

Literature review: smoking and coronary artery disease



Cigarette smoking highly boosts the risk of coronary artery disease (CAD), and the associated risk is particularly high in subjects with diabetes mellitus (DM) (Mühlhauser, 1994). The prevalence of smoking worldwide is one and quarter billion adult smokers, 10% of them reside within South East Asian countries. Smoking prevalence in these countries is a range from 12.6% to 40% in Singapore and Laos, respectively. Malaysia is recording 21% adult current smokers (Southeast Asia Tobacco Control Alliance (SEATCA), 2008). Cigarette smoking is estimated to cause more than five million deaths, making it the leading cause of preventable mortality worldwide (Peto et al., 1996). Atherosclerotic cardiovascular disease, chronic obstructive pulmonary disease (COPD) and lung cancer consider the three relevant causes of smoking related mortality (Centers for Disease Control Prevention, 2008). It has well known that cigarette smoking increases the risk of microvascular complications in DM (ie, nephropathy, retinopathy, and neuropathy) probably by its metabolic effects (worsening diabetes control and insulin resistance) in combination with increased inflammation and endothelial dysfunction. It appears to be stronger in type 1 diabetic patients, while the enhanced risk for macrovascular complications, coronary heart disease (CHD), stroke, and peripheral vascular disease, is most pronounced in type 2 diabetic patients (Eliasson, 2003, Haire-Joshu et al., 1999, Solberg et al., 2004).

Smoking cessation can safely and cost effectively be recommended for all patients, and it is a gold standard against which other preventive behaviors should be evaluated. Stopping smoking at any age has a considerable impact on improving life expectancy, reducing morbidity and reducing health care costs associated with treating smoking related conditions (Asaria et al.,

2007, Ward, 2008), but effective strategies are lacking cessation support (Everett and Kessler, 1997). There are several treatment interventions have been identified as essential to achieve cessation. These interventions include brief counseling by multiple health care providers, use of individual or group counseling strategies, and use of pharmacotherapy (Haire-Joshu et al., 1999).

Smoking cessation medicines are among the most cost-effective disease prevention interventions available (Fiore, 2000). There are several types of them assist in smoking cessation are available. (Wu et al., 2006). The 2008 update to Treating Tobacco Use and Dependence, a Public Health Service-sponsored Clinical Practice Guideline Panel identified seven first-line (FDA-approved) medications (bupropion SR, nicotine gum, nicotine inhaler, nicotine lozenge, nicotine nasal spray, nicotine patch, and varenicline) and two second-line (non-FDA-approved for tobacco use treatment) medications (clonidine and nortriptyline) as being effective for treating smokers (Fiore et al., 2008). The most commonly used formulation is nicotine replacement therapy (NRT). It reduces motivation to smoke and many of physiological and psychomotor withdrawal symptoms usually experienced during an attempt to quit smoking, and therefore, may increase the likelihood of remaining abstinent (Gourlay and McNeil, 1990, West and Shiffman, 2001). NRT is currently recommended as a safe intervention to general populations and higher-risk groups, including pregnant and breastfeeding women, adolescents, and smokers with cardiovascular disease (National Institute for Health and Clinical Excellence (NICE), 2008). Systematic reviews show that all forms of NRT have been proven to be effective (Fiore et al., 2008) and it

increase quit rate one and a half to two fold in comparison with placebo.

There are many studies provide good evidence that smoking cessation pharmacotherapy enhance the success of quit smoking attempt (Cahill et al., 2008, Fiore et al., 2008, Hughes et al., 2007, Stead et al., 2008).

Unfortunately, there are insufficient evidences to recommend one delivery system over another.

