Notes on antidepressant use in cancer patients – clinician guidelines

**Use of antidepressants in cancer-related depression**

Antidepressant treatment of cancer patients is under-utilized, as often the patient’s distress is seen as a normal response to abnormal circumstances which requires psychological assistance only. Cancer patients often have complex physical symptoms relating to the disease and its treatment and become physically and psychologically depleted during the course of their illness. Many patients, particularly those with advanced disease, may not meet full DSM V criteria for Major Depression, but will nevertheless benefit from antidepressants. Antidepressant therapy tailored to the symptom profile can improve mood and also address some of the common symptoms of anxiety, insomnia, anorexia, nausea, agitation, loss of motivation, pain and hot flushes. Antidepressants also have a beneficial effect on immune functioning.

Choice of antidepressant will depend on:
- Symptom profile (hence receptor profile of the drug)
- Co-morbid physical and psychiatric illness
- Drug interactions
- Contraindications
- Early vs advanced disease
- Understanding of the biology of the drug
- Prescriber familiarity

**SSRIs**

Many GPs prescribe this group of drugs as first-line treatment for depression following an extensive campaign at the time of their introduction. This may be appropriate in early cancer diagnosis, but common side-effects of nausea, diarrhoea, insomnia, disturbances in sexual function and agitation make them unsuitable for very ill patients who may already suffer these symptoms. Cytochrome P450 activity, particularly 2D6 inhibition, leads to interference with other drugs which are metabolized through this enzyme.

- **Sertraline** - useful in patients with mild-moderate depression who may have irritability, anxiety, obsessional features, post-trauma syndromes, at doses of 50-200mg. Do not use with patients on Tamoxifen because moderate 2D6 inhibition interferes with metabolism to its active metabolite.
- **Citalopram** – has a long half-life and weak antihistaminic activity which has some anxiolytic and sedative action. Do not use at doses >40mg because of Q-T prolongation. Has 2D6 inhibition.
- **Escitalopram** – the left enantiomer of Citalopram; has a more predictable response at lower doses, less antihistaminic activity and less 2D6 inhibition – safe to use with Tamoxifen.
- **Do not use paroxetine** (Short T ½ -> discontinuation symptoms, potent 2D6 inhibitor), **fluoxetine** (long T ½, 2D6 and others), **fluvoxamine** (broad CYT P450)
SNRIs
Increase synaptic noradrenalin and serotonin and may also boost dopamine in the dorsolateral prefrontal cortex by inhibiting noradrenalin transporters. Pseudo-anticholinergic effects (dry mouth, constipation, urinary retention) may occur, but not to the degree of tricyclic antidepressants.

- **Venlafaxine** – although it has a short T½, XR forms mitigate discontinuation syndromes although they may still be unpleasant. Used in doses of 75-225mg in this population. Hypertension may be a problem.
- **Desvenlafaxine** – the active metabolite of venlafaxine; a ‘clean’ drug with low CYP450 metabolism, renal metabolism and low protein binding. Useful for hot flushes as well as depression, in doses of 50-100mg in slow release form. Is metabolized through conjugation hence CYP450 interactions not a problem.
- **Duloxetine** – a useful drug in cancer patients as has FDA approval for pain as well as being an effective antidepressant in doses of 60mg (starting at 30mg). Does not cause hypertension but should not be used in patients with alcoholism or renal or liver impairment. Has 2D6 and 1A2 potential for interactions.

NaSSA

- **Mirtazapine** – an analogue of the older tetracyclic mianserin, this drug has distinct advantages in advanced disease and palliative care, but side effects of sedation and increased appetite with weight gain make it less useful for the ambulant population. Its receptor profile has noradrenergic and specific serotonergic activity (enhancing 5HT1A-mediated serotonergic activity and blocking 5HT2 and 5HT3), antagonizes adrenergic alpha2 autoreceptors and heteroreceptors, thereby not causing sexual side effects, postural hypotension and constipation or diarrhea and reducing nausea and vomiting.

Melatonin-active agents

- **Agomelatine** – not a great deal of experience in the cancer population. May be useful for milder depressions with sleep disturbance where monoaminergic agents not tolerated. Liver function needs to be monitored.

Combination antidepressants

- **Mirtazapine with venlafaxine/desvenlafaxine/duloxetine** – combinations of these medications allows specific targeting of desired symptoms and synergistic boosting of antidepressant effect. In advanced disease, problematic weight loss, nausea and anorexia, insomnia and anxiety can be alleviated with 30-45mg mirtazapine and fatigue improves with a small dose of SNRI eg 37.5–75mg venlafaxine XR or 30mg duloxetine. The combination does not appear to cause serotonergic syndrome. There are conflicting views among psychiatrists about the use of combination antidepressants.

Dr Di Clifton, Medical Director Psychosocial Cancer Care St Vincent’s Hospital Melbourne
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Other antidepressants

- **Tricyclics** – the broad receptor profile of this group of drugs makes them unsuitable as antidepressants in this population. The use of opiates raises the anticholinergic load and TCA’s may precipitate delirium and aggravate problems of dry mouth and constipation. In addition the anti-α1 adrenergic properties may increase risk of falls in more frail patients. Pain specialists still use small doses of amitriptyline or doxepin, but duloxetine or desvenlafaxine are alternatives.

- **MAOIs** – there is no indication for this group of medications in the complex care of cancer patients because of risk of drug interactions. Occasional survivors with atypical refractory depression respond to MAOIs, as with the general population.

Psychostimulants

- **Methylphenidate** – may be used where life expectancy is short to improve mood and energy.

Note:

**Procarbazine**, used in the treatment of brain tumours, can cause a serotonergic syndrome with some antidepressants because of weak MAOI activity. **Tramadol**, an opiate-like anti-inflammatory, can cause serotonergic syndrome in combination with antidepressants. Practitioners are advised to check all drug combinations.

CAVEAT

These notes are based on my personal experience in an oncology and palliative care setting and my reading of the literature on antidepressants. There are no robust studies of currently available antidepressants in this complex, multifactorial field. These notes will need revision as more information, choices and experience evolve.