Management of Depression and Insomnia

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Mental health problems in the world & in Singapore

- 450 million suffer from mental disorders
- 1 in 4 persons will develop a mental or behavioural disorder in their lifetime
- Anxiety & Depression: 6.5% of population
- Minor Psychiatric Illness: 15.7% of population

Mental disorders in primary care

- 25% of patients have a mental disorder
- 88% of patients with mental disorder seek primary care first
- Diagnosis missed half the time for depression, more for eating disorders and alcoholism

Depression usually untreated or undertreated in Primary Care

- Untreated
- Treated Appropriately (only 1/6)

Obstacles to diagnosis

- Insufficient time
- Presentation with somatic symptoms
- Competing problems
- Stigmatization
- Minimization

Presentation influences psychiatric diagnosis in primary care

Bridges KW, Goldberg DP. J Psychosom Res. 1985;29:563-569.
Physical complaints are rarely organic


The Medical Model of Depression


Neurobiology of Depression

Serotonin-related symptoms

Norepinephrine-related symptoms

Impulse • Appetite
Aggression

Motivation • Zest
Energy • Social drive


Diagnostic Criteria for Major Depressive Disorder

• Five or more of the following for at least 2 weeks
  - Depressed mood*
  - Loss of interest or pleasure*
  - Appetite/weight change
  - Sleep disturbance
  - Psychomotor disturbance
  - Fatigue or low energy
  - Feelings of worthlessness or inappropriate guilt
  - Impaired ability to think or concentrate
  - Recurrent thoughts of death or suicide

* At least one of these symptoms must be present.


Depression and Comorbidity

Prevalence of Depression as a Concomitant Condition

- Cancer: 25%
- Diabetes: 32.5%
- Postpartum: 10%–20%
- Poststroke: 32%
- Post-myocardial infarction: 16%


Non-Pharmacologic Therapies

- Psychological Interventions
- Social Intervention
- Electroconvulsive Therapy (ECT)
Antidepressants
- Used in both anxiety and depression
- Effective in mild, moderate or severe depression
- 60-70% response rate in depression
- Effectiveness comparable between and within classes
- Improvements seen in 2 weeks; sometimes up to 4-8 weeks

Antidepressants: TCAs
- Older and time-tested, cheap
- Problems of anticholinergic side-effects, postural hypotension and sedation
- Toxic in overdose; cardiac effects
- Imipramine, amitriptyline, clomipramine and dothiepin (prothiaden)
- Dose 10 – 150 mg/day
- Usual effective dose 25-100 mg/day
- Once daily at night; titrate up 25 mg/day

Antidepressants: SSRIs
- Newer, costlier
- Safer in overdose
- Less problematic side-effects
- Broad spectrum of activity
  - Depression
  - Anxiety
  - OCD
  - PTSD
- Side effects
  - Overstimulation, insomnia (early)
  - Sexual – erectile dysfunction
  - GI effects

Antidepressants: MAOIs
- Phenelzine, Tranylcypromine
- MAO inhibition causes NE accumulation
- Postural hypotension, dietary restrictions, drug interactions, sexual dysfunction

Antidepressant Classes

Pharmacologic Classes
Antidepressant Classes

<table>
<thead>
<tr>
<th>Class</th>
<th>Example</th>
<th>Action</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNRI</td>
<td>Venlafaxine</td>
<td>Inhibits 5HT and NE reuptake</td>
<td>Same as SSRIs (low doses), hypertension, insomnia, agitation, headache (high doses)</td>
</tr>
<tr>
<td>NARI</td>
<td>Nefazodone</td>
<td>Serotonin antagonist &amp; reuptake inhibitor</td>
<td>Somnolence, asthenia</td>
</tr>
<tr>
<td>NARI</td>
<td>Sertraline</td>
<td>Serotonin reuptake inhibitor</td>
<td>Somnolence, asthenia</td>
</tr>
<tr>
<td>NaSSA</td>
<td>Mirtazapine</td>
<td>Alpha2, 5HT1, 5HT2, 5HT3 antagonist – Enhances NE &amp; 5HT neurotransmission</td>
<td>H1 antagonism – sedation, weight gain</td>
</tr>
<tr>
<td>NDRI</td>
<td>Bupropion</td>
<td>NE and Dopamine reuptake inhibitor</td>
<td>Stimulation, agitation, nausea, insomnia, seizures (4/1000)</td>
</tr>
<tr>
<td>NaSSA</td>
<td>Trazodone</td>
<td>5HT antagonist</td>
<td>Sedation, postural hypotension, nausea</td>
</tr>
</tbody>
</table>

