North Metropolitan Area Mental Health Service
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DRUG BULLETIN

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Smoking Cessation in Psychiatric Patients

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Smoking and Psychiatric Patients

The Department of Health in Western Australia including Graylands Hospital will become smoke-free in January 2008. As a high prevalence (50-90%) of smoking exists in psychiatric populations compared with the general population[1], use of nicotine replacement therapy (NRT), particularly for persons who smoke heavily becomes important. In addition to the standard precautions recommended for NRT, consideration should be also be given to the potential for worsening of mental state in psychiatric patients and the effects on concomitant psychotropic medication. Although this bulletin focuses on NRT for managing nicotine withdrawal, it is recognised that a comprehensive treatment plan including counselling and behaviour modification is important in managing and maintaining abstinence from smoking[2, 3].

Nicotine Withdrawal

In addition to craving for cigarettes, the nicotine withdrawal syndrome includes four or more of the following within 24 hours of smoking cessation[4]:

- Dysphoric or depressed mood
- Insomnia
- Irritability, frustration, or anger
- Anxiety
- Difficulty concentrating
- Restlessness or impatience
- Decreased heart rate
- Increased appetite

Nicotine Replacement Therapy

NRT is used to relieve nicotine cravings and withdrawal associated with smoking cessation but provides nicotine levels lower than those associated with smoking. **Table 1 lists the various forms of NRT that will be available on hospital formularies as of 1st January 2008.** NRT should only be used for those who smoke more than 10 cigarettes per day[2]. There is no evidence to suggest that low dependence smokers benefit from NRT. All forms of NRT are considered equally effective and choice should be based on patient preference, ease of administration and specific product contraindications[5]. The NRT patch is considered the first-line treatment option at Graylands Hospital due to the ease of once-daily administration. **Figure 1 outlines the recommended pathway for assessment and management of nicotine dependence at Graylands Hospital.**

In addition to the forms of NRT that will be included on the formulary, nicotine gum, sublingual tablets and 16-hour patches are also marketed in Australia. Bupropion (also non-formulary) is the only non-nicotine drug licensed for smoking cessation. Bupropion has limited applications for inpatients on smoke-free wards, as it must be commenced at least 7 days before smoking is stopped.

Combination and High-Dose Nicotine Replacement Therapy

Some high dependence smokers may continue to experience withdrawal symptoms even with the use of NRT at maximum recommended doses. Although the manufacturers do not recommend combination NRT, studies have shown that combining a nicotine patch with a *pro re nata (prn)* form of nicotine (e.g. inhaler, lozenge, sublingual tablet or gum) for

intermittent cravings may be more efficacious than monotherapy in some patients[6]. There are no data available regarding the maximum dose of *prn* nicotine when used in combination with a patch. However, toxicity from NRT is unlikely given that cigarette smoking produces much more elevated plasma nicotine levels compared to NRT. Dose of combination therapy should be titrated according to patient withdrawal symptoms and tolerability. Combination therapy may be considered for patients continuing to experience significant withdrawal symptoms with monotherapy. Some studies have shown a small benefit in using a higher than maximum dose of NRT in treating some high-dependence smokers[5]. If either of these strategies are employed, patients should be carefully monitored for nicotine toxicity.

Duration of Treatment

There is limited safety data on the use of NRT for longer than 12 weeks. All clinical studies to date have been in patients that have had a desire to quit smoking. Duration of treatment has not been established for smokers that require NRT due to smoking bans.

Contraindications

The following contraindications apply to all forms of NRT[2]; there are also precautions specific to the individual forms of NRT (**see Table 1**). When considering the contraindications and precautions, it should be noted that NRT delivers nicotine at levels lower than cigarette smoking and exposure to carbon monoxide and other harmful substances is eliminated. Clinicians should also conduct a careful risk-benefit analysis of prescribing versus not-prescribing NRT.

Cardiovascular disease

NRT is contraindicated in patients with unstable or worsening angina pectoris, Prinzmetal angina, severe cardiac arrhythmias, and those who have recently suffered a myocardial infarction or cerebrovascular accident[2].

Pregnancy

Nicotine is category D in pregnancy, and the manufacturers contraindicate its use[2]. Nicotine use during pregnancy may decrease foetal growth, as does cigarette smoking. It is not clear whether other adverse effects of smoking during pregnancy are also associated with NRT use. If behavioural interventions are unsuccessful, and NRT is utilised, care should be taken to ensure that the dose is minimised but consistent with the previous level of smoking.

Lactation

The manufacturers of all forms of NRT advise against its use in lactation[2]. Nicotine from NRT is excreted into breast milk, with a milk to plasma ratio averaging 2.9, which is similar to an equivalent level of cigarette smoking[7]. Effects in the neonate from smoking and nicotine include: colic, irritability, apnoeic episodes and immune system impairment[7]. If NRT is considered in lactation, the risk of exposure of the infant to nicotine from NRT should be weighed against the risks associated with the infant's exposure to nicotine, cigarette-derived toxic substances and cigarette smoke from continued smoking by the mother.

Patients less than 18 years

NRT has not been adequately studied in these patients and should be used with caution[2].

