UNIT NO. 4

MANAGEMENT OF MAJOR DEPRESSION

Dr Nelson Lee

ABSTRACT

Mood disorders, in particularly Major Depressive Disorder are perhaps the most common psychiatric disorders encountered in a family practice setting. In milder cases psychological interventions may be all that is needed to manage the depression. Medication may be needed if the depression is more severe. Once an assessment including suicide assessment has been done, the primary care physician establishes a therapeutic relationship with the patient. He has 4 treatment options: watchful waiting, psychological interventions, pharmacotherapy, and referral to a psychiatrist. A combined approach of establishing a therapeutic relationship, psycho-education, and appropriate use of psychotropic medications give the best results. The primary care physician needs to know the indications for referral to a psychiatrist.

Keywords: Major Depressive Disorder; Psychological interventions; Antidepressants

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INTRODUCTION

Mood disorders, in particularly Major Depressive Disorder (MDD) are perhaps the most common psychiatric disorders encountered in a family practice setting. Large epidemiological studies suggest that major depressive disorder has a lifetime prevalence of 16.6%, occurring with approximately twofold higher frequency in women compared with men.[1] The point prevalence of MDD has been reported to be 10% in the primary care setting, 15-20% in the nursing home population, and 22% to 33% in medically ill patients.[2] MDD also agreegates in families, it is 1.5 to 3 times more common in individuals with first degree biological relatives affected with MDD compared with the general population[3].

Managing depression in the primary healthcare setting is a potentially fulfilling and highly possible provided that the patient is not severely ill. Many patients feel that treatment in this setting is more reassuring and less stigmatising. They often already have good rapport with the treating doctor which helps speed up the therapeutic process.

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NELSON LEE, Medical Director and Consultant Psychiatrist, The Psychological Wellness Centre

MANAGEMENT STRATEGIES

Once an assessment including suicide assessment has been done (as described in Unit 3), the primary care physician establishes a therapeutic relationship with the patient. He has 4 treatment options: watchful waiting, psychological interventions, pharmacotherapy, and referral to a psychiatrist.[2,5]

ESTABLISH A THERAPEUTIC RELATIONSHIP AND PSYCHOEDUCATION

The establishment of a therapeutic relationship is often very helpful to a depressed patient. Family Practitioners are usually very skilled in establishing rapport with the patients.

Maintain good eye contact and have an attentive body language by leaning forward and provide affirmative nods as the patient speaks. Very often it is not only what is said that is important but how it is said. Maintain a warm, relaxed tone and this will encourage your patient to be more forthcoming and receptive towards you. It is often a source of great relief just to be able to find an empathetic medical professional who is willing to listen without judging and who aims to understand.

Allow the patient to ventilate and avoid providing direct solutions but instead increase their awareness of their own perceptions and resources, and to help them problem solve. This would lead to increased self-esteem and help develop independence and confidence to meet future challenges positively. It would also be good to summarise and paraphrase what the patient has said. It helps to consolidate their thoughts and it also helps them feel understood

Psycho-education by helping the patient understand their condition better can help debunk myths about the condition and de-stigmatise fears associated with having a mental condition. I found it helpful to use simple analogies like diabetes in helping patient's to understand that depression like diabetes is due to a shortage of chemicals in the body, in this case serotonin in the brain, much akin to that of insulin in diabetes. Helping medicalise the condition also avoids patients seeing themselves as weak and this can go a long way in helping the patient accept treatment.

WATCHFUL WAITING

In the primary care setting there will be a number of patients who have a depressed state that fail to meet the standard of 4 or more distinct symptoms beyond depressed mood and anhedonia. Should antidepressives be prescribed? A scanty literature does not support antidpressive efficacy in such patients. The attending physician's judgment about whether symptoms will spontaneously resolve will determine whether

medication is needed. Current data suggest that active treatment with antidepressives be considered only for those individuals with more segvere functional impairment and a 4 to 8 week trial of support, education, and when appropriate, exercise for all others.[6, 5]

PSYCHOLOGICAL INTERVENTIONS

When is psychotherapy a better choice than pharmacotherapy? If the patient has overwhelming neurovegetative symptoms he or she needs pharmacotropic medications. If on the other hand, the patient has a barrage of negative thoughts or a severe life crisis psychotherapy may be more useful.

