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RESEARCH ARTICLE

NICOTINE REPLACEMENT THERAPY- A REVIEW

Biju B. Joseph

Prof., Dept. of Oral Medicine and Radiology ACDSR Kerala, Kerala University of Health Sciences.

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Abstract

Tobacco use has detrimental effects on health, including oral health. The emergence and increasing popularity of newer tobacco and nicotine products make tobacco use one of the major public health problems in the world. Tobacco use increases the risk of oral diseases such as oral cancer, oral mucosal lesions, periodontal disease, and dental caries, among many other oral diseases and conditions. The dental office is an excellent venue for providing cessation intervention.

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Introduction:-

Nicotine addiction is the major factor impeding smoking cessation and long-term Abstinence. Smoking is a major contributor to health inequalities IN WORLD.^{1,2,3}

Smoking, a global issue, exacerbates poverty by diverting funds from essentials, while second-hand smoke poses health risks indoors. Second-hand smoke causes serious cardiovascular and respiratory diseases, including coronary heart disease and lung cancer, and kills around 13 million people prematurely every year. The addiction to tobacco and related products poses a great challenge to healthcare providers⁴. The tobacco epidemic is one of the biggest public health threats the world has ever faced. Globally, 1.25 billion people use tobacco, and 80% of them live in low- and middle-income countries (LMICs), where the burden of tobacco-related illness and death is heaviest. Tobacco use kills more than 8 million people per year . Furthermore, tobacco use imposes a heavy economic burden throughout the world.

Cigarette smoking is one of the most important causes of illness and premature death. The tobacco problem in India is very complex, due to large use of an array of smoking forms well as smokeless tobacco products.^{5,6}

Tobacco use is the single greatest preventable cause of death in the world. Tobacco use is often incorrectly perceived to be solely a personal choice. This is contradicted by the fact that when fully aware of the health impact, most tobacco users want to quit but find it difficult to stop due to the addictiveness of nicotine. The toxicity of smoking is attributed to other components in cigarettes, it is the pharmacological effects of nicotine that lead to tobacco addiction. Pharmacological interventions for tobacco cessation continue to evolve with our growing knowledge of the neurochemical basis of nicotine addiction . Nicotine is the main alkaloid of tobacco smoke and the principal modulator of the psychopharmacological effects associated with addiction. The addiction to tobacco and related products poses a great challenge to healthcare providers. A wide range of ailments caused by tobacco are one of the substantial threats the general population is facing. It continues to be the substance causing maximum health damage globally.⁷

Corresponding Author:- Biju B. Joseph

Address:- Prof., Dept. of Oral Medicine and Radiology ACDSR Kerala, Kerala University of Health Sciences.

The damaging and harmful effects of tobacco usage on oral health are now well recognized. These include, in particular, a higher prevalence and severity of periodontal diseases among smokers. Tobacco use has also been directly implicated in numerous oral morbidities, including oral cancer, stomatitis nicotina, oral leukoplakia, periodontitis, gingival recession and soft-tissue changes as well as lead to nicotine addiction and dependence.

Nicotine is the main active ingredient in tobacco products that reinforces individual to tobacco addiction behaviour. the toxicity of smoking is attributed to other components in cigarettes, it is the pharmacological effects of nicotine that lead to tobacco addiction.

Therefore, pharmacological interventions for tobacco cessation continue to evolve with our growing knowledge of the neurochemical basis of nicotine addiction. Tobacco has been regarded as a potential risk factor for oral diseases such as oral potentially malignant disorders and oral cancers. The prevention and control of tobacco use is one of the rising issues globally. Tobacco cessation is one of the method which helps in improving the life expectancy and reducing the morbidity.

