INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH

IJCMPR

Available Online at http://www.journalcmpr.com

REVIEW ARTICLE

TOBACCO CESSATION INTERVENTIONS CURRENT CONCEPTS: AN OVERVIEW

Ankita Piplani

Department of Public Health Dentistry, Postgraduate Institute od Dental Sciences, Rohtak

ARTICLE INFO

Article History:

Received 15th October, 2016
Received in revised form 7th November, 2016
Accepted 16th December, 2016
Published online 28th January, 2017

Key words:

Nicotine Relacement therapy, Tobacco cessation, Bupropion, Varenicline, Clonidine, Nicotine Dependence.

ABSTRACT

Background: Tobacco is a modern day epidemic that poses substantial health burden and is the single greatest preventable cause of death in the world. The physical addiction to tobacco is a key factor in continued tobacco use. Approximately 40 % of the smokers attempt to quit annually, yet less than 5% do, hence tobacco addiction is best considered as a chronic relapsing diseases. **Objectives:** To compile, collate and provide evidences regarding effectiveness of various models of tobacco cessation therapies for quitting of tobacco habits. **Materials and Method:** Articles required for the narrative review were collected from the searches in the electronic data bases such as PubMed, PubMed Central, Google Scholar. Various effective pharmacological and behavioral interventions are there to assist people to overcome the addiction. In pharmacotherapy several effective medications are available for treating tobacco addiction and their ability to reduce tobacco use and related diseases is potentially large. Clonidine and nortriptyline are effective but they are regarded as second-line drugs due to their side effects. Nicotine replacement therapy (NRT), varenicline and bupropion SR are regarded first-line medications. The review aims to summarize literature on various pharmacological interventions currently used to treat tobacco dependence.

INTRODUCTION

Tobacco has become a major public health challenge in the world because of its association with increased morbidity and mortality.(Jorenby D 2002) Worldwide there are nearly 1.2 billion users of nicotine and tobacco products.(Jain R 2013) The high prevalence of smoking is due to dependence producing effect of nicotine that promotes regular smoking by making it difficult to quit and further sustaining exposure to the other 4000 harmful chemicals that are present in tobacco smoke which harms almost every organ of human body.(Garrett BE 2001) Nicotine present in tobacco binds to the nicotinic acetylcholine receptors located in the brain, autonomic ganglia, and neuromuscular junctions. Such binding leads to the release of a number of neurotransmitters and hormones including dopamine, serotonin, nor-epinephrine, acetylcholine, vasopressin, and beta-endorphin. The release of these substances modulates many of the subjective, cognitive, and behavioral effects associated with smoking, such as increase in pleasure, improved mood, increased attention, enhanced cognition and motor performance, and weight loss. As a result of this neuro adaptation, cessation of tobacco use results in a withdrawal syndrome, characterized by depressed mood, insomnia, irritability, frustration or anger, anxiety, difficulty concentrating, restlessness, decreased heart rate, and increased appetite or weight gain. Thus, nicotine addiction is maintained not only by the subjective positive effects, but also by the desire to avoid the negative symptoms associated with nicotine withdrawal. This is proved by the fact that, approximately 40% of the smokers attempt to quit annually, yet less than 5% do.(Kotlyar M 2002) This illustrates the powerful force of tobacco addiction which necessitates health professional help with various interventions to achieve permanent abstinence.(Tonnesen P 2009)

MATERIALS AND METHOD

A thorough literature search was performed to understand and identify the updates in the field of pharmacological treatment of tobacco dependence. Electronic databases like Pubmed, Pubmed Central, Google Scholar were searched from January 2000 to December 2015 for the relevant literature using keywords “Nicotine Relacement therapy, Tobacco cessation, Bupropion, Behavioral intervention, Varenicline, Clonidine, Nicotine Dependence.” Out of 23724 articles which appeared 52 articles were considered for review. Systematic reviews, narrative reviews, clinical trials, comparative studies and reports/guidelines of international health agencies were included for review.

5 A’s methodology to help patients of tobacco use:

Health professionals are in strong position to help tobacco users in quitting this habit because approximately 70 percent of smokers visit a physician during any given year, and 90 percent over five years and an equal percentage visit dentists.(Carpenter MJ 2013) To help health professionals in treating

patients of tobacco use, National Cancer Institute has developed recommendations often referred to as "the four As" in 1989. Later on the Agency for Health Care Policy and Research recommended a 5-step approach in 1996 which was similar to the original approach by the National Cancer Institute, except for the additional step of assessing the patient's willingness to stop.(Karnath B 2002)

Ask about smoking

Tobacco use must be approached as a health problem just like any other health condition. Therefore everyone who approaches for health care should be asked about tobacco use before advising him to quit or offering assistance to quit.(WHO 2010)

