The nicotine patch: guidelines for practical use

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Four nicotine transdermal patches are now or will soon be available in Australia and are a valuable aid to smoking cessation. This article reviews the latest information on nicotine patches, compares the patch to nicotine gum and provides medical practitioners practical guidelines for the use of nicotine patches in smoking cessation.

■ The role of nicotine replacement with nicotine gum is well established in smoking cessation. However, there are many difficulties associated with its use and it has been shown to be of questionable efficacy in the general practice setting.[1] More recently, nicotine transdermal patches have been found to be an effective aid to smoking cessation in studies overseas[2-10] and in Australia,[11] and appear to offer a number of advantages over nicotine gum.

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Smoking is a complex addiction with both pharmacological and psychosocial elements. Nicotine replacement therapy with the patch alleviates the addiction to the drug nicotine by delivering a fairly steady plasma concentration of nicotine. This provides constant protection from withdrawal symptoms and craving for cigarettes while the patient focuses on changing the behavioural aspects of the smoking habit.

Available patches

Nicabate and Nicotinell patches are already available in Australia; Prostep and Nicorette patches are expected to be approved for marketing during 1994 (see Table 1). All of the patches are self-adhesive and have been scheduled S4 – that is, available on prescription only. Recommended courses of the nicotine patch consist of a number of weeks using the full strength treatment patch and a weaning period (except for Prostep) using one or two different strengths of weaker patches. The cost of the available patches is no more than the cost of cigarettes over the same time period.

Three of the patches – Nicabate, Nicotinell and Prostep – deliver nicotine over a full 24 hours and are designed to provide continuous protection from nicotine withdrawal. Nicorette is a 16-hour patch which is removed at bedtime to mimic more closely the nicotine intake pattern in the smoker.

There are two types of delivery system which determine the rate of nicotine release. Nicabate uses a rate-limiting membrane, which provides a steady, predictable rate of nicotine release. The other three patches have a matrix layer from which nicotine diffuses directly into the skin at a rate determined to a large degree by the permeability of the skin. The rate of nicotine delivery of these patches may therefore vary more widely from one patient to another depending on the skin type and the location of the patch.

Pharmacokinetics of the nicotine patch

After each application, plasma nicotine levels rise to a peak over several hours and then slowly decline over the period of application (see Figure 1). The time to reach peak plasma concentrations of nicotine is fastest for Nicabate at four hours[12] and is about eight to nine hours for the other patches.[13-15] Twenty-four-hour patches provide moderate protective levels the next morning. The 16-hour patch results in low plasma concentrations of nicotine throughout the night and subtherapeutic levels on waking.

The average plateau nicotine levels for the larger patch sizes are approxi-

Nicotine replacement therapy with the patch alleviates the addiction by delivering a fairly steady plasma concentration of nicotine.

Table 1. Nicotine transdermal patches in Australia

Trade name (Manufacturer or distributor)	Application period per patch (hours)	Patch size (cm^2)	Nicotine absorbed in application period (mg)	Recommended duration of patch use: Each patch (weeks)	Recommended duration of patch use: Total course (weeks)	Delivery system	Pack size	Average retail price* $
Nicabate (Marion Merrell Dow)	24	22	21	6	10	Rate-limiting membrane	7	30.50
		15	14	2			7	27.50
		7	7	2			7	25.00
Nicotinell (Ciba-Geigy)	24	30	21	4	12	Matrix	7/28	33.90/123.40
		20	14	4			7/28	31.30/113.90
		10	7	4			7/28	28.70/104.00
Prostep (Wellcome)	24	33†	22	6 to 8‡	6 to 8‡	Gel matrix	14	N/A
		17†	11	6 to 8‡			14	N/A
Nicorette (Kabi Pharmacia)	16	30	15	12§	16§	Adhesive matrix	N/A	N/A
		20	10	2§			N/A	N/A
		10	5	2§			N/A	N/A