SNRI (Serotonin Norepinephrine Re-uptake)
- Dual Mechanism of action
- Useful as second line drug
- Also useful in painful somatic symptoms
- Examples Duloxetine, Venlafaxine
- Side effects similar to SSRIs
- Need to monitor BP for Venlafaxine
- Duloxetine has approval for diabetic neuropathy

NaSSA (Noradrenergic and Specific Serotonergic)
- Mirtazepine (Remeron)
  - Alpha-2 adrenergic receptors that normally inhibit the release of the neurotransmitters norepinephrine (noradrenaline) and serotonin, thereby increasing active levels in the synapse
  - Mirtazapine is a potent antagonist of 5-HT2 and 5-HT3 receptors. Reducing side effects of sexual dysfunction and GI effects
  - Prominent anti-histamine effect. Weight gain and sedation prominent

Choosing An Antidepressant
- Cost
- Symptom profile
  - E.g. Sleep disturbance, risk of overdose, obsessive symptoms, prominent anxiety
- Side effect profile
  - E.g. Anticholinergic effects, cardiotoxicity, sexual effects, weight gain
- Previous history of response/non response (patient/family)
- Dosing schedule

Dosages and Treatment
- Dosages typically similar for adult primary care and psychiatric patients
- Acute treatment: 8 to 12 weeks
- Maintenance treatment: 6-12 months symptom-free
- "The dose that makes them well is the dose that keeps them well"

Management Guidelines
- Adequate dose of antidepressant therapy
- Adequate duration: 8-12 months
- Prophylaxis at full dose for recurrent depression
  - 2 or more episodes
  - Prominent family history
  - Significant suicide risk
Initiating therapy

- May start with full dose or half-dose
- May need to cover with short-term BZPs to manage anxiety and insomnia initially
- Response takes 10 to 21 days, sometimes longer
- Side effects usually settle within a week
- Beware the "one-dose" patient

Suboptimal response?

- Increase to maximum tolerable dose
- Maintain for adequate duration
  - 4-8 weeks
- Deal with psychosocial stressors
- Manage anxiety
  - Relaxation techniques
    - Progressive muscle relaxation and imagery
  - Short-term benzodiazepines
    - Xanax, Ativan
- Beware the "one-dose" patient

Suboptimal response?

- Consider switch within class first
- Then consider switch outside class
- Augmentation
  - Lithium, Thyroxine, Antipsychotics
- ECT
- Avoid combining antidepressants

Monitoring

- No specific blood monitoring required for antidepressants
- Venlafaxine requires BP monitoring
- Continuous monitoring of disease symptoms

Prognosis

10-yr relapse rate (1st-time major depressives)

50%!!
Generalists Give Good Care for Mood Disorders

- 85-95% depressed patients treated by PCP successfully without referral
- Prognosis of patients treated by PCP’s better than that of patients treated by psychiatrists

What is insomnia?

- One or more of the following symptoms:
  - Difficulty falling asleep
  - Waking up frequently during the night with difficulty returning to sleep
  - Waking up too early in the morning
  - Unrefreshing sleep
  - Perception of poor quality sleep even if true sleep was obtained

What do you do to manage your sleep disorder?

Sleep Hygiene

- Temperature:
  - Optimal temperature for sleep is quite cool, around 15.6 to 20 degrees Celsius
  - Temperatures in this range help to facilitate the decrease in core body temperature that in turn initiates sleepiness
Bed: Should only be used only for sleep, with activities such as work, reading and even worrying kept outside the bedroom.

- Sharing a bed often leads to poor quality sleep because people are regularly disturbed by their loved ones during the night.
- On average, couples suffered up to 50% more disturbances when sleeping with their partners than they did on their own.