Adverse Effects

The adverse effects of NRT are usually mild and transient and may be related to smoking cessation itself. Side effects common to all forms of NRT include dizziness, headache, nausea, vomiting, hiccups, abdominal pain and myalgia[2]. Tachycardia, chest pain, anxiety and blood pressure changes occur infrequently; arrhythmias occur rarely[2]. Local transient reactions specific to the different forms of NRT are common and are listed in **Table 1**. NRT should be stopped if severe adverse reactions occur.

While chronic smokers can tolerate doses of nicotine that may be toxic to non-smokers, use of higher than recommended doses can result in overdose symptoms. Nicotine toxicity presents as pallor, cold sweat, nausea, salivation, vomiting, abdominal pain, diarrhoea, headache, dizziness, disturbed hearing and vision, tremor, mental confusion and weakness[2].

Assessing Nicotine Dependence

The level of nicotine dependence determines the dose of NRT required. The following categories of nicotine dependence are based on the Fagerstrom Test for Nicotine Dependence, and can be used to determine NRT requirements[3] (**see Table 1**).

- **High dependence:**

  Waking at night to smoke or smoking within the first 5 minutes of waking;

  Usually >30 cigarettes per day.

- **Moderate dependence:**

  Smoking within 30 minutes of waking;

  Usually 20-30 cigarettes per day.

- **Low-moderate dependence:**

  Not needing to smoke within the first 30 minutes of waking;

  Usually 10-20 cigarettes per day.

- **Low dependence smokers:**

  Less than 10 cigarettes per day.

Table 1: NRT usage guide[2]

	Dose (monotherapy)	Directions for use	Practice points
Nicotine patches 24 hour patches (21mg, 14mg, 7mg)	**Moderate and highly dependent smokers:** Week 1-4: 21mg Week 5-8: 14mg Week 9-12: 7mg **Low-to-moderately dependent smokers**: Week 1-4: 14mg Week 5-12: 7mg	▪ Apply to a cool, clean, dry, non-hairy site on the upper body or outer part of the arm. ▪ Press on patch firmly for 20 seconds after applying. ▪ Avoid any area with skin folds. ▪ Site of application should be rotated daily. ▪ Wait one hour after applying patch before swimming, bathing or showering.	▪ Avoid in patients with generalised chronic dermatological disorders, such as psoriasis, chronic dermatitis or urticaria. ▪ 24-hour patch can be removed at night if sleep disturbance or vivid dreams occur. ▪ Cutting patches into smaller sizes is not recommended ▪ Used patches still contain nicotine, they should be folded over and placed in the protective pouch that contained the new patch and be disposed in a way that avoids inadvertent poisoning. ▪ Local erythema and itching is common with the nicotine patch in the first 2 weeks of therapy
Nicotine lozenges 2mg, 4mg	**Moderate and highly dependent smokers:** 4mg **Low-to-moderately dependent smokers**: 2mg Week 1-6: 1 lozenge every 1-2 hours. Week 7-9: 1 lozenge every 2-4 hours. Week 10-12: 1 lozenge every 4-8 hours. Thereafter, a lozenge should be taken in situations were there is a strong temptation to smoke. Maximum dose is 15 lozenges daily	▪ The lozenge should be moved from one side of the mouth to the other and repeated until the lozenge is completely dissolved over 20-30 minutes. ▪ Lozenge should not be chewed or swallowed whole. ▪ Food and drink should be avoided while the lozenge is in the mouth.	▪ Lozenges contain aspartame, avoid in patients with phenylketonuria. ▪ Gastric, oral, oesophageal or pharyngeal inflammation may be worsened. ▪ Transient sore throat, mouth irritation and hiccups on initiation are common with nicotine lozenges.
Nicotine inhaler 10mg	Dose is self-titrated; A cartridge should be used when the user feels an urge for a cigarette or feels the onset of withdrawal symptoms. Most smokers will use 6 to 12 cartridges per day. Use should be gradually reduced to zero after 12 weeks.	▪ Insert cartridge into the mouthpiece before use. ▪ Shallow puffs are taken approximately every two seconds or alternatively 4 puffs can be taken every minute. ▪ Inhalation or puffing on the mouthpiece releases nicotine, which is absorbed through the buccal mucosa. ▪ 20 minutes of intense use removes all nicotine from the cartridge.	▪ Contraindicated in patients with menthol hypersensitivity. ▪ Avoid in patients with asthma or throat conditions. ▪ Spent cartridges still contain nicotine; they must be disposed of in a way that avoids inadvertent poisoning. ▪ Coughing, throat and mouth irritation and hiccups are common at the start of therapy.

