating so. There was an amendment in Drugs & Cosmetics Act, 1940 vide notification published in the Gazette of India vide G.S.R. 443(E) and 444(E) dated 30.04.1992, mentioning that manufacture and sale of all cosmetics and all Ayurvedic drugs licensed as toothpastes/toothpastes containing tobacco have been prohibited. However, recent studies Journal of Toxicology reported the presence of nicotine in some toothpastes.⁵

Tobacco control polices in India:

The Government of India enacted 'Cigarettes and Other Tobacco Products (Prohibition of Advertisement and Regulation of Trade and Commerce, Production, Supply and Distribution) Act, 2003 (COTPA)' to prohibit the consumption of cigarettes and other tobacco products, various provisions of this Act have been enforced since 1st May 2004. The key features of the COTPA are as follows:

- (i) Ban on smoking in public places, including indoor workplaces.
- (ii) Ban on direct and indirect advertising of tobacco products.
- (iii) Ban on sale of tobacco products to minors (less than 18 years of age).
- (iv) Ban on sale of tobacco products within a radius of 100 yards of educational institutions.
- (v) Display of mandatory pictorial health warnings on all tobacco product packages.
- (vi) Testing of tobacco products for tar and nicotine.

The Smoke-free Rules were revised in October, 2008, redefining 'public places' so as to include all workplaces and authorizing personnel responsible for enforcement of law for maintaining smoke-free public places across the country.³

Epidemiology:

The National Survey on Drug Use and Health (NSDUH) includes a series of questions about the use of tobacco products, including cigarettes, chewing tobacco, snuff, cigars, and pipe tobacco. Cigarette use is defined as smoking "part or all of a cigarette." For analytic purposes, data for chewing tobacco and snuff are combined as "smokeless tobacco."⁶

Epidemiology of smoking in India:

The use of chewing tobacco is reaching at dangers in endemic levels in India, student's professionals, taxi drivers, young and old all takes it. A recent study identified use this bad habit by nearly 70% of college student in several Indian cities.⁷

Fig.1: Percentage distribution of tobacco use according to gender³

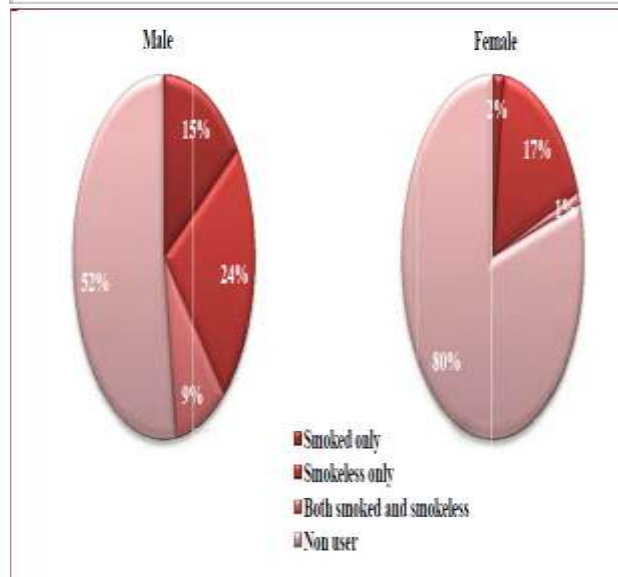
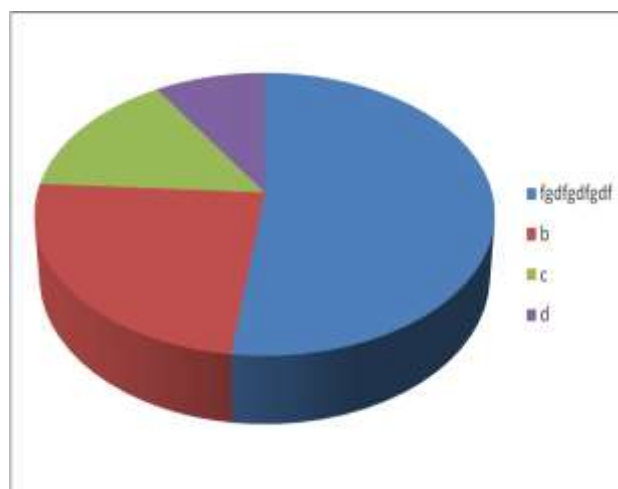


Fig. 2: Percentage distribution of daily cigarette smokers by no. of cigarette smoked on average per day according to gender³

