Smoking Cessation: Mental Health

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Introduction

• smoking rates have halved in Australians since 1980s
• smoking rates have remained high (32%) in people with mental illness
  – even higher in people with schizophrenia

Best practice for smoking cessation

• 3%-5% successful quit cold turkey
• NRT at least doubles quit rates compared to unassisted quitting
• interventions that combine pharmacotherapy and behavioural support increase smoking cessation success in a wide range of settings and populations
  – clinicians should encourage smokers to use both
Nicotine Replacement Therapy (NRT)

- NRT
  - established safety and efficacy record
  - at least doubles quit rates compared to unassisted quitting
  - reduces cravings and physical withdrawal symptoms
  - best result = NRT + behavioural advice
  - for at least 8 weeks
  - no evidence for weaning
  - can be started 2 weeks before ‘quit date’ - increases quit rates by 35%
Combination therapy

• combination therapy ↑ quit rates further
• combining the nicotine patch with an intermittent form of NRT
• patch provides steady protection against background cravings
• intermittent form gives quick, flexible relief
  > if possible, take in anticipation of smoking trigger
• well tolerated; adverse effect profile similar to mono-therapy
NRT formulation choices

**Topical NRT**

- patches

**Intermittent NRT**

- chewing gum
- lozenge/mini lozenge
- inhalator
- mouth spray (Quickmist®)
- oral films
Drug Interactions

- many interactions identified; varying clinical significance
- chemicals in tobacco smoke can interact by two mechanisms
- dose adjustments
  - **pharmacokinetic**- usually poly-carbons not nicotine
    - stimulation of hepatic enzymes
    - antipsychotics, warfarin & caffeine
  - **pharmacodynamic**- largely due to nicotine
    - alter the expected response or actions of other drugs
    - beta-blockers, insulin

Dose adjustments may be required and based on clinical presentation and according to medical review.
Pharmacokinetic Interactions

• usually due to polycyclic aromatic hydrocarbons from tobacco smoke inducing hepatic enzymes
  • cytochrome CYP450 isoenzymes- primarily 1A2
  • this enzyme metabolises several clinically important drugs such as antipsychotics, warfarin & caffeine
  • inter-individual variability in drug metabolism
Pharmacokinetic Interactions

• CYP1A2 activity higher in heavy smokers (≥20/day).
• induction varies depending on:
  • bioavailability of polycarbons in tobacco smoke
  • extent of inhalation
• enzyme induction rapidly reversed when a patient abruptly stops smoking, with a new steady state of CYP activity reached after approximately one week
• 5 cigarettes per day may be enough for enzyme system induction

Nb. The effect of smoking on hepatic enzymes is not related to nicotine so NRT does NOT influence CYP1A2 activity.

Induction (smoking)

- *induction* of enzymes (smoking) may result in an ↑ in the metabolism of many drugs that are substrates, and cause a subsequent ↓ in plasma concentrations and requirement for **higher** dose.

Inhibition (smoking cessation)

• *inhibition* (smoking cessation) may result in a ↓ in the metabolism, and cause an ↑ in plasma concentrations necessitating a reduction in dose

Clinical Relevance

• **HIGH** - documented interactions with clinically important effects in a number of patients and/or drugs metabolised principally through CYP1A2 which have a narrow therapeutic index.

• **MODERATE** - documented interactions with minor or no clinical effects, or isolated reports of clinically important effects and/or drugs metabolised partly by CYP1A2 with a narrow TI and/or drugs metabolised principally by CYP1A2 with a wide therapeutic index

• **LOW** - theoretical interaction without documented cases and/or drugs metabolised partly by CYP1A2 with a wide therapeutic index
Clozapine

• What happens when your client smokes.
  – increased metabolism and decreased plasma concentrations
  – may need higher doses
  – clinical relevance- HIGH

• What happens when your client stops smoking
  – decreased metabolism and increased plasma concentrations
  – may need lower doses

• What do you need to do
  – monitor trough plasma level before and for two weeks after stopping smoking or sooner if side effects develop
  – be alert for increased adverse effects (e.g. hypotension, dizziness & sedation) and if they occur consider dose reduction
Olanzapine

