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# Smoking Cessation Interventions; Pharmacological Aids

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**Abstract**
Tobacco dependence is a chronic condition that usually requires repeated intervention.

Effective interventions exist that can produce long-term cessation at up to double the rate achieved by smokers without treatment. Because of the potential health benefits and availability of effective interventions every smoker should be offered intervention that at a stage involve pharmacotherapy. Because pharmacotherapies enhance the quit rates of most other cessation methods every smoker should be offered appropriate pharmacotherapy to support cessation attempts, unless contra-indicated. . A number of pharmacotherapies are effective and safe. Nicotine replacement therapy, Anti-depressants and other drugs are effective cessation aids.

More intervention research is needed to evaluate the effectiveness of other cessation methods such as acupuncture and hypnotherapy.

Tobacco dependence meets accepted criteria for a drug dependence disorder. In most users, tobacco produces tolerance, a well-characterised withdrawal syndrome, and an inability to control future use [(1)].Thus tobacco dependence warrants medical treatment just as do other dependence disorders and other chronic diseases.

Although many smokers succeed in quitting on their own, this is usually after several attempts. Over 90 per cent of unaided quit attempts are not successful[1,2]. Use of appropriate pharmacotherapies could double or triple cessation rates.

**Types of pharmacotherapy**

A variety of pharmacological interventions for treating tobacco product dependence have been evaluated in recent years. These include:

• Nicotine replacement therapies such as widely used gum and patches and less common aerosol inhalers, nasal sprays and lozenges (not all available in Saudi Arabia);

• Anxiolytic medications which might reduce the anxiety symptoms associated with withdrawal;

• Some classes of anti-depressants, including bupropion (Zyban), now available for use in Australia as well as the US and UK; and

• A variety of other pharmaceutical therapies such as clonidine, nortriptyline, mecamylamine, naltrexone and silver acetate.

**Nicotine replacement therapy**

The aim of nicotine replacement therapy (NRT) is to replace some of the nicotine from cigarettes without the harmful constituents contained in tobacco smoke. NRT reduces withdrawal symptoms associated with smoking cessation and makes it easier to avoid smoking by replacing some, but not all, of the nicotine obtained from smoking [3]. Nicotine replacement therapy (NRT) is considered a cornerstone of smoking cessation in the US,[4] and the UK [5].

There are several different forms of nicotine replacement therapy; chewing gum (2mg and 4mg doses), trans-dermal patches (16 hour and 24 hour in varying doses), nasal spray, inhalers and sublingual tablets and lozenges. Nicotine chewing gum and trans-dermal patches are the most frequently used and researched forms of nicotine therapy.

Nicotine chewing gum contains a nicotine resin complex that is absorbed directly through the buccal mucosa, resulting in plasma concentrations which are approximately half that produced by smoking a cigarette . It is available either as a 2 mg or 4 mg preparation, and in many countries, including Australia, is sold without a prescription from a medical practitioner.

Trans-dermal patches are available in several different sizes, and deliver between 7 mg and 22 mg of nicotine over a 24-hour period, resulting in plasma levels similar to the trough levels seen in heavy smokers [2].

Nicotine gum, nicotine trans-dermal patch, nicotine nasal spray , nicotine inhaler and nicotine sublingual tablets/lozenges all increase quit rates at five to 12 months approximately two-fold compared with placebo and regardless of the setting [4,6]. One study that directly compared four of the six products found no difference in abstinence rates or withdrawal discomfort, although compliance was lower for inhaler and nasal spray [7]. Highly dependent smokers (20 or more cigarettes per day) benefit more from 4 mg than 2 mg gum [6].

Wearing a patch only during waking hours (16 hours/day) is as effective as wearing it for 24 hours/day [6]. Eight weeks of patch therapy was as effective as longer courses and there was no evidence that tapered therapy was better than abrupt withdrawal [6,8].

