Treatment for Anxiety Disorders in Primary Care

Dr Terence Leong
Associate Consultant
Dept of Psychological Medicine
Why treat in primary care?

1) Common
   - Half of primary care patients fulfilled criteria for an ICD-10 mental disorder, and the top 3 are:
     . Somatoform disorders 35.9%
     . Anxiety disorders 16.4%
     . Mood disorders 13.5% (Toft et al 2005)

2) Co-morbidity
   - Anxiety disorders had the highest co-morbidity rate of 89% for another mental diagnosis

3) Lower drop-out rates worldwide

4) Family Physician as Main Healthcare Provider
Treatment of Anxiety Disorders

1) Pharmacological (main focus of talk)

2) Psychological

3) Social
Stepped Care Approach for Treatment of Anxiety Disorders

- Step 1: Recognition and diagnosis
- Step 2: Treatment in primary care
- Step 3: Review and consideration of alternative treatments
- Step 4: Review and referral to specialist
- Step 5: Care in mental health service

NICE Guidelines 2004
Steps 2 and 3:

- Step 2: Start Treatment in primary care
- Step 3: Review and consideration of alternative treatments

NICE Guidelines
Key Treatment Considerations

- Mild cases: do not need medications. Try psychological and social interventions instead

- Moderate to severe cases: a Combined Approach involving both medications and psychosocial interventions is best

- Pharmacotherapy is indicated if
  - Symptoms are moderate to severe
  - Significant impairment of social, occupational and role functioning
Pharmacological

They're anti-anxiety pills...

But I'm afraid to take them!!
Guidelines on Pharmacotherapy

• **A)** SSRI as first line: start at a lower dose than for depression, and increase dose gradually (reason: initially may worsen anxiety)

  ➔ If no improvement on high dose after 4-6 weeks:

• **B)** Switch to another agent (another SSRI, SNRI or TCA) & increase gradually

  ➔ If no improvement on high dose after 6-12 weeks:
    Consider Referral

• Beta-blocker: Propranolol 10-20 mg bd/tds prn for Generalized Anxiety Disorder or Performance Anxiety

NICE Guidelines
Pharmacological treatment

Before prescribing consider:
- age, gender → dose
- previous treatment response → which agent
- patient’s preference → compliance
- risk of self-harm or accidental overdose → SSRI preferred
- possible interactions with concomitant medications → escitalopram, mirtazapine
- cost → cheaper agent may be just as good
If starting medications, inform patients:

- Antidepressants may be required in higher doses & for longer duration for anxiety

- Need to start at low doses & increase slowly

- Delay in onset of effect (4-12 wks)

- Need to take medication as prescribed

- Side-effects (common S/E, Serotonine Syndrome)

- Discontinuation symptoms
Serotonin Syndrome

- High doses
- Two or more serotonergic drugs
- During switching of antidepressant (no wash out): esp when switching from fluoxetine
- Drug interactions (tryptophan, MAOI, Selegiline, amphetamines, meperidine, other antidepressants, St John’s Wort, lithium)
- Can mimic anxiety before other sx develop!!
  - Confusion and agitation
  - Flushing, shivering, sweating and hyperthermia
  - Hyperreflexia and clonus
Discontinuation symptoms

• Not associated with tolerance or craving

• Most common discontinuation/withdrawal symptoms are:
  dizziness, numbness and tingling, gastrointestinal disturbances, headache, sweating, anxiety and sleep disturbances

* Esp. with agents with short half lives such as paroxetine
What about Benzodiazepines?

1) Always Short Term & Minimum Effective Dose, on a prn basis

2) Ask yourself what is the reason you’re prescribing them:
   - Anxiety?
   - Insomnia?
   - Alcohol withdrawal?
   - Muscle relaxation?
   - Other?
Reasons for Prescribing BZDs

- Anxiety: 91.1%
- Insomnia: 59.4%
- Alcohol withdrawal: 57.2%
- Muscle relaxation: 56.1%
- Other: 23.9%

Maine Benzodiazepine Study Group, 2004, Physician Survey
Reason to Prescribe >90 Days