* Based on 'list price' to wholesaler plus average wholesale markup of 13% plus average pharmacy markup of 50%.
† Both patch strengths for treatment use. Weaning period not recommended.
‡ This information was provided at the time of writing but may change.
§ Recommended duration of use overseas – Australian recommendations were not available at time or writing.
N/A = Not available at time of writing.

mately one-half to one-third of the average smoking level, depending on the particular patch used. Highest average blood levels over the 24 hour period are achieved by Nicabate (17 ng/mL),[12] followed by Nicotinell (13 ng/mL),[13] Prostep (11 ng/mL)[14] and Nicorette (8 ng/mL).[4,15] In comparison, hourly use of 2 mg nicotine gum achieves lower average blood levels of 8 to 10 ng/mL, or about one-third of the levels of smoking.[16]

Efficacy

The use of the nicotine patch approximately doubles the success rate of smoking cessation interventions at six and 12 months, compared with the use of a placebo patch. An analysis of 10 placebo-controlled studies of the nicotine patch[2-11] shows that at six months, 22.6% of active patch users were abstinent compared with 11% of placebo users.

Success rates are higher when the patch is combined with a more comprehensive smoking cessation programme. Six month abstinence rates for active patch users average 25% when they are participating in a comprehensive programme,[7-11] compared with 19.6% when they are only given brief advice.[2,4-6]

It is not possible to say whether one patch is more effective than the others because of the differences in the design of the trials. No studies directly comparing the different patches have yet been conducted.

Nicotine craving and withdrawal

Most studies have demonstrated a significant reduction in cigarette craving, especially in the first few weeks after quitting. Morning craving may be more effectively relieved by 24-hour patches than by 16-hour patches because of the higher plasma concentrations of nicotine on rising.

Withdrawal symptoms are also reduced, although certain symptoms are helped more than others. The nicotine patch is most effective in relieving negative mood states (such

Further information

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Average plateau nicotine levels for the larger patch sizes are approximately one-half to one-third of the average smoking level.

as irritability, anger, frustration, and anxiety), as well as difficulty in concentrating and thinking about cigarettes. However, there is little effect on non-mood related withdrawal symptoms, such as hunger or constipation.

Side effects

Generally, the nicotine patch is well tolerated and compliance is high. The most common side effects are skin reactions: transient itching, burning and tingling occur in up to 50% of subjects. This is usually minor and requires no treatment. Mild to severe erythema with or without oedema of the skin occurs in one of every four or five patients and can be minimised by rotating application sites. A small percentage of people experience contact dermatitis or skin sensitisation which may require cortisone cream or cessation of therapy. Skin reactions tend to occur after three or four weeks of use.

The most common systemic side effects with 24-hour patches are disturbed sleep (up to 30% of patients) and vivid dreams (up to 26% of patients). These do not appear to occur with the 16-hour patch. If they persist, the 24-hour patch may be removed at bedtime, or a lower strength patch can be used. Other adverse effects represent the pharmacological effects of nicotine and are uncommon because these patients were accustomed to higher nicotine levels from smoking.

Contraindications and safety

The risks of nicotine from the patch must be weighed against the considerable adverse effects of smoking. The nicotine patch results in lower plasma concentrations of nicotine (Figure 1) than smoking and does not introduce carbon monoxide and the many chemicals and tars that are contained in cigarette smoke. Therefore, correct use of the nicotine patch is safer than continuing to smoke.

Contraindications to the use of the patch are listed in Table 2. While the use of the nicotine patch in patients with absolute contraindications may be associated with increased risk, the level of risk is less than for smoking. Nonetheless, prescription of the patch in these situations is not approved at present.

The nicotine patch may be used cautiously where relative contraindications apply. It is especially important to select smokers who are motivated and to consider starting with a patch with a low dose of nicotine. A study of 156 patients with stable coronary artery disease with a 14 mg patch reported no increase in cardiac symptoms or complications among the active patch users.[17]

Transdermal nicotine probably has a low risk of dependence although there is no research evidence to support this. Plasma concentrations of nicotine rise more slowly and are lower than with smoking. There are no reinforcing peaks of nicotine and the craving–reward cycle is broken.

