

## MEDICATION USE IN DEPRESSION

Indications for the use of antidepressants are discussed in “Treatment” section above.

When confronted with the wide range of available antidepressants, remember that despite marketing claims to the contrary:

- ❖ *All antidepressants are equally effective for most depressions at a group level (though note that there is some evidence to support use of TCA, SNRI, NASSA in melancholia)*
- ❖ *All antidepressants take equally long to be effective (usually 2-6 weeks)*
- ❖ *It's best to be familiar with the use of a small number of antidepressants*

When initiating antidepressants it is important to persist to allow **an adequate trial**. Three factors make up an adequate trial

- ❖ **Dose:** An average level for that agent, as recommended by the PI.
- ❖ **Duration:** Three weeks to six weeks
- ❖ **Compliance:** Confidence that the patient is compliant

### **Choice of antidepressants**

#### **Past response**

The best predictor of future response is past response. Previous response to a particular antidepressant overrides most other considerations.

If a patient has not previously had antidepressants, a family history of response to a particular antidepressant (eg in a parent or sibling) may guide choice. It may indicate a greater biological responsiveness to that agent, as well as providing a foundation of greater patient confidence.

#### **Side effect profile**

The second consideration in medication choice is side effect profile. Although newer agents are well tolerated overall, many individuals experience significant side effects.

For those on other medications, the risk of interactions or cumulative side effects should be minimised. Where continued role functioning and alertness is critical (eg some occupations, roles, parenting) sedating side effects are best avoided. Medications with sexual side effects are best avoided in those with a biological or psychological sensitivity to sexual difficulties.

#### **Symptom profile**

Certain patterns of depressive symptoms may respond to particular antidepressants. Evidence for this is limited, and at times these may be based on convention and analogies with older medications rather than on systematic trials. Past response and side effect profile are more powerful factors, and most antidepressants will be effective for a wide range of presentations.

These are summarised in the table which follows:

## ***Do benzodiazepines have a role?***

As in other conditions, benzodiazepines should be used sparingly and for brief periods. They have potential for dependence and abuse. It is also possible that their use may limit new learning and slow the effectiveness of psychological treatments.

They should never be used alone for treatment of depression. Their anxiolytic effects may mask some depressive symptoms, but the depression will not resolve.

The main indication for benzodiazepine use in depression is for initial control of insomnia. Most non-sedating antidepressants will improve the insomnia associated with depression, but this response may take several weeks. If insomnia is present but a non-sedating antidepressant such as an SSRI is preferred (eg due to past response), a hypnotic such as Temazepam (*Normison*) 10-20mg nocte or Nitrazepam (*Mogadon*) 5-10mg nocte may be useful in the initial weeks of treatment.

**Anxiety symptoms associated with depression should not usually be treated with a benzodiazepine. CBT is the treatment of choice for these symptoms. Most antidepressants are effective in reducing anxiety.**

## **Other medications**

A number of other medications are used in treating depression where additional symptoms are present or where first-line treatment has been ineffective. Most should usually be used after specialist consultation.

### **Antipsychotics**

These must be used where psychotic symptoms are present. They may also be effective in reducing severe anxiety, and boosting or augmenting other antidepressants where there has been incomplete response. Conventional antipsychotics such as Haloperidol (*Serenace*) and Chlorpromazine (*Largactil*) should be used cautiously due to their side effect profile, including the risk of irreversible movement disorders. Newer agents with more favourable side effect profiles, such as Olanzapine (*Zyprexa*), Quetiapine (*Seroquel*) or Risperidone (*Risperdal*), are preferable.

### **Mood stabilisers**

Lithium Carbonate (*Lithicarb*), Carbamazepine (*Tegretol*) and Sodium Valproate (*Epilim*) are all effective mood stabilisers. They may be used to treat depression occurring in Bipolar Affective Disorder as well as to prevent recurrence of depression or mania in that disorder. In other depressions they may be used to augment the effect of antidepressants where treatment has been ineffective. Newer anticonvulsants such as Vigabatrin may have similar effects but have not yet been systematically studied. Lamotrigine is a useful agent in bipolar depression, but needs to be introduced over 6 weeks due to risk of Stevens-Johnson Syndrome.