• What happens when your client smokes.
  – increased metabolism and decreased plasma concentrations
  – may need **higher** doses
  – clinical relevance - **MODERATE**

• What happens when your client stops smoking
  – decreased metabolism and increased plasma concentrations
  – may need **lower** doses

• What do you need to do
  – be alert for increased adverse effects (e.g. hypotension, dizziness & sedation) and if they occur consider dose reduction
Chlorpromazine

• What happens when your client smokes.
  – increased metabolism and decreased plasma concentrations
  – may need higher doses
  – clinical relevance- MODERATE

• What happens when your client stops smoking
  – decreased metabolism and increased plasma concentrations
  – may need lower doses

• What do you need to do
  – be alert for increased adverse effects (e.g. hypotension, dizziness & sedation) and if they occur consider dose reduction
Caffeine

• What happens when your client smokes.
  – increased metabolism and decreased plasma concentrations
  – may need **higher** doses
  – clinical relevance- **HIGH**

• What happens when your client stops smoking
  – decreased metabolism and increased plasma concentrations
  – may need **lower** doses

• What do you need to do
  – advise client that caffeine intake needs to be reduced by half to avoid excessive caffeine levels
SSRIs

• What happens when your client smokes.
  – fluvoxamine is the only SSRI expected to interact with smoking
  – increased metabolism and decreased plasma concentrations
  – may need higher doses
  – clinical relevance- LOW

• What happens when your client stops smoking
  – decreased metabolism and increased plasma concentrations
  – may need lower doses

• What do you need to do
  – be alert for increased adverse effects (e.g. hypotension, dizziness & sedation) and if they occur consider dose reduction
• What happens when your client smokes.
  – serum levels of amitriptyline, clomipramine, imipramine, nortryptyline are lower in smokers
  – increased metabolism and decreased plasma concentrations
  – concentration of free drug rises, which appears to offset the effects
  – clinical relevance- LOW

• What happens when your client stops smoking
  – decreased metabolism and increased plasma concentrations

• What do you need to do
  – be alert for increased adverse effects (e.g. hypotension, dizziness & sedation) and if they occur consider dose reduction
Pharmacodynamic Interactions

• largely due to the nicotine
• alter the expected response or actions of other drugs
• such interactions may increase the risk of adverse events
Benzodiazepines

• What happens when your client smokes.
  – clients who smoke may experience less drowsiness
  – likely due to stimulation of CNS from smoking
  – clinical relevance- LOW

• What happens when your client stops smoking
  – less stimulation of CNS

• What do you need to do
  – clients may experience an enhanced effect including a risk of CNS depression. Consider dose reduction
Methadone

• What happens when your client smokes
  – methadone can increase smoking and satisfaction from smoking
  – clients who smoke may experience less drowsiness
  – likely due to stimulation of CNS from smoking
  – nicotine affects endogenous opioid system; smoking enhances the effect of methadone on opioid withdrawal symptoms
  – clinical relevance- MODERATE

• What happens when your client stops smoking
  – methadone can potentiate nicotine withdrawal

• What do you need to do
  – reducing methadone when a patient is trying to quit smoking can be detrimental
  – be alert for signs of opioid toxicity and if they occur consider dose reduction
Oral contraceptives

• What happens when your client smokes.
  – smoking increases the adverse effects of the oral contraceptive pill especially risk of clots, stroke and myocardial infarction
    > Risk of CV death 19.4 per 100,000 vs 3.03 per 100,000
  – be aware for symptoms such as severe sudden chest pain, shortness of breath, severe pain or swelling in one leg, sudden blurred vision or loss of sight, or sudden severe headache
  – in women over 35 years who smoke more than 15 cigarettes/day

• What happens when your client stops smoking
  – decreased risk of adverse effects
Summary

• stopping smoking is just as important in mental health patients
• tobacco smoking can affect drug metabolism via pharmacokinetic & pharmacodynamic mechanisms
• a change in smoking status can render patients at risk of serious adverse effects
• patients should be regularly monitored with regards to smoking and extent of tobacco use and doses of relevant medications adjusted accordingly
References

• Tang J, Law M, Wald N. How effective is nicotine replacement therapy in helping people to stop smoking? BMJ 1994;308:21-26