Review Article

Smoking cessation in primary care: a tool for the general practitioner

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Abstract

Tobacco smoking is one of the leading causes of morbidity and mortality worldwide. In Saudi Arabia, the prevalence rate of smoking has been estimated up to 28%. However, nationwide primary-care smoking cessation programs are not fully implemented. Several pharmacotherapies have been proven to be effective as smoking cessation aids. In this article, a summarized approach to smokers presenting to primary care will be discussed with a focus on first-line pharmacotherapy used in smoking cessation.

KEY WORDS: Smoking, cessation, primary care, Saudi Arabia

Introduction

Tobacco smoking is one of the leading causes of death and morbidity worldwide.[1–5] The Centers of Disease Control (CDC) estimates about 480,000 smoking related deaths per year in the United States, which includes about 90% of lung cancer deaths and 80% of chronic obstructive pulmonary disease-related deaths.[1] Moreover, cigarette smoking results in approximately 5.1 years of potential life lost and about $96.8 billion in productivity losses annually in the United States.[2] Cigarette smoking affects and harms almost every organ of the body, and smokers are at increased risk of cardiovascular disease (ischemic heart disease and stroke), respiratory disease (chronic obstructive disease), and cancer (almost anywhere in the body).[1]

In Saudi Arabia, the prevalence of cigarette smoking has been estimated to be between 17.5% and 28% while being predominantly among male subjects.[6–9] Similar figures have been reported in the United States and China (20.6% and 28%, respectively).[10,11]

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Quitting smoking reduces the risk of cardiovascular disease, stroke, and lung cancer.[1] Furthermore, it is expected to improve productivity while reducing the number of potential life lost per year. Several strategies can be utilized to effectively increase smoking cessation rates. These include quitlines, mass media campaigns, taxation on tobacco products, laws enforcing smoking-free practice, subsidizing smoking cessation treatments, and integrating treatment of tobacco dependence into routine primary care.[12]

Approach to Smokers in Primary Care

Smoking is a complex habit that involves both physical and psychological dependence. Several factors contribute to the habit of smoking and, at the same time, can be barriers when deciding to quit. These include physical addiction, behavioral factors, and emotional factors [Figure 1]. Smoking initiation is likely to occur in the context of psychological distress (e.g., stress and depression) and risk-taking behavior.[13] In addition, reduced self-efficacy and peer pressure increase the chances of smoking among adolescents.[14] On the other hand, having a high level of social support is protective against engaging in substance use.[14,15] Other factors influencing smoking initiation include adverse childhood events and certain personality characteristics such as hostility and neuroticism.[16] It is, therefore, essential to address those factors once identified in order to successfully assist smokers in quitting.

During the quitting process, smokers go through a number of stages commonly known as the cycle of change [Figure 2].

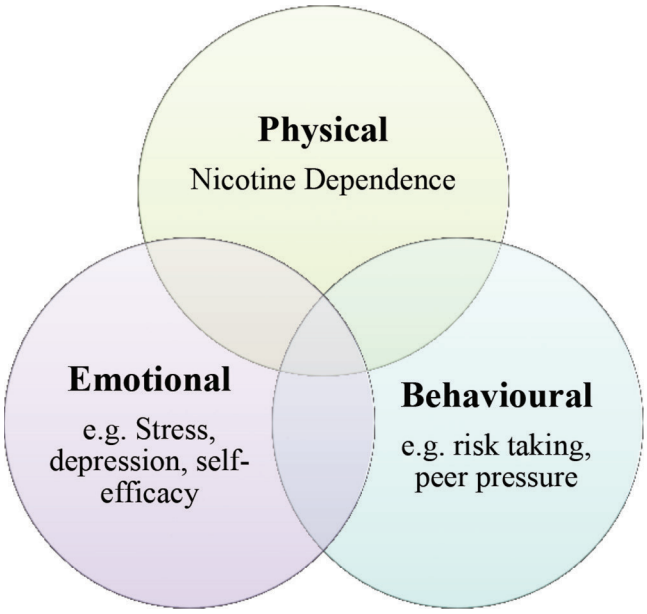

Figure 1: Factors contributing to smoking.