Comparison of the nicotine patch with the gum

The nicotine patch is compared with nicotine gum in the box on page 108. The major benefit of the patch is its ease of use and higher patient com-

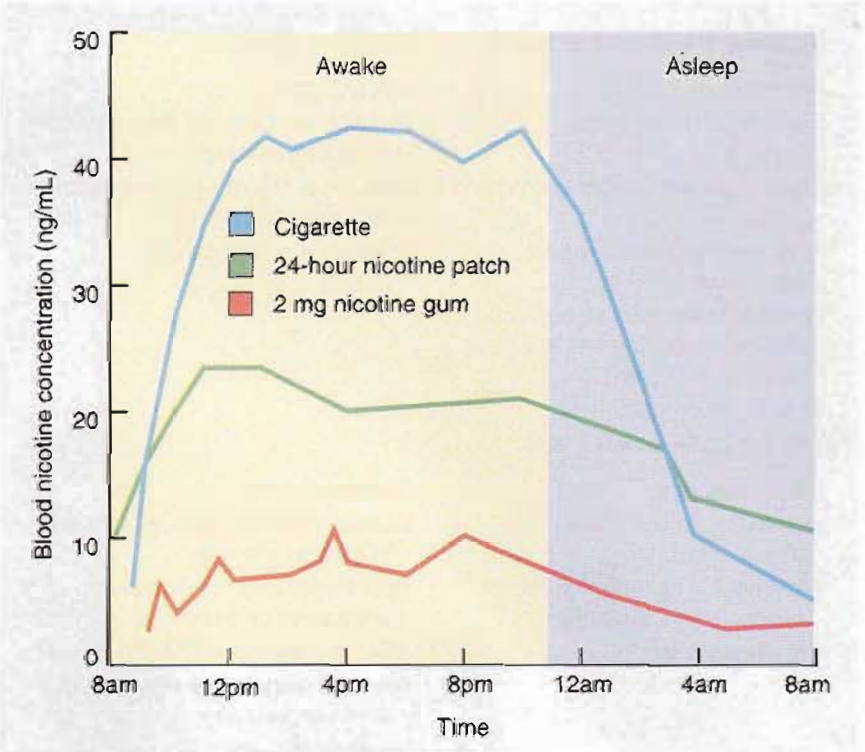

Figure 1. Blood nicotine concentrations while awake and asleep from the use of half-hourly cigarettes, a 24-hour nicotine patch and hourly 2 mg nicotine gum.

Illustration adapted from information appearing in *The New England Journal of Medicine, Journal of Clinical Pharmacology* and *Clinical Pharmacology and Therapeutics.*

Source: Smoking data adapted from Benowitz NL,[3] nicotine patch data adapted from Gorsline J, Gupta SK, Dye D, Rolf CN,[12] and nicotine gum data adapted from Benowitz NL, Jacob III P, Savanapridi C.[16]

The use of the nicotine patch approximately doubles the success rate of smoking cessation interventions at six and 12 months.

pliance compared with nicotine gum. The gum tends to be underused by most patients who do not use enough pieces or who do not continue to use them for an adequate length of time. Long term dependence is also a concern with the gum – up to 25% of abstainers are still using the gum at one year, although the harm from this is less than for smoking.

The nicotine patch also appears to be more effective than nicotine gum. In the 10 studies of the nicotine patch referred to previously, the interventions were 2.2 times more effective when the active patch was used compared with placebo, at a mean of 8.3 months follow up (n = 3,096). By comparison, in a meta-analysis of nicotine gum trials,[1] the active gum group was found to be only 1.3 times more effective than placebo at six months follow up (n = 1,756).