Combinations of different forms of NRT are more effective than one form alone where abstinence rates at six and 12 months were higher for combination of nicotine patches and inhaler than placebo patches and inhaler as well as (25% vs 22.5% at six months, 19.5% vs 14% at 12 months) [9] , while the combination of bupropion and nicotine patch is more effective than nicotine patch alone [10].

**Side effects**

• For nicotine gum, most side effects are relatively mild and transient, including mouth soreness, hiccups, indigestion, jaw ache and unpleasant taste. In less than two per cent of users, more severe side effects are irritability, lightheadedness, headache, excessive salivation and anorexia.

• For nicotine patches, minor skin irritation at the patch site is reported by up to half of patch users and insomnia by up to a quarter of users. Comparatively rear side effects include headache, dizziness, fatigue, gastrointestinal distress, sweating, limb pain and palpitations.

• Nasal spray causes nose, throat or eye irritation in most users. More serious side effects in up to a quarter of users include nausea, headache, dizziness and cold hands and feet.

• Nicotine inhalers cause throat irritation and coughing in up to 50 per cent of users. Less common side-effects include nausea, bad taste in the mouth, dizziness, gastrointestinal disturbances and oral burning sensation[1].

**Contra-indications**

• Although there has been concern about the safety of NRT in smokers with cardiac disease, empirical studies have shown the nicotine patch is safe in patients with stable cardiac disease [4,11].

The US clinical guidelines [4] recommend use of NRT with caution in those within two weeks post-myocardial infarction, those with serious arrhythmias and those with worsening angina.

**Dependency**

• The UK guidelines recommend NRT or bupropion for people who smoke 10 cigarettes or more [5]. The US and Scottish guidelines recommend that all smokers be offered appropriate pharmacotherapy, with NRT or bupropion as a first choice unless contraindicated [4].

**Pregnancy**

The US [4], UK [5] and Scottish [12] guidelines cautiously recommend NRT when a pregnant woman is otherwise unable to quit and when the likelihood of quitting, with its potential benefits, outweighs the risk of NRT use or continued smoking.

A small non-random trial of nicotine patch use by pregnant women beyond 24 weeks found no adverse effect on fetal status [13].

**Availability of NRT**

NRT is currently available in the form of nicotine patch (7mg, 14mg and 21mg strength) which is available without prescription from pharmacists. This provides smokers with an opportunity to receive advice from pharmacists at the point of purchase.

Barriers to access should be reviewed and addressed. The UK recently elected to make NRT available through a wider range of retail outlets and settings (ie not restricted to pharmacies). Saudi Arabia should consider this also. Proponents of wider distribution outlets for NRT argue that it should be as readily available as cigarettes themselves and more accessible to smokers wanting to quit.

There is no subsidisation of the cost of NRT for consumers in Saudi Arabia. A smoker using the patch for 10 weeks (an average course) will incur a cost of approximately 600 SR. This is comparable for many smokers to the cost of purchasing cigarettes over the same period.

If NRT is made available at a reduced cost , the use of NRT will increase, where there is evidence to suggest that reducing out-of-pocket costs for NRT increases both use of NRT therapies and cessation outcomes [14].

**Anti-depressants**

Bupropion SR; is a non-nicotine aid to smoking originally developed and marketed as an anti-depressant. It is sold as Zyban in USA, UK and Australia. It blocks the re-uptake of dopamine and norepinephrine centrally.

Use of bupropion SR approximately doubles cessation rate compared to placebo (30.5%, (95% CI 23.2, 37.8) versus 17.3% (15).

When used for smoking cessation bupropion is initiated one to two weeks before the target quit date and is generally continued for three months.

Bupropion is contra-indicated in people with a seizure disorder, a current or prior diagnosis of anorexia nervosa or bulemia, use of a monoamine oxidase (MAO) inhibitor within the previous 14 days or using other medications that contain bupropion.

Nortriptyline is a tricyclic antidepressant that blocks uptake of norepinephrine and serotonin .Use of nortriptyline is estimated to triple smoking abstinence rates at five months or more compared to placebo cessation rate 30.1% (95% CI 18.1, 41.6) versus 11.7% [(15)].