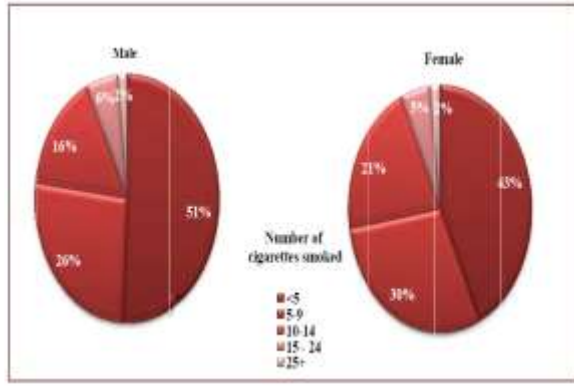


Fig. 3: Percentage distribution of daily bidi smokers by no. of bidi smoked on average per day according to gender³

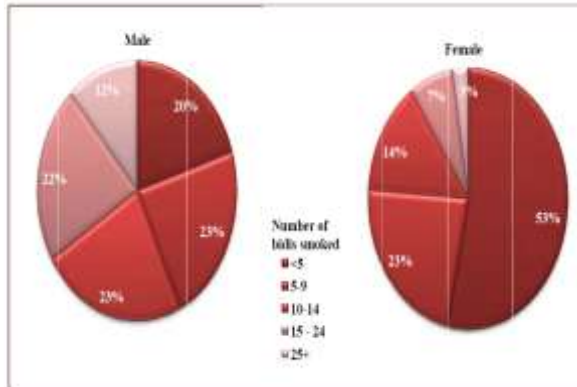


Fig. 4: Percentage distribution of smokers by interest in quitting smoking³

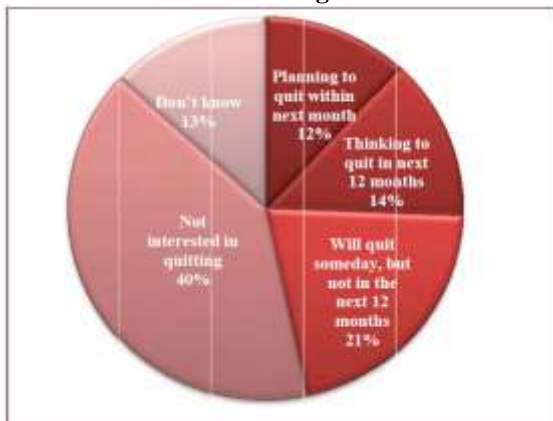
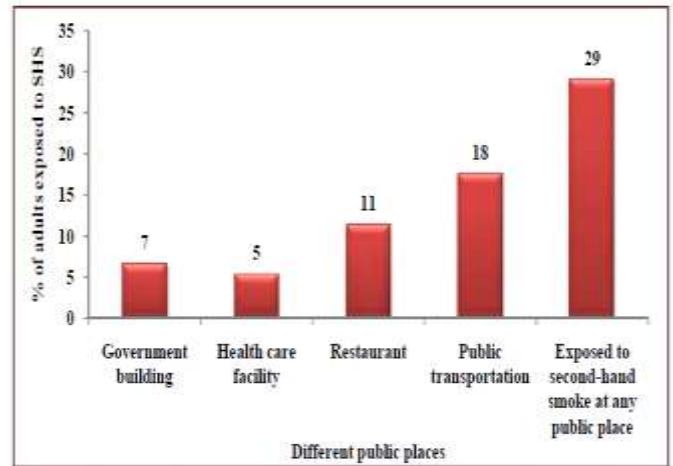


Fig. 5: Exposure to SHS among adults at different public places³



Treatment of smoking cessation:

Interventions to aid smoking cessation are among the most important treatments that can be offered to smokers to improve their current and future health and reduce the risk of premature death. In the year 2000, an estimated 4.83 million premature deaths worldwide were a direct consequence of smoking.¹²

The smoking cessation treatment are categorized into three category, these are as follows in following figure. (Fig .