Advice about smoking cessation

Integrating tobacco cessation into primary health care and other routine medical and dental visits provides the health-care provider with opportunities to remind users that tobacco harms their health. Repeated advice at every visit reinforces the need to stop using tobacco. Benefits of quitting smoking and adverse effects of smoking has to be discussed. Advise should be given on health, economic and family point of view. Smokers should be educated about power of addiction and temporary nature of withdrawal symptom. It is crucial that smokers should be told about withdrawal symptoms like depressed mood, craving, insomnia, irritation, poor concentration, restlessness, increased appetite, which are caused by brain changes due to repeated tobacco use and are most severe during the first week and last two to four weeks after stopping tobacco.(WHO 2010)

Assess the patient's willingness to stop smoking

After advising, willingness to quit should be assessed in every patient. Assessment for nicotine dependence has to be done to identify need for pharmacotherapy.(WHO 2010)

The Fagerström Tolerance Questionnaire was developed by Karl-Olov Fagerström. This instrument was modified to the Fagerström Test for Nicotine Dependence by Todd Assessment of nicotine dependence can be done with Fagerstrom Test for Nicotine Dependence. This is a standard instrument for assessing the intensity of physical addiction to nicotine. Heatherton, *et al*. in 1991. The test was designed to provide an ordinal measure of nicotine dependence related to smoking. It contains six items that evaluate the quantity of cigarette/bidi consumption, the compulsion to use, and dependence. Behavioral interventions should be provided at all levels of nicotine dependence and pharmacotherapy can be provided in patients with moderate to high dependence.(Heatherton TF 1991)

The smokers who are not ready to quit smoking immediately or has failed in their quit attempt 5R's strategy should be applied in them which consist of:-

1. ***Relevance*:** The relevance of quitting smoking should be made understandable to person in his/her own context.
2. ***Risks*:** The smoker should be helped to identify personalized potential health risks and to stratify both acute and long-term risks.
3. ***Rewards*:** The smoker should be showed personal benefits of stopping smoking.
4. ***Road-blocks*:** The barriers or obstacles that might impede the success of a quit attempt should be identified.
5. ***Repetition*:** Smoking cessation interventions should be delivered repeatedly, whenever the smoker is found not willing/ready enough to quit smoking.(Karnath B 2002)

Fagerstrom Test for Nicotine Dependence

	PLEASE TICK (✓) ONE BOX FOR EACH QUESTION	
How soon after waking do you smoke your first cigarette?	Within 5 minutes 5-30 minutes 31-60 minutes	☐ 3 ☐ 2 ☐ 1
Do you find it difficult to refrain from smoking in places where it is forbidden? e.g. Church, Library, etc.	Yes No	☐ 1 ☐ 0
Which cigarette would you hate to give up?	The first in the morning Any other	☐ 1 ☐ 0
How many cigarettes a day do you smoke?	10 or less 11 – 20 21 – 30 31 or more	☐ 0 ☐ 1 ☐ 2 ☐ 3
Do you smoke more frequently in the morning?	Yes No	☐ 1 ☐ 0
Do you smoke even if you are sick in bed most of the day?	Yes No	☐ 1 ☐ 0
	Total Score	
SCORE	1- 2 = low dependence 3-4 = low to mod dependence	5 - 7= moderate dependence 8 + = high dependence

Assist

Patients should be assisted in their quit attempts with pharmacotherapy and counseling. Counseling is required for helping patients with a quit plan which includes:-

1. Setting a quit date usually within 2 weeks, enlisting support and understanding of family and friends, anticipating challenges especially in first few weeks and removing tobacco products from environment.
2. Providing practical counseling (eg problem solving and skills training) which includes:-stressing abstinence, reviewing past quit experience, educating about withdrawal symptoms and simple ways of handling them, reviewing relationship of alcohol to tobacco use, pointing out that having other smokers in the home will increase the difficulty, helping to obtain support from family, friends and coworkers.
3. Recommending Pharmacotherapy:- Pharmacotherapy along with MI can increase the abstinence of smoking among smokers.

Currently several effective medications are available for treating tobacco addiction and their ability to reduce tobacco use and related diseases is potentially large. Agents such as clonidine and nortriptyline are effective but they are regarded as second-line drugs due to their side effects. Nicotine replacement therapy (NRT), varenicline and bupropion SR are regarded first-line medications.(Tonnesen P 2009)

Pharmacological Interventions for smoking cessation

Nicotine Replacement Therapy

The most well studied and well documented pharmacological approach to help smokers manage the signs and symptoms of nicotine dependence and withdrawal is the therapeutic use of nicotine replacement therapies (NRT) which was approved in early 1980s. Nicotine replacement therapy (NRT) reduces tobacco consumption by decreasing physiological and psychomotor withdrawal symptoms through delivery of nicotine.(Wadgave U 2016)