- Chronic anxiety: 69.4%
- Serious mental health dx: 42.8%
- Chronic insomnia: 30.6%
- Other: 23.3%
- Extendid crisis: 20.6%
- Never: 12.8%

Maine Benzodiazepine Study Group, 2004, Physician Survey
# Dosage Conversion Table for Benzodiazepines

<table>
<thead>
<tr>
<th>Benzodiazepines</th>
<th>Dosages (mg)</th>
<th>Half-life (hours)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam <em>(Dormicum)</em></td>
<td>5-7.5</td>
<td>1.8 to 6 (active metabolite)</td>
</tr>
<tr>
<td>Alprazolam <em>(Xanax)</em></td>
<td>0.5</td>
<td>6-12</td>
</tr>
<tr>
<td>Lormetazepam <em>(Loramet)</em></td>
<td>1-2</td>
<td>10-12hrs</td>
</tr>
<tr>
<td>Lorazepam <em>(Ativan)</em></td>
<td>1</td>
<td>10-20</td>
</tr>
<tr>
<td>Bromazepam <em>(Lexotan)</em></td>
<td>5-6</td>
<td>10-20</td>
</tr>
<tr>
<td>Nimetazepam <em>(Erimin)</em></td>
<td>5</td>
<td>14-30</td>
</tr>
<tr>
<td>Clonazepam <em>(Rivotril)</em></td>
<td>0.5</td>
<td>18-50</td>
</tr>
<tr>
<td>Clorazepate <em>(Tranxene)</em></td>
<td>15</td>
<td>36-100</td>
</tr>
<tr>
<td>Diazepam <em>(Valium)</em></td>
<td>10</td>
<td>36-200 (active metabolite)</td>
</tr>
<tr>
<td>Flurazepam <em>(Dalmadorm)</em></td>
<td>15-30</td>
<td>40-250</td>
</tr>
</tbody>
</table>

*Includes metabolites - in hours
Role of benzodiazepines

Discourage patients from long term BDZ use
- High risk of dependency
- Side effects
- Tolerance & withdrawal
- Benzodiazepines are associated with worse outcomes in long-term (increased incidence of depression & cognitive decline)
Tolerance

- Time-dependent decrease in effect

- Neurochemical basis unclear

- Varying rates for different behavioral effects:
  - sedative and psychomotor effects diminish first (e.g. few weeks)
  - memory and anxiety effects persist despite chronic use

Limitations on the use of benzodiazepines in anxiety and insomnia: are they justified? Lader et al., European Neuropsychopharmacology, 1999
Long-term effects on Cognition

• Stewart (2005): long-term BZD use affects several cognitive functions:
  - Ability to learn new material
  - Visuospatial deficits
  - Changes in explicit memory
  - Attention/concentration difficulties

• Amnestic effects: delayed recall

• The higher the lipid solubility, the greater the likelihood of memory damage
  - Low lipid solubility (clonazepam) → less likely to impair memory
  - High lipid solubility: diazepam, triazolam, alprazolam, lorazepam

Cognitive effects of long-term benzodiazepine use: a meta-analysis
Barker et al., CNS Drugs, 2004
Dependence

- 90% of long-term users (>8mo-1yr) experience significant withdrawal

- Common: insomnia, fatigue, headache, muscle, twitching, tremor, sweating, dizziness, tinnitus, difficulty concentrating, nausea, depression, abnormal perception of movement, irritability

- Rare: Seizures, delirium, confusion, psychosis, triggering of depression, mania, OCD.

Cognitive effects of long-term benzodiazepine use: a meta-analysis
Barker et al., CNS Drugs, 2004
How do you recognize patients at risk for dependency?

- Use of High Potency BDZs (e.g. dormicum, erimin, alprazolam, lorazepam)
- Higher daily dose needed to control symptoms
- High pre-taper levels of anxiety and depression
- Other substance dependence/abuse
- Personality disorders
- Not motivated to discontinue use

Cognitive effects of long-term benzodiazepine use: a meta-analysis
Barker et al., CNS Drugs, 2004
Socio-Economic Costs of Inappropriate Benzodiazepine Prescribing

- Associated with substance abuse
- Increased mortality from overdose and suicide
- Increased risk of accident/traffic, falls and fractures in elderly
- Increased risk of aggressive behaviour and/or domestic disharmony
- Increased risk to foetus, infants, children
- Contribution to job loss, unemployment, loss of work through illness
- Cost of medical consultations, hospital admissions/ investigations
- Dependence and withdrawal reactions

Frequency and risk factors of potentially inappropriate medication use in a community-dwelling. Lechevallier-Michel et al., Journal of Clinical Pharmacology, 2005
Guidelines worldwide

- **UK:** Benzodiazepines are indicated for the short-term relief of anxiety or insomnia that is severe. Benzodiazepines can cause or exacerbate depression and increase the risk of suicide.