Literature review

This review will cover the aims of this research. Globally, it was estimated that there are about 1.3 billion smokers, half of whom will die from smoking-related diseases (Shafey et al., 2009). While in Malaysia, the Third National Health and Morbidity Survey has reported some decline in smoking statistics among general population (18 years and above) in Malaysia with an overall smoking rate of 21.5%; male and female smoking rates of 46.4% and 1.6%, respectively (Ministry of Health, 2006). To our knowledge, there is limited information about the prevalence of smoking among diabetes mellitus patients, but it seems to be mirror to general population, at least for young adults. Findings from the national Behavioral Risk Factor Surveillance System show that the prevalence of smoking in young adults with diabetes mellitus is similar to the prevalence in the general population (Ford et al., 2004). Other study in the United States found the age-adjusted prevalence of smoking was 27.3% and 25.9% among people with and without diabetes, respectively. The prevalence of smoking did not differ significantly between participants in both groups when they were stratified by age, sex, race, or education (Ford et al., 1994). Few studies examined the prevalence of tobacco use with diabetic patients, information that is critical for targeting

prevention efforts. There is no estimated prevalence for smoking in diabetes mellitus patients in Malaysia.

Few studies was conducted about the knowledge and awareness of diabetic patients towards smoking cessation and its pharmacotherapies. There is a survey done in the United Kingdom to investigate awareness of pharmacotherapeutic aids to smoking cessation in diabetic cigarette smokers. A structured questionnaire-based interview was held by research nurse individually with current smokers in a private room. Of 597 diabetic patients attending a routine clinic, one hundred diabetic patients were current smokers. The majority of them were type 2 diabetic patients (96%). There were 66% and 54% had heard about NRT and bupropion, respectively. Those who had heard about NRT, only 49% considered it safe with diabetes, while who knew of bupropion 39% thought it unsafe in diabetic patients. Approximately 84% were aware of the UK National Health Service (NHS) quit line, but only 8% had used it. The authors conclude that this subpopulation has poor knowledge and awareness of NRT and bupropion as aids to quit smoking (Gill et al., 2005).

A qualitative study done in the United States, aimed to investigate beliefs about cigarette smoking and smoking cessation among Urban African Americans with Type 2 Diabetes. Focus groups and a short survey were used to assess cigarette use patterns, perceived smoking health effects, preferences for treatment, and attitudes toward smoking cessation among this subpopulation. Twenty five participants were included in this study. The mean age was (SD) 48. 5 years ($\pm 10. 23$), 60% female, smoked 20. 9($\pm 12. 54$) cigarettes per day. Regarding the beliefs and knowledge about smoking <https://assignbuster.com/literature-review-smoking-and-coronary-artery-disease/>

and diabetes, Participants believed that smoking increased their risk for all health outcomes, though there was not a clear understanding of how. Furthermore, they believed smoking decreased their appetite and quitting smoking makes you gain weight, and that it would negatively affect diabetes. Regarding beliefs and opinions about stopping most participants desired to quit and believed it was important to quit, but were not motivated to quit or confident they could achieve cessation (Janet L. Thomas et al., 2009).

Another study established in the United States, aimed to assess what smokers believe about the health risks of smoking and the effects of smoking filtered and low-tar cigarettes, as well as their awareness of and interest in trying so-called reduced risk tobacco products and nicotine medications. It was conducted between May and September 2001. They gathered data on demographic characteristics, tobacco use behaviors, awareness and use of nicotine medications, beliefs about the health risks of smoking, content of smoke and design features of cigarettes, and the safety and efficacy of nicotine medications. The findings of this study showed a substantial percentage of respondents either answered incorrectly or responded " don't know" to questions about health risks of smoking (39%), content of cigarette smoke (53%), safety of nicotine (52%), low-tar cigarettes and filtered cigarettes (65%), additives in cigarettes (56%), and nicotine medications (56%). The smokers' characteristics most commonly associated with misleading information when all six indices were combined into a summary index were as follows: those aged 45 years or older, smokers of ultra-light cigarettes, smokers who believe they will stop smoking before they

experience a serious health problem caused by smoking, smokers who have never used a stop-smoking medication, and smokers with a lower education level. Those who believed they would stop smoking in the next year were more knowledgeable about smoking. The authors conclude that smokers are misinformed about many aspects of the cigarettes they smoke and stop smoking medications (Cummings et al., 2004).

Unfortunately, there is a dearth of information on the efficacy of smoking cessation pharmacotherapies in diabetic patients because large-scale studies involving this group do not report results separately for them. Additionally, there are few direct head to head comparison studies among them in this subgroup population.