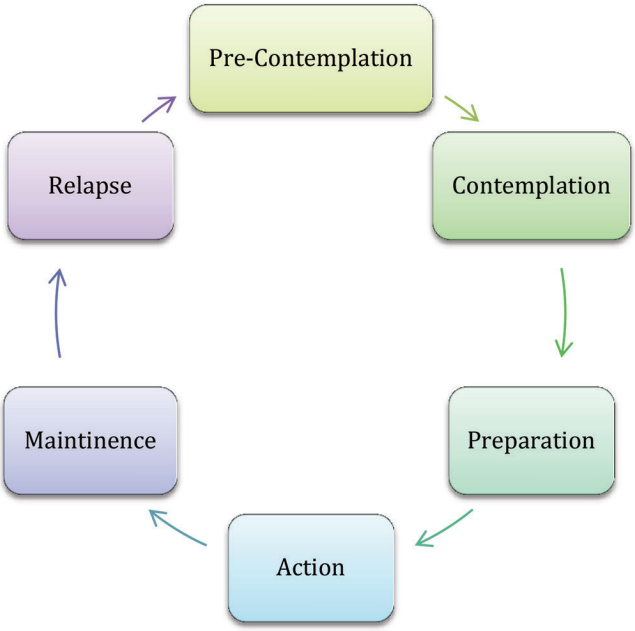

Figure 2: Stages of change.

Understanding those stages can help physicians offer support to their patients and help smokers understand the changes they are going through.[17]

During the first stage, smokers are in denial, may not see that cessation advice apply to them, and are not considering a change (precontemplation). In the second stage, smokers are usually ambivalent about changing, considering the change but worried about giving up their enjoyed behavior (contemplation). During the next stage (preparation), smokers try to change and experiment small changes while preparing to make a specific change. This is followed by the action stage, during which smokers will be practicing a new behavior. The action stage is followed by the maintenance stage where a commitment to continue change is sustained. This is often followed by a relapse stage where old behaviors are resumed, and the circle is repeated from there.[17] It is also worth mentioning that, each time a person repeats this cycle, they learn from their previous relapse experience.

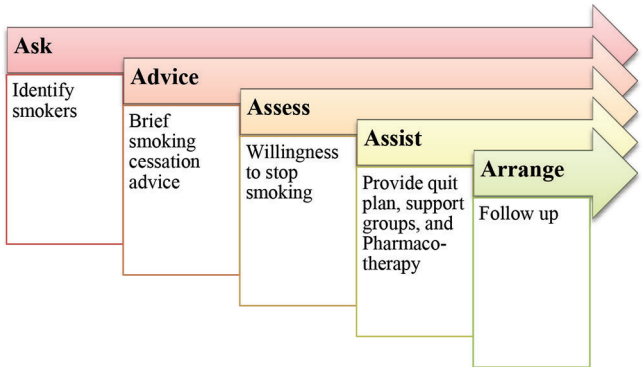

Figure 3: The 5 A's of smoking cessation advice.

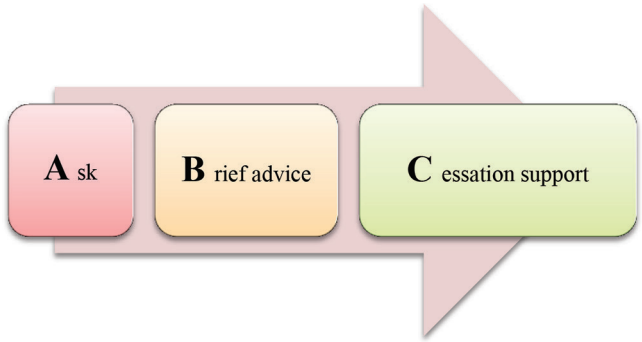

Figure 4: ABC smoking cessation advice.

It is important for physicians to support their patients through each stage in that cycle. For example, in the first two stages of change, a physician may address the patient's lack of readiness, explain the advantages and disadvantages of making the change, and personalize the patient's risk (e.g., using CVRA risk score). In the next two stages, the physician should offer support (e.g., social groups), arrange regular follow-up, identify factors leading to relapse, and generously praise their patients for not smoking.[17] Supporting patients during the relapse period, explaining that it is a normal part of lifestyle changing behavior, and learning from their previous experience are also crucial.