Treatment of smoking cessation

1.Nicotine replacement therapy	2.Non nicotine replacement therapy(medication)	3.Novel therapy
<ul style="list-style-type: none"> • Transdermal nicotine patch • Nicotin nasal spray • Nicotine gum • Nicotine lozenge 	<ul style="list-style-type: none"> • Bupropian • Varenicline • Nortriptyline • Clonidine • Cystine • Mecamylamine 	<ul style="list-style-type: none"> • Vaccines(nicvax) • Electronic cigratte • Behavioral treatment • Moblile apps for smoking cessation • Herbal treatment

Nicotine replacement therapy (NRT):

Nicotine replacement therapy is following, including uses, advantages, disadvantages, precaution and side effects.¹³ (Table)

PRODUCT	USE	ADVANTAGE	DISADVANTAGE	PRECAUTION	SIDE EFFECT
Nicotine patch	16- and 24-hour preparations available; apply each day to clean, dry, hairless skin; start high-dose (21 mg/24 h) patch if 410 cigarettes per day; taper to mid-dose (14 mg) in 4 – 6 weeks, then low-dose (7 mg) for 2 weeks	Place and forget; no prescription needed in most countries; can decrease morning cravings if worn at night	Passive—no action to take when craving occurs	Not recommended to use while smoking; caution in unstable cardiac disease (recent heart attack)*	Skin reaction (50% of patients mild, 10% causing discontinuation); rotate site each day; rash improved with hydrocortisone cream; vivid dreams or sleep disturbance can occur if worn overnight
Nicotine gum	Chew every 1 – 2 hours as needed; chew and park; 2 and 4 mg strength (4 mg if around 1 pack /day)	Able to use as needed; can self-dose; no prescription needed in most countries	Not pleasant to chew, poor compliance	Avoid food and acidic drinks 15 minutes before and while using (decreases absorption)	Jaw ache; nausea; Hiccups

Nicotine inhaler	Puff as needed; use up to 16 cartridges/day less needed if using combination therapy; orally absorbed – no need to inhale deeply	Can use as needed; mimics hand – mouth behavior	Costly, visible; requires very frequent puffing to achieve therapeutic levels; poor compliance; prescription in some countries	Avoid food and acidic drinks 15 minutes before and while using	Cough, throat Irritation (40%), usually mild
Nicotine nasal Spray	1 – 2 sprays per hour; do not sniff/inhale— tilt head back and spray; aim away from nasal septum	Use as needed; rapid relief of symptoms	Cost; requires prescription in some countries; very poor compliance	Asthma, rhinitis, sinusitis, nasal polyps	Nasal irritation (80 – 90%); possible dependence (10 – 20%)
Nicotine lozenge	2 and 4 mg (4 mg if smoke within 30 min of waking); dissolve in mouth; do not Chew.	Ease of use, No prescription needed in most countries	Poor compliance	Avoid food and acidic drinks 15 minutes before and while using	Hiccups, nausea, heartburn

Non nicotine replacement therapy:

In this therapy some medication are use stopping smoking. This has been shown to increase the likelihood of successful outcomes, with the more intensive the support the greater the abstinence rates. If available, smokers should be referred to local smoking-

cessation services. These provide good value for money, and offer the best chance of success. These services are especially important for those smokers with smoking-related disease who are typically more dependent.^{12, 13}

Drug name	Dose	Effect	Mechanism of action	ADR
Bupropion	150 mg /day for first three days and 300 mg/day after third day	Anti-depressant	Increase dopamine level	Dry mouth, insomnia, nausea, and headache, seizure, severe hypersensitivity reaction.
Nortriptyline	25 mg/day	Anti-depressant	Inhibits the reuptake of noradrenaline and	dry mouth, , light-headedness,

			serotonin neurotransmitter	shakiness, and blurred vision, Urinary retention, constipation, sexual difficulties, and seizure.
Clonidine	Start with 0.1 mg/day, and then are gradually increased, up to 0.4 mg/day.	alpha-2 adrenoceptor agonist	Reduces sympathetic activity by decreasing noradrenaline release	postural hypotension, dizziness, dry mouth, Depression, sleep disturbance and constipation

Novel therapy:

This therapy is the discovering new therapeutic uses for existing molecules designed to developed and benefit to human use.

