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A review on current therapies and its problems in smoking cessation

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Abstract

Smoking is likely the most preventable reason for ailments and premature death in the world. In 2010 it was estimated that approximately there are 120 million smokers in India. Around 70% of tobacco smokers are willing to stop, yet just 2-3% prevail with regards to doing so for all time every year. The first line pharmacotherapies normally used for smoking cessation include Nicotine substitution products (gum, transdermal patch, nasal spray, inhaler, and lozenge), varenicline and bupropion. Non-pharmacological therapies such as patient education, Counselling when used by physicians along with pharmacotherapies are found to increase the cessation rates by two folds within a single year. Blend pharmacotherapies are expanding the smoking restraint rates and furthermore lessens the withdrawal manifestations and are demonstrated to be as powerful as monotherapies. Physicians assume a significant job in the smoking discontinuance process. Significant rates of quitting smoking are accomplished when non-pharmacologic help is joined with pharmacological interventions. New treatment options such as nicotine vaccines are found to have better therapeutic effects and abstinence rates on smokers compared to other pharmacotherapies available. This review article deals with the available therapies (pharmacological and non-pharmacological) for smoking cessation along with the limitations and adverse effects associated with different pharmaceutical formulations.

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INTRODUCTION

Smoking is likely the most preventable reason for ailments and premature death in the world. In 2010 it was estimated that approximately there is 120 million smokers in India (Caponnetto *et al.*, 2012). From the World Health Organization (WHO) report, 12% of cigarette smokers in the world are from India. The death rates due to tobacco-related illnesses are more than 1 million. Demises are essentially brought about by different malignancies such as lung cancer, ischemic coronary illness and persistent obstructive lung disorder (US Department , 2004), (Figure 1). According to the findings from 2015, the quantity of men smoking tobacco in India expanded to 108 million, prompting 36% expansion during 1998-2015. Historically, the vast majority of the smoked tobacco in India is as bidis, in which tobacco wrapped inside a Tendu leaf. Around 70% of tobacco smokers are willing to stop, yet just 2-3% prevail with regards to doing so for all time every year (Jha *et al.*, 2008).

Addictive properties of nicotine create a huge problem for people who are ready to quit. More than 80% of cigarette users who attempt to stop smok-

Table 1: Next-Generation Nanoparticle-Based Nicotine Vaccines

Vaccine	Developer	Nanoparticle platforms
SEL-068	Selecta Biosciences	Biodegradable polymeric particles
DNA scaffolded nicotine vaccine	Arizona State University	Self-assembled DNA scaffold
Liposome nicotine Vaccine	Scripps Institute and Virginia Tech	Liposomes
Hybrid Nanoparticle-based nicotine vaccine (NanoNicVac)	Virginia Tech	Lipid-polymer hybrid nanoparticles

ing are found towards relapsing inside the primary month of forbearance, and just 5% of smokers stay abstinent as long as a half year. The pharmacological impact of nicotine on the postsynaptic nicotinic acetylcholine receptor assumes a significant job in tobacco dependence. Along these lines, pharmacotherapy for tobacco reliance is fundamental to improve the achievement rates.

Current approaches to smoking cessation are pharmacotherapy and counseling. The blend of Counseling and medicine is having a preferable remedial impact on patients over either alone. Clinicians should use both counseling and medication to people making a quit endeavor. Smoking termination therapies are the greatest profitable intercessions in clinical setup (Healton and Fiore, 2008).

Smoking Cessation Treatment

Dependence to tobacco is a long-term situation that requires continuous treatment. When an individual is dependent on nicotine, termination is very troublesome (Anderson *et al.*, 2002). Numerous clients undergo manifold efforts to quit, without treatment which expands the achievement rates. Phases of-progress model is the best method used for deciding a patient's readiness to stop tobacco. This representation uses 5 motivational stages to achieve a behavioral change

1) pre-consideration (no plan to stop in the next 6 months)

2) contemplation (considering to quit within the next half year)

3) planning (actively preparing to stop inside the following 30 days)

4) achievement (fruitful restraint for a half year)

5) continuation (effective forbearance for > a half year) (Farkas *et al.*, 1996; Lancaster and Stead, 2017).

Smoking discontinuance treatment is demanding and conduct mediations alone had just constrained achievement. So pharmacotherapy is exceptionally dependent to assist in smoking termination. The most well-known pharmacologic treatment is nicotine replacement therapy(NRT). But at present antidepressant therapy is also being focused as a treatment option (Hughes *et al.*, 2007). The 5 A's and 5 R's concerning smoking discontinuance in a patient-specialist setting is as follows (Figures 2 and 3).