In an open-label, randomized trial conducted in Belgium, France, the Netherlands, the United Kingdom, and the United States, compared varenicline with transdermal NRT for smoking cessation. Participants were randomized to receive either 12 weeks of varenicline or 10 weeks of transdermal NRT (Aubin et al., 2008). The primary end point was continuous abstinence rate (CAR) during the last 4 weeks of each treatment. Secondary end points were CARs from the last 4 weeks of treatment through weeks 24 and 52 and the 7-day point prevalence of abstinence assessed at the end of treatment, week 24, and week 52. The Minnesota Nicotine Withdrawal Scale (MNWS) and The modified Cigarette Evaluation Questionnaire (mCEQ) measures of craving, withdrawal, and smoking satisfaction were assessed at baseline and at each weekly visit through week 7 (or at early termination).

Data were analyzed in both the prespecified primary analysis population (all randomized participants who received at least 1 dose of study drug: 376 varenicline, 370 NRT) and the all-randomized population (378 varenicline, 379 NRT). CARs were significantly higher in the last 4 weeks of treatment of varenicline group compared with NRT group (55.6% vs 42.2%, respectively; Odds ratio (OR) = 1.76; 95% CI, 1.31-2.36; $P < 0.001$). At week 24, there was no significant difference in CARs (32.2% and 26.6%; OR = 1.33; 95% CI, 0.97- 1.82). At week 52, CARs were not significantly higher for varenicline over to NRT in the primary analysis population, although the difference in CARs remain significant through week 52 in all-randomized population analysis (25.9% vs. 19.8%; OR = 1.44; 95% CI, 1.02-2.03; $P = 0.04$). The 7-day point prevalence of abstinence at week 12 was significantly higher for varenicline compared with NRT (62.0% vs 47.0%, respectively; OR = 1.71; 95% CI, 1.27-2.30; $P < 0.001$). The differences in 7-day point prevalence of abstinence were not significant at week 24 or week 52.

For weeks 1 through 7, the average scores of MNWS and mCEQ for cravings, withdrawal symptoms, and the reinforcing effects of smoking were significantly lower with varenicline compared with NRT (all population analysis, $P \leq 0.001$). Varenicline group had significantly lower MNWS subscale scores for negative affect and restlessness compared with NRT (both, $P < 0.001$); there was no difference between varenicline and NRT in the subscale scores for increased appetite or insomnia.

A guideline "Treating Tobacco Use and Dependence: 2008 Update" is a product of the Tobacco Use and Dependence Guideline Panel. This guideline contains strategies and recommendations designed to assist clinicians; <https://assignbuster.com/literature-review-smoking-and-coronary-artery-disease/>

tobacco dependence treatment specialists; and health care administrators, insurers, and purchasers in delivering and supporting effective treatments for tobacco use and dependence (Fiore et al., 2008). A meta-analysis displayed the effectiveness of the first-line smoking cessation medications compared with placebo at 6 months post-quit. They determined the estimated abstinence rate and odds ratio at 6 months post-quit (95% CI) compared with placebo estimated abstinence rate of 13.8% and estimated odds ratio of 1.0. Varenicline had the highest estimated abstinence rate and odds ratio (33.2% and 3.1), while nicotine gum had the lowest estimated abstinence rate and odds ratio (19.0% and 1.5).

Another multicenter, randomized, double-blind, placebo-controlled trial compared the efficacy and safety of varenicline with placebo for smoking cessation in 714 smokers with stable cardiovascular disease that had been diagnosed for > 2 months. Participants received either varenicline (1 mg twice daily) or placebo at ratio 1: 1, along with smoking-cessation counseling, for 12 weeks. Follow-up lasted 52 weeks. The primary end point was carbon monoxide-confirmed CAR for last 4 weeks of treatment. The secondary outcomes were the CAR from week 9 through 52; CAR for weeks 9 to 24 and 7-day point prevalence of tobacco abstinence at weeks 12 (end of drug treatment), 24, and 52. The CAR was higher for varenicline than placebo during weeks 9 through 12 (47.0% versus 13.9%; odds ratio, 6.11; 95% CI, 4.18 to 8.93) and weeks 9 through 52 (19.2% versus 7.2%; odds ratio, 3.14; 95% CI, 1.93 to 5.11). The varenicline and placebo groups did not differ significantly in cardiovascular mortality (0.3% versus 0.6%; difference, -0.3%; 95% CI, -1.3 to 0.7), all-cause mortality (0.6% versus 1.

