Is Varenicline More Effective in Long Term Abstinence from Smoking than Nicotine Replacement Therapy (NRT)? A Review

Amit Kumar1, Manjunath BC2, Adarsh Kumar2, Vipul Yadav4, Bhavna Sabbarwal5, Mansi Mendiratta5, Madhavi Wig7

1, 6, 7 Postgraduate Student, Department of Public Health Dentistry, Postgraduate Institute of Dental Sciences, Rohtak
2 Senior Professor and Head, Department of Public Health Dentistry, Postgraduate Institute of Dental Sciences, Rohtak
3 Professor, Department of Public Health Dentistry, Postgraduate Institute of Dental Sciences, Rohtak
4 Assistant Professor, Department of Public Health Dentistry, Postgraduate Institute of Dental Sciences, Rohtak

Abstract

Background: Long term abstinence from smoking is the objective of tobacco cessation therapy. Varenicline, FDA approved a novel beta 4 alpha 2 nAChR partial agonist may offer more benefits. Objectives: To assess the effectiveness and evidence of varenicline over nicotine replacement therapy in extended term abstinence to smoking. Search strategy: A systematic literature survey was carried out identify in electronic database such as PubMed, MEDLINE; Database of Reviews of Effects (DARE); in English language using MeSH terms ‘Varenicline’ ‘Nicotine Replacement Therapy’ ‘Abstinence’ of last 10 years from 2008 to 2020. Selection criteria: We included randomized controlled trials which compared Varenicline when compared with NRT. Results: Initially 182 articles were filtered out, selection of 7 articles by independent reviewer were done. Data from each study were extracted by one reviewer and independently checked for accuracy by a second reviewer. At two years, 28.8% of participants who were prescribed varenicline and 24.3 percent of those who were prescribed NRT quit; the adjusted odds ratio was 1.26 [95 percent confidence interval (CI): 1.23 to 1.29], P 0.0001. At 24 weeks, the RR for varenicline versus NRT for abstinence was 1.25. (95 percent CI 1.14 to 1.37; 8 trials, 6264 people; moderate-quality evidence). Conclusions: An 8-week course of varenicline tends to result in a higher rate of abstinence for up to three years than a similar course of NRT in clinical practice.

Keywords: Varenicline, smoking cessation; NRT (Nicotine Replacement Therapy); Abstinence.

INTRODUCTION

Smoking cessation greatly reduces the risk of tobacco-related morbidity and mortality at all ages [1], including older smokers who have relatively poor health conditions and higher nicotine addiction levels [2, 3]. Smokers aged 65 and up can benefit up to 3.7 years in life expectancy after quitting. Nicotine replacement therapy (NRT) and varenicline, according to the US Preventive Services Task Force, are successful smoking cessation aids [4]. When compared to a placebo or non-NRT control group, NRT helps smokers quit smoking with a 53 percent–68 percent higher chance of quitting [4-6]. In two head-to-head clinical trials (the EAGLES review and an open-label trial in the United States), as well as in clinical settings, varenicline was found to be more successful than NRT in achieving abstinence [1, 6-8]. Tobacco reduction treatment aims for long-term abstinence from smoking. Varenicline, FDA approved in 2006 a novel alpha 4 beta 2 nAChR partial agonist may offer more benefits. There is little evidence that varenicline and nicotine replacement therapy (NRT) are beneficial for long-term smoking cessation. Nicotine, which is found in tobacco products, is now recognised as being as addictive as heroin or cocaine [9].

The rates of smoking cessation tend to vary by age. Older smokers have a better chance of quitting successfully than younger smokers [10], likely because they are more motivated, have a higher participation rate, and have more health issues [9, 10]. According to a meta-analysis of clinical trials, smokers aged 50 and up have a 3-fold greater risk of maintaining abstinence with pharmacological intervention [10]. However, the efficacy of varenicline versus NRT in older smokers has...
not been studied. The efficacy of varenicline in comparison to NRT could be influenced by sex and nicotine dependency level, according to new evidence [9, 10].

Nicotine causes the brain to release dopamine and other neurotransmitters, reinforcing the smoker's addiction to nicotine. Cardiovascular Disease is the main cause of preventable death, with people having a 70% risk of dying from coronary heart disease and lung disease. Due to the addictive nature of nicotine, quitting is extremely difficult, with up to 60% of people relapsing within the first year. Smoking, in addition to its positive reinforcement properties, can become a self-medicating behaviour with long-term habituation, reducing negative affect and modulating withdrawal symptoms [10]. Smokers that have life-threatening illnesses that could be caused in part by their cigarette use still have a hard time quitting, with as many as 70% of those who survive a heart attack resuming smoking within a year (40 percent while still in the hospital) and about 50% of lung cancer patients resuming smoking after surgery [10]. So, this review was undertaken to assess the effectiveness and evidence of varenicline over nicotine replacement therapy in long term abstinence to smoking.