Counseling smokers in general practice and even giving a short advice can be part in assisting them to stop.[18,19] Counseling addresses psychosocial factors associated with smoking while ensuring appropriate follow-up. Pharmacotherapy, on the

Table 1: First-line pharmacotherapies for smoking cessation

	First-line pharmacotherapies for smoking cessation[20,25–30]			
	Strength	**How to use**	**Side effects**	**Contraindications**
NRT patches	Heavy smokers (>20cigs/day) start with 21mg/24hr. Light smokers (<20cigs/day) start with 14mg/24hr.	Apply patch on a clean, dry and fresh site each time. Step-down down dose every 3-4 weeks. Duration of treatment (8-12 weeks).	Itchiness and erythema at patch site. Insomnia.	Hypersensitivity to nicotine.
NRT gum	Light smokers: 2mg/piece (max. 20 pieces/day). Heavy smokers: 4mg/piece (max. 10 pieces/day).	Chew gum until taste is strong. Rest gum between cheek until taste fades then chew again.	Nausea and dyspepsia. Mouth soreness.	Hypersensitivity to nicotine.
NRT Lozenge	Light smokers: 2mg/piece. Heavy smokers: 4mg/piece. Maximum 15 pieces/day	Place between gum and cheek and allow it to dissolve. Move from side to side at times. Do not chew or swallow.	Nausea and dyspepsia. Mouth soreness.	Hypersensitivity to nicotine.
Bupropion SR	150 mg (maximum daily dose of 300mg)	Start 1-2 weeks before quit date. Start with150 mg once daily for three days then150 mg twice daily thereafter. Duration of treatment is 12 weeks.	Headache, insomnia, dry mouth and loss of appetite (usually early on, and improve with time).	Hypersensitivity to bupropion. Epilepsy / seizure disorder. History of anorexia/ bulimia. Concurrent use of mono-amine-oxidase inhibitors. Patients on linezolid or IV methylene blue.
Varenicline	0.5 mg and 1 mg	Start 1-2 weeks before quit date. 0.5 mg once daily for 3 days followed by 0.5 mg twice daily for 4 days then1 mg twice daily thereafter. 12 weeks course. May continue for another 12 weeks as maintenance.	Nausea is very common but usually is mild-moderate and improves with time. May cause neuro-psychiatric symptoms and patients should be monitored closely.	Hypersensitivity to varenicline.

other hand, addresses the problem of nicotine dependence and withdrawal symptoms (e.g., headache, irritability, and fatigue). Indications of nicotine dependence include smoking within 30 minutes of waking, smoking more than 10 cigarettes per days, and showing a history of withdrawal symptoms during previous quit attempts.

The 5-A's structured smoking cessation advice (*A*sk, *A*dvice, *A*ssess, *A*ssist, and *A*rrange) is one approach in delivering a brief advice to smokers in the United States.[20] It starts by "asking" to identify tobacco smokers, then "advising" using a personalized advice to quit smoking, followed by "assessing" the patient's willingness to quit and "assisting" them to quit by providing a quit plan (quit date, social support, and pharmacotherapy), and, finally, "arranging" regular follow-up [Figure 3].

Another simple Approach is the ABC brief advice that is used in New Zealand.[21] This approach consists of: Asking about and documenting every patient's smoking status; providing Brief advice to every one who smokes; and offering every one who smokes Cessation support (including behavioral support and pharmacotherapy) [Figure 4].

First-Line Pharmacotherapy for Smoking Cessation

Interventions that combine pharmacotherapy and behavioral support increase the success rate of smoking cessation.[22] First-line pharmacotherapies include nicotine replacement therapy (NRT), varenicline, and bupropion[20,23,24] [Table 1].

Nicotine Replacement Therapy

NRT is one of the oldest and a widely used smoking cessation aid. The chief mechanism of action of NRT is considered to be through the stimulus of nicotinic receptors in the brain and the consequent release of dopamine. This in turn helps in the reduction of nicotine withdrawal symptoms in smokers who abstain from smoking.[31] Several studies have demonstrated the efficacy and success rate of NRT.[31–34] NRT nearly doubles smoking cessation rates when compared with non-pharmacological interventions.[31] In a Cochrane review by Stead et al., NRT increased the chances of quitting smoking by 50%–70%.[32]

The use of NRT is associated with mild side effects. These range from localized erythema and skin irritation (for patches), nausea and dyspepsia (for gums and lozenges), and mouth and throat soreness (for inhalers and sprays).[35] NRT is generally safe to use, especially when compared with nicotine obtained from cigarettes, which is mixed with harmful combusted tobacco substances.[31] Moreover, NRT does not appear to increase the risk of serious cardiovascular events and is safe to use in smokers with stable cardiovascular disease.[31,36] However, caution should be taken when using NRT with smokers with acute cardiovascular disease (e.g. myocardial infarction and stroke) as it can cause vasoconstriction.[31]