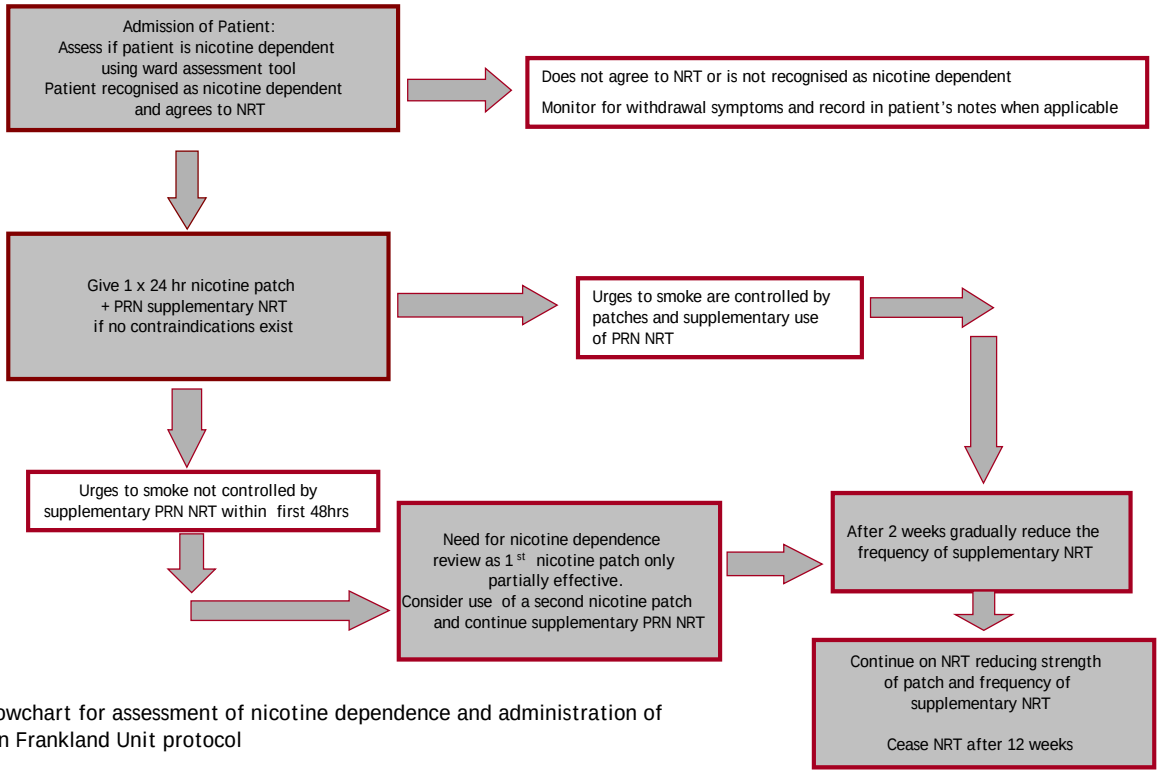

Figure 1: Flowchart for assessment of nicotine dependence and administration of NRT based on Frankland Unit protocol

Concomitant Drug Considerations

Table 2: Psychotropic-smoking drug interactions[2, 8, 9]

Drug	Effect of cigarette smoking
Chlorpromazine	Decreased plasma level by 24%
Clozapine	Decreased plasma level by 28%
Haloperidol	Decreased plasma level by 70%
Fluvoxamine	Decreased plasma level by 44%
Imipramine	Decreased plasma level*
Olanzapine	Decreased plasma level by 50%
Propranolol	Decreased plasma level by 50%

*Unknown value

The polycyclic aromatic hydrocarbons in cigarette smoke, *not* nicotine, are potent inducers of the cytochrome (CYP) P450 isoenzyme system, particularly CYP1A2[8]. Cessation of smoking reverses the effects of 1A2 induction and is usually complete in 1-3 weeks[10]. Reversal of 1A2 induction can lead to an increase in the plasma level of a substrate drug. This effect is clinically significant for drugs that are predominantly metabolised by 1A2. An example is clozapine, where a mean increase of up to 72% of clozapine plasma levels was observed in one study following smoking cessation[11]. Dose reductions of drugs that are affected by cigarette smoking may need to be considered to reduce the risk of toxicity and dose-dependent adverse effects. Psychotropic drugs that are major substrates for CYP 1A2 are listed in **Table 2**.

As well as the psychotropic drug interactions listed in **Table 2**, other important drug interactions with cigarette smoking involve caffeine, flecainide, mexiletine, theophylline, and warfarin[8]. In addition, patients with diabetes mellitus may require lower doses of insulin as a result of an increased rate of insulin absorption due to improved subcutaneous blood flow[8]. Consideration should be also given to the possibility of worsened antipsychotic-induced extrapyramidal side effects (EPSEs) following smoking cessation, as nicotine provides a protective effect against EPSEs by increasing dopaminergic neurotransmission[1].

Conclusions

NRT has been effectively used to manage smoking withdrawal symptoms reported in smoke-free psychiatric hospitals[12-14]. However, evidence from mandatory cessation programs in other psychiatric inpatient institutions shows that use of NRT alone does not lead to high long-term abstinence rates[12-14]. If long-term abstinence is a goal of therapy, NRT must be combined with a comprehensive behavioural modification program.

This bulletin was written by Karolinka Golebiewski and Henry Lie and was reviewed by members of the Graylands Pharmacy Department and Dr Viki Pascu.

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References available on request

Comments are welcome at the email address: DrugInformation.Graylands@health.wa.gov.au