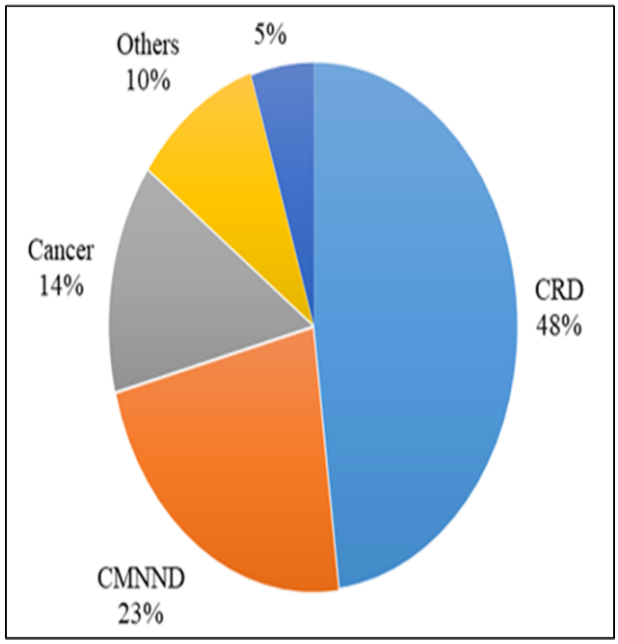

Figure 1: Distribution chart showing the different causes of tobacco deaths

Mechanism of Action

Mechanism of NRT in Giving Up Smoking

The mechanism of activity of NRT is believed to be by incitement of neural nicotinic acetylcholine receptors (nAChR) in the ventral tegmental part of the brain, thereby leads to the delivery of dopamine in the nucleus accumbens. This activity of nicotine from nicotine replacement products prompts a decrease in nicotine withdrawal side effects in nor-

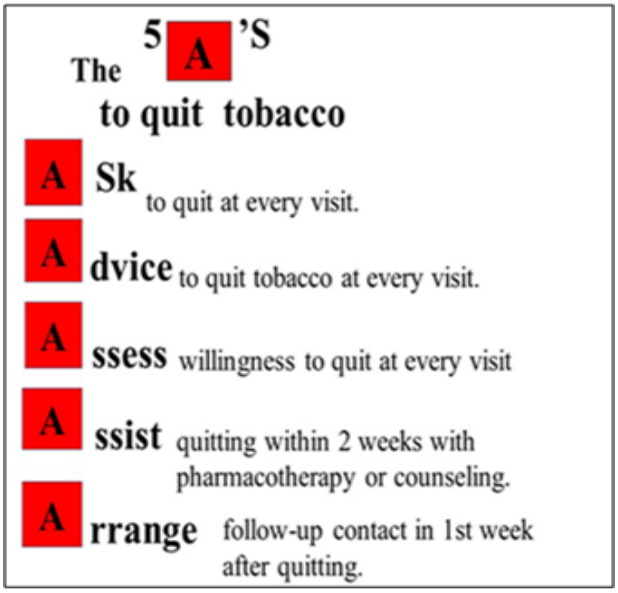

Figure 2: Five A's: Basic consideration and queries to initiate a discussion regarding smoking cessation in a patient-doctor setting

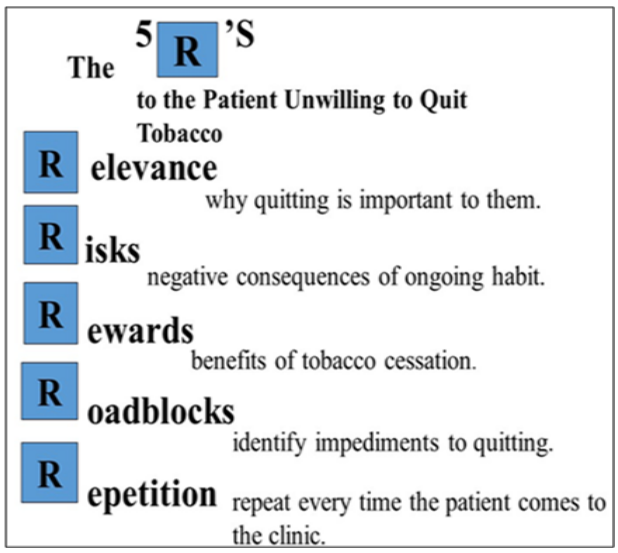

Figure 3: Five R's: For assessment of the patient's understanding regarding the risks of tobacco usage and benefits of smoking cessation is critical

mal smokers who refuse to smoke. NRT likewise gives a less rewarding effect on tobacco products. Complete elimination of withdrawal symptoms isn't accomplished with NRT because none of the accessible nicotine delivery systems mimic the fast and significant levels of arterial nicotine attained when tobacco smoke is breathed in. The accessible pharmaceutical nicotine products undergo systemic venous absorption and do not, therefore, achieve rapid systemic arterial delivery. From a cigarette within a fraction of seconds, high portions of nicotine arrive at the cerebrum. Compared to nicotine delivery from a cigarette, pharmaceutical products accomplish lower levels for a considerable length of time (nasal spray or oral products such as gum, inhalator, sublingual tablet, or lozenge) to hours (transdermal patches) (Torrijos and Glantz, 2006), (Figure 4).

Mechanism of Non-NRT in Giving Up Smoking

Anti-depressants and nicotine receptor agonists are the commonly available non-NRT for smoking cessation. It is found that some antidepressants act on neurotransmission pathways of nicotine, for example, the hindrance of dopamine reuptake by acting on the dopamine transporter framework decreases the dopamine inadequacy experienced in nicotine withdrawal and furthermore hinder the nicotine receptors independently depending upon their antidepressive effects. Nicotine receptor agonists help the patient in smoking cessation using a combination of two effects: first, they help in keeping up moderate degrees of dopamine accordingly diminishing the withdrawal side effects symptoms along with reducing the satisfactory feeling obtained when smoking (Hughes *et al.*, 2005), (Figure 4).