Keeping regular hours and habits:
- If you can't fall asleep within 15 to 20 minutes, leave the bedroom and do something relaxing such as reading or listening to soft music.
- Your sleep-wake patterns are regulated by an internal ‘clock’ that dictates when you feel sleepy; only return to bed when you feel sleepy again.
- Avoid long afternoon naps.

Avoidance of stimulants and stimulation activities close to bedtime (vigorous exercise, intense work and exciting TV programmes):
- Avoid heavy meals or spicy foods 2 to 3 hours before bedtime.
- Avoid using alcohol as a sleep aid.
- Stress management and relaxation.
- Exercise regularly.

Drug treatment:

Drug Treatment:
- Benzodiazepines
- Newer short acting hypnotics:
  - Zopiclone
  - Zolpidem
- Antihistamines
- Psychiatric drugs e.g. anti-depressants, anti-psychotics

Benzodiazepines (BZP):
- Anti-anxiety
- Hypnotic/sedative
- Anticonvulsant
- Muscle relaxant effect
- Effect can be short acting or long acting.
Sedation:
- Anxiolytic properties
- Behavioral disinhibitory effects:
  - Euphoria, Impaired judgment, Loss of self-control
- Exert such effects at dosages that cause minor CNS depression
- Anterograde Amnesia

Hypnosis
- ↓ Latency of sleep onset
- ↑ Stage 2 NREM Sleep i.e. light sleep
- ↓ REM sleep duration:
  - may cause anxiety, irritability, rebound ↑ REM sleep
- However, usage > 2 week:
  - tolerance of effects on sleep

Dependence
- Psychologic & Physiologic
  - Psychological Reliance
  - Physiological dependence: Withdrawal syndrome upon abstinence
- Affected by T1/2
- Less likely if:
  - taken once a day
  - long acting drug taken
  - taken for short periods
  - if taken only when necessary

Short-acting BZP
- More likely to produce withdrawal symptoms in long term use, especially if taken several times a day or patients with personality problems
- Examples:
  - Midazolam- Dormicum
  - Lorazepam- Ativan
  - Alprazolam- Xanax
  - Bromazepam- Lexotan

Long-acting BZP
- Examples:
  - Diazepam-Valium
  - Nitrazepam-Mogadon
  - Chlordiazepoxide-Librium
  - Chlorazepate-Tranxene
  - Flurazepam-Dalmadorm

The Newer short acting hypnotics
- Zolpidem (Stilnox®) and Zopiclone
  - Mechanisms of actions differ
  - Speed on Onset: Approx 30 minutes
  - Medium Acting: Approx 8 hours
  - No hangover effect
  - Preserves sleep architecture
  - Minimal rebound nightmares
  - Minimal addictive potential
Zolpidem (Stilnox®)
- The absence of active metabolites, and the rapid elimination prevents any drug accumulation
- Short duration of action and absence of next-day residual effects
- Generally well tolerated and effective in elderly patients

Side effects (Australian Adverse Drug Reactions Bulletin, Vol 26, No 1, Feb 2007)
- Visual hallucinations
- Amnesia
- Sleep walking
- Automatic behaviour ‘while asleep’ e.g. binge eating and house painting

Important points before starting any benzodiazepines.
- Take a complete history including alcohol, legal and illegal drug history. Caution when starting benzodiazepines on patients with history of drug and alcohol abuse
- Limited to 2 to 4 weeks; use the lowest effective dose
- Inform patient at the start of treatment of limited duration

Important points before starting any benzodiazepines.
- Inform patient of side effects and potential problems like dependence
- When in doubt, issue small quantities at a time
- Encourage all patients with dependency to withdraw and consider referring to the IMH Addiction Medicine Department/CAMP
- Treat any underlying causes like depression, panic disorder, etc
- Consider alternatives like psychological intervention and a referral to psychologist

· With the update on prescribing benzodiazepines guidelines on September 2008, it is important for you to be familiar with our local MOH guidelines
Non-drug option

- Cognitive behavioural therapy (CBT)
  - Help patients change the behaviours and thoughts that can get in the way of a good night’s sleep
  - Cognitive part: teaches you to change the anxiety-producing thoughts that interfere with your ability to sleep
  - Behavioural part: aims at actions that impair your ability to sleep, such as spending too much time in bed