Sedation, dry mouth and lightheadedness are common side effects affecting at least half of users [(1)]. Extreme caution is advised if used in patients with cardiovascular disease due to risk of arrhythmias, changes in contractility and blood flow.

Nortriptyline is an efficacious smoking cessation treatment. It may be used under a doctor's supervision as a second line agent to treat tobacco dependence [(15)]. When used for smoking cessation treatment is initiated two to four weeks before the quit date and continued for around 12 weeks[(1)].

Fluoxetine; is a potent and selective inhibitor of neuronal serotonin reuptake. It is sold as Prozac . Fluoxetine reduces food intake and increases resting energy expenditure, resulting in moderate body weight loss during use [(16)] and reduction of weight gain in smoking cessation [(17)] . Use of fluoxetine significantly increased abstinence rate from 20% in the placebo to 30% in two treatment groups at six months follow-up in a multi-centre trial [(18)].

Fluoxetine, compared to placebo, increased the likelihood of abstinence at one and three months amongst smokers with minor depression but not those with little or no depression [(19)]. Fluoxetine was used in conjunction with cognitive-behavioural therapy.

When used for smoking cessation, treatment is initiated two weeks before the target quit date and is generally continued for at least three months.

Fluoxetine may aid smoking cessation in depressed smokers [(19)].

**Other pharmacological aids**

Clonidine is a centrally acting adrenergic agonist that dampens sympathetic nervous system activity. The main rationale for use is to reduce tobacco withdrawal symptoms, especially craving. It is used primarily as an antihypertensive medication. It may be

administered transdermally or orally. Smokers using clonidine are started on the drug several days before quitting and maintained on a fixed daily dose for several weeks.

The usefulness of clonidine is limited by appreciable sedation and postural hypotension [20]. Local skin irritation is common with transdermal clonidine. Adverse effects if ceased abruptly include nervousness, agitation, headache and tremor, accompanied by a rapid rise in blood pressure and elevated catecholamine levels.

Mecamylamine is a nicotine antagonist. The rationale for use is its potential to block the rewarding effect of nicotine, therefore reducing smoking.No evidence for its effect on smoking cessation if used alone, but in combination with nicotine, it may be superior to nicotine alone [21].

Naltrexone is a long acting opioid antagonist. In humans, smoking one or two cigarettes significantly increases plasma endorphin levels, leading to the theory that endogenous endorphins may reinforce smoking behaviour [22]. Clinical trials failed to detect a significant difference in quit rates between naltrexone and placebo[23].

Anxiolytics; they increase production of dopamine, serotonin and norepinephrine, low levels of which are associated with urge to smoke and the anxiety that occurs with nicotine withdrawal .There is no consistent evidence that anoxiolytics aid smoking cessation [24].

**Silver acetate**

Silver acetate produces an unpleasant taste when combined with cigarettes, acts as an aversive therapy. It is sold in the form of gum, lozenge and spray. There is little evidence for a specific effect of silver acetate in promoting smoking cessation [25].

**Other interventions**

Acupuncture; is promoted for a range of health related issues and problems, including smoking cessation. The most commonly cited rationale for use of acupuncture in smoking cessation is that it relieves the discomfort of nicotine withdrawal [1]. There is no evidence of a specific effect of acupuncture in smoking cessation other than as a placebo effect as there was no difference in cessation rates between 'active' acupuncture and 'inactive' or sham acupuncture procedures [26,27].

Hypnotherapy ; is proposed to act as an aid to smoking cessation by influencing underlying impulses to weaken the desire to smoke, strengthen the will to stop and/or increase concentration and increase ability to focus on a treatment program [28].

Most of the studies in the scientific literature are either case reports or poor quality, uncontrolled trials that show a great variability in quit rates (4-88%) six months after treatment [29,30]. Therefore, there is insufficient evidence to recommend hypnotherapy as a specific treatment for smoking cessation.

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