Psychological interventions in the primary care setting include the following:

- Supportive Counselling
- Interpersonal therapy
- Cognitive-Behaviour Therapy (CBT)
- Behavioural Therapy (BT)
- Other psychological therapies e.g. psychodynamic therapy

Supportive Counselling and Psycho-education

Supportive counseling focuses on helping the individual explore any problems they may have and to develop was to resolve them.

Interpersonal therapy

As its name suggests, interpersonal therapy focus on interpersonal relationships and explore links between depressed mood and a severe life crisis (e.g., marital strife, job loss, or loss of a loved one, interpersonal relationships with significant others, and long term difficulties in forming and maintaining relationships).[7,8,5] Interpersonal therapy helps generate new skills for asserting personal needs and engaging more constructively, even confrontationally, with significant others at work and at home.[5]

Cognitive Behaviour Therapy (CBT)

CBT is perhaps one of the psychological interventions with the biggest evidence base. CBT is a form of psychological therapy, conceptualised by pioneers such as Aaron Beck and Albert Ellis, which has been in use since the 1950s. It is based on the concept that how we think, feel and act are inter-related.

For example, a student who has failed an examination may think, "I am stupid and useless and will never amount to anything". This thought makes disempowers him and makes him feel depressed and dejected. Because he feels this way, he acts by avoiding future examinations, and eventually drops out of school, which reinforces his notion that he is indeed stupid and useless.

The goal of CBT is to break this sort of self-fulfilling prophecy. CBT is particularly applicable in cases of depression, because there often are a lot of automatic negative thoughts that can trigger dysfunctional feelings and actions. It is usually conducted over 8 – 12 hourly sessions, and the patient needs to be able to commit to regular attendance, active participation and homework assignments. The therapist will help the patient to identify their negative thoughts and replace them with more flexible and salutary cognitions. By adopting a more positive way of thinking, the patient will be better equipped, in the long term, to cope with problems in daily life. In the primary care setting, the number of sessions may be reduced to six and are called brief psychological therapy[4]. Studies suggest that a combination of CBT and medication is the most effective treatment for depression in the long-term.[2]

Behavioural Therapy (BT)

Behavioural interventions include contextual approaches based on functional analyses (contingency management and behavioural activation, social skills training, self control therapy, and problem solving therapy (PST), and behavioural marital therapy (BMT).[8]

Other psychological therapies

Although short-term psychodynamic and emotion-focussed psychotherapies may also be efficacious in treating major depressive disorfer, less evidence supports these strategies for the treatment of depressed patients.[8,2] In psychodynamic therapy, the approach is to bring repressed thoughts and feelings into consciousness and to develop new ways of tolerating and coping with the emotional pain.[7]

PHARMACOTHERAPY

The mainstay of pharmacotherapy for depression are the antidepressants. These are effective in both anxiety and depression. In terms of efficacy, all the various anti-depressants are actually equal or close to equal at about 60-70%. They vary more in terms of their side-effect profiles, drug interactions and time to onset of action.[9] Most anti-depressants would take on the average 2-4 weeks to take effect and this should be explained to the patient at the onset, some patients may start to feel changes as early as after the first week. It may however take 8-12 weeks for the full effect of the medication to be felt.

The short term side effects usually also subside after this time, so it may be helpful to tell the patient about these so they know what to expect. I have found compliance to be better when the patient is educated about this beforehand. Of course it may not be necessary to explain every single side effects but the more commonly experienced ones should be dealt with so that the patient is able to anticipate these should they arise.

Commonly Used Classes of Antidepressants

The common examples of the commonly used classes of antidipressants, actions and precaustions are summarized in Table 1.