Electronic cigarette:

Electronic cigarettes (EC) are devices designed to deliver nicotine without tobacco smoke by heating a solution of nicotine, flavouring, additives and propylene glycol and/or vegetable glycerine Invented by Lik Hon in Hong Kong in 2003.¹⁴ It has increased rapidly across the country and globally. Perceived and marketed as a “healthier alternative” to conventional cigarettes, few data exist regarding the safety of these

devices and their efficacy in harm reduction and treatment of tobacco dependence; even less is known about their overall impact on population health. Studies show that the vapor generated from electronic cigarettes has variable amounts of nicotine and potential harmful toxins, although at levels lower than in conventional cigarettes. The long-term carcinogenic and lung function effects of electronic cigarettes are not known. Although some data demonstrate that electronic cigarettes may be effective in reducing conventional cigarette consumption,¹⁴

Comparison of toxin levels in conventional and electronic cigarettes is follows in Table G¹⁴

Comparison of toxin levels in conventional and electronic cigarettes

Toxins	Conventional cigarette($\mu\text{g}/\text{cigarette}$ in mainstream smoke)	Electronic cigarette(μg per 15 puffs)	Average ratio(Conventional: Electronic)
Carbonyl compound			
Formaldehyde	1.6-52	0.20-5.61	9
Acetaldehyde	52-140	0.11-1.36	450
Acrolein	2.4-62	0.07-4.19	15
Toluene	8.3-70	0.02-0.63	120
Nitrosamines			
N'-Nitrosomocoline	0.005-0.19	0.00008-0.00043	380
NNK(Nicotine-derived nitrosamine ketone)	0.012-0.11	0.00011-0.00283	40

Behavioral treatment:

The Public Health Service (PHS) of the U.S Department of Health and Human Services, and lead by the Surgeon General, has periodically released a series of guidelines related to the behavioral treatment of tobacco use. The most recent set of guidelines was released in 2000 in response to new, effective clinical treatments for tobacco dependence that were identified since the previous set of guidelines was published in 1994.¹¹

Following are the PHS Clinical Practice Guidelines for effective tobacco cessation treatments;

- Tobacco use screening and brief intervention in routine medical care provided by a variety of providers—including physicians, nurses and dentists.
- Face-to-face intensive counseling treatments.
- Proactive telephone counseling.
- Effective pharmacotherapy should be used for smoking cessation except in the presence of special circumstances (e.g., pregnancy, certain medical co-morbidities).

- Long-term smoking cessation pharmacotherapy should be considered as a strategy to reduce the likelihood of relapse.

The Guidelines also identify a number of key findings that clinicians should utilize. These include:

- Tobacco dependence is a chronic condition that often requires repeated intervention. However, effective treatments exist that can produce long-term or even permanent abstinence.
- Because effective tobacco dependence treatments are available, every patient who uses tobacco should be offered at least one of these treatments.
 - a. Patients willing to try to quit tobacco use should be provided treatments identified as effective in this guideline.
 - b. Patients unwilling to try to quit tobacco use should be provided a brief intervention designed to increase their motivation to quit.
 - It is essential that clinicians and health care delivery systems (including administrators, Insurers and purchasers) institutionalize the consistent identification, documentation, and treatment of every tobacco user seen in a health care setting.
 - Brief tobacco dependence treatment is effective, and every patient who uses tobacco should be offered at least brief treatment.
 - Tobacco dependence treatments are both clinically effective and cost-effective relative to other medical and disease prevention interventions.¹¹

Recent technology for treatment:

Some mobile application for smoking cessation; Mobile phones have shown some promise in helping people quit smoking and modifying other health behaviors. Most of these phone-based interventions have relied on the text-messaging feature of mobile phones and consisted of a series of short and sometimes interactive set of text messages that guide a person through the process of behavior change. However, with the proliferation of smart phones, there are new possibilities for using mobile phones as tools for health promotion. Smart phones have powerful operating systems that can run computer programs or applications (apps), in addition to the standard features of mobile phones. Among smart phones, the i-Phone is notable because since its release in 2007, third parties have been able to create apps for the i-Phone operating system and distribute them to the public through a common online website, the Apple iTunes store. To date, the Apple iTunes store has released more than 100,000 i-Phone apps, which have been downloaded by consumers more than 3 billion times. Of the applications that have been released, 20 have

previously been identified as smoking cessation apps. Few studies have examined the content quality of i-Phone apps for a given health behavior or condition. The present study examines the content of existing i-Phone apps as they apply to smoking cessation. Of interest is the degree to which these apps adhere to established best practices in smoking cessation, their popularity among i-Phone users, and the relationship between these variables.