Therapies for Smoking Cessation

Non Pharmacological Therapies for Smoking Cessation

Non-pharmacologic termination approaches include mediations such as providing instructions to patients, self-improvement materials, and giving (Regalado-Pineda *et al.*, 2007). Doctors assume a significant job in the smoking discontinuance process. It is discovered that 70% of cigarette smokers consult family doctors every year. Studies have discovered that even concise (5-10 minutes) guidance on cessation by doctors during the medical clinic visit improves end rates compared with no assistance).

Counseling consists of face-to-face sessions and also accompanied by telephonic conversations for support. It is discovered that gathering guiding is more successful than other smoking cessation therapies (Cahill *et al.*, 2016).

Self-help material is also found to enhance renounce rates among smokers related to individuals who receive no intercession, however, the impact is extremely moderate. Proactive phone advising, in which the advocate starts the customer contact, subsequently upgrades the advantage of the phone guiding in examination with responsive directing, where the customer is starting the contact. Internet-based cigarette termination projects are likewise seen as successful in smoking discontinuance, still, more research is going around (Swartz, 2006).

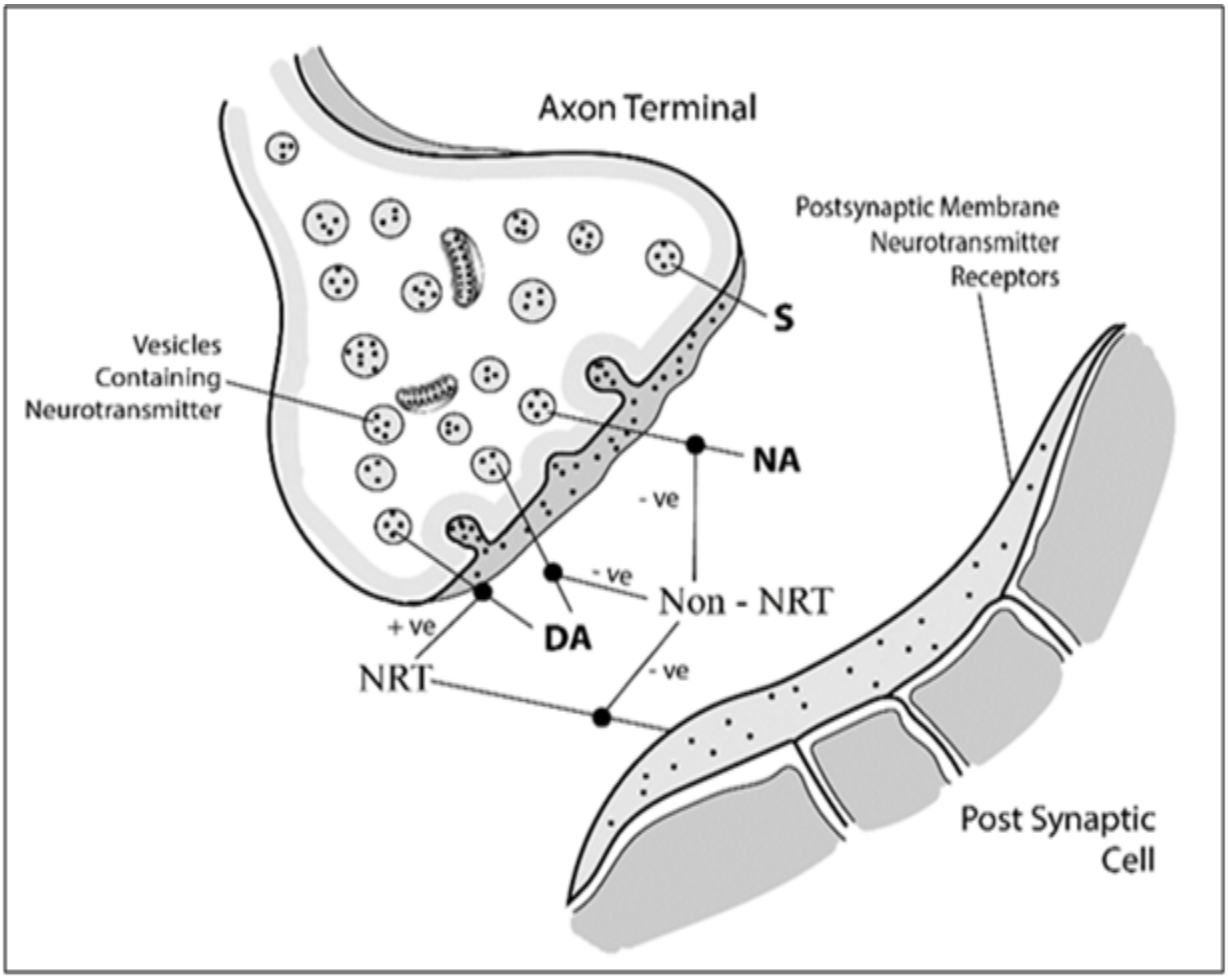

Figure 4: Mechanism of Action NRT and Non-NRT

Pharmacotherapies for smoking cessation

The most elevated quit rates are accomplished when non-pharmacologic help is joined with pharmacological interventions. Three classes of prescription are endorsed as helps for smoking termination (nicotine substitution, bupropion [Zyban, additionally sold under the exchange name Wellbutrin to treat depression], and Varenicline [Chantix]). 2 others are likewise accessible as off-name (nortriptyline and clonidine), with reported viability and are prescribed as substitution treatments according to the present rules (Fiore *et al.*, 2000), (Figure 5).