Forms of Nicotine Replacement Therapy

NRT is available in various forms like gum, trans dermal patch, nasal spray, oral inhaler and tablet. Trans dermal Patch is a slow sustained release form of nicotine delivery. Other products like gum, nasal spray, oral inhaler, and tablet are acute dosing forms of nicotine. They provide general craving relief and breakthrough craving relief with immediate release of nicotine.(Wadgave U 2016)

Transdermal patch

Nicotine patches are applied to the skin and deliver nicotine through the skin at a relatively steady rate. Patches are available in a range of dosages, which permits higher dependent smokers to use the strongest patches and lower-dependent smokers to use a lower. The range of dosages allows users to gradually decrease their nicotine intake over a period of several weeks or longer to enable a gradual adjustment of their bodies to lower nicotine levels and ultimately to a nicotine-free state. They are available in different doses, and deliver between 5mg and 22mg of nicotine over a 24-hour period.(Wadgave U 2016)

Acute Dosing Nicotine Products

Acute-dosing products have the benefit that both the amount and timing of doses can be titrated. Control over the timing of self-dosing enables smokers to use NRT medications as “rescue medication” when they encounter particularly strong cravings or threats to abstinence. Acute dosing nicotine products include gum, lozenge, sublingual tablet, oral inhaler, and nasal spray.(Wadgave U 2016)

Nicotine Gum

Nicotine chewing gums are the first available form of NRT. They are available in 2mg and 4mg formulations. Gum taken orally is used by “Chew and Park Method.” The gum is chewed slowly until tingling sensation is felt in the mouth, then chewing of the gum should be stopped and it is parked against the cheek, after a minute when the tingling is almost gone, it should be chewed again. Acidic beverages have been shown to interfere with buccal absorption of nicotine; therefore, patients should avoid acidic beverages (eg, soda, coffee, beer) for 15 minutes before and during chewing gum.(Fiore MC 2000)

Nicotine Lozenge

The lozenge is available in 2mg and 4mg formulations. Instructions for use and dosing are similar to nicotine gum, but the lozenge is not chewed; it dissolves in the mouth over approximately 30 minutes.(Wadgave U 2016)

Nicotine Sublingual tablet

The tablet is placed under the tongue from where the nicotine in the tablet is absorbed sublingually.(Wadgave U 2016)

Nicotine Oral inhaler

It consists of a mouthpiece and a plastic cartridge containing nicotine. The vapor inhaler was designed to satisfy behavioral aspects of smoking, namely, the *hand-to mouth ritual*, while delivering nicotine to reduce physiological withdrawal symptoms produced by tobacco withdrawal. Although termed an “inhaler” the majority of nicotine is delivered into the oral cavity and very little nicotine is delivered to the lung. As the absorption is primarily through the oral mucosa, the rate of absorption is similar to that of nicotine gum.(Wadgave U 2016)

Nicotine Nasal spray

It was designed to deliver doses of nicotine more rapidly through nostrils. Nicotine nasal spray is absorbed into the blood rapidly relative to all other NRT forms.(Wadgave U 2016)

Contra-indications for NRT

There are no contra-indication for nicotine replacement except in case of allergy (rare for patch users, exceptional for oral form users). Precautions should be taken in the case of children under 18 years, recent severe cardiac events, and pregnancy.

Adverse effects, precautions, warnings, drug interactions

The risks of nicotine medications are similar as those of nicotine in tobacco. There is no added risk due to partial or total replacement of nicotine provided by tobacco compared to that provided by substitutes. The intake of nicotine medications removes hundreds toxins contained in the smoke and constitutes an overall health benefit compared to tobacco use. Nicotine replacement therapy may have side effects, like

e.g. common side effects (more than one person in 100) like headaches, dizziness, hiccups, sore throat, irritation or dryness of mouth, nausea, vomiting, digestive disorders, uncommon side effects (more than one person in 1000) like palpitations, rare side effects (more than one person in 10,000) are generally moderate and are not comparable with the consequences of smoking. It is always safer to take nicotine replacement therapy than tobacco.(Fiore MC 2000)

Risk of dependence on oral substitutes

There is a risk to maintain nicotine addiction using oral nicotine replacement. This health risk is considerably lower with NRT than smoking tobacco. The risk of addiction is highest with tobacco, much lower with oral tobacco, even lower with oral nicotine replacement therapy and virtually absent with nicotine patches.(Fiore MC 2000)

Clinical Evidence showing efficacy of Nicotine Replacement therapy for smoking cessation

A cochrane review by Stead *et al* (Stead LF 2012) of 117 trials comparing NRT to controls found that NRTs increases the rate of quitting by 50% to 70% regardless of setting. The risk ratio (RR) of abstinence for any form of NRT relative to control was 1.60 (95% confidence interval [CI] 1.53 to 1.68). The pooled RRs for each type were 1.49 (95% CI 1.40 to 1.60, 55 trials) for nicotine gum; 1.64 (95% CI 1.52 to 1.78, 43 trials) for nicotine patch; 1.95 (95% CI 1.61 to 2.36, 6 trials) for oral tablets/lozenges; 1.90 (95% CI 1.36 to 2.67, 4 trials) for nicotine inhaler; and 2.02 (95% CI 1.49 to 2.73, 4 trials) for nicotine nasal spray. One trial of oral spray had an RR of 2.48 (95% CI 1.24 to 4.94).
Various randomized controlled trial (Shiffman S 2009, Batra A 2005, Wennike P 2003, Molyneux A 2003) comparing NRT with control also showed that NRT is well tolerated & effective in promoting smoking cessation.