### **Other augmentation agents**

In some treatment resistant depressions augmentation with other agents (eg Thyroid Hormone) has been effective in some patients. Such augmentation should only be initiated after specialist consultation.

## **Patient information and education**

The success of antidepressant treatment depends on much more than pharmacology. Good communication is vital to ensure initiation and compliance. In depression, apprehension and misinformation may be great, while concentration and information processing ability may be impaired. Successful treatment may require

### **Steps for improving compliance**

*Explanation and rationale*

*Dispelling misperceptions*

*Encouraging a long-term view*

*Explaining possible side effects*

*Giving relevant support material*

persistence for several weeks before signs of improvement are seen, and side effects may be maximal in the first weeks of treatment, peaking before signs of improvement.

Steps which can be taken to improve compliance with antidepressants include:

### **Explanation and rationale**

The diagnosis of depression and reasons for antidepressant use should be explained.

### **Dispelling misperceptions**

Antidepressants are often viewed with suspicion. Common concerns include that they may be addictive, that they will create a false "high" and that depression will recur on cessation. A useful analogy can be to see antidepressants as like a splint or plaster in treating a fracture, providing stabilisation to allow internal healing processes to take place. It can be useful to explain that antidepressants are not stimulants, and a non-depressed person taking them will feel no benefit.

### **Encouraging a long-term view**

Expectations of immediate benefit should be reduced. A trial of antidepressants can be explained as a medium-term investment requiring several weeks of persistence prior to seeing a return. Foreshadowing that 10-20% of people may require a change of antidepressant due to side effects or non-response can prevent loss of hope later.

### **Explaining possible side effects**

Possible side effects should be explained. Many peak in the initial weeks of treatment and then subside. Giving the patient some forewarning and allowing them a level of control about whether to persist with side effects or change to a different agent can be effective.

### **Giving relevant support material**

Even the best crafted explanation may not be remembered the next day. The use of written or audiovisual materials about diagnosis and treatment will significantly enhance compliance. They may also provide the patient with a useful device for explaining and validating their condition to family and supports.

Many drug companies provide sophisticated and useful patient support materials. Where these are free of excessive promotion they are a useful adjunct to treatment.

## **Treating the subtypes of depression**

### **a) Mixed anxiety and depression**

A mix of anxiety and depressive symptoms may be more common than either syndrome on its own and is usually associated with non-melancholic depression. These illnesses are typically chronic, with exacerbations associated with periods of increased stress.

The most effective medications are SSRIs. Venlafaxine (*Efexor*) and Moclobemide (*Aurorix*) may also be useful. Benzodiazepines should be avoided.

### **b) Severe or melancholic depression**

Although a minority of cases (5-10% of all depression) the increased risk means identification is critical. Major risk factors include a strong family history of depression (including bipolar disorder). It is more common in the elderly, and is associated with cerebrovascular disease. When occurring in a young person (< 40), be alert to the possibility of a bipolar illness.

The most effective medications are probably Venlafaxine (*Efexor*) or the tricyclics such as *Prothiaden*. Some have argued that SSRI's are less effective in this group. A minority of patients will require ECT, which is highly effective in this group.

### **c) Post-natal depression**

This occurs in 10-20% of all women in the 12 months post-partum. It is usually non-melancholic, but a small proportion will experience psychosis. Risk factors include previous history of depression, poor social supports, ambivalent attitude towards pregnancy and motherhood, poor relationship with own mother, pre and perinatal complications, primiparous women.

Always consider risk issues for both mother and baby. Choice of medication will depend on whether mother is breastfeeding (see below).

### **d) Depression as part of a Bipolar Affective Disorder**

A Major Depressive episode may form one part of a bipolar affective disorder, where history reveals episodes of clinical or subclinical mania. Melancholic and psychotic symptoms are more common in depressions occurring in this context

The major risk in treatment of this group is that antidepressants may precipitate a swing into mania, or trigger "rapid cycling" with more frequent switching between states. Antidepressants should only be used with mood stabiliser cover, and treatment of this group should usually involve specialist consultation

### **e) Depression and substance use**

The use of alcohol, in particular, complicates the presentation of depression. Alcohol dependence can lead to depression, and persons who are depressed may self-medicate with alcohol. In young persons, cannabis dependence may present with amotivation,

lethargy and withdrawal, thus mimicking depression. In older persons, benzodiazepine use may precipitate depression or complicate its treatment.