- **Canada:** Continuous use of benzodiazepines should not exceed two weeks.

- **New Zealand:** Short-term treatment with benzodiazepines may be beneficial but use for more than four weeks could well be harmful.

- **Denmark:** Prescription of benzodiazepines should be restricted to a maximum of two weeks (sleeping pills) or four weeks (anxiolytics)

Maine Benzodiazepine Study Group, 2004, Physician Survey
Singapore (CPG 2008)

- Use antidepressants to treat anxiety

- Benzodiazepines should not be first line treatment: only for short-term relief (2-4 weeks) of anxiety or sleep disturbance

- Treatment duration should be limited as benzodiazepines are addictive

- **How to stop**: change currently used benzodiazepine to equivalent dose of Diazepam (max 40mg) and reduce slowly over several months (reduce by 1/8th of total dose every fortnight)
## Comparison of Anxiolytic Medication

<table>
<thead>
<tr>
<th>Agent</th>
<th>Positive</th>
<th>Negative</th>
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| SSRI  | Well tolerated  
Treats comorbid depression  
Low risk of mortality in overdose | Slow onset of effect (4-12 wks)  
May worsen anxiety symptoms initially |
| BZD   | Quick onset of effect  
Well tolerated | Sedation  
Recurrence & Rebound anxiety  
Withdrawal effects  
Risk of dependence |
| TCA   | Treats comorbid depression | Cardiotoxicity  
Anticholinergic effects  
Risk in overdose |
| MAOI  | Treats comorbid depression | Low tyramine dietary requirement  
Risk of hypertensive crisis |
| RIMA  | Reduced dietary restrictions compared to MAOI | Less effective than MAOI |
Drug-drug interactions:

- BZD
  - respiratory depression with CNS depressants such as alcohol, barbiturates, opioids
  - sedation with mirtazapine
  - ataxia and dysarthria with lithium
  - delirium with clozapine
How to avoid drug interactions

1) Advise patient not to combine BZD with alcohol

2) Discuss with patient the potential for abuse and dependency and monitor BZD use

3) Do not use propranolol when patient uses calcium inhibitors, when patient has DM and when patient has cardiac problems
Pharmacotherapy of Anxiety in Elderly

- First identify: primary medical cause, medication, dementia, etc.
- Avoid TCA and mirtazapine → associated with hypotension → risk for falls
- BZD also associated with falls
- Start in lower dose & increase very slowly
Pharmacotherapy of Anxiety in Children

- Always psychological interventions first!

- Limited number of SSRIs in lower doses
  - Fluvoxamine, sertraline, fluoxetine
  - Do not use venlafaxine or paroxetine → associated with high incidence of suicidal ideation
Pharmacotherapy of Anxiety during Pregnancy

- TCA lowest known risk in pregnancy, but higher fetal toxicity risk
- Lowest risk SSRI: fluoxetine
- SSRIs after 20 weeks GA associated with persistent pulmonary hypertension in neonate and discontinuation syndrome
- Paroxetine in 1st trim. associated with fetal heart defects
- Benzodiazepines 1st trim. with cleft palate
Pharmacotherapy of Anxiety Disorders during Lactation

- Best sertraline, paroxetine, amitriptyline

- Not
  - fluoxetine --> in higher doses in breast milk: short and medium term adverse effects found
  - Long-acting BZD --> floppy infant syndrome; sedation, lethargy, impaired respiration and withdrawal
Psychological Treatments