Bupropion (Amfebutamone)

Bupropion hydrochloride was introduced in 1997. It is the first non –NRT intervention which was recommended by FDA as a first line drug for smoking cessation.(Karnath B 2002) It was originally developed as an antidepressant drug. It is a weak inhibitor of the neuronal uptake of nor-adrenaline and dopamine but not serotonin. In addition, bupropion has been shown to release dopamine and inhibit neuronal nicotinic receptors in the brain.(Molyneux A 2003) Hence, bupropion acts by increasing brain levels of dopamine and norepinephrine, which simulates the effect of nicotine on these neurotransmitters and hence affects brain reward system.(Karnath B 2002) Bupropion can be used in tobacco users with or without the history of depression.(WHO 2010)

Dose

The recommended dose is 150 mg once daily for 3 days, then 150mg twice daily for 7 to 12 weeks with an interval of at least 8 hours between the two doses. It can be given with transdermal nicotine. Patients with hepatic or renal diseases should be treated with reduced dosage of bupropion.(Karnath B 2002)

Prescribing practice

Bupropion is started while the person is still using tobacco. The person can completely quit in two weeks after initiating bupropion.(WHO 2010)

Adverse Effects

Common adverse effects includes dry mouth, agitation, insomnia, anorexia, weight loss, headaches, lowering of seizure threshold (at doses above 600mg/day) and dizziness.(7) Rarely allergic reactions can occur including skin rashes, fever, muscle and joint pain.(WHO 2010)

Contraindications

Bupropion is contraindicated in patients with bulimia or anorexia nervosa, in patients with seizure disorders, in cases of tumour of central nervous system, persons who are undergoing unsupervised withdrawal of alcohol or benzodiazepines, below 18 years and persons on monoamine oxidase inhibitors. In addition it should be used with caution to patients with risk factors for seizures. Lactating mothers should be advised not to continue breastfeeding infants while taking bupropion.(WHO 2010 ,Bundy C 2004)

Clinical evidence showing efficacy of Bupropion in smoking cessation

Various studies have documented the role of bupropion in smoking cessation. A Cochrane review by Hughes *et al*(Hughes JR 2014) on 65 trials showed bupropion significantly increased long-term cessation (44 trials, N = 13,728, risk ratio [RR] 1.62, 95% confidence interval [CI] 1.49 to 1.76). Th review also stated that there is insufficient evidence that adding bupropion (12 trials, N = 3487, RR 1.19, 95% CI 0.94 to 1.51) to nicotine replacement therapy (NRT) provides an additional long-term benefit. Based on a limited amount of data from direct comparisons, bupropion appear to be equally effective and of similar efficacy to NRT (bupropion versus NRT 8 trials, N = 4096, RR 0.96, 95% CI 0.85 to 1.09). Bupropion was well tolerated, there was no significant increase in the rate of serious adverse events amongst participants taking bupropion.
Other randomized controlled trials (Cox LS 2012, Croghan IT 2007, Evins A 2005, Covey LS 2007, McCarthy DE 2008, Dalsgareth OJ 2004, Tonnesen P 2003, Ahluwalia JS 2002, Dale LC 2001) conducted to compare bupropion with placebo showed that the bupropion was effective in promoting continuous abstinence whether used alone or in combination with NRT as compared to placebo.

Varenicline

Varenicline was approved for smoking-cessation treatment in 2006, under the trade name Chantix (Pfizer). Varenicline, a newly approved agent for smoking cessation, offers a new option to patients who cannot tolerate the adverse effects associated with NRT and bupropion and in patients with contraindications to such therapies (e.g seizures). Varenicline has a high affinity and high selectivity for binding at the α4β2 receptor. Varenicline is a highly water-soluble salt, similar in structure to nicotine. Varenicline also binds with moderate affinity at the serotonin receptor, which is responsible for the adverse effect of nausea that occurs with the agent. It acts by i) releasing dopamine and creating similar reinforcing effects (against action), but not to the full extent that nicotine does because of its partial binding of the receptor; and (ii) binding to the nicotine receptor (antagonist action) and blocking the effects of nicotine. It maintains moderate levels of dopamine to counter withdrawal symptoms, and reduces both the urge to smoke and the negative mood.(Potts LA 2007)