First Line Pharmacotherapies

Nicotine Replacement Therapy(NRT)

Nicotine substitution therapy is often used as a constituent in smoking discontinuance treatments. These products act lessening the physiological and psychomotor withdrawal indications experienced with smoking discontinuance, accordingly increases abstinence rates (Goldstein *et al.*, 1989). NRT is typically begun from a booked quit day, from which the smoker will be abstinent from smoking. The idea is to restore nicotine to decrease the force of withdrawal.

Nicotine Gum

A commercially available OTC medication that comes in 2-mg and 4-mg portion and is bitten for 1 to 2 hours to achieve the highest everyday portion of 60 mg. In this, nicotine is bound to a gum and is discharged while biting. Roughly half of the nicotine in the gum is discharged in the mouth and retained through the mucosa. The day by day portion is 10 pieces, and the prescribed length of treatment is 1 to 3 months. Patients are told to bite nicotine gum gradually until they feel gentle shivering, which shows nicotine discharge. The patient should then place the gum between the cheek and gums of the teeth for seven minutes before biting it once more.

Acidic nourishments or drinks can reduce the transport of nicotine from the gum since nicotine is ionized at low pH and consequently it avoids ingestion over the buccal mucosa Unfavorable impacts of nicotine gum include temporomandibular joint [TMJ] disease, trauma to dental applications, a sore jaw,