4%; difference, -0.8%; 95% CI, -2.3 to 0.6), cardiovascular events (7.1% versus 5.7%; difference, 1.4%; 95% CI, -2.3 to 5.0) (Rigotti et al., 2010).

Nides and his colleagues conducted a multicenter, double-blind, placebo-controlled, trial to evaluate the efficacy and tolerability of three varenicline doses in adult smokers. Bupropion hydrochloride was included as an active control. Participants were randomized to receive varenicline 0.3 mg once daily, varenicline 1 mg once daily, varenicline 1 mg BID, bupropion SR 150 mg BID, or placebo for 7 weeks, with the option of participation in follow-up through week 52. The varenicline groups received active drug for 6 weeks, followed by placebo for 1 week. The primary efficacy outcome in this study was CAR for any 4-week period from baseline through week 7. Secondary efficacy outcomes involved the 4-week CAR for weeks 4 through 7, 4 through 12, 4 through 24, and 4 through 52; cravings and withdrawal symptoms, assessed using the MNWS and the brief Questionnaire of Smoking Urges (QSU-brief); reinforcing effects of smoking, assessed using the mCEQ; and changes in body weight (Nides et al., 2006). The findings of this study presented that the patients treated with varenicline (except of those who received varenicline 0.3 mg once daily) or bupropion SR had significantly higher CARs for any 4 weeks compared with placebo ($P < 0.001$ and $P = 0.002$, respectively). The CARs for any 4 weeks were 48.0% for varenicline 1 mg BID (OR = 4.71; $P < 0.001$), 37.3% for varenicline 1 mg once daily (OR = 2.97; $P < 0.001$), 33.3% for bupropion SR (OR = 2.53; $P = .002$), and 17.1% for placebo. No statistical comparison was performed between the varenicline and bupropion SR groups. Only varenicline 1 mg BID was significantly more efficacious than placebo throughout the entire follow-up

period ($P \hat{=} 0.01$). Varenicline 0.3 mg once daily and varenicline 1 mg once daily were significantly more efficacious than placebo through week 7 ($P \hat{=} 0.05$), and bupropion SR was significantly more efficacious than placebo through week 12 ($P \hat{=} 0.05$). Scores on the MNWS and QSU-brief indicated reductions from baseline in cravings with varenicline 1 mg BID compared with placebo at each weekly time point during active treatment (week 2: $P < 0.01$; weeks 1 and 3-6: $P < 0.001$). Varenicline 1 mg BID was also associated with consistent improvements from baseline (the day before the TQD) to week 1 in scores on several subscales of the mCEQ compared with placebo, including satisfaction (mean change, -4.82; $P < 0.05$), enjoyment of respiratory tract sensations (mean change, -0.84; $P < 0.05$), and aversion (mean change, 0.82; $P < 0.05$). (The mCEQ was not used beyond week 1 of the active-treatment period.) There were no significant differences on any of the mCEQ measures between the lower doses of varenicline and placebo (Nides et al., 2006).

Rationale/Justification

Few studies examined the prevalence of tobacco use with diabetic patients, information that is critical for targeting prevention efforts. To our knowledge, there is no estimated prevalence for smoking in diabetes mellitus patients in Malaysia.

Most people today recognize major health risks from smoking, but this general knowledge does not necessarily translate into a belief that one is personally at high risk of becoming seriously ill as a consequence of smoking. Furthermore, general awareness of health risks does not mean that people are adequately informed about smoking in ways that might influence <https://assignbuster.com/literature-review-smoking-and-coronary-artery-disease/>

their smoking behavior. Because the knowledge, beliefs, and preferences of smokers facilitate maximum receptivity to programs, these are important considerations when developing effective cessation interventions. Therefore, we will investigate smokers' knowledge about the health risks of smoking and their awareness of nicotine medications.

Unfortunately, there is a dearth of information on the efficacy of smoking cessation pharmacotherapies in diabetic patients because large-scale studies involving this group do not report results separately for them. Additionally, there are few direct head to head comparison studies among them in this subgroup population.