Table1. Classes of anti depressants

Class	Examples	Action	Precautions
Tricyclic antidepressants	Amitriptyline, Imipramine, Clomipramine, Nortryptyline, Dothiepin	Inhibit serotonin & NE uptake; anticholinergic-antimuscuranic; alpha1-adrenergic antagonist; anithistamine	Anticholinergic effects, postural hypotension, confusion, weight gain, CVS effects, toxicity in overdose
MAOIs	Phenelzine, Tranylcypromine	MAO inhibition causes NE accumulation	Postural hypotension, dietary restrictions, drug interactions, sexual dysfunction
SSRIs	Fluoxetine, Fluvoxamine, Paroxetine, Citalopram, Escitalopram Sertraline	Selectively inhibits 5HT reuptake	Agitation, akathisia, anxiety, insomnia, sexual dysfunction, GI effects, withdrawal effects
SNRI	Venlafaxine, Duloxetine	Inhibits 5HT and NE reuptake	Same as SSRIs (low doses), hypertension, insomnia, agitation, headache (high doses)
NaSSA	Mirtazapine	Alpha2, 5HT1, 5HT2, H1 antagonism → Enhances NE & 5HT neurotransmission	H1 antagonism – sedation, weight gain
NDRI	Bupropion	NE and Dopamine reuptake inhibitor	Stimulation, agitation, nausea, insomnia, seizures (4/1000)

(1) Selective serotonin reuptake inhibitors (SSRIs)

Selective serotonin reuptake inhibitors (SSRIs) are a family of antidepressants considered to be the current standard of drug treatment. SSRIs are said to work by preventing the reuptake of serotonin (5HT) by the presynaptic nerve, thus maintaining higher levels of 5-HT in the synapse.

(2) Serotonin-norepinephrine reuptake inhibitors (SNRIs)

Serotonin-norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine (Effexor) and duloxetine (Cymbalta) are a newer form of antidepressant that works on both norepinephrine and 5-HT. The dual action of these drugs may ake them more activating and may also be helpful in helping patients who may be suffering from chronic pain[10].

(3) Noradrenergic and specific serotonergic antidepressants (NASSAs)

Noradrenergic and specific serotonergic antidepressants (NASSAs) form a newer class of antidepressants which purportedly work to increase norepinephrine (noradrenaline) and serotonin neurotransmission by blocking presynaptic alpha-2 adrenergic receptors while at the same time minimising serotonin related side-effects by blocking certain serotonin receptors. The only example of this class in clinical use is mirtazapine (Remeron).

(4) Norepinephrine-dopamine reuptake inhibitors

Norepinephrine-dopamine reuptake inhibitors such as bupropion (Wellbutrin, Zyban) inhibit the neuronal reuptake of dopamine and norepinephrine (noradrenaline).

(5) Tricyclic antidepressants (TCAs)

Tricyclic antidepressants are the oldest and include such medications as amitriptyline and dothiepin. Tricyclics block the reuptake of certain neurotransmitters such as norepinephrine (noradrenaline) and serotonin.

(6) Useful information about other classes of antidepressants

Venlaflaxine (Effexor), Duloxetine (Cymbalta) and Mirtazepine (Remeron) also target the Noradrenaline system. Mirtazepine does not have sexual dysfunction as one of its side effects and is helpful for patients who experience this with the other drugs. There is however prominent sedation as well as weight-gain, which should be explained to the patient so they may watch their diets. These effects are mainly brought about by the anti-histamine properties of this agent.

Bupropion (Wellbutrin) can be more agitating, especially in patients with co-occurring anxiety, but is helpful for patients with problems of poor drive and motivation arising from the depression. It has also been marketed as Zyban for smoking cessation.

(7) Newer antidepressants that have entered the market

Desvenlafaxine (Pristiq) is a newer anti-depressant which also belongs in the SNRI group of medications. It is the major active metabolite of venlafaxine. Aglomelatine (Valdoxan) is a novel anti-depressant in that it targets both serotonin and melatonin receptors. It has a significantly lower incidence of both sexual dysfunction and weight gain and may be helpful in restoring sleep architecture.[11]

More details on the SSRIs and TCAs

The SSRI's are the most commonly used as well as the tricyclic antidepressants as they have been around the longest and are still rather commonly used.

Selective Serotonin re-uptake inhibitors (SSRI)

SSRIs are recognised as first-line medication for the treatment of depression. They work by increasing the amount of postsynaptic serotonin in the brain. They are generally preferred over tricyclic antidepressants because they are equally effective, but have fewer or more tolerable side effects, and are much less lethal in cases of overdose.

Although all the SSRIs are functionally similar, they are structurally diverse. This is the reason why a patient may respond better to one SSRI than another. Individual SSRIs also have slightly different benefits and effects. For example, fluoxetine has an energising effect and is good for patients who feel lethargic, while fluvoxamine is more sedating and is better for patients who have difficulty falling asleep. Escitalopram is favoured for patients who are already on more complicated drug regimes due to other medical conditions, because it causes few drug-drug interactions.