It is essential to address the issues of substance use as part of the management of depression. This might include specific drug and alcohol counselling or a detoxification program.

There is evidence to suggest that antidepressants are less effective when a person is concurrently abusing alcohol or illicit drugs. Therefore a concerted effort should be made to encourage the person to cease or substantially reduce the amount consumed prior to commencing an antidepressant.

#### **f) Adolescents and young people**

Depression is common in this age group and is generally under-recognised. It is likely to be multifactorial, involving significant family and developmental issues, and is often precipitated by a crisis (e.g. relationship breakup or failing exams). Drug and alcohol problems may often be associated.

Depression may be more difficult to detect in younger people, because of greater reluctance to seek help, greater need for sensitive interviewing and greater likelihood of atypical depressive symptoms such as boredom, irritability and pain.

Melancholic or psychotic features are rare, but if present may indicate an evolving Bipolar Affective Disorder. If these are present, urgent referral to specialist mental health service should occur.

Antidepressants should rarely, if ever, be used in isolation in adolescents, but should be combined with psychosocial interventions.

#### **g) Depression in the elderly**

Depression occurs commonly in the elderly. 'Late-onset' depression (i.e. first episode after 50) tends to be associated with organic pathology, such as cerebrovascular disease and degenerative brain disease. Also consider iatrogenic depression secondary to medications (e.g. corticosteroids, antihypertensives).

Melancholic and psychotic features occur more commonly in the elderly. Typical psychotic features in the elderly are delusions of guilt, poverty or somatic illness. These symptoms may be vague or not disclosed. The GP should have a high index of suspicion where there is significant agitation or slowing, where milder concerns about money or health are expressed, where the patient is unusually difficult to reassure or where there is a failure to respond to adequate doses of an antidepressant. It is critical that psychotic features such as delusions or hallucinations are recognized (see Assessment section). Psychotic depression will not respond to antidepressants alone, and is associated with a much higher risk of morbidity and mortality.

## **h) Depression and Personality Disorder**

Patients with serious personality disorder tend to have high rates of comorbid depression, which is often missed due to focussing on the 'acting out' elements of the personality disorder, such as intense anger and deliberate self-harm.

It is essential to ask about symptoms of depression in this group. Vegetative symptoms like change in appetite, sleep and libido may be more sensitive markers than cognitive symptoms such as helplessness and hopelessness, which tend to be chronic in this group.

Whilst simple, short-term psychological strategies can be useful for this group of patients, some will require more comprehensive psychological therapy. This may be an indication for referral to a specialist mental health service.

Medication has been demonstrated to be useful in patients with personality disorder and comorbid depression. It is important to avoid losing hope. Focus on those aspects of the presentation, such as depression, that can be treated.

### ***Pregnancy and breastfeeding***

The decision to continue or initiate medication during pregnancy requires careful thought. Most antidepressants fall into medium to low-risk categories. Therefore possible risks of treatment need to be weighed against the risk to the mother and foetus of untreated depression. Psychosocial treatments from support to specific CBT should always be the first choice. However, in patients with severe depression, melancholia or significant suicide risk, antidepressant use may be indicated.

If a patient on antidepressants discovers they are pregnant, a decision to cease treatment should not be made without review of the seriousness, rate of onset and degree of risk posed by the previous depressive episode. Specialist assessment should usually be sought in these situations.

#### ***Risk to Foetus of Antidepressants taken by mother:***

<b>Category</b>	<b>Description</b>	<b>Agents</b>
A	Extensive human use with no proven risk	None
B1	Low risk. Animal studies show no increased risk	None
B2	Low risk. Limited animal studies	Fluoxetine, Mianserin, Tranylcypromine, Venlafaxine
B3	Animal studies have shown fetal damage. Human risk uncertain	Moclobemide, Phenlazine, Citalopram, Nefazodone, Sertraline, Paroxetine
C	Reversible harmful effects	Benzodiazepenes, tricyclics
D	Risk of malformations	Lithium, Carbamazepine, Valproate, Clonazepam

The postpartum period is the highest risk period for development of depression, and the question of prescribing during breastfeeding often arises. If in any doubt in dealing with this question you should feel welcome to make a referral for assessment and advice.