Objectives

General objectives

Determine the prevalence of smoking among diabetic patients in outpatient clinic at General Hospital Penang.

To investigate diabetic smokers' knowledge about the health risks of smoking and their awareness of nicotine medications.

To estimate direct head-to-head comparison between varenicline and nicotine patch regarding to their efficacy in smoking cessation.

Specific objectives

Determine the prevalence of smoking among diabetic patients.

To assess the knowledge of diabetic smokers about the health risks of smoking and their awareness of nicotine medications.

To compare between varenicline and NRT in the abstinence rate of smoking.

To compare between varenicline and NRT in the cravings and withdrawal symptoms, assessed using the MNWS and QSU-brief.

To compare between varenicline and NRT in the reinforcing effects of smoking, assessed using the mCEQ.

To compare between varenicline and NRT in changes in body weight.

Research Methodology

Study design

This study comprises different types of study design according to the different objectives.

For estimating the prevalence of the smoking among DM patients, it will be achieved by review the medical records for all diabetic patients who attend the diabetic outpatient clinic during 2010. Besides assessing the smoking status, we will collect also specific demographic and diabetic-related data. Any medical records does not contain information about smoking status will be excluded.

The second objective in investigating knowledge and awareness of diabetic smokers about the health risks of smoking, smoking cessation and smoking cessation pharmacotherapies, the study design it will be cross-sectional survey. All the diabetic smoker patients who attend the outpatient diabetic clinic at General Penang Hospital in 2011 will be invited to participate in the survey. The questionnaire will be either distributed or interviewed by the

clinical staff. The questionnaire will be based on another study. More detailed information on how the survey was conducted can be found elsewhere (Cummings et al., 2004). The questionnaire will be divided to two sections involving: socio-demographic, tobacco-related and diabetes-specific health information; knowledge and awareness towards the health risks of smoking and their knowledge of smoking cessation and smoking cessation pharmacotherapies.

The sociodemographic information will include (age, sex, race ... etc); diabetic-related information, it will contain: type of diabetes, type of diabetic treatment, duration of diabetes; while for smoking related information will involve: number of cigarettes smoking per day, age started smoking, duration of smoking, are there any attempt to stop smoking for any period of time, Are there other smokers in the household.

To compare treatment effect of varenicline and nicotine patch in abstinence rate of smoking cessation for diabetic smoker patients and to investigate the impact of the smoking cessation on the diabetic control. The study design will be randomised, open-label, parallel group study. The participants will be randomized in a 1: 1 ratio either to varenicline or nicotine patch treatments. Subject who will receive varenicline will administer 0.5 mg/day for 3 days, 0.5 mg twice daily for 4 days, then 1 mg twice daily thereafter. Full dosing was achieved by the target quit date (TQD) and continues up to 12 weeks. Participant who will receive nicotine patch applied transdermal patches each morning starting on the TQD for 10 weeks. Doses of NRT were 21 mg/day for the first 6 weeks, 14 mg/day for 3 weeks, then 7 mg/day for 3 weeks.

We choose these two treatments (nicotine patch and varenicline) for several reasons. Nicotine patch is the most commonly used pharmacotherapy for smoking cessation (Burton et al., 2000, Pierce et al., 1995, West et al., 2001). Given that many smokers in general population use this treatment to quit smoking, it is important to determine treatment effect of other agents relative to the patch. Furthermore, recent data suggest that there is decline in the efficacy of nicotine patch over the previous 10 years (Irvin et al., 2003, Jorenby et al., 1999, Pierce and Gilpin, 2002). Varenicline is selected in this study because yet there is limited studies published about the effectiveness of this treatment in the diabetic smoker population. Also, varenicline was found to be the highest efficacy in the 2008 PHS Guideline meta-analysis (odds ratio 3.1) comparing to placebo (Fiore et al., 2008). Finally, smokers could be encouraged to seek out this prescribed agent, and insurers and health care systems could be encouraged to make this treatment more widely available, if it could be demonstrated that varenicline is more efficacious than over-the-counter medication (such as nicotine patch).

In this study we will collect three types of end points: efficacy, measuring of craving and withdrawal symptoms, and investigating the impact of smoking cessation on diabetic outcome.

