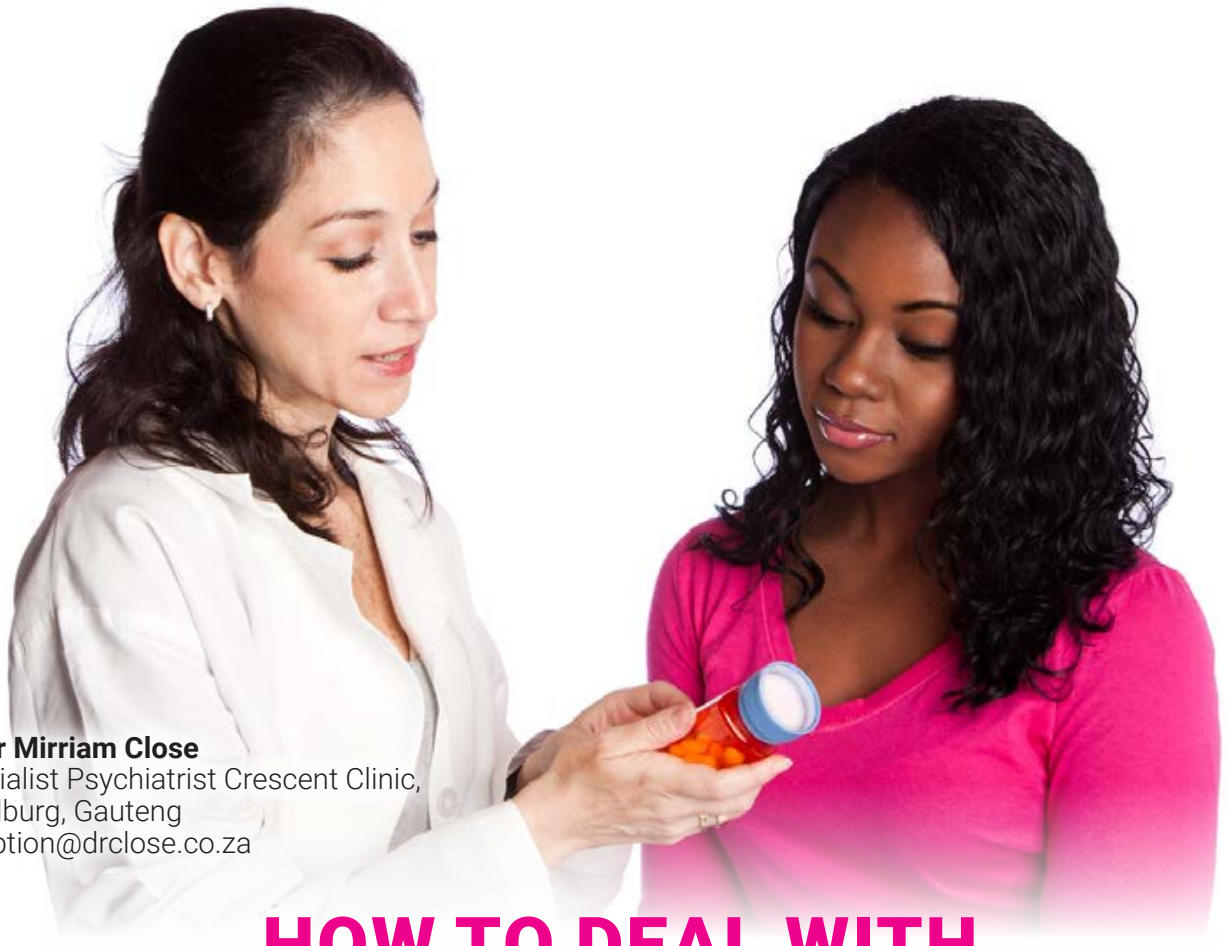

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HOW TO DEAL WITH ANTIDEPRESSANT SIDE EFFECTS

Available antidepressants have provided safe and effective management of mood and anxiety disorders. However, side effects may remain as a limiting component to symptom resolution. The presence of side effects could contribute to treatment discontinuation in up to 23% of patients, suboptimal response by limiting dose escalation and negative impact on quality of life.

The management of adverse effects would therefore contribute to improved patient adherence, comfort and symptoms remission. Common side effects include sexual dysfunction, gastrointestinal difficulties, weight gain, apathy, somnolence and fatigue and sleep disturbances. Psychiatric complications with central nervous system changes may occur. Peripheral side effects and other serious side effects are important considerations with regards to the utilisation of antidepressants.

