# How to start antidepressants

Original article by: May Su

The antidepressants that would be used as a first line agent would usually be a selective serotonin re-uptake inhibitor (SSRI), venlafaxine or mirtazapine. The choice would be determined by the symptoms of the patients and the side-effect profile that would be tolerable. At times, a side effect of a medication may be used as an advantage. See the antidepressant matrix for a single page overview. Furthermore see the list of antidepressants available in Australia.

Of "first line" agents, a few generalisations can be made:

**SSRIs, venlafaxine and mirtazapine:**

- The base effective dose is equivalent to one tablet daily;
- "start low, go slow": start with a half tablet daily for 4-6 days (except fluoxetine which has very long half life and can be started as one tablet daily);
- then increase to one tablet daily;
- the dose can be increased to at least 2 tablets daily (though there is no "rule of thumb" of the maximum safe daily dose - each drug is different).

Before starting a patient on an antidepressant, discuss side-effects. The most common side effects are nausea, headache, sexual dysfunction, agitation and sleep disturbance. It is useful to emphasise that early side-effects like agitation, sleep disturbance and nausea often settle after the first few days to week of treatment and it is important to press on.

The principle is to "start low, go slow". Start at "half dose" for 4 days and increase to the full dose afterwards. For elderly patients, it may be appropriate to continue on the "half dose" until review. Warn patients that this is a long term medication, usually of a minimum of 18-24 months for a first episode.

Initially patients should be reviewed weekly or fortnightly. This is to assess side effect profile, continuing risk and for supportive therapy. Patients need to be aware that it usually takes 4-6 weeks before they receive a reasonable effect from antidepressants, although there should be some effect by two weeks of therapy (3-4 weeks for fluoxetine due to long half life). If there is no noticeable effect by 2 weeks, the dose should be increased (increase the dose by 50-100%). If response is unsatisfactory at 6 weeks, increase the dose again. If there is no effect at all at the 6 week mark (despite having increased the dose), it may be worthwhile to change antidepressants. Otherwise review progress at 4 weeks after each dose adjustment.

The most common reason for poor response to antidepressants is not using a reasonably high dose, or not trialing for long enough. There is some evidence that fluoxetine (and hence SSRIs) work at the level of neurogenesis (1). They don't work quickly.

There is a risk of relapse if precipitously ceasing antidepressants. Suddenly stopping antidepressants can also cause significant withdrawal effects, so weaning over several weeks is the preferred method.

Antidepressants do not necessarily have to be continued indefinitely. If patients have been

symptom free, then it is not unreasonable to consider a trial off antidepressant after 18-24 months, however they must be warned of risk of relapse and withdrawal.

SSRIs are highly effective. There has been some bad press in the past few years related to increased risk of suicide with SSRIs. The main reason for this is that SSRIs (in fact all antidepressants) take longer to improve mood than they take to improve the other symptoms of depression such as amotivation. This is an issue for the severely depressed patient who has had significant suicidal ideations, or even plans, but mainly lacks the concentration and interest to carry out the attempt. As the antidepressants act, the patient's functional ability improves while they may still have symptoms of nihilism and low mood. This is when they require closer monitoring regarding risk to self or others. A study showed that patients with depression on SSRIs had around twice the number of suicide attempts compared to those on placebo, though there was no statistical significance for fatal attempts. Furthermore, there was no statistical significance between SSRIs and TCAs (though paroxetine was on the edge of significance).

**Choice of antidepressants - by side-effects:**

Avoidance of drug interactions:

- citalopram
- sertraline
- venlafaxine
- mirtazapine
- avoid: *fluoxetine*

Avoidance of sedation:

- any of the SSRIs except fluvoxamine
- venlafaxine
- avoid: *mirtazapine*

Patient with insomnia (sedation may be a useful side-effect):

- mirtazapine
- fluvoxamine is relatively sedating for an SSRI

Patient with severe anxiety with their depression:

- mirtazapine
- avoid: *venlafaxine*

Patients with severe depression:

- venlafaxine and;
- mirtazapine may be "stronger" than the SSRIs.
- avoid: *moclobemide*

Avoidance of sexual side-effects:

- moclobemide
- mirtazapine

## Choice of antidepressants - by patient group

Elderly patient with polypharmacy:

- citalopram
- sertraline
- mirtazapine

Otherwise healthy adult:

- All the SSRIs are usually well tolerated;
- sedation and weight gain may be an issue with mirtazapine.

Pregnant or breastfeeding woman:

- Best evidence of safety with TCAs and fluoxetine;
- most SSRIs are probably safe;
- there are lower levels of sertraline and paroxetine in breast milk compared to fluoxetine but this is of unknown significance.
- avoid in pregnancy: *paroxetine* (recent research showing a statistically significant increase in cardiovascular malformations - see more below) (2) (3).

Sexual side-effects:

- Can try to switch to another SSRI;
- mirtazapine has no sexual side-effects but sedation and weight gain may be issues;
- moclobemide has no sexual side-effects by relatively less effective.

In adolescents and children:

- Poor evidence base for most medications (specialist referral recommended);
- fluoxetine.

## Reference links:

(1) Huang GJ., Herbert J. Stimulation of neurogenesis in the hippocampus of the adult rat by fluoxetine requires rhythmic change in corticosterone. *Biol Psychiatry*. 2006 Apr 1;59(7):619-24. Epub 2005 Dec 2.

(2) Therapeutic Goods Administration (TGA). Caution over antidepressant paroxetine during pregnancy [media release]. 7 September 2005. [download PDF :: 30 Kb]

(3) GlaxoSmithKline. Paroxetine and pregnancy [website]. http://www.gsk.com/media/paroxetine_pregnancy.htm

Updated: Michael Tam (19 June 2003)

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