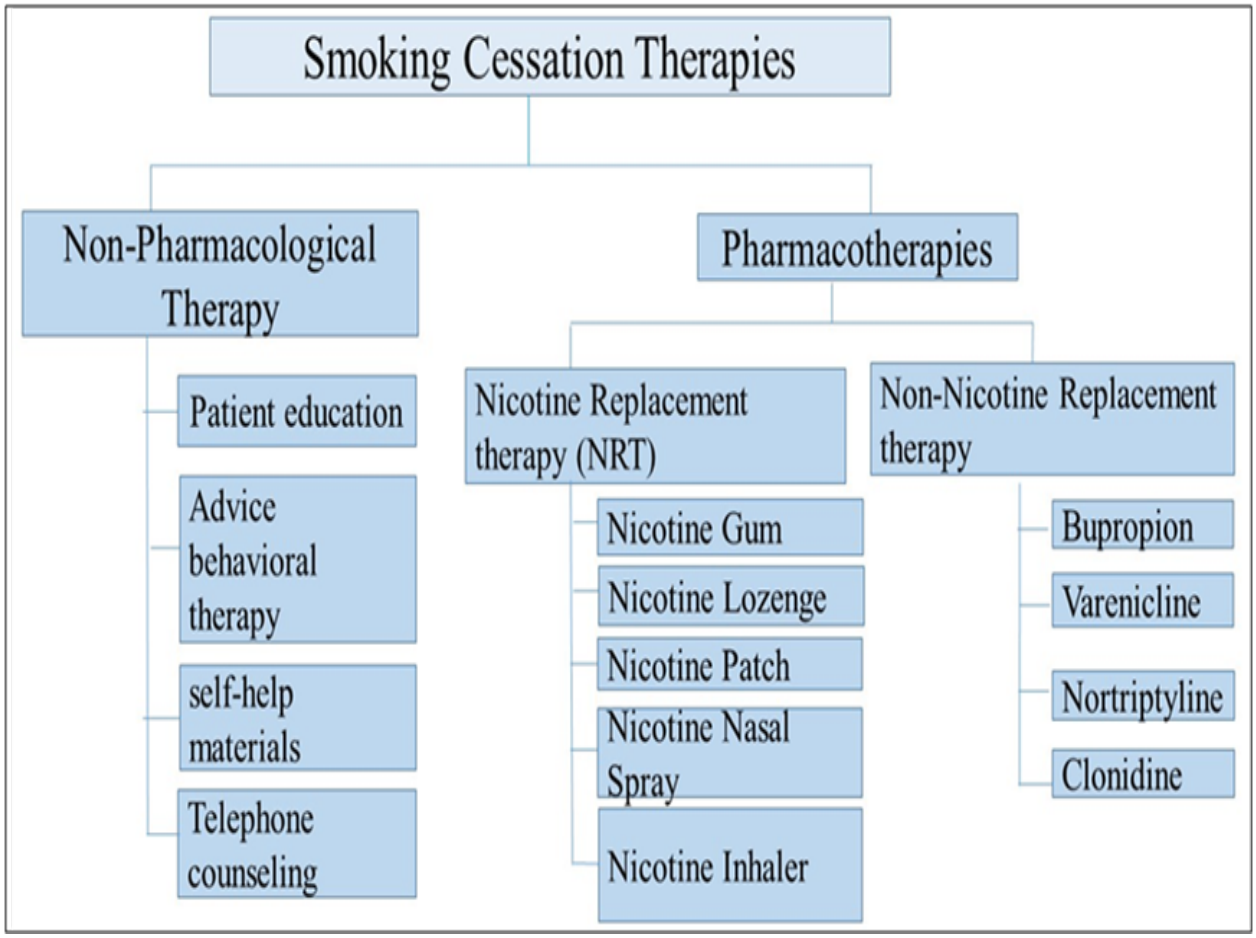

Figure 5: Classification of Smoking Cessation Therapies

oral disturbance or ulcers, and overabundance salivation. When nicotine from the gum is swallowed it causes hiccups and systemic absorption of nicotine is found to cause nausea, vomiting, abdominal pain, constipation, looseness of the bowels, palpitations, and cerebral pain. Nicotine gum isn't prescribed for patients with poor dentition (Rennard *et al.*, 2013).

Nicotine Lozenge

Nicotine lozenge is also an OTC drug similar to that of nicotine gum but chewing is not required. Nicotine lozenge is having similar dosing, absorption and duration of therapy concerning that of gum. Formulations are accessible in 2 mg and 4 mg dose.

The dosage of lozenge is as follows; Week 1-6: 1 lozenge in 1-2 hours after waking, weeks 7-9: 1 lozenge for every 2-4 hours, weeks 10-12: 1 lozenge each for 4-8 hours.

Patients are advised not to have food or take beverages for 15 minutes before administering the medication and the day by day portion ought not to surpass 20 lozenges for every day. Adverse effects of the formulations are sleeplessness, nausea, headache and cough (Bhattacharyya *et al.*, 2008).

Nicotine Patch

It is a transdermal patch that delivers nicotine into the body through the skin. It is considered as one of the safest NRTs available. They are simple to administer and sustain the therapeutic level of nicotine for 12 to 24 hours, along these lines accomplishing 40% to half nicotine blood levels to that of a smoker of 30 cigarettes for each day. he patches are accessible in 21-mg, 14-mg, and 7-mg dosages. The doses are selected based on the number of cigarettes an individual is smoking per day. Least a month of treatment is required to accomplish long term abstinence. Most fixes are applied during the night to give sufficient blood levels of nicotine when the smoker gets up. Mainly relapse is found during this time because of low levels of nicotine during awakening. The possibility of withdrawal manifestations is high which will make a propensity for the smoker to smoke in the wake of enlivening. Both are likely decreased by keeping up with nicotine levels during the night. Extended usage of fix has not been noticed, which proposes that slow kinetics of nicotine delivery with transdermal systems is not enough to sustain addiction. Regular reactions

