The Rational Use of Anti-depressants in Primary Care

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Introduction

A great variety of anti-depressants is now available in Hong Kong (Table 1) and clinicians are sometimes confused as to how to select the most suitable medication for the most appropriate patient.

Table 1 Classes of Anti-depressants

1. First generation
   a. TriCyclic Anti-depressants (TCAs) e.g., amitriptyline, etc.
   b. Tetracyclic Anti-depressants e.g., maprotiline, etc.
   c. MonoAmine Oxidase Inhibitors (MAOIs) e.g., phenelzine, etc.
2. Second generation
   a. Selective Serotonin Reuptake Inhibitors (SSRIs): e.g., fluoxetine, citalopram, escitalopram, etc.
   b. Others e.g., amineptine (DA agonist), trazodone (weak SSRI), mianserin (5HT antagonist), etc.
3. Third generation
   a. Serotonin & Noradrenaline Reuptake Inhibitor (SNRI) e.g., venlafaxine, etc.
   b. Noradrenaline and Specific Serotonergic Antidepressant (NaSSA) e.g., mirtazapine
   c. Reversible Inhibitor of Monoamine Oxidase A (RIMA) e.g., moclobemide
   d. SSRI selective serotonin (5HT) blockere.g, nefazodone
   e. Others, selective serotonin reuptake agonist e.g., tianeptine, DA & Na reuptake inhibition e.g., bupropion, etc.

Key: DA=dopamine, 5HT=serotonin, Na=noradrenaline

For a rational approach to medication, the STEPS principles (Preskorn, 1998a) are particularly relevant, and they are discussed below.

1. Safety

The most important aspect of safety is the toxic side-effects of the medications. For example, tricyclics can induce cardiac arrhythmia, and the SSRIs may induce the Serotonin Syndrome (Lejoyeux, et al 1994). Secondly, contra-indications in using the medications have to be considered especially in the presence of other disorders such as psychotic disorder, hepatic or renal diseases, etc. For example, venlafaxine may not be suitable for patients with unstable hypertension. This then involves the safety margin in over-dosage such as delirium caused by tricyclics overdose. Besides, one must explore the possibility of drug-drug interactions including the ‘cheese reactions’ between the MAOIs and tyramine containing food. Interactions between anti-depressants e.g., TCAs with MAOIs can also result in hypertensive crisis. Sometimes, this involves the drug effects on the cytochrome P450 isoenzymes (Preskorn 1998b) e.g., fluoxetine and tricyclics used in combination can lead to toxic levels of tricyclics.

2. Tolerability

Tolerability refers mainly to adverse events or side-effects. One should not only concentrate on the short-term effects, but also the long-term consequences e.g., the effects of excessive weight gain. Other relevant issues include effects on alertness and sleep, appetite and sex; psychiatric adverse events such as agitation or manic swing; cognitive dysfunction and sex-related problems.

Furthermore, one has to consider drug withdrawal effects. After long-term treatment with the SSRIs, the discontinuation syndrome (Shatzberg et al, 1997) can occur especially for the short-acting ones like paroxetine and fluvoxamine.

It should be noted that some side-effects can be beneficial e.g., mirtazapine can relieve insomnia and poor appetite, while the SSRIs can even cure premature ejaculation.

3. Efficacy

So far, most anti-depressants have similar efficacy (about 65%) though differences occur if compliance is considered. Generally speaking, compliance is much better for the second and third generation anti-depressants.

The timing of onset of efficacy should also be considered. There was an impression that venlafaxine in high doses had an earlier onset of anti-depressive effect, and escitalopram (a purer form of citalopram) may theoretically work faster than others. Augmentation (e.g., with a stimulant) or combination therapy (e.g., lithium plus SSRIs) are sometimes allowed for refractory depression. Quite often, depressive patients have other co-morbid symptoms e.g., obsessions, anxiety, etc., and specific anti-depressants have differential effects on them. For example, the SSRIs are useful for coexisting panic disorder.

4. Price

Generally speaking, if different medications have identical effects (and side-effects) then the least costly one should be chosen. The most objective way of testing the relative costs of each medication is through ‘cost-analyses’ such as cost-benefits, cost-effectiveness and cost-utility comparisons. For example, though the SSRIs are more expensive than TCAs, they are found to be of similar or even higher cost-effectiveness.
5. Simplicity

For demented and elderly patients, a once daily scheme is desirable. This however depends on the half-life of individual medications. For example, escitalopram can be taken once a day while fluvoxamine is often taken twice daily to maintain the stable blood level.

Simplicity also means there is no need for constant drug adjustment. Normally, a one-tablet SSRIs regime is sufficient but TCAs have to be increased steadily until a therapeutic window is reached. If dose titration is mandatory, then the flexibility in such adjustment is also an important element.

Certain anti-depressants specified that they should be taken with food or at particular timing, and a few cannot be taken without prior physical checkup.

Besides the STEPS criteria, other factors affecting the choice of anti-depressants should also be considered, including past clinical response, the doctor’s experience in the use of particular medications, and perhaps the affordability of the consumers.

Conclusion

Within the plethora of modern pharmaceuticals, the clinicians must apply a rational choice in choosing the most appropriate medicines for their depressed patients.

References