Nicotine replacement therapy (NRT) aims to temporarily replace much of the nicotine from cigarettes to reduce motivation to smoke and nicotine withdrawal symptoms, thus easing the transition from cigarette smoking to complete abstinence. Nicotine replacement therapy (NRT) aims to reduce motivation to consume tobacco and the physiological and psychomotor withdrawal symptoms through delivery of nicotine^{8,9,10}

Most tobacco users want to quit but find it difficult to stop due to the addictiveness of nicotine. Interventions for tobacco cessation are important in enabling tobacco users to stop using, which includes pharmacological and nonpharmacological approaches to aid tobacco cessation. Pharmacological approaches include nicotine replacement therapy (NRT) and non nicotine medications (bupropion and varenicline). Out of the various chemicals identified in tobacco smoke, nicotine is the main active ingredient in tobacco products, which is highly toxic and potentially lethal that reinforces the individual to tobacco addiction behavior. Nicotine is mostly absorbed through the buccal mucosa, and the absorption rate depends on the route of administration such as cigarette smoking and inhalation¹¹.

Mechanism Of Action Of Nicotine

Nicotine acts by the stimulation of neural nicotinic acetylcholine receptors (nACh receptors) in the ventral tegmental area of the brain. Stimulation of nACh receptors also leads to the activation of the central, peripheral nervous system, and nonneuronal tissue. This causes the release of dopamine in the nucleus accumbens.

Mechanism Of Nicotine Addiction

The average nicotine content of a cigarette is 10–14 mg, only 10% of which enters the systemic circulation, resulting in peak plasma concentrations of 300–500 nM. The amount of nicotine binding to plasma proteins is negligible (5%); its half-life is about 2 h. Inhaled nicotine from tobacco smoke enters the circulation through the lungs. The accumulation of the nicotine in the brain starts approximately 7 s after inhalation. Nicotine binds to nACh receptors in the brain that leads to a release of adrenaline and dopamine. This improves mood and reinforces the behavior. Nicotine induces pleasure and reduces stress and anxiety. Smokers use nicotine to control their mood, and for arousal, it also improves concentration. The presence of different types of nACh receptors, receptor upregulation, and receptor desensitization has influence on various physiological effects.

Mechanism of action NRT

The primary indication for NRT is to aid smoking cessation by reducing nicotine-withdrawal symptoms. In a study conducted by nancy r etal, it appears that NRT was used primarily to reduce nicotine-withdrawal symptoms (and perhaps to improve no-smoking policy compliance) without attention to the smokers' ultimate goal.³

The main mode of action of NRT is thought to be the stimulation of nicotinic receptors in the ventral tegmental area of the brain and the consequent release of dopamine in the nucleus accumbent. This and other peripheral actions of nicotine lead to a reduction in nicotine withdrawal symptoms in regular smokers who abstain from smoking. NRT may also provide a coping mechanism, making cigarettes less rewarding to smoke. It does not completely eliminate the symptoms of withdrawal, however, possibly because none of the available nicotine delivery systems reproduce the rapid and high levels of arterial nicotine achieved when cigarette smoke is inhaled Evidence for effectiveness. The most recent Cochrane reviews suggest that NRT leads to a near doubling of cessation rates achieved by non-pharmacological intervention, irrespective of the level of that intervention.³

Who should receive NRT.

Nicotine replacement therapy, preferably in conjunction with behavioral support should generally be offered to any regular cigarette smoker prepared to make a quit attempt. NRT is relatively unlikely to help smokers who are not motivated to quit or do not experience or expect to experience nicotine withdrawal symptoms. Motivation to quit, and Dependence³.

Nicotine-replacement therapy was prescribed more often to smokers with nicotine-withdrawal symptoms and to heavier smokers, who are more nicotine dependent and therefore more likely to develop nicotine withdrawal, but it was prescribed regardless of a patient's intention to stop smoking. Smokers with more nicotine-withdrawal symptoms, who are known to be less successful in quitting smoking, were also more likely to receive NRT. Since nicotine is the main factor responsible for the addiction to cigarette smoking, its rapid rates of absorption and entry to the brain are believed to be key factors responsible for the high abuse potential of this drug.¹²

Patient Contra indication

Nicotine-replacement therapy is relatively contraindicated in smokers with recent myocardial infarction, unstable angina, and serious ventricular arrhythmias. Hepatic impairment: For smokers with moderate liver function impairment, as indicated by a Child-Pugh score of 7, the total clearance of nicotine is reduced by approximately 40% to 50. Renal impairment: Nicotine clearance is decreased by approximately 30% in patients with moderate renal impairment and approximately 50% in subjects with severe renal impairment.