Some patients may have unrealistic expectations of antidepressants, and may quickly become non-compliant when these expectations are not met. In order to prevent this, it is a good idea to inform them that:

- It may take two to four weeks before their mood improves palpably
- They may experience side effects, such as initial nervousness, sedation, abdominal discomfort, nausea and sexual dysfunction but these are usually transient even if they occur.
- They should not abruptly stop their medication, because this causes risk of discontinuation syndrome. This may present as fatigue, irritability, worsening of depression, headache, dry mouth, tremor and paraesthesia

Table 2. The SSRIs

Generic name	Trade name(s)	Starting dose	Dose (mg day)
Fluoxetine	Prozac, Magrilan	10-20	20-60
Fluvoxamine	Faverin, Luvox	25-50	50-300
Escitalopram	Lexapro	5-10	10-20
Sertraline	Zoloft	25-50	50-200
Paroxetine	Seroxat, Paxil	12.5-25	25-75

Tricyclic Antidepressants (TCAs)

TCAs are an older class of antidepressants. Compared to SSRIs, they have greater effect on adrenergic, muscarinic, histaminergic and dopaminergic receptors. Although they are as effective as SSRIs, they cause more side effects, such as sedation, dry mouth and urine retention. They have a narrow therapeutic index, and may cause death by cardio- and neurotoxicity in overdose.

In spite of this, TCAs are sometimes very effective for patients who have treatment-resistant depression, neuropathic pain or insomnia. Examples of commonly-used ones are amitriptyline, dothiepin and imipramine.

Phases of treatment: response, remission and duration of treatment

The management of the patient with MDD can be framed in the context of 3 phases:

Acute phase. The acute phase of treatment is focused on the acutely depressed patient. Patients should be given an adequate course of treatment. In cases of treatment failure (that is, no response after 4-8 weeks of treatment), raising antidepressant doses to the optimal tolerable level should be considered before switching to another drug. For partial responders, combination of antidepressant medications can be considered before switching medications. The psychiatrist colleague may need to be consulted. ECT may be needed for severe depression, presence of psychotic features or catatonia.

Remission phase. Once the symptoms are in remission, it is generally recommended that the patient be kept on treatment for another 6 months to a year for the first episode. Remember that the dose that gets them well is also the dose that keeps them well and drug doses should not be tapered till the end of the treatment period.

The maintenance phase. Patients with a second episode should be treated for a year to two, and patients with more recurrent episodes or very severe episodes of depression should be put on long-term treatment.

REFERRAL TO THE PSYCHIATRIST

There are cases in which referral to a psychiatrist is indicated. This is particularly so for patients who are suicidal or homicidal, or who are so severely ill that they have become psychotic (having hallucinations or odd beliefs) or stuporous (refusing to talk, eat or drink). These patients require urgent psychiatric treatment.

Some patients may be suffering from other psychiatric conditions that will necessitate more intensive treatment. Common conditions include anxiety disorders, mania, drug misuse, eating disorders and dementia.

Other patients may be treatment-resistant or belong to a special group (e.g. pregnant, pediatric or geriatric patients). It is likely that these patients will also require specialist care, but they may be referred on a non-urgent basis to a psychiatric clinic if there is no immediate threat to safety.

A summary of situations when referral is recommended are:

- Suicide risk is present
- Need for hospitalisation
- Failure of adequate medication trial
- Complicated medical or psychiatric morbidity including antepartum or postpartum depression
- Need for combined medication & psychotherapy
- Evaluation for pharmacotherapy
- Need for ECT.

CONCLUSIONS

Depressive disorders are common. Many can be treated in the GP setting. A strategy of establishing a therapeutic relationship, psychoeducation, and the consideration of the 4 options of watchful waiting, psychotherapy, pharmacotherapy, and referral to the psychiatrist provides a framework of caring for this group of patients in primary care.

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LEARNING POINTS

- **Depressive disorders are common.**
- **Many patients with depressive disorder can be treated in the GP setting.**
- **A combined approach of establishing a therapeutic relationship, psycho-education, and appropriate use of psychotropic medications give the best results.**
- **Know the indications for referral to a psychiatrist.**