SEXUAL DYSFUNCTION

Upon direct enquiry of sexual disorder symptoms, the prevalence occurs in 58% of patients. Certain antidepressants, such as the selective serotonin re-uptake inhibitors (SSRI) medications are deemed problematic, with paroxetine presenting with the higher side effects profile.

The approach to the management of the side effects includes:

- Obtaining a comprehensive history, including the baseline sexual functioning and noting concerns relating to the choice of antidepressant treatment.
- Dose reduction of the antidepressant medication, with consideration of the impact on the mood or anxiety.
- Timing of sexual activity prior to the next dose minimises sexual side effects.
- The alternative antidepressants, with noted efficacy on depressive symptoms and fewer sexual side effects include: bupropion, agomelatine, desvenlafaxine, moclobemide, trazodone and vortioxetine.
- Erectile dysfunction treatment includes the phosphodiesterase type 5 inhibitors such as sildenafil.
- Steroid therapies including oestrogen and testosterone may be utilised as augmentation strategies to counter antidepressant side effects.

GASTRO-INTESTINAL DIFFICULTIES

In 17% to 26% of patients utilising antidepressant medications, nausea and stomach complaints with SSRI medications, are prevalent. Venlafaxine and vortioxetine are associated with increased nausea. The management includes:

- Slow-release formulations, if available.
- Dose administration at night may ameliorate symptoms.
- Divided dosing regimens, to be taken with small amount of food may assist with symptoms.
- Ginger-containing foods and beverages or sugar-free candy may be utilised.
- Anti-emetic medications and proton pump inhibitors may be used to treat side effects.
- Diarrhoea is documented to occur in 16% of patients on SSRI medication. Although usually transient, it may persist. The management includes anti-diarrhoeal agents, lactobacillus acidophilus culture or psyllium which might be beneficial.
- Constipation occurs in 11% to 12.5% of individuals. Paroxetine

is the SSRI most associated with this side effect. Management includes optimised water and fibre intake together with appropriate constipation medication regimens including stool softeners.

WEIGHT GAIN

Weight gain presents as a complex factor with regards to antidepressant management. The increased weight may represent improvement of depressive symptoms and resolution of a loss of appetite, residual symptoms of unresolved depressive disorder, medication related symptoms or another, independent factor.

- Paroxetine is associated with weight increase in contrast to placebo.
- Mirtazapine and venlafaxine demonstrated weight gain side effect profile.
- Fluoxetine and citalopram do not demonstrate significant weight changes.
- Less weight gain is noted with bupropion. Newer antidepressant agents including agomelatine and vortioxetine are associated with less weight gain effects.
- Topiramate, an anticonvulsant, has weight decreasing effects.
- Effective lifestyle modifications would be an important component of weight management.

FATIGUE AND SOMNOLENCE

Drowsiness is a common side effect occurring in 10% to 38% of depressed outpatients. In descending frequency of occurrence of symptoms, mirtazapine, trazodone and SSRI presented with fatigue and somnolence.

Management of drowsiness includes:

- Assessment of sleep patterns and counseling on sleep hygiene measures.
- A shift in antidepressant dosing schedule from morning to nighttime administration.
- Divided dosing or use of a slower release preparations are effective strategies.
- Psycho-stimulant augmentation may be considered.
- Graduated increase in exercise would also help reduce fatigue.

INSOMNIA

Due to the stimulating effect of certain medications of the serotonin noradrenaline re-uptake inhibitor (SNRI) class and bupropion, insomnia may be a side effect. Sedating antidepressant medication may therefore be utilised to counter this side effect. Insomnia is reported in 12% to 22% of depressed outpatients.

Management of antidepressant-induced insomnia includes:

- Educating patients on sleep hygiene.
- Modification of use of caffeine and stimulants.
- Changing the timing of doses to the morning.
- Adding adjunctive medications including melatonin, trazodone, mirtazapine, and/or low doses of anticonvulsants and atypical antipsychotics.

APATHY

A complaint of dullness, lack of motivation or feeling numb may be a side effect of long-term antidepressant usage. Although an elusive symptom, it may herald relapse or represent residual depressive symptoms.

The management of apathy includes:

- Usage of stimulating medications.
- A dose reduction of the causative antidepressant or switching may be considered.

DISCONTINUATION SYNDROME

An abrupt dose reduction of antidepressant medication may present with a discontinuation syndrome, simulating antidepressant side effects.

To minimise this occurrence:

- A cross-titration down of one antidepressant and optimisation of the replacement medication.
- The utilisation of fluoxetine, as a longer acting antidepressant to cover a shorter-acting antidepressant, may minimize withdrawal side effects.

