Canterbury District Health Board
Te Poari Hauora o Waitaha

Clinical Pharmacology Bulletin

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Smoking Cessation in Psychiatric Patients

Psychiatric patients are often highly nicotine dependant and find it difficult to stop smoking, making it important to individualise therapy. Factors to consider include patient preference of therapy, previous experience, co-morbidities, other drugs, and adverse drug reactions (ADRs). Most patients do not experience a worsening in psychiatric condition with cessation; however, closer monitoring is required.

Nicotine withdrawal

Nicotine is a psychoactive drug that has agonist activity at nicotinic-acetylcholine receptors in the central nervous system. It results in physical dependence and tolerance. Absence of nicotine may result in cravings, mood changes, irritability, anger, anxiety, reduced concentration, headaches and weight gain.

Types of treatment:

- **Counselling:** an essential part of smoking cessation. Use with pharmacotherapy is superior to either intervention alone.
- **Pharmacotherapy:** nicotine replacement therapy (NRT), bupropion, varenicline and nortriptyline. Efficacy between drugs is similar. When combined with behavioural therapy, the chances of abstinence long-term are approximately doubled. Efficacy of combinations of drugs is unclear and may result in additive ADRs. However, they may be useful in some patients. See table for overview of pharmacotherapy.

NRT - works as a long-acting agonist on nicotine receptors to ameliorate withdrawal symptoms. Varying forms of administration exist and are equal in efficacy. Use of a patch plus a short-acting form (e.g. gum) may increase efficacy. NRT is inexpensive and used first-line in psychiatric patients.

Varenicline - is a partial agonist of α4β2- nicotinic-acetylcholine receptors, reducing symptoms of withdrawal and craving. It prevents nicotine from exerting rewarding and reinforcing effects. Varenicline is predominantly renally cleared unchanged.

Antidepressants

These modulate neural pathways that underlie nicotine addiction and alleviate depressive symptoms caused by withdrawal.

Bupropion - enhances noradrenaline/dopamine in CNS and appears to antagonise nicotinic-acetylcholine receptors. Action may be independent of antidepressant effects. Bupropion is an inhibitor of the hepatic isoenzyme CYP450 2D6.

Nortriptyline - a tricyclic antidepressant (TCA) that increases availability of serotonin and noradrenaline in the CNS. Smoking cessation action may be independent of antidepressant effect.

Other antidepressants - evidence for efficacy of other TCAs, selective serotonin reuptake inhibitors (SSRIs), venlafaxine, moclobemide or St John's wort in smoking cessation is lacking.

Significant pharmacokinetic interactions:

CYP2D6 inhibition

Bupropion + SSRIs/TCAs: bupropion inhibits CYP2D6 and is likely to increase concentrations of other drugs metabolised by this enzyme (e.g. SSRIs, TCAs, risperidone). The interaction with venlafaxine is not thought to be clinically significant.

Nortriptyline + SSRIs: fluoxetine and paroxetine inhibit CYP2D6 and are likely to significantly increase TCA concentrations.

CYP1A2 metabolised drugs (e.g. clozapine, olanzapine, haloperidol): Smoke from cigarettes induces CYP1A2. Smoking cessation may result in reduced clearance of drugs metabolised by this enzyme, especially clozapine.

Significant pharmacodynamic interactions:

Psychiatric ADRs: bupropion / varenicline

Bupropion is dopaminergic and may theoretically antagonise the antidopaminergic effects of antipsychotics. ADRs such as mania, delusions, paranoia and suicidal behaviour have been reported. Use with particular caution in patients with bipolar disorder.

Varenicline has not been studied in patients with serious psychiatric disorders. ADRs such as depression, agitation, anxiety, suicidal ideation and psychosis have been reported in patients with and without psychiatric disorders. Close monitoring is recommended and consider a psychiatric referral.

Seizures: bupropion / nortriptyline + antipsychotics / venlafaxine / TCAs / SSRIs: All lower seizure threshold. A maximum dose of 150mg bupropion daily is recommended.

Anticholinergic ADRs: TCAs and antipsychotics. Both act on anticholinergic receptors resulting in additive effects.

Insomnia: varenicline + TCAs / atypical antipsychotics: Varenicline causes insomnia and may negate sedative effects.

Cardiotoxicity: nortriptyline + venlafaxine / atypical antipsychotics. Nortriptyline (high-dose), venlafaxine and atypical antipsychotics can prolong QT interval and may have an additive effect.

Serotonin toxicity / risk of bleeding: nortriptyline + SSRIs / venlafaxine. Concomitant use of drugs that increase serotonin concentrations increase the risk of serotonin toxicity and bleeding (due to antiplatelet effect of serotonin).

Both nortriptyline and bupropion (unlicensed indication) are antidepressants and may be considered for the use in depression to treat both depressive and nicotine withdrawal symptoms.

Overview of Smoking Cessation Pharmacotherapy

Drug	Dosing	Benefits	Interactions / Cautions in Psychiatric Patients
NRT	Various - see Medsafe datasheets/CDHB bulletin Duration: 8-12 weeks	Inexpensive. Various types. Well tolerated.	Dermatological reactions (with patch use). Poorly controlled vascular disease (e.g. recent stroke, myocardial infarction).
Varenicline	Day1-3: 0.5mg daily Day 4-7: 0.5mg BD[a] Day 8+ : 1mg BD[a] Duration: 12 weeks	Minimal interactions (renally cleared).	Psychiatric ADRs (e.g. depression, agitation, anxiety, suicidal ideation, psychosis). Insomnia[a]. Dose reduce in renal impairment.
Bupropion[b]	Day 1-3 150mg daily Day 4+ : 150mg BD[a] Duration: 7–12 weeks	Antidepressant.	CYP2D6 inhibition - significant drug interactions. Psychiatric ADRs (e.g. delusions, paranoia, mania, suicidal ideation) Risk of seizures (1 in 1000).
Nortriptyline[b]	Day 1- :75-100mg daily Duration: 12 weeks	Inexpensive. Antidepressant.	QT prolongation. Cardiotoxicity (higher doses). Anticholinergic ADRs. Serotonin toxicity.

(a) Insomnia can be minimised by avoiding dosing at bedtime, provided there are at least 8hrs between doses (b) Start 1-2 weeks before stopping smoking