With the proliferation of smart phones such as the Smartphone, are being used in novel ways to promote smoking cessation. Each app was independently coded by two reviewers for its approach to smoking cessation and adherence to the U.S. Public Health Service’s 2008 Clinical Practice Guidelines for Treating Tobacco Use and Dependence. Each app was also coded for its frequency of downloads. Apps for smoking cessation rarely adhere to established guidelines for smoking cessation. It is recommended that current apps be revised and future apps be developed around evidence-based practices for smoking cessation.¹⁵

Some mobile apps for smoking cessation are as follows³;

For android phone:

Apps name	Cost	Discription
Quit smoking - QuitNow	Free	Offers real-time stats about last cigarette smoked, amount of cigarettes avoided, and money saved
Stop! Quit Smoking - LITE,	Free	Includes a community system for support from other quitters. Offers real-time display of money and time saved
Quit Smoking: Cessation Nation,	Free	Allows for support from over 17 million people who are also trying to quit. Informs you of health improvements

		and offers games to distract from cravings
Get Rich or Die Smoking	Free	Includes a sophisticated rewards system and a community to chat with other quitters.

		quitting, and tips to avoid smoking
Smoke Free	Free	Provides reminders for time passed since last cigarette and tracks the length of cravings.

Time To Quit Smoke	Free	Informs you of how much time has passed since your last cigarette, how much money was saved, and allows for customized widget display on desktop for convenient achievement display
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Quits	Free	Offers help for quitting any bad habit. Keeps track of how many days since last cigarette and amount of money saved.
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Some hazards on smoking cessation:

Tobacco is a plant with green foliage and tubular flowers. Biologically titled *Nicotiana tabacum*, it derives its name from Jaen Nicot, the French ambassador to Portugal who brought it back with him as a medicine in 1560. In 1800, it was used for smoking achieving worldwide popularity as Spanish sailors carried it with them in their travels planting its seeds in a variety of places there are strong evidences that smoking behavior is related to social factors, particularly the influence of parents and peer groups. Taste and smell also influence the inclination to smoke where exciting sensory organs in the lips, mouth and throat provide sensations of touch, taste and irritation. Also, it has been suggested that high negative mood variability is a risk factor for future smoking escalation and that its mood-stabilizing effects may reinforce and maintain daily cigarette use among youths.¹⁶ Smoking causes harmful effects during some disease. These are,

Smoking cessation during pregnancy:

Cigarette smoke contains thousands of chemicals, many of which are reproductive toxins. The foremost toxin in cigarette smoke is carbon monoxide, a potent fetal toxin. Some smokers—because of nausea and vomiting during pregnancy—may be unable to tolerate oral formulations, and in that case patch use is preferred. If patches are used, it is recommended that they be used for 16 rather than 24 hours, to minimize

For WINDOS phone:

APPS name	Cost	Description
Kick Smoking	Free	Focuses on helping you resist cravings and keeping track of health benefits of quitting. Provides a craving timer and records the number of cravings resisted
Stop Smoking	Free	Keeps track of the places you smoke regularly and keeps track of the number of cravings resisted
Quit Smoking	Free	Includes check of current health status, timeline for

total daily exposure to the fetus. The initial selection of the strength of the patch should be similar or higher than the patch strength that would have been selected for a non pregnant female. Bupropion is an alternative pharmacotherapy to nicotine replacement therapy. Bupropion is contraindicated in women with risk factors for seizures or a history of eating disorders. It also is recommended that all patients be reported to a bupropion registry.¹⁷

Smoking cessation during respiratory disease:

Smoking cessation is the one of the most important ways to improve the prognosis of patients with respiratory disease. The Task Force on guidelines for smoking cessation in patients with respiratory diseases was convened to provide evidence-based recommendations on smoking cessation interventions in respiratory patients.

Based on the currently available evidence and the consensus of an expert panel, the following key recommendations were made.

1) Patients with respiratory disease have a greater and more urgent need to stop smoking than the average smoker, so respiratory physicians must take a proactive and continuing role with all smokers in motivating them to stop and in providing treatment to aid smoking cessation.

2) Smoking cessation treatment should be integrated into the management of the patient's respiratory condition.

3) Therapies should include pharmacological treatment (i.e. nicotine replacement therapy, bupropion or varenicline) combined with behavioural support.