Pregnancy considerations: Nicotine, hydrogen cyanide, and carbon monoxide are the harmful substances in tobacco smoke, which pose severe risks to the developing fetus. Therefore, pregnant individuals should be particularly cautious about exposure to these toxic compounds.

Older patients: When prescribing NRT for older patients, initiating NRT at the lower end of the recommended dose range is prudent. This approach considers the increased likelihood of impaired hepatic, renal, or cardiac function, as well as the presence of comorbid medical conditions often observed in this age group¹³

Adverse Effects.

Gastrointestinal (GI) symptoms such as abdominal pain, dyspepsia, hiccups, diarrhea, nausea, and vomiting. Central nervous system symptoms such as headache. Cardiovascular system symptoms such as palpitations and hypertension. Neuropsychiatric symptoms such as depression, back pain, dizziness, nervousness, drooling, shakiness, cold sweats, hypertension, increased heart rate, and vivid dreams. Nose and oral ulcers and irritation due to the absorption of NRTs through the oral or nasal mucosa. Excess salivation and swelling of the lips, throat, and tongue are the additional adverse effects of nicotine. Skin rash or irritation in some individuals due to transdermal patches of NRT. For patients experiencing skin irritation, the application of topical hydrocortisone 1% cream or ointment can provide relief. Hiccoughs, GI disturbances, and jaw pain associated with nicotine gum. Sore throat, coughing, dry lips, and mouth ulcers due to administering nicotine sublingual tablets. The nicotine nasal spray has adverse drug reactions such as a runny nose and nasal irritate. Throat irritation, oral dryness, gastric reflux, and nausea, vomiting due to administering oral NRT products, as concluded in a recent meta-analysis. Patients are advised to promptly notify their healthcare providers if they experience any of the mentioned adverse effects to ensure the safety and well-being of individuals undergoing NRT. Furthermore, healthcare providers should provide counselling to patients, emphasizing that all forms of nicotine have addictive potential, and there exists a possibility of developing a psychological and physical dependence on NRT, although significantly less than smoking tobacco.¹³

Drug-Drug Interactions.

Nicotine interactions are observed with adenosine, cimetidine, and varenicline. Adenosine might amplify the chronotropic effects of nicotine. Cimetidine can lead to elevated serum nicotine concentrations, potentially resulting in toxicity. When varenicline is coadministered with NRT, there is an increased risk of experiencing sleep disturbances, nausea, and cutaneous adverse drug reactions. These reactions may include localized erythema, itching, and worsening preexisting acne.

Forms of Nicotine Replacement Therapy

Nicotine replacement therapy (NRT) helps smokers quit by providing controlled nicotine doses. Tobacco, containing harmful substances like tar and nicotine, leads to addiction and health risks. NRT substitutes nicotine from smoking

with products like patches, gums, and tablets to alleviate cravings and withdrawal symptoms.⁴ NRT products are available in a number of forms as follows: chewing gum, transdermal patch, nasal spray, oral inhaler, and tablet¹¹.

Existing WHO guidelines.

The need to provide interventions and supportive systems to help tobacco users quit as a key component of a comprehensive tobacco control approach to reduce the prevalence of tobacco use three types of tobacco cessation medicine (NRT, bupropion and varenicline) have been included in the WHO Model Lists of Essential Medicines.⁵

Dental considerations in NRT

Health professionals have a pivotal role in the cessation of tobacco. Clinicians can induce a major difference even with a minimal intervention and also there would be an association, which exists between the intensity of intervention and outcome of tobacco cessation.¹⁴ Dentists being oral health care providers are first to encounter tobacco related changes in patient's mouth. It is a professional as well as moral responsibility of a dentist to help the patients in quitting the habit by spreading awareness among them. Dentist needs to be well aware of different modes of tobacco cessation. Nicotine Replacement Therapy (NRT) is one of these methods.¹⁵ Medical professionals have responsibilities to reduce the prevalence of tobacco use among their patients, including dentists. A study conducted by Ather et al found study identified several important aspects in this regard, including a relatively low prevalence of smoking among medical students as compared to the general population.¹⁶