The primary outcome for efficacy in the study it will be self-reported CAR, confirmed by exhaled CO levels of 6 ppm or below, during the last 4 weeks of treatment (varenicline and NRT, weeks 9-12 after TQD)

The secondary is the CAR from the last 4 weeks of each treatment until 6 months. Other secondary outcomes are 7-day point prevalence of tobacco

abstinence at weeks end of drug treatment and at 6 months. Continuous abstinence define as self-reported abstinence from any tobacco- or nicotine-containing product during the specific period and it will be verified by carbon monoxide (CO) level \leq 10 ppm. If the CO level is more than 10 ppm will be classified as a smoker regardless of self-reported abstinence. Point prevalence abstinence define as self-reported abstinence from any tobacco- or nicotine-containing product in the past 7 days that was not contradicted by expired air CO > 10 ppm. These are traditional standards for assessing efficacy of smoking cessation interventions (Fiore et al., 2008, Hughes et al., 2003).

The Minnesota Nicotine Withdrawal Scale (MNWS) (Cappelleri et al., 2005) will be used to assess urge to smoke, depressed mood, irritability, anxiety, poor concentration, restlessness, increased appetite and insomnia. The modified Cigarette Evaluation Questionnaire (mCEQ) (Cappelleri et al., 2007) will be used to assess smoking satisfaction, psychological reward, aversion, enjoyment of respiratory tract sensations and craving reduction. The two previous questionnaires will be administered baseline visit and at each weekly visit through week 6 (after TQD) and at the end of treatment or at termination for participants who discontinued the study before week 6 (TQD). While the MNWS will be administered to all participants, the mCEQ will be administered only to participants who report smoking since their last completed questionnaire.

Furthermore, we will assess the level of the nicotine dependence by using the Modified Fagerström Test for Nicotine Dependence (Heatherton et al., 1991) that range to three score ranges: (0-3) score indicate to low
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dependent, (4-6) score indicate to moderate dependent and (7-10) score indicate highly dependent. It will be administered at the baseline of the study.

Schematic presentation of study design:

Screening all diabetic patients' medical records to estimate prevalence of smoking among them

Interviewed structured questionnaire for all diabetic smoker to:

To know characteristics of diabetic smoker (sociodemographic, diabetic history and tobacco use history)

Investigate the knowledge towards smoking cessation and its pharmacotherapies

Patients who attend quit smoking clinic Assessed for eligibility

Excluded:

Did not meet entry criteria

Withdrew consent

Randomized at ratio 1: 1

Allocated to Varnicline (2mg or 1mg)

(For 12 weeks) and arrange for quit date

Allocated to nicotine Patch

(For 12 weeks) and arrange for quit date

Follow up at the end of treatment (12 weeks) and at 6 months to assess:

Abstinence rate of smoking cessation

the cravings and withdrawal symptoms

the reinforcing effects of smoking

changes in body weight

Analysis

Inclusion criteria

The inclusion criteria it will be varying among the different objectives:

For investigating the knowledge and awareness towards smoking cessation and its pharmacotherapies, smoker and ex-smoker diabetic patients (either type I or II) of both sexes aged ≥ 18 years will be included.

For the direct comparison between nicotine patch and varenicline, Diabetic smokers of both sexes aged ≥ 18 years who smoke ≥ 10 cigarettes/day and willing to quit smoking.

Exclusion criteria

Patient is currently using any form of tobacco other than cigarettes; any form of NRT or other smoking cessation therapy.

Significant depression requiring behavioral counseling and those using medications with psychoactive effects (e. g., antidepressants, antianxiety

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agents). other active psychiatric diseases because of previously identified limitations with delivery of the specific counseling intervention in such subjects.

History of skin allergies or evidence of chronic dermatosis.

Patient has medical contraindications for any of the study medications.

Pregnant, breastfeeding women or at risk of becoming pregnant.

Drug abuse or HIV infected patient.

Recent (â%œ3 months) history of myocardial infarction, angina pectoris, serious cardiac arrhythmia, or other medical conditions that the healthcare provider deemed incompatible with study participation.

Participation within the last 12 months in a formal smoking cessation program.