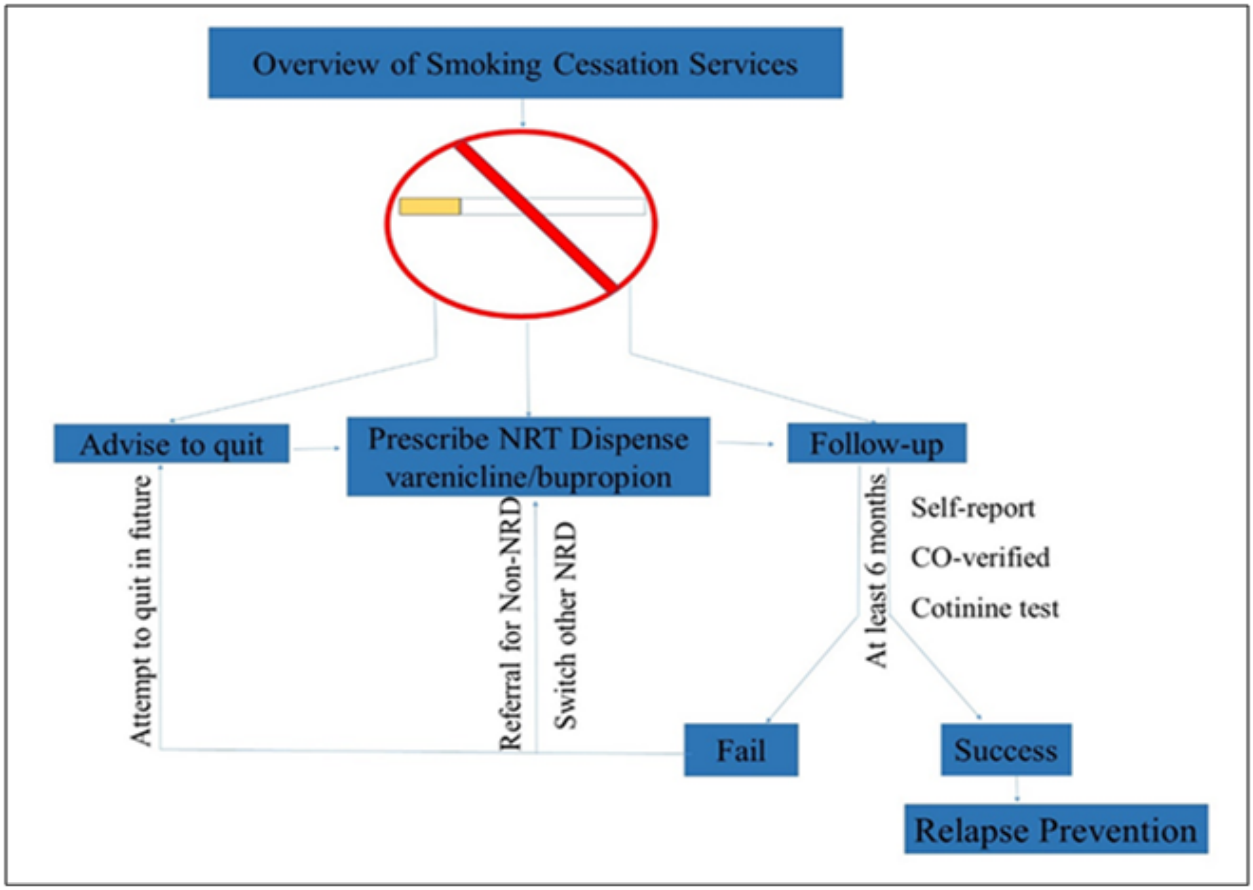

Figure 6: Overview of Smoking Cessation Services

of nicotine fix are skin annoyance,burning, lightheadedness, headache, sickness Skin irritation can be diminished by turning the fix sites (Helge and Denelsky, 2000).

Nicotine Nasal Spray

Compared to gum or patch, nicotine nasal spray distributes nicotine more quickly. The medication is sprayed towards the lower nasal mucosa from where it is ingested. It is obtainable by prescription in a measure of 10 ml. Each 0.05-ml the formulation conveys 0.5 mg of nicotine to each nostril approaches one dose(1mg). The prescribed dose is 1 to 2 sprays each hour for 6 to about two months. Patients are recommended not to go beyond five doses for every hour or 40 dosages for every day. The majority of the patients require around 15 dosages per day, with a steady reduction in the number of doses within a specified period. Since this dosage form conveys a lot of nicotine quickly, it might be valuable for vigorously dependent smokers. Regular unfavorable impacts incorporate nasal annoyance, rhinorrhea, wheezing and throat disturbance (Schneider *et al.*, 1996).

Nicotine Inhaler

It is a physician endorsed drug comprising of a plastic cartridge containing nicotine that fits on a mouthpiece. To rise to the measure of nicotine acquired from 1 cigarette, approximately 80 inhalations are required. From the 10 mg cartridge of nicotine, 4 mg can be breathed in and 2 mg taken into the body. Regular dosing is 6 to 16 cartridges for each day for 6 to 12 weeks, trailed by a slow decrease of more than 6 to 12 weeks. Patients are advised not to use more than 16 cartridges per day. The adverse effects include throat irritation, stomach upset, pain in jaw, neck or back, rhinitis and local irritation (VeryWell mind, 2018).

Bupropion

The first non-nicotine treatment for smoking cessation. An aminoketone antidepressant for the treatment of the manic depressive disorder repurposed for smoking termination therapy. It is found to have both noradrenergic and dopaminergic activity (Wilkes, 2008). Cigarette smoking leads to nicotine ingestion into the circulation system and crosses the blood-brain barrier. This causes the delivery of dopamine into the synaptic cleft of the dopaminergic, pleasure-seeking pathways in the brain. Bupropion is believed to put forth its main effect by inhibiting this dopamine reuptake, probably by its impact on the dopamine transporter sys-

tem. Dopamine reuptake hindrance in the core accumbens diminishes the dopamine insufficiency experienced in nicotine withdrawal and may clarify the constricting impact bupropion has on nicotine withdrawal manifestations. At the postsynaptic acetylcholine nicotinic receptor, bupropion antagonizes the impact of nicotine and has been appeared to obstruct the pharmacological impacts of nicotine in vivo. Altogether these actions of the medication may bring about lessening of withdrawal manifestations. One potential advantage of bupropion is that it causes less weight gain when associated with other smoking termination treatments (Warner and Shoaib, 2005).

Therapy is started with 150 mg day by day for 3 days, trailed by 150 mg twice daily. During the first week of therapy, patients remain to smoke until a stable bupropion level has been established. In the second seven-day stretch of treatment, patients are encouraged to quit smoking. Treatment is normally proceeded for 3-4 months and in certain patients up to 1year. For chronic smokers who have backslid or couldn't accomplish forbearance with nicotine substitution prescription alone, at that point a blend of bupropion and nicotine substitution treatment is given. Common adverse effects are insomnia, nausea/vomiting, dizziness, anxiety, and constipation (Boshier *et al.*, 2003).