However a study conducted by Tanuja et al found that subjects had an ample knowledge regarding NRT use in tobacco cessation, it does not reflect their current attitude and preparedness.¹⁷ There is an urgent and pressing need for sensitization and training of dental professionals for treating nicotine dependence. Hence, sensitization and training programs are mandatory for the dental professionals especially during student phase.¹⁸

Tobacco use is a modifiable risk factor for oral disease. Dental professionals are able to reduce the burden of oral and overall health by influencing tobacco use. Brief interventions in dental clinics were effective in motivating patients to quit, a lack of confidence on the effectiveness was a significant barrier. Globally, the majority of dental students recognized themselves as role models in society and believed they should receive training. However, few reported receiving such formal training.¹⁹

Dental professionals can play important role in preventing adverse oral health effects by promoting smoking cessation. Dental students should also take a detailed history regarding tobacco smoking routinely, should motivate, encourage, and counsel their patients to quit this habit. In India, most dentists or health care professionals in the field do not ask or suggest methods to quit tobacco. This can be attributed to the fact that in India, no separate education or training is given to dental professionals during their course for helping individuals to quit tobacco. No such exposure during this learning phase could lead to the passive tobacco cessation guidance or services offered by these professionals. According to Severson et al. Hastreiter et al. and Tomar et al. in their studies regarding dental office practice for tobacco users, only a minority of the respondents in their study maintained records or advocated tobacco cessation practices among their clients. According to Severson et al., 40% of all the smokers make some attempt to quit in response to some advice from the general population.¹⁷

Health care settings have become increasingly attractive as an avenue for tobacco cessation and health care providers play a credible role in promoting tobacco cessation. As future dentists, dental students do have an important role in promoting tobacco cessation. Assessing their attitude, practice and constraints related to tobacco cessation promotion in dental patients is important, in order to provide a better service to the country's health care system. It is the responsibility of dental professionals to educate the patients about the oral health hazards of tobacco and to encourage patients to quit tobacco use while they seek for oral health care.^{20,21,22,23}

Dependence on tobacco or nicotine is a chronic condition that warrants interventions by all healthcare providers, including oral healthcare providers. Patients need multiple attempts to successfully achieve abstinence. A study by Babb et al. found that 68% of adult smokers wanted to stop smoking, 55% made a past-year quit attempt, and about 7% quit smoking. The dental office is an excellent venue, and the entire dental team needs to be involved in tobacco cessation. Integration of tobacco cessation by the electronic health record system with automated clinical reminders is a useful tool. Tobacco cessation in oral health settings is both feasible and effective. Incorporating behavioural interventions for tobacco cessation within routine oral examinations help tobacco users quit. However, the reach

and use of existing smoking cessation interventions remain low. There are gaps in the utilization of programs, policies, and resources that can improve cessation rates and help smokers quit.²⁴

Brief chair side-based interventions can come a long way in motivating and assisting tobacco users to quit smoking. Dental chair time is managed by routine inclusion of the tobacco history, assessment of readiness to quit and providing the desired cessation therapy. The same is reinforced again in the subsequent visit. Incorporation of smoking cessation intervention as a routine component of dental care is missing in usual dental practices. All dental institutions have responsibilities to provide necessary professional skills required by the dental health professionals to provide smoking cessation counselling confidently²⁵.

Long-term addiction to tobacco is the leading behavioral cause of premature mortality and morbidity and seems to become the leading mortality cause in the world by 2030. Dentists and the dental team in particular, due to having regular patient visits and the eligibility for initial detection of tobacco oral side effects as well as its effects on the general health, play an effective role as reliable health care providers in motivating patients for smoking cessation and even smoking prevention. Recent advancements include five key components of interventions in the centers of patient care, which included asking patients regarding smoking, counseling the patients for quitting smoking, assessing their willingness to quit smoking, helping them to quit smoking using both consultation and treatment, and lastly, planning to quit smoking and follow-up. Mecklenburg and Watt et al., studies proved that the dental care team possess a prominent position as health care providers considering patient interaction and may play an effective role through providing 2-3 minutes of consultation for smoking cessation to smokers to facilitate smoking cessation as part of their routine dental activities.