In vivo studies have found the dopamine response to varenicline to be 32–60% of the response to nicotine. With this partial agonist–antagonist profile, the varenicline

competitively inhibits nicotine, thus blocking the effects of nicotine at the α4β2 receptor site. Therefore, varenicline alleviates the symptoms of nicotine craving and withdrawal by its agonist activity and inhibits the effects of repeated nicotine exposure by its antagonist activity.(Potts LA 2007)

Dose

Varenicline is available in 0.5- and 1-mg tablets. The recommended dose is 0.5 mg once daily for days 1–3 to 0.5 mg twice daily for days 4–7, with a final dosage of 1 mg twice daily. Varenicline should be initiated one week before setting the "quit date." Varenicline is indicated for 12 weeks of treatment.(Potts LA 2007)

Side effects

Varenicline is usually well tolerated. Mild to moderate nausea and vomiting are the most common adverse effects, occurring in approximately 30% of patients. Other common adverse effects seen are headache, insomnia and abnormal dreams.(Potts LA 2007)

Contraindications

Varenicline is not recommended for pregnant women, children or people with a mental illness.(Potts LA 2007)

Clinical evidence showing effectiveness of Varenicline for smoking cessation

A cochrane review conducted by Cahill *et al*(Cahill K 2016) of 15 trials comparing varenicline with placebo for smoking cessation showed that the pooled RR for continuous or sustained abstinence at six months or longer for varenicline at standard dosage versus placebo was 2.27 (95% CI 2.02 to 2.55; 14 trials, 6166 people, excluding one trial evaluating long term safety). Varenicline at lower or variable doses was also shown to be effective, with an RR of 2.09 (95% CI 1.56 to 2.78; 4 trials, 1272 people). The pooled RR for varenicline versus bupropion at one year was 1.52 (95% CI 1.22 to 1.88; 3 trials, 1622 people). The RR for varenicline versus NRT for point prevalence abstinence at 24 weeks was 1.13 (95% CI 0.94 to 1.35; 2 trials, 778 people). The two trials which tested the use of varenicline beyond the 12-week standard regimen found the drug to be well-tolerated during long-term use. The main adverse effect of varenicline was nausea, which was mostly at mild to moderate levels and usually subsided over time.

Various randomized controlled trial showed varenicline to be effective in significantly increasing abstinence rates. In all the trials varenicline was well tolerated.(Potts LA 2007, Gonzales D 2006, Jorenby DE 2006, Nides M 2006, Aubin HJ 2008, Tsai ST 2007)

Clonidine

Clonidine is a central alpha 2 adrenergic agonist that has been used mostly as an anti-hypertensive. Stimulating alpha2 receptors results in decreased release of norepinephrine, hence results in reduced sympathetic activity.

Due to this uncertainty, its side effect profile, and the possibility of a withdrawal reaction upon discontinuation, clonidine is currently recommended as second-line pharmacotherapy for smoking cessation in the Agency for Healthcare research and Quality (AHRQ) clinical practice guidelines.(Glassman AH 1988, Glassman AH 1993, Kotlyar M 2002)

Dose

0.1 to 0.45 mg/day have been used for smoking cessation. (Glassman AH 1988, Glassman AH 1993)

Side Effects

Due to the risk of a withdrawal reaction characterized by sympathetic rebound resulting in incresed blood pressure, clonidine must be tapered off slowly when discontinued. (Glassman AH 1988, Glassman AH 1993)

Clinical evidence of clonidine for smoking cessation

Several studies have found that clonidine is effective in increasing quit rates among women but not among men, whereas others have found some efficacy in both male and female smokers. Still other studies have failed to find that clonidine is superior to placebo in promoting smoking cessation, regardless of gender. (Glassman AH 1988, Glassman AH 1993, Hilleman DE 1993, Wei H 1988, Niaura R 1996, Davison R 1988, Prochazka AV 1992, Franks P 1989, Nana A 1998)

Despite being extensively studied, the role of clonidine as an aid to smoking cessation remains unclear. Clonidine appears to have beneficial effects in some smokers with the greatest benefits possibly occurring in women. Due to this uncertainty, its side effect profile, and the possibility of a withdrawal reaction upon discontinuation, clonidine is considered a second-line pharmacotherapy in assisting smokers with a cessation attempt.(Kotlyar M 2002)

Nortriptyline

Nortriptyline is one of the two agents recommended as second-line pharmacotherapy in the most recent AHRQ clinical practice guidelines. The lack of a smoking cessation indication and its side effect profile resulted in nor-triptyline being recommended as second-line therapy in the AHRQ clinical practice guidelines.(Kotlyar M 2002)