Of further importance is the finding that the use of nicotine gum in the subgroup of general practice trials is of doubtful value.[1] This may be because of the lack of time available to provide adequate instructions on the correct use of the gum in general practice. Therefore, because it is so simple to use, the nicotine patch may prove to be even more effective than the gum in the general practice context.

Comparison of the nicotine transdermal patch with nicotine gum

Nicotine transdermal patch	Nicotine gum
Advantages	**Advantages**
Higher abstinence rates	Flexible dosage – can be adjusted according to needs
Ease of use and simple instructions	More rapid response to unexpected or occasional triggers
High compliance and patient acceptance	Provides a substitute oral activity
Provides continuous steady-state plasma concentrations and constant protection	
Socially acceptable	
Low risk of dependence likely	
Disadvantages	**Disadvantages**
Skin reactions and sleep disturbances	Questionable evidence that it works in general practice
Fixed dose – no provision for sudden urges to smoke	Poor compliance – tends to be underused by patients
Greater expense	Special chewing technique required
	Chewing related side effects (e.g. sore jaw, nausea)
	Unpleasant taste
	Difficulties with dentures
	Less socially acceptable
	Reduced effectiveness while drinking and eating

For best results from the gum, a fixed dosage schedule (e.g. hourly) is preferred to the ad lib method. Careful instructions should be given to smokers and the 4 mg gum should be used for the more dependent smoker.

Although the nicotine patch will probably replace the gum for most smokers requiring nicotine replacement therapy, nicotine gum will continue to have a role in certain situations:

- for patients who are intolerant of the patch, especially those with skin sensitivity
- for patients requiring occasional doses to cope with specific triggers, such as an acute, stressful situation
- to increase nicotine levels when using the patch, for example, on rising from sleep
- for relapse prevention. After quitting smoking, patients can carry nicotine gum with them and use it as a safety valve to help prevent 'slips'.

Selection of patients for the nicotine patch

Not all smokers should be given the nicotine patch. Suitable candidates are those who are motivated to quit, those who are dependent on nicotine and those who are free from important contraindications. We suggest the following steps to assess whether patch use is appropriate (see Table 3).

- *Step 1.* Identify patients who smoke – actively seek this information and raise the subject in a nonconfrontational way.
- *Step 2.* Assess the patient's motivation to quit. Although most smokers (80 to 90%) want to quit, only 10% are actually motivated and ready to quit at any time, 30% are unsure or ambivalent ('contemplators') and 60% are not ready ('precontemplators').[18,19] Use of the patch should only be considered for the group that is

The most common systemic effects are disturbed sleep and vivid dreams with the 24-hour patch, but not the 16-hour patch.

Table 2. Contraindications to the nicotine transdermal patch

Absolute

Recent acute myocardial infarction
Unstable angina
Severe cardiac arrhythmia
Recent cerebrovascular disease
Pregnancy and lactation

Relative

Stable ischaemic heart disease, peripheral vascular disease or cerebrovascular disease
Psoriasis, eczema, urticaria
Hyperthyroidism, insulin dependent diabetes mellitus, phaeochromocytoma
Liver or renal disease
Peptic ulcer

Table 3. Practical guidelines for intervention using the nicotine patch

Patient selection

Identify patients who smoke
Assess the patient's motivation to quit
Assess the patient's dependence on nicotine
Consider contraindications to the nicotine patch

Intervention

Explain rationale of the patch
Provide instructions and discuss side effects
Select patch strength and duration of course
Provide brief behavioural advice, such as that contained in the *Smokescreen for the 1990s* programme [20]
Follow up

ready to quit. To categorise patients according to their readiness to quit, ask: 'How do you feel about your smoking?', as discussed in the *Smokescreen for the 1990s* programme (see Figure 2),[20] and discuss the issues with your patient. If necessary, ask: 'Are you ready to quit now?'

- *Step 3.* Assess the patient's dependence on nicotine. A quick assessment in a medical consultation can be made by asking the following three questions:[10]

– Do you smoke more than 20 cigarettes a day?