Physicians hardly consult or assist smokers for smoking cessation owing to lack of education, confidence and skills, and other barriers regarding the intervention of smoking cessation. Ebne et al. showed that the resistance and lack of cooperation of patients and lack of cooperation between dental centers and supporting organizations of smoking cessation were the most limitations regarding the implementation of smoking cessation programs. Also, Johnson et al.'s study in the UK showed that the most common barriers to implementing such programs were the limited time of the dentist and the lack of training facilities.²⁰

A multidisciplinary team approach, has the following multipronged components of biochemical monitoring at each session, assessment of nicotine dependence, spirometry for lung function, pharmacologic and individualized behavioural change communication therapy, social and family support, short and long-term follow-up and relapse prevention and management. Dental health professional plays a pivotal role in the multidisciplinary team of tobacco cessation.²¹

The dental team is well placed to undertake public health interventions; involvement would mean a radical change of approach to practice for most dentists and their teams. The adoption of such changes is likely to be determined by two main factors: whether the profession dental team can play a more general public health role, and whether it is economically possible for a dental team to make this change. The dental students and dental team members are in an ideal position to give their patients specific and authoritative, information concerning the adverse oral effects of tobacco use, interventions for tobacco cessation by non-physicians, including oral health professionals, may increase tobacco abstinence rates. However, the counselling procedures are still in its budding stage, the lack of tobacco-dependence education during dental training might be the reason. The Cochrane review concluded that behavioral tobacco cessation interventions delivered by dental professionals might increase abstinence rates among cigarette users and smokeless tobacco users. Development of strategies to integrate tobacco cessation counselling within the dental profession is a crucial aspect, this was the observation made by a study conducted by Talluri et al. Tobacco cessation is a skill that has to be developed and mastered by our dental graduates which will further help prevent serious, life threatening illnesses^{26,27},

Dental professionals, such as dentists and dental therapists/hygienists have a special role in identifying smokers: odour and teeth stains are obvious revealing signs.. Dentists are in a unique position to motivate and assist their patients to quit tobacco use and smoking. The current approach to the management of tobacco smoking addiction revolves around a combination of education, counselling, and pharmacotherapy. The prevention and control of tobacco use are increasing issues of global importance,. These measures are aimed at reducing the effect of tobacco related morbidity and mortality by preventing the initiation of tobacco smoking by the non-users and cessation of tobacco smoking among current users and chronic smokers.^{28,29,30,31, 32}

A key objective of the Government and all health professionals is to eliminate or to reduce the impact of tobacco usage on the wider population. The paradigm for cessation has changed over the years with a shift toward viewing addiction as a disease and the contemporary approach toward the management of tobacco addiction centers around a combination of education, counseling, and pharmacotherapy. Nicotine replacement products (NRPs) are the collective name for a range of over-the-counter medications containing pure nicotine, designed to aid users of tobacco products in reducing their intake of such products, or to achieve a total cessation of use.³³

Tobacco cessation interventions provided by oral healthcare providers can be classified into three categories, which include brief educational, behavioral, and pharmacological interventions. The interventions can be used alone or in combination.²⁴ Regular exposure to workshops and CDE programs are suggested for incorporating tobacco cessation practices effectively into dental practice.^{34,35} There is an urgent need to sensitize and train health professionals at the community level in the treatment of nicotine dependence as most people cannot afford to go to a specialist tobacco cessation clinic, nor can the Government afford to run them^{16,37-50}

Conclusion:-

Nicotine replacement therapy (NRT) describes a group of products delivering nicotine that are licensed for the relief of withdrawal as an aid to smoking cessation. NRT use for smoking reduction, to support temporary abstinence, for long-term use should also be enabled and NRT products should be made as widely available as cigarettes. Dentists are well placed in tobacco smoking cessation as they provide preventive and curative services on a regular basis. By expanding the dental examination, diagnosis, and treatment to include tobacco cessation, a potentially life-saving measure is added to an established service. Enhancing motivation is an important part of the overall treatment for tobacco addiction. Dental professionals should try to advocate for the implementation of the World Health Organization(WHO) framework convention in tobacco control .

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