This agent is an effective antidepressant in the tricyclic antidepressant (TCA) class of medications and mechanism of action is via the inhibition of the re-uptake of nor-epinephrine and serotonin with a greater effect on norepinephrine re-uptake.(Oates J 2001)

Side effects

Side effects of the TCAs are due to blocking muscarinic cholinergic receptors (dry mouth, blurred vision, constipation, and urinary retention), H1 histamine receptors (sedation, drowsiness, weight gain), and alpha1 adrenergic receptors (orthostatic hypotension). (Oates J 2001)

As TCAs can cause cardiac conduction delays that can result in arrhythmias in susceptible individuals or in overdose situations, nortriptyline should be avoided in patients at risk. (Oates J 2001)

Clinical Evidence of using Nortriptyline for Smoking Cessation

The efficacy of nortriptyline as a smoking cessation aid has been assessed in a double-blind placebo controlled studies, enrolling approximately two hundred patients.(Oates J 2001) As with bupropion, subjects with a major depressive episode at the time of enrollment were excluded to ensure that any effect seen was independent of nortriptyline's antidepressant effect. Study demonstrated that nortriptyline significantly increased

smoking cessation rates when compared to placebo. Hall *et al* [(46)] reported six month quit rates of 24 percent vs. 12 percent for nortriptyline and placebo treated subjects, respectively, while Prochazka *et al* [(Prochazka 1998)] reported one-year quit rates of 14 percent vs. 3 percent favoring nor-triptyline over placebo.

These two studies evaluating a total of 413 subjects suggest that nor-triptyline is likely to be useful in assisting smokers with the smoking cessation attempt.

The lack of a smoking cessation indication and its side effect profile resulted in nor-triptyline being recommended as second-line therapy in the AHRQ clinical practice guidelines.[(Kotlyar 2002)]

Arrange

Follow up contacts has to be arranged to see the motivated person again after a week. Follow up is most important around the quit date. If a personal visit is not possible follow up should be arranged on telephone. A second follow up contact is advisable in the first month. Subsequently a monthly contact for the next six months is ideal. The patient must be instructed appropriately whom to contact in case of a lapse, side effects of medicine, or when having difficulties to deal with cravings or stress.[(John RM 2009)] Actions to be taken during follow-up contact are:- success should be appreciated; if tobacco use has occurred, situations has to be reviewed; recommitment to total abstinence should be elicited; patient should be reminded that a lapse can be used as a learning experience; helping patients to identify problems already happened and how to face challenges in the future; pharmacotherapy use and problems associated with it need to be assessed; referral to more intensive treatment, if required, should be considered.[(Anderson JE 2002)]

CONCLUSION

Tobacco cessation assumes the most important role in the present time as it causes 1 in 20 deaths among women and 1 in 5 deaths among men between the ages 30 and 69 years.[(Jha P 2008)] However, smoking cessation remains uncommon in India as only about 5% of the men aged 45–59 years were ex-smokers in 2010.[(Jha P 2015)] A psychological, emotional and behavioral dependence were found to be the most important barriers in quit attempts.[(Gupta SD 2014)] All these barriers were due to addiction potential of nicotine present in tobacco, hence WHO had acknowledged the importance of integrating tobacco control programmes into health systems. By adopting a guideline-based approach to universally identify and helping those patients who use tobacco, health professionals can reduce the rates of smoking and its consequences among their patients.