1) Supportive Counselling

- Empathic listening & showing understanding
- Validation
- Self Esteem building
- Normalization
- Naming the problem / emotions
- Reframing situation from more positive angle
- Skills building
- Giving advice
- Modeling adaptive behavior
- Providing anticipatory guidance
- Promoting autonomy & coping strategies
- Forming crisis plans: what, when, who, how
Psychological Treatments

2) Behavioural therapy:
   - Relaxation Exercises
     - Controlled Breathing Exercises
     - Guided Imagery
     - Progressive Muscle Relaxation
   - Activity Scheduling
   - ABC Charting (Antecedent, Behaviour, Consequences)
   - Controlled worry period
   - Coping Skills
   - Stress Management

3) Others:
   CBT, Psychodynamic, Solution-Focussed, Narrative therapy, Mindfulness & Acceptance
Social Interventions

- Diet & Lifestyle
- Self Care Time
- Financial
- Family, Marriage & Children
- Work-Life Balance
- Housing (esp. elderly living alone)
- VWOs, Family Service Centres
- Building of Social Network & Support
Psychological Treatments

Step 4: Review & Referral to specialist

1) Review:
   - Correct Diagnosis?
   - Co-morbidity present? If so, treated?
   - Have you tried 2 trials of antidepressant treatment at optimal dose for 12 weeks each?

2) Refer if:
   . Diagnosis Unclear
   . Suspect Organic Cause
   . Poor or no response to the 2 trials of medication
   . Severe anxiety or distress
   . Multiple or serious co-morbidities
   . Substance dependence
   . Polypharmacy
   . Risk of Harm to self or others
   . Marked Socio-occupational impairment despite treatment
Case 1

- You have successfully treated a young lady suffering from an Anxiety Disorder with Paroxetine. As she is well, she stopped taking it. Soon after, she experienced giddiness, headache, strange sensations on her skin, nausea, diaphoresis and insomnia. Which of the following statements is true?
A) Withdrawal Symptoms
B) Discontinuation Syndrome
C) The symptoms may persist and lead to mortality
D) Fluoxetine can be used to treat these symptoms
A) False. SSRIs are not addictive
B) True. It’s due to abrupt cessation of an antidepressant with short half life
C) False. They usually resolve within a few days and are not life-threatening.
D) True. Fluoxetine can be used to treat discontinuation syndrome, then tailed off gradually. Alternatively, a short course of low dose benzodiazepines can be given.
Case 2

- Your regular patient admits to being dependent on Dormicum 6 tabs per day. He is motivated to quit with your help. You are confident that he does not doctor-hop and will comply with your advice. He is medically stable. What will you do?
A) Ask him to stop all benzodiazepines immediately
B) Prescribe dormicum for now, but gradually reduce it and stop it within a few months
C) Prescribe an equivalent dose of diazepam, reduce it gradually and stop within a few months
D) Refer to an Addictions Specialist
Answers

A) Risky: may lead to withdrawal seizures, delirium etc
B) Should change to equivalent dose of diazepam
C) Correct
D) It is possible to do outpatient detoxification in primary care, esp. since there is already a good doctor-patient relationship.
Case 3

- You have diagnosed a patient with Panic Disorder (moderate severity). She found the xanax you prescribed very helpful and relieved her panic attacks well. But she is not keen to continue with the SSRI you prescribed concurrently as it made her anxious instead. What will you do?
A) Prescribe only xanax, but on a prn basis only with advice not to abuse it
B) Counsel her that SSRI is the first line treatment and ask her to continue at the same dose.
C) Reduce the dose of SSRI by half, then increase it gradually over the next few weeks.
D) Stop the xanax
Answers

A) Tolerance will inevitably develop and she will need increasing doses of xanax. Iatrogenic dependence will occur.

B) She is very sensitive to the side effect of SSRI. Initially SSRIs can increase anxiety and she will need to start on a lower dose before increasing.

C) Correct approach

D) Stopping xanax abruptly will lead to a relapse
Take home message

• Anxiety disorders are common, if left untreated they are costly for individuals and society

• Be cautious with benzodiazepines

• A range of effective interventions are available, pharmacotherapy is just one of them

• Consider Combined Therapy (medications + psychosocial interventions)
Thank you for your attention!

Help Patients to Overcome:

F E A R

False Expectations Appearing Real