NRT comes in several forms. Of which, patches, gums, and lozenges are readily available for sale in supermarkets in some countries (e.g., United Kingdom).[25,31] The choice of NRT method should be discussed with patients as per their preference and after explaining possible side effects of each method. All forms of NRT have demonstrated to be efficacious as smoking cessation aids.[32] However, it is worth mentioning that NRT does not completely remove withdrawal symptoms, given that all forms of NRT are absorbed in a slower fashion compared with nicotine delivered by smoked cigarettes, which reach high levels in the blood via arterial absorption.[24,31]

Nicotine 24-hour patches come in three different strengths (7, 14, and 21 mg), which are initiated according to smoking status (light vs. heavy smoking). The 24-hour patches are used once daily, and it is advisable to use a new patch on a fresh site to minimize side effects.[26] The course of treatment is usually 12 weeks and should not be less than 8 weeks.[25,26] Nicotine patches are used in a stepdown approach during the course of treatment.[26] Nicotine gums come in two strengths (2 and 4 mg). Smokers are advised to chew the gum until the taste is strong; after that the gum is rested between gums and cheek and then chewed again when the taste has faded. Nicotine lozenges are placed between the gum and cheek and allowed to dissolve. These come in three strengths (1, 2, and 4 mg).

Bupropion SR

Bupropion was initially approved by the Food and Drug Administration in 1997 as an antidepressant and now is licensed for use in smoking cessation.[37] The exact mechanism of bupropion is not fully understood. Bupropion is known to enhance both noradrenergic and dopaminergic neurotransmission and inhibit reuptake of norepinephrine transporter and dopamine transporter in the central nervous system.[38] A more recently discovered pharmacological property of bupropion is its affinity for nicotinic receptors. This is thought to contribute to its antidepressant effects and to its effectiveness in smoking cessation by reducing nicotine craving and withdrawal symptoms.[39,40]

The efficacy of bupropion has been documented by a large number of studies with quit rates between 23% and 33% at 1 year.[41–45] Along with its needed effects, bupropion may cause some unwanted effects. Common early side effects include headaches, insomnia, dry mouth, and loss of appetite. Most of these side effects go away after the first week of use.[46] Bupropion may cause seizures, which is estimated to occur in about 1 in 1000 patients (0.1%), especially in people with certain medical conditions; so, this drug is absolutely contraindicated in patients with a history of epilepsy.[46] Medications that can lower seizure threshold include antimalarials, antidepressants, antipsychotics, hypoglycemic agents, and sedating antihistamines.[27,28]

When using bupropion, smokers should set a quit date, and bupropion is started 1–2 weeks before that quit date (i.e., while the patient is still smoking). This is because bupropion normally takes about 1 week to reach its steady state. Dosing of bupropion is started as 150 mg once daily for the first 3 days; this is then subsequently increased to 150 mg twice daily (with a minimum of 8 h between doses and a maximum daily dose of 300 mg). Bupropion can be taken with or without food and should be swallowed and not crushed.[27,28] The duration of treatment is usually 7–12 weeks with a goal of complete abstinence of smoking. If treatment is not effective at 12 weeks, the medication should be stopped and treatment strategy reevaluated.[28]

Varenicline

Varenicline is a highly selective nicotine receptor binder. It works as a partial agonist to alpha-4-beta-2 nicotinic acetylcholine receptors where it binds with high selectivity and affinity, thus reducing symptoms of craving and withdrawal.[47] Moreover, it has an antagonist effect on the same receptors where it blocks nicotine binding to receptors, thus blocking the rewarding and reenforcing effects of smoking.[47,48]

Varenicline is probably the most effective smoking cessation aid currently available in the market. Several studies have demonstrated the effectiveness and superiority of varenicline compared with placebo and other smoking cessation aids.[48–53] The continuous abstinence rate for varenicline at 3 months (last 4 weeks of treatment) is about 43%–55% and at 1 year (weeks 9–52 of treatment) is 21%–26%.[48,52,53] This can be compared with 20%–29% at 3 months and 14%–16% at 1 year for bupropion.[52,53]

Varenicline is generally safe to use, with mild to moderate nausea being the most common side effect.[54,55] Concerns have been raised about neuropsychiatric side effects and, particularly, suicidal risk when using varenicline. However, several studies did not establish a direct correlation.[56–59] Moreover, in a randomized-controlled study by Anthenelli et al.,[59] varenicline increased smoking stopping rates among adults with stable depression without worsening the signs of anxiety or depression.