CENTRAL NERVOUS SYSTEM

- Epileptogenic potential may considered higher for tricyclic antidepressants and bupropion. Therefore, in a patient with a predisposition or concern with regards to epilepsy, these medications are to be used with caution.
- The SSRI medication have been shown to be associated with increased risk of extrapyramidal symptoms. The management would include adjusting the dose, switching the medication or utilisation of other effective treatments.
- Neuroleptic malignant syndrome has been attributed to the usage of antidepressant medication, or the withdrawal of the medication. As an urgent condition, hospitalisation and specific management would be required.
- Although antidepressants may be beneficial with regards to cognitive optimisation, there is limited evidence to suggest impairments in certain cognitive parameters. Neurocognitive assessments would be beneficial to clarify these aspects.
- Headaches are common initiation symptom of SSRI antidepressants which is usually transient. Conservative management would be recommended.

SERIOUS SIDE EFFECTS

- Serotonin syndrome, as a potentially life-threatening condition, requires urgent management. Serotonin syndrome manifests with myoclonus, hyperreflexia, sweating, shivering, incoordination, and mental status changes. To minimise the risk of a serotonin syndrome, with the usage of two or more serotonergic agents, a discontinuation of the replaced medication and a wash-out period should occur.
- Bleeding may occur with SSRI medications.
- Cardiac complications, seizures or agranulocytosis may occur with tricyclic antidepressants.

PSYCHIATRIC COMPLICATIONS

With regards to antidepressants, the initiation, usage or discontinuation may mimic or potentiate various other psychiatric manifestations.

- Monitoring for suicidality and clinical worsening is required. Should these effects occur, stopping or switching the medication may be necessary. Referral for urgent psychiatric care would be warranted.
- Tricyclic antidepressants, bupropion and venlafaxine are associated with highest mortality rates in overdose. Of the SSRI medications, fluoxetine and sertraline are the safer options when considering safety in overdose profile.
- Anxiety symptoms may present on initiation. Slow and low dosage optimisation may assist with this side effect.
- A presentation may occur whereby patients experience feeling numb or blunted. Dosage of the antidepressant is to be reviewed and adjusted, if possible.
- Antidepressants may potentiate mixed or manic symptoms in the presence of Bipolar Disorder. Various management options exist including: stopping the antidepressant, switching to another antidepressant with less potential to cause phase changes such as bupropion and optimising the mood stabilising medication.
- Paradoxical effects have been noted to occur with fluoxetine and sertraline. This entails the resumption of depressive symptoms during the maintenance phase of antidepressant treatment or the emergence of new symptoms and exacerbation of the initial clinical presentation. The management includes a discontinuation of the antidepressant.

PERIPHERAL EFFECTS

PERIPHERAL EFFECTS	CAUSATIVE ANTIDEPRESSANT	MANAGEMENT
Tremor	SSRI Venlafaxine	• Moderate caffeine intake. • Consider antipsychotic or other medication side effect. • Utilisation of ß-blockers.
Orthostatic hypotension	Trazodone	• Reduce or discontinue medication. • Rise slowly from seated position. • Use medication at night.
Hyponatraemia	SSRI- fluoxetine, citalopram and escitalopram Venlafaxine	• Monitor at risk population such as elderly patients. • Fluid restriction. • Diuresis to be considered.
Adverse cutaneous drug reactions	Tricyclic Antidepressants SSRI	• Reduce or discontinue medication. • Antipruritic and/or topical or oral steroids. • Hospitalization if severe.
Ophthalmic Concerns	SSRI	• Eye drops usage for dry eyes. • Monitor and complete a • risk assessment for previous history and age with regards to glaucoma. • Monitor visual concerns for development of cataracts.
Dry Mouth	Tricyclic Antidepressants	• Regular sips of water. • Chewing sugar-free gum. • Avoiding acidic beverages. • Usage of a suitable mouthwash.
Sweating	Bupropion SNRI	• Reduce or switch medication. • Usage of anti- andrenergic or anti- cholinergic treatments.
Hepatotoxicity	Agomelatine Duloxetine Venlafaxine	• Citalopram and escitalopram are safer alternatives. • Monitor liver function tests prior to dose initiation, as per guidelines or after dose increments.
Genito-urinary	SSRI Duloxetine	• Adjust or discontinue medication. • Mirtazapine may be considered for management of SSRI- associated urinary retention.

Although antidepressant side effects may occur, effective management approaches are available to reduce the impact. Various strategies can be utilised including monitoring symptoms, using alternative options and conservative treatments that are symptom targeted.Education and advice for patients with regards to side effects has shown to be valuable. This would serve to minimise the risk of discontinuation and optimise the potential of beneficial antidepressant usage. The information would serve to reassure patients and provide knowledge to optimally manage their conditions and medications. MHM

References available upon request