Varenicline

It is an exceptionally specific $\alpha 4\beta 2$ nicotinic acetylcholine receptor partial agonist established for smoking discontinuance therapy. Treatment is begun one-week earlier than the objective quit date. Therapy is begun with 0.5mg once day by day orally for 3 days, afterward 0.5mg twice daily for 4 days pursued by 1mg twice day by day for 3 months. Therapy up to 6 months is required for obtaining a reduced relapse. Compared to bupropion, varenicline is having better efficacy in accomplishing restraint from smoking and also in deferring smoking reversion. Most regular unfriendly responses related with varenicline are sickness, sleeping disorder, syncope, and skin reactions. Patients ought to be observed for changes in conduct, aggressiveness, distress, discouraged state of mind, self-destructive ideation, and suicide endeavors. Patients taking varenicline are recommended to be alert for developing new or declining indications of cardiovascular sickness (Food and Administration, 2013). Un intended wounds from falls and vehicular mishaps have likewise been accounted for with varenicline. In this manner, the FDA has given a warning concerning working on heavy machinery while utilizing varenicline (Moore *et al.*, 2008).

Second Line Pharmacotherapies

Nortriptyline

An IInd generation tricyclic antidepressant used for the treatment of major depression, also utilized for smoking discontinuance treatments at doses of 75-100 mg for each day. The helpful impact of nortriptyline in smoking discontinuance isn't seen however, it is claimed to be due to the noradrenergic effects on nicotine. It is a nicotine receptor antagonist, and have a comparative component of activity to that of bupropion in smoking discontinuation therapies, but the therapeutic effect produced by nortriptyline is less than that of bupropion. Common side effects of nortriptyline are sedation, dizziness, sleep deprivation, obscured vision, constipation, and sickness. These side effects happen often in patients being treated for depression, and less prevalent with the quantity used for smoking cessation (Hughes *et al.*, 2005).

Clonidine

Clonidine is marketed as an antihypertensive agent but also found to be viable in diminishing manifestations of nicotine withdrawal. An overall improvement in tobacco withdrawal symptoms such as craving, anxiety, restlessness, tension, and hunger, etc are found with clonidine therapy. A transdermal patch (0.1–0.3 mg/day) and oral (0.15–0.45 mg/day) dosage forms of clonidine is established to be better aids for giving up smoking. Dose-related adverse effects include dry mouth, bradycardia, dizziness, drowsiness and postural hypotension (Gourlay *et al.*, 2004).

Additional Drugs

Buspirone

Buspirone is an anxiolytic agent, that has been utilized in smoking termination treatment to get rid of nicotine withdrawal signs. A dose of 15-30 mg/day is used for smoking cessation therapy. Adverse effects associated with buspirone are dizziness, drowsiness, nausea.

Naltrexone

Naltrexone is a μ-opioid receptor antagonist accepted for the treatment of both narcotic and liquor addiction. It is mainly used for smoking cessation therapies in depressed female smokers. It is found to be effective when combined with a nicotine patch. Common adverse reactions associated with naltrexone are laziness, discomfort, and abdominal pain (O'Malley *et al.*, 2006).

Mecamylamine

Mecamylamine is a ganglionic cholinergic blocker used for lowering blood pressure. It is used for

smoking cessation therapy due to its nicotine antagonism and thereby reducing the tendency to smoke. The daily dose is 2.5-20mg/day. Drowsiness, postural hypotension, and constipation are the side effects associated with mecamylamine ((Lancaster and Stead, 2000).

Combination Pharmacotherapy

With all the principal line treatments one half to two-thirds of smokers are relapsing within 1 year.Combination pharmacotherapies are increasing the smoking self-restraint rates and also decrease the withdrawal indications and are demonstrated to be as viable as monotherapies. Two types of mix pharmacotherapy are commonly used.

1. Treatment using altered forms of NRT (eg. nicotine fix + nicotine gum)
2. Therapy with two medications such as a non-nicotine medication and NRT (eg. bupropion SR + nicotine patch)

Combination therapy using two different drugs provides an enhancement in therapeutic properties. The blend of bupropion SR and varenicline improves the adequacy of varenicline and furthermore expands the capacity of bupropion to decrease the weight addition occurring after quitting smoking. For smoking cessation, only the combination of bupropion SR plus nicotine patch is accepted by the FDA (Healton and Fiore, 2008).

Combination of Nicotine Replacement Therapy (NRT)

There are two sorts of blend NRT termed as consecutive and simultaneous therapy. Consecutive therapy provides initially a stable nicotine dose required to achieve abstinence (nicotine patch) followed by the desired dosing to prevent relapse (Sweeney *et al.*, 2001) . Simultaneous NRT therapy provides a passive nicotine delivery through long-acting NRT (i.e. nicotine fix) and followed by active delivery using a short-acting NRT (i.e. lozenge, inhaler, nasal spray, gum, and lozenge). Improved treatment efficacy and increased withdrawal symptom relief are obtained from combination NRT therapy and also high serum concentration of nicotine is achieved.

Combination Treatment of Non-Nicotine Pharmacotherapy and NRT

Bupropion sustained-release (SR) plus NRT

In an experimental study of 1504 smokers, it was found that bupropion SR plus nicotine patch group had higher smoking forbearance rates contrasted to nicotine patch group, and also and furthermore blend treatment with bupropion SR in addition to nicotine inhaler also had better effect compared to either agent alone. Additionally, mix treatment of bupropion SR in addition to nicotine lozenge was also found to be superior to monotherapies (Smith, 2009).