4) Respiratory physicians should receive training to ensure that they have the knowledge, attitudes and skills necessary to deliver these interventions or to refer to an appropriate specialist. 5) Although the cost of implementing these recommendations will partly be offset by a reduction in attendance for exacerbations, etc., a budget should be established to enable implementation.¹⁸

Smoking cessation during diabetes:

Cigarette smoking predicts incident type-2 diabetes, but smoking cessation leads to higher short-term risk. For smokers at risk for diabetes, smoking cessation should be coupled with strategies for diabetes prevention and early detection. an extensive body of literature consistently identifies

cigarette smoking as a risk factor for incident diabetes. Therefore, smoking cessation should decrease diabetes risk among current smokers, perhaps by reducing systemic inflammation, which is a well-established risk factor for incident diabetes. However, smoking cessation is also

associated with substantial weight gain, which could tip the balance toward increased risk.¹⁹

Smoking cessation during male infertility:

Smokers may not experience reduced fertility, males with marginal semen quality may benefit from quitting smoking. Also, smokers should quit smoking for the sense of responsibility for their future generation as tobacco smoke contains numerous mutagenic substances. Smoking reduces sperm production, sperm motility, sperm normal forms and sperm fertilizing capacity through increased seminal oxidative stress and DNA damage.¹⁶

Smoking cessation during tuberculosis:

Smoking prevalence is high in western countries as in USA 20% of adults are smokers¹, comparative figure from India varies from 15-50% among men. 17 % of total smokers and 1/3 tubercular patient of the world reside in our country, Smokers are 2-4 times more prone to get tubercular infection¹ as well as it increase the T.B. mortality by nine fold, around 50% of death due to tuberculosis in Indian men attributed to smoking⁴. Tuberculosis with smoking is a double trouble as it helps in spreading the infection, change the latent tuberculosis in clinically active stage, as well as aggravates the severity also^{4,5}. It was also reported that extra pulmonary tuberculosis more prevalent in smokers. Therefore a case control study was done to assess the impact of tobacco smoke on sputum status as well as clinical radiological profile of tubercular patient.²⁰

Smoking cessation during substance abuse treatment:

Tobacco relative to other substances of abuse. Tobacco remains responsible for greater morbidity than alcohol and all other drugs combined (U.S. Department of Health and Human Services, 2000). To put the death toll and morbidity of the different substances in perspective, a 1995 study in Canada (Single, Rehm, Robson, & Truong, 2000) found those 34,728 deaths and 194,072 admissions to hospital were attributed to tobacco. In contrast, 6,507 deaths and 82,014 admissions to hospital were attributed to alcohol, and 805 deaths and 6,940 admissions to hospital were due to illicit drugs. Patients in substance abuse treatment frequently smoke cigarettes and often die of tobacco-related causes. Substance abuse treatment programs too often ignore tobacco use. Many patients have expressed interest in stopping smoking, although they may be ambivalent about smoking cessation during substance abuse treatment. This article provides a review of tobacco cessation literature and successful methods of intervention. Research supports two key findings: (a) smoking cessation during substance abuse

treatment does not impair outcome of the presenting substance abuse problem and (b) smoking cessation may actually enhance outcome success. We will discuss how to incorporate smoking cessation.²¹

Smoking cessation during Coronary Heart Disease:

Components in the blood, called platelets, stick together along with proteins to form clots. Clotting prevents blood loss and infection after an injury. Chemicals in cigarette smoke cause blood to thicken and form clots inside veins and arteries, even when clotting isn't needed to prevent bleeding or infection. Smoking also promotes the formation of plaque in the walls of arteries and clots can form where there is plaque. This is especially dangerous when arteries are already narrowed from smoking, because the clots can easily block those arteries. When arteries are blocked, the oxygen to nearby organs is cut off. Coronary heart disease occurs when arteries that carry blood to heart muscles are blocked by clots. This blockage can lead to a heart attack and sudden death.²²

Conclusion

Smoking is a major cause of ill-health and premature death among people in many countries and this is increasing rapidly. Even in countries many child and females are already affected by smoking through passive manner for example through their husbands/parents spending scarce resources on cigarettes, their constant exposure to second-hand smoke and, increasingly, having to cope with a spouse's death from smoking. Now days the health problems associated with smoking get increases day by day. In this review report we focused on epidemiological status of India. Treatment like nicotine replacement therapy and medication of antidepressants and recent treatment with new technologies such as electronic citrates and mobile apps for smoking cessation. We also focused Some hazards on smoking cessation like during pregnancy, respiratory disorder, diabetes, male infertility, tuberculosis, Coronary Heart Disease and during substance abuse treatment. Finally, we concluded that this review highlights the recent data regarding pharmacotherapy and advanced therapy such as electronic cigarette and mobile apps are promoting smoking cessation and strong comprehensive tobacco control policies are to be implemented for controlling the hazardous health effect and premature death which is occurring due to active and passive smoking.

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