References

1. Jorenby D. Clinical efficacy of bupropion in the management of smoking cessation. *Drugs.* 2002; 62(2):25–35.
2. Jain R, Majumder P, Gupta T. Pharmacological intervention of nicotine dependence. *Biomed Res Int*. 2013;(3):1-8.
3. Garrett BE, Rose CA, Henningfield JE. Tobacco addiction and pharmacological interventions. *Expert Opin Pharmac other*. 2001; 2 (10):1545-55.
4. Kotlyar M, Hatsukami DK. Managing nicotine addiction. *J Dent Educ. 2002*; 66:1061–73.
5. Tonnesen P. Smoking cessation: How compelling is the evidence? A review. Health Policy. 2009; 91(1):S15–S25.
6. Carpenter MJ, Jardin BF, Burris JL, Mathew AR, Schnoll RA *et al.* Clinical strategies to enhance the efficacy of nicotine repla cement therapy for smoking cessation: a review of the literature. *Drugs*. 2013; 73(5):407-26.
7. Karnath B. Smoking cessation. *Am. J. Med*. 2002; 112:399–405.
8. World Health Organization. Helping People Quit Tobacco: *A Manual for Doctors and Dentists.* 2010.
9. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom Test for Nicotine Dependence: a revision of the Fagerstrom Tolerance Questionnaire. *Br J Addict.* 1991; 86(9):1119-27.
10. Wadgave U, Nagesh L. Nicotine Replacement Therapy: An Overview. *Int J Health Sci*.2016 ;10(3):425-35.
11. Fiore MC, A clinical practice guideline for treating tobacco use and dependence: A US Public Health Service report. The Tobacco Use and Dependence Clinical Practice Guideline Panel, Staff, and Consortium Representatives. *JAMA*. 2000 Jun 28;283(24):3244-54.
12. Stead LF, Perera R, Bullen C, *et al*. Nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev*. 2012;11(11): CD000146.
13. ShiffmanS, FergusonSG, StrahsKR. Quitting by gradual smoking reduction using nicotine gum: a randomized controlled trial. *Am J Prev Med.* 2009;36(2):96-104.
14. Batra A, Klingler K, Landfeldt B, Friederich HM, Westin A *et al*. Smoking reduction treatment with 4-mg nicotine gum: a double-blind, randomized,placebo-controlled study. *Clin Pharmacol Ther*. 2005;78(6):689-96.
15. Wennike P, Danielsson T, Landfeldt B, Westin A, Tonnesen P. Smoking reduction promotes smoking cessation: results from a double blind, randomized, placebo-controlled trial of nicotine gum with 2-year follow-up. *Addiction*. 2003;98:1395-1402.
16. Molyneux A, Lewis S, Leivers U, Anderton A, Antoniak M *et al*. Clinical trial comparing nicotine replacement therapy (NRT) plus brief counselling, brief counselling alone, and minimal intervention on smoking cessation in hospital inpatients. *Thorax*. 2003;58(6):484-8.
17. Bundy C. Changing behaviour: Using motivational interviewing techniques. *Journal of the Royal Society of Medicine.* 2004;44 (97):43–47.
18. Hughes JR, Stead LF, Hartmann-Boyce J, Cahill K, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database Syst Rev*. 2014 Jan 8;(1):CD000031.
19. Cox LS, Nollen NL, Mayo MS, Choi WS, Faseru B *et al*. Bupropion for smoking cessation in African American light smokers: a randomized controlled trial. *Journal of the National Cancer Institute.* 2012;104:290-298.
20. Croghan, IT, Hurt RD, Dakhil SR, Croghan GA, Sloan JA *et al*. Randomized comparison of a nicotine inhaler and bupropion for smoking cessation and relapse prevention. *Mayo Clinic Procedings.* 2007; 2:186−195.
21. Evins A, Cather C, Deckersbach T, Freudenreich O, Culhane M, Olm-Shipman C *et al*. Double-blind, placebo