Nortriptyline plus NRT

In a 6-month study on 158 smokers, combination therapy of nortriptyline plus nicotine patch increased smoking abstinence rates compared to that of monotherapy (Prochazka *et al.*, 2004). In a clinical study regarding the comparison of nortriptyline in addition to nicotine substitution product vs nicotine replacement alone, the desires to smoke and nicotine withdrawal side effects were comparable in both the treatment group.

Varenicline plus NRT

Varenicline alone has a limited therapeutic effect on smoking cessation therapy and furthermore not entirely replaces the dopaminergic impact of smoking, guiding to a continuous desire to smoke cigarettes. Thus combination therapy of an NRT along with varenicline is needed to decrease both withdrawal manifestations and desire to smoke to achieve complete abstinence (Moore *et al.*, 2008).

New Trends in Smoking Cessation

The existing drugs for smoking cessation have low levels of efficacy, and there is a wide change in progress rates and also linked with remarkable aftereffects. Subsequently, there is an extraordinary need for progressively viable medications to help smokers in achieving long term continence.

Nicotine vaccines (First generation Conjugate and Next Generation Nanoparticle-Based Nicotine Vaccines)

Nicotine immunizations act by inducing the immune system to create antibodies coordinated against nicotine acquired from smoking tobacco, subsequently considered as a therapeutic agent in smoking cessation. The antibodies produced by the nicotine vaccine reduce plenty of the nicotine's behavioral and physiological effects, which holds nicotine in the blood and minimizes its delivery in brain. Compared to traditional pharmacological therapies, nicotine vaccine has several major advantages such as;

1. No need of frequent administration and long term efficacy is obtained from the prolonged existence of antibodies in the blood
2. Minimum adverse effects associated with vaccines (Hu *et al.*, 2016).

3. Less price compared to other formulations. In conventional vaccines, a nicotine counterpart is conjugated by a covalent bond to a carrier protein in sequences to be recognized by the immune system. It is the little subatomic weight and the basic structure of nicotine, which makes it incompetent to produce an immune response.

The original conjugate nicotine immunizations have limitations such as poor identification and internalization by immune cells, trouble in consolidating with atomic adjuvants, low bioavailability and low immune constancy (Zhao *et al.*, 2017b). Subsequently, nanoparticles have been considered as a conveyance vehicle for antibodies which will beat a significant number of the disadvantages related with conjugate nicotine immunizations and also a stronger immune response can be induced with this next-generation nicotine vaccine. Contrasted with original conjugate nicotine antibodies, the nanoparticle-based nicotine immunizations present numerous favorable circumstances:

1. The particulate nature can impersonate the geometry of normally existing pathogens, (for example, microscopic organisms and infections), thus enhanced recognition by the immune system.
2. Enhanced catch and introduction by antigen-showing cells can be accomplished by adjusting the physicochemical properties, (for example, size and surface charge).
3. Molecular adjuvants can be effectively joined, viably conveyed, and proficiently discharged in a controllable way, thereby reducing systemic toxicity and increasing the magnitude of the immune response (Ilyinskii *et al.*, 2016; Zhao *et al.*, 2017a), (Table 1).

Cytisine

Cytisine is a plant alkaloid derived from the *Cytisus laburnum,* that has been marketed as a medication for smoking cessation. It is an incomplete agonist of the $\alpha 4\beta 2$ nicotinic acetylcholine receptor(nAChRs). It is considered as one of the most practical human services intercessions to assist in smoking cessation along with other non-pharmacological therapies. Treatment is started with 1 capsule each 2 h (maximum: 6 capsules/day) for initial 3 days, trailed by 1 capsule every 3 h (most extreme: 4 capsules/day) for days 13-16 and finally, at the end of day 21-25, the dose is reduced to 1–2 capsules/d. The adverse reactions associated with cytisine include weight gain, stomachache, dyspepsia, sickness, vertigo, and sleeping disorders (West *et al.*, 2011).

Overview of Smoking Cessation Services

The smoking cessation services underwent by a health care provider in a health care set up initially provide an advice to quit followed by prescribing and dispensing either NRT or Varenicline/bupropion or combined therapy. Then follow up for at least 6 months is done to determine the success or failure of the therapy within the patient. (Figure 6).

CONCLUSIONS

The death rates due to tobacco-related illnesses are more than 1 million. The available pharmacotherapies include NRT and Non-NRT's. Pharmacotherapies alone is not an effective option for smoking cessation. Clinical Physicians also have an important role in smoking cessation therapies along with pharmacological interventions. Physicians should understand the smoking status of an individual and should provide adequate behavioral therapies and counseling followed by pharmacotherapy to help them quit. Compared to monotherapies combination therapies of two NRT's or an NRT and Non-NRT (bupropion or varenicline) are found to be effective. New treatment options such as nanoparticle-based nicotine vaccines are found to have better therapeutic effect and abstinence rates on smokers compared to other pharmacotherapies available.

Conflict of Interest

None.

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