– Do you smoke your first cigarette within 30 minutes of waking?

– Have you experienced strong cravings or withdrawal symptoms during a previous attempt to quit?

A more detailed assessment can be made by using the Fagerström Test for Nicotine Dependence.[21]

- *Step 4.* Consider contraindications to the use of the patch (see Table 2).

Practical guidelines for nicotine patch intervention

We recommend the following practical guidelines for assisting smoking patients to quit using the nicotine patch (see Table 3).

Figure 2. Categorisation of patients according to their motivation or readiness to quit smoking.
Source: Smokescreen for the 1990s.[20]

Continuing to smoke while using the patch may increase the risk of nicotine toxicity and adverse cardiac events.

Explain the rationale for the use of the patch

The nicotine patch is only an aid to smoking cessation and will only relieve craving and withdrawal symptoms. It is important that patients do not have unrealistic expectations and do not see the patch as a 'magic cure'.

Provide instructions and discuss side effects

Patients must stop smoking first

Patients must stop smoking before using the patch. Continuing to smoke while using the patch may increase the risk of nicotine toxicity and adverse cardiac events, especially for patients with established (or silent) cardiac disease.

Describe correct application

Patients should apply the patch on the morning of 'quit day' to a clean, dry, non-hairy area of skin, generally on the upper chest or back or the outer upper arm. Twenty-four-hour patches should be replaced at the same time each day. Sixteen-hour patches are removed at bedtime. The site of application for all patches should be rotated each day. Patches can be worn while bathing or swimming.

Discuss possible side effects

Side effects should be discussed, especially skin reactions and sleep disturbances.

Select patch strength and duration of course

Patch strength

While the standard patch doses will be appropriate for most smokers, certain patients may require individualised dosing. Nicabate delivers the highest blood nicotine level and may be more effective for the more dependent or obese smokers. (Obese men have been shown to have lower plasma concentrations of nicotine than nonobese men.) These patients may also need multiple patches or the addition of nicotine gum, especially when withdrawal symptoms are not relieved by the full strength patch. On the other hand, a weaker starting patch may be more appropriate for people who smoke less than 15 cigarettes a day, smokers weighing less than 45 kg or where relative contraindications apply, such as stable cardiac disease.

Duration of course

Recommended treatment courses range from four to 12 weeks with weaning periods of four to eight weeks, depending on the patch used (see Table 1). A weaning period is not recommended for Prostep. While

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continued

the optimal duration of treatment is at present unclear, the course should provide adequate time for the withdrawal symptoms to abate and for the patient to learn coping strategies to maintain abstinence. More dependent smokers may require a longer course.

Provide brief behavioural advice

The nicotine patch is an adjunct to advice and counselling and only assists in alleviating the pharmacological addiction. The doctor can help the smoker address the psychosocial aspects of the smoking habit by: setting a quit day; identifying smoking triggers; discussing alternatives and substitutes to smoking; addressing the patient's concerns about quitting (such as weight gain); discussing health issues; and providing written materials. These steps are part of the *Smokescreen for the 1990s* programme.[20]

Follow up

Arrange further follow up visits to issue the patient further prescriptions and to assess the patient's progress, beginning one week after the quit day. It is important to review any side effects from patch use and to assess the adequacy of nicotine replacement. Increase the dose of nicotine if required. Those who attend follow up visits are more likely to be long term abstainers.[22]

Conclusion

Medical practitioners can help smoking patients who are motivated and dependent on nicotine to quit by using nicotine transdermal patches and behavioural advice. Use of the patch doubles the cessation rate of smoking interventions when compared with placebo. Correct use of the patch is safe and well tolerated, and reduces craving for cigarettes and withdrawal symptoms. The patch has many advantages over the nicotine gum and probably has greater efficacy, especially in general practice. It is likely to supersede nicotine gum for those quitters who require nicotine replacement therapy. ■

A list of reference is available on request to the editorial office.

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