Varenicline can be started in a similar fashion to bupropion by setting a quit date and starting the medication 1 week before the quit date while still smoking.[29] Varenicline comes in two strengths (0.5 and 1 mg). It is usually started in a gradual fashion to reduce side effects. On the first 3 days of treatment, it should be given as 0.5 mg once daily. This is titrated to 0.5 mg twice daily on days 4–7. After that, it is given as 1 mg twice daily until the end of the treatment course, which is usually 12 weeks.[29,30] A further 12-week course can be give for successful candidates as maintenance to prevent relapse.[28,29,60] Moreover, for those who fail a treatment course, varenicline can be used at another attempt with comparable quitting rates.[61]

Second-Line Pharmacotherapies

Nortriptyline and clonidine are second-line pharmacotherapies that can be considered when first-line therapies fail.[20] Nortriptyline is a tricyclic antidepressant that is given in doses of 75–100 mg daily for 8–12 weeks as a smoking cessation aid.[62] Its side effects include dry mouth, blurred vision, drowsiness, and palpitations, which make it less tolerated by patients.[24,62] On the other hand, clonidine is a centrally acting antihypertensive that has been reported to reduce withdrawal symptoms in tobacco addiction.[63] It can be given in doses of 0.25–0.75 mg daily as dermal patches for a period of up to 12 weeks for smoking cessation.[24] As for nortriptyline, its prominent side effects (dry mouth, dizziness, orthostatic hypotension, and sedation) make it less favorable to use among smokers [24,63] Other alternative therapies include acupuncture and hypnotherapy.[20] However, these are not readily available in Saudi Arabia.

Use of Smoking Cessation Aids in Special Conditions

Pregnancy

None of the available pharmacotherapy for smoking cessation is completely safe for use during pregnancy. Pregnant women are advised to stop smoking, and guidelines suggest offering them intense smoking cessation advice and counseling.[64] The risk from cigarette smoking outweighs the harm from NRT (given other toxins in combusted tobacco and higher nicotine concentrations). In pregnant women failing to stop quitting after counseling, NRT can be used (with preference to short-lasting forms, e.g., gums and lozenges) after a detailed advice on risks and benefits from NRT versus continuing to smoke.[64]

Diabetes

The American Diabetes Association recommends smoking cessation as part of routine care.[65,66] Smoking cessation with or without pharmacological intervention can alter the pharmacokinetics and dynamics of insulin absorption, and, hence, diabetic patients using pharmacological interventions as smoking aid should monitor their blood sugars more closely.[47] Hypoglycemia and uncontrolled diabetes can lower the seizure threshold for diabetic smokers, and, therefore, it is not advised to use bupropion for such patients, especially if on insulin or oral hypoglycemic medications. On the other hand, diabetic patients who smoke can safely use NRT although it may result in fluctuations in blood sugars (affects insulin absorption via vasoconstriction), and they need to monitor their blood sugars more frequently.[26]

Cardiovascular Disease

NRT is vasoconstrictor and should not be given in acute scenarios for patients who just experienced a myocardial infarction or stroke.[31] It is otherwise safe to be used in smokers with stable cardiovascular conditions.[31,36] Some concerns were raised about varenicline regarding a small increased cardiovascular risk, which should be discussed with patients.[30] However, no clear evidence of harm has been demonstrated in studies examining that risk.[36,64,67]

Chronic Kidney Disease

Dose adjustments (reduction) are needed for varenicline for patients with chronic kidney disease (creatinine clearance < 30 mL/min) as it is almost entirely secreted by the kidneys. In such patients, the maximum recommended daily dose is 1 mg/day.[30,64]

Mental Illness

Bupropion has been shown to be effective in smokers with depression.[64] However, it should not be used concomitantly or within 14 days of discontinuing monoamine oxidase inhibitors as it can increase the risk of hypertensive reactions.[28] Cautions have been issued regarding neuropsychiatric events with varenicline. But, several studies did not show a direct causal relationship.[23,57,58,64] Nonetheless, patients should be warned about such events and should consult their primary-care physician should they experience any mood changes or suicidal thoughts.[64]

Conclusion

Tobacco smoking is a leading but preventable cause of morbidity and mortality. Smokers should be offered cessation advice and counseling at every encounter with their primary-care physician. The 5-A's and ABC approaches are effective and easy to use in primary-care setting. Primary-care physicians should offer support to smokers during their cycle of change. All forms of first-line pharmacotherapies have proven to be effective in smoking cessation with varenicline being the

most effective at present. Precautions should be taken when prescribing smoking cessation medications (e.g., bupropion and varenicline). However, adverse events are not enough to mitigate their use.

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