controlled trial of bupropion sustained-release for smoking cessation in schizophrenia. *J Clin Psycho pharmacol.* 2005;25:218–25.
22. Covey LS, Glassman AH, Jiang H, Fried J, Masmela J, LoDuca C: A randomized trial of bupropion and/or nicotine gum as maintenance treatment for preventing smoking relapse. *Addiction.* 2007;102:1292-302.
23. McCarthy DE, Piasecki TM, Lawrence DL, Jorenby DE, Shiffman S, Fiore MC, Baker TB. A randomized controlled clinical trial of bupropion SR and individual smoking cessation counseling. *Nicotine Tob Res.* 2008;10(4):717-29.
24. Dalsgareth OJ, Hansen NC, Soes-Petersen U, Evald T, Hoegholm A *et al*. A multicenter, randomized, double-blind, placebo-controlled, 6-month trial of bupropion hydrochloride sustained-release tablets as an aid to smoking cessation in hospital employees. *Nicotine Tob Res.* 2004;6:55- 61.
25. Tønnesen P, Tonstad S, Hjalmarson A, Lebargy F, Van Spiegel PI *et al*. A multicentre, randomized, double-blind, placebo-controlled, 1
year study of bupropion SR for smokingcessation. *J Intern Med.* 2003;254(2):184-92.
26. Ahluwalia JS, Harris KJ, Catley D, Okuyemi KS, Mayo MS. Sustained release bupropion for smoking cessation in African Americans: a randomized controlled trial. *JAMA.* 2002; 288:468–474.
27. Dale LC, Glover ED, Sachs DP, Schroeder DR, Offord KP *et al*. Bupropion for smoking cessation : predictors of successful outcome. *Chest.* 2001;119(5):1357-64.
28. Potts LA, Garwood CL. Varenicline: the newest agent for smoking cessation. *American Journal of Health-System Pharmacy*. 2007;64(13):1381–1384.
29. Cahill K, Lindson-Hawley N, Thomas KH, Fanshawe TR, Lancaster T. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev*. 2016 May 9;(5):CD006103.
30. Gonzales D, Rennard SI, Nides M, Oncken C, Azoulay S *et al*. Varenicline, an a4ß2 nicotinic acetylcholine receptor partial agonist vs sustained-release bupropion and placebo or smoking cessation: a randomized controlled trial. *JAMA*. 2006;296:47-55.
31. Jorenby DE, Hays JT, Rigotti NA *et al* . Efficacy of varenicline, an a4ß2 nicotinic acetylcholine receptor partial agonist vs placebo or sustained-release bupropion or smoking cessation: a randomized controlled trial . *JAMA*. 2006; 296:56-63.
32. Nides M, Oncken C, Gonzales D, Rennard S, Watsky EJ, Anziano R, Reeves KR. Smoking cessation with varenicline, a selective alpha4- beta2 nicotinic receptor partial agonist: results from a 7-week, randomized, placebo- and bupropion-controlled trial with 1-year follow-up. *Arch Intern Med*. 2006;166:1561–1568.
33. Aubin HJ, Bobak A, Britton JR, Oncken C, Billing CB *et al*. Varenicline versus transdermal nicotine patch for smoking cessation: results from a randomised, open-label trial. *Thorax*. 2008;63:717-24.
34. Tsai ST, Cho HJ, Cheng HS, Kim CH, Hsueh KC *et al*. A randomized, placebo-controlled trial of varenicline, a selective alpha4beta2 nicotinic acetylcholine receptor partial agonist, as a new therapy for smoking cessation in Asian smokers. *ClinTher*. 2007;29:1027-39.
35. Glassman AH, Stetner F, Walsh BT, Raizman PS, Fleiss JL . Heavy smokers, smoking cessation, and clonidine: results of a doubleblind, randomized trial. *JAMA*. 1988;259:2863-6.
36. Glassman AH, Covey LS, Dalack GWl. Smoking cessation, clonidine, and vulnerability to nicotine among dependent smokers. *Clin PharmacolTher*. 1993;54:670- 9.
37. Kotlyar M, Hatsukami DK. Managing nicotine addiction. *J Dent Educ*. 2002;66:1061–73.
38. Hilleman DE, Mohiuddin SM, Delcore MG, Lucas BD, Jr. Randomized, controlled trial of transdermal clonidine for smoking cessation. *Ann Pharmacother*. 1993;27:1025- 8.
39. Wei H, Young D. Effect of clonidine on cigarette cessation and in the alleviation of withdrawal symptoms. *Br J Addict.* 1988;83:1221-6.
40. Niaura R, Brown R, Goldstein M, Murphy J, Abrams D. Transdermal clonidine for smoking cessation: a doubleblind randomized dose-response study. *Exp Clin Psychopharmacol.* 1996;4:285-91.
41. Davison R, Kaplan K, Fintel D, Parker M, Anderson L *et al*. The effect of clonidine on the cessation of cigarette smoking. *ClinPharmacolTher*. 1988;44:265- 7.
42. Prochazka AV, Petty TL, Nett L, Silvers GW, Sachs DP *et al*. Transdermal clonidine reduced some withdrawal symptoms but did not increase smoking cessation. *Arch Intern Med.* 1992;152:2065-9.
43. Franks P, Harp J, Bell B. Randomized, controlled trial of clonidine for smoking cessation in a primary care setting. *JAMA*. 1989;262:3011-3.
44. Nana A, Praditsuwan R. Clonidine for smoking cessation. *J Med Assoc Thai*. 1998;81:87-93.
45. Oates J, Brown N. Antihypertensive agents and the drug therapy of hypertension. In: Hardman J, Limbird L, eds. Goodman and Gilman's the pharmacological basis of therapeutics. New York: McGraw-Hill, 2001:871-900.
46. Hall SM, Reus VI, Munoz RF, Sees KL, Humfleet G *et al*. Nortriptyline and cognitive-behavioral therapy in the treatment of cigarette smoking. *Arch Gen Psychiatry*. 1998;55:683-90.
47. Prochazka AV, Weaver MJ, Keller RT, Fryer GE, Licari PA *et al*. A randomized trial of nortriptyline for smoking cessation. *Arch Intern Med.* 1998;158:2035-9.
48. John RM, Sung HY, Max W. Economic cost of tobacco use in India. Tob Control. 2009; 18(2):138–143.
49. Anderson JE, Jorenby DE, Scott WJ, Fiore MC. Treating tobacco use and dependence: an evidence-based clinical practice guideline for tobacco cessation. *Chest* 2002;121:932–941.
50. Jha P, Jacob B, Gajalakshmi V, Gupta PC, Dhingra N *et al*. A nationally representative case-control study of smoking and death in India. *The New England Journal of Medicine.* 2008;358:1137–1147.
51. Jha P, MacLennan M, Yurekli A, Ramasundarahettige C, Palipudi K *et al*. Global hazards of tobacco and the benefits of smoking cessation and tobacco taxes in Cancer. Disease Control Priorities. 3rd Edition 2015:175–93.
52. Gupta SD, Purohit N, Bhati DK, Kundu AS. Smoking cessation: exploring predictors of change in smoking behavior in Indian male population. *Journal of Substance Use*. 2014;19(6):410-415.