MATERIAL AND METHODOLOGY

We included all reviews that included pharmacotherapy (varenicline or NRT) for smoking cessation. These are usually adult smokers, of either gender, and of any nationality and ethnicity. We have included all the data from those reviews which focus on populations of smokers, e.g., adults with mental health problems, smokeless tobacco users [11], or pregnant women [9], as such reviews cover a range of interventions beyond the pharmacotherapies which are the subject of this overview.

However, trials of pharmacological interventions which target specific groups of smokers, settings, intervention delivery and cessation techniques are included within the relevant sections of this overview, classified by the type of intervention.

Search strategy: A systematic literature survey was carried out to identify in electronic database such as PubMed, MEDLINE; Database of Reviews of Effects (DARE); in English language using MeSh terms ‘Varenicline’ ‘Nicotine Replacement Therapy’ ‘Abstinence’ of last 10 years from 2010 to 2020. (Figure-1). Characteristics of all the includes studies were tabulated (Table-1).

Selection criteria: We included randomized controlled trials which compared Varenicline when compared with NRT.

Fig-1: Flowchart depicting the search strategy employed for the review
RESULTS
Initially 182 articles were filtered out, selection of 7 articles by independent reviewer were done. Data from each study were extracted by one reviewer and independently checked for accuracy by a second reviewer. Findings revealed that at 2 years, 28.8% of participants prescribed varenicline and 24.3% of those prescribed NRT quit; adjusted odds ratio was 1.26 [95% confidence interval (CI): 1.23 to 1.29], P < 0.0001. (Table 2) The RR for varenicline versus NRT
for abstinence at 24 weeks was 1.25 (95% CI 1.14 to 1.37; 8 trials, 6264 people; moderate-quality evidence). Four trials which tested the use of varenicline beyond the 12 weeks of standard regimen found the drug to be well-tolerated during long-term use. Point prevalence of quit rates at 3, 6 and 9-months and 1, 2 and 4-years after exposure is represented as graph (Table-3).

Table-2: Odds-ratios and 95% confidence intervals for the association between prescription of varenicline versus NRT and smoking cessation

| Odds-ratio (95% confidence interval) | 3-months | 6-months | 9-months | 1-year | 2-years | 4-years |
|--------------------------------------|---------|---------|---------|--------|--------|--------|
| 1.42 (1.37 to 1.48)                  | 1.45    | 1.40    | 1.35    | 1.26   | 1.19   |

Table-3: Point prevalence quit rates by instrumental variable condition at 3, 6 and 9-months and 1, 2 and 4-years after exposure

DISCUSSION

NRT, bupropion, and varenicline are all widely available, both on prescription and, in the case of NRT, over the counter. In the United States and the European Union, they are approved as first-line treatments for use as smoking cessation aids, and they are widely recommended in many national guidelines.

Different treatments use different mechanisms, but the underlying principles are as follows:

i. To alleviate the cravings and withdrawal symptoms that are frequently associated with a quit attempt, and/or

ii. Smoking's reward can be reduced by indirectly disrupting dopamine release or desensitising receptors, and/or

iii. To provide some positive reinforcement other than through the use of a cigarette.

It should be noted that the precise mechanisms underlying some therapies are still being researched.

The following are thought to be the major mechanisms of action, either alone or in combination:

i. To block nicotine or blunt nicotine’s effects on its receptors or receptors in nicotine-affected
pharmacological pathways; these include bupropion, vaccines, mecamylamine, the nicotine receptor partial agonists (varenicline, cytisine, diacnrine), selective type 1 cannabinoid receptor antagonists (rimonabant, taranabant), and the opioid antagonists.

ii. To alleviate withdrawal symptoms: these include nicotine replacement therapies, lobeline, varenicline, Nicobrevin; To compensate for the effects of nicotine: these include anxiolytics, antidepressants, clonidine, bupropion; Aversive therapy: silver nitrate; • Sensory replacement: Nicobrevin.

Baker and colleagues [17] discovered that varenicline had the same effects as NRT on smoking abstinence after 26 weeks; the odds ratio was 1.3. (95 percent confidence interval, 0.9 to 1.9). Aubin and colleagues found similar effects between the two medications after a year. [1.4 (95% confidence interval 0.99 to 1.99)].

In contrast, Anthenelli and colleagues 2016 [1] concluded that at 24 weeks, those given varenicline had higher rates of abstinence than those given NRT.; odds ratio (and 95% confidence interval) were 1.5 (1.3 to 1.8).

Cahill and colleagues [18] conducted a network meta-analysis of randomised controlled trials, which revealed that varenicline is the most effective smoking cessation medication for up to 12 months.; odds ratio (and 95% confidence interval) were 1.6 (1.3 to 1.9).

However, because of differences in treatment delivery and participant characteristics, the efficacy of treatments in clinical trials may differ from their effectiveness in everyday clinical settings. Furthermore, abstinence for 6 to 12 months does not guarantee longer-term abstinence (> 24 months). A systematic review of RCTs discovered that 30% of participants who reported quitting at the 12-month follow-up relapsed in the following years.

CONCLUSION
Eight-week course of varenicline appears to yield higher abstinence rate up to 3 years than a similar length course nicotine replacement therapy in routine clinical practice.

Conflict of Interest Statement: Nil

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