

ABSTRACT

Bipolar disorder is a chronic relapsing and remitting disorder. Poorly controlled bipolar disorder results in increased morbidity with a poorer quality of life. There is increased suicide risk. Long-term treatment and support are required to minimise the risk of recurrence and optimise quality of life, and social and personal functioning. The core features of bipolar disorder – its recurrent and cyclic nature – can make it a challenging illness to manage. Whilst medications do play a large role in the management, pharmacologic treatment is further complicated by the risk of inducing opposite or polar changes in mood state. Psychosocial interventions should not be neglected.

Keywords: Bipolar disorder, Management, Mood stabilizers, Antidepressants, Psychological intervention

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INTRODUCTION

Bipolar is a complex disorder. The core features of bipolar disorder -- its recurrent and cyclic nature -- can make it a challenging illness to manage. Pharmacologic treatment is further complicated by the risk of inducing opposite or polar changes in mood state.

Nonetheless, it can be very fulfilling to treat in a primary care setting as stable patients can have a very good quality of life.

The benefits of treatment by a primary care physician are multifold. Treatment is easily available, there is less stigmatization and there is a chance for good rapport with the physician that not only improves compliance but allows for early relapse warning.

PHARMACOLOGICAL THERAPIES

The drug treatment of an acute manic or hypomanic episode depends on the severity of symptoms. Acute manic and mixed episodes of sufficient severity can constitute medical emergencies requiring hospitalization to ensure safety and enhance rapid recovery.

In the initial management of acute behavioural disturbance or agitation, the short-term use of a benzodiazepine (such as lorazepam) should be considered as an adjunct to the treatment.

If a patient develops acute mania, treatment options include starting an antipsychotic and/or mood stabilisers such as valproate or lithium. Options include:

- prescribing an antipsychotic if there are severe manic symptoms or marked behavioural disturbance as part of the syndrome of mania.
- prescribing mood stabilisers (Lithium, Valproate, lamotrigine or carbamazepine).
- Or a combination for more complex cases.

Bipolar depression is associated with the same substantial risks of morbidity and mortality as major depressive disorder. Pharmacologic agents with mood-stabilizing properties form the foundation of treatment of this illness, but psychotherapy can be helpful.

Managing depressive symptoms in bipolar disorder has some similarities to managing unipolar depression. However, in bipolar disorder antidepressants carry the risk of 'switching' or inducing a manic episode. There is therefore only a limited role for maintenance treatment with antidepressants in bipolar depression.

Patients with bipolar disorder typically experience more fluctuations in both the severity and duration of symptoms than people with unipolar depression, this result in higher morbidity.

When initiating antidepressant treatment for a patient who is not on a mood stabiliser, prescribers should explain the risks of switching to mania. Antidepressant treatment should begin at a low dose and be increased gradually if necessary. Furthermore, such treatment should be given for the minimum duration required to achieve a stable, normal mood state.

ELECTROCONVULSIVE THERAPY (ECT)

Electroconvulsive therapy (ECT) is recommended only to achieve rapid and short-term improvement of severe symptoms after an adequate trial of other treatment options has proven ineffective and/or when the condition is considered to be potentially life-threatening, in individuals with:

- severe depressive illness.
- catatonia.
- a prolonged or severe manic episode.

AGITATED BEHAVIOUR

The management of disturbed behaviour in bipolar disorder should start with psychosocial and environmental interventions aiming to de-escalate any potential violent situations.

Severe behavioural disturbance in people with bipolar disorder should normally be treated first with oral medication,

such as lorazepam or an antipsychotic, or a combination of an antipsychotic and a benzodiazepine. Intramuscular medications may be required in severe cases. An urgent referral to a psychiatrist or hospital is necessary.

MAINTENANCE PHASE

Bipolar disorder is a chronic relapsing and remitting disorder. Studies have shown that poorly controlled bipolar disorder results in increased morbidity with a poorer quality of life. There is increased suicide risk. Long-term treatment and support are required to minimise the risk of recurrence and optimise quality of life, and social and personal functioning. The primary long-term treatments are pharmacological (mood stabilisers), but psychosocial interventions do have an important role to play.

MOOD STABILIZERS

Antiepileptics (sodium valproate, lamotrigine and carbamazepine)

Antiepileptics (sodium valproate, lamotrigine and carbamazepine), are used as mood stabilisers in the treatment of bipolar disorder. However, it has been reported by the US FDA that patients taking antiepileptic drugs have about twice the risk of suicidal thoughts and behaviours (0.43%) compared with patients receiving placebo (0.22%). Even though this is still a small risk, it is recommended by the FDA that clinicians explain the benefits and risks of antiepileptic use.

Sodium Valproate

Sodium valproate has been found to be superior to placebo in the treatment of acute mania in two randomised controlled trials and in a systematic review. There is no difference in efficacy among sodium valproate, lithium and carbamazepine in the treatment of acute mania.

A Cochrane systematic review of valproate showed no significant difference in preventing relapse as compared to lithium.

Its benefit at prevention of depressive episodes is marginal as well.

Carbamazepine

Two randomized controlled trials have found carbamazepine to be more effective than placebo in the treatment of acute mania. However, the use of carbamazepine should be balanced with its potential side effects.

Lamotrigine

A systematic review showed that lamotrigine significantly reduced depressive relapses. A randomised controlled trial with bipolar I patients found that after stabilization, continuation

with lamotrigine delayed the onset of the next depressive episode. Unfortunately, there is little evidence that it helps with manic relapses.

Lithium

Although lithium salts have been in use for various conditions since the 1800s, the use of lithium in the treatment of bipolar disorder was discovered in 1949. However, the United States Food and Drug Administration (FDA) only approved it for the treatment of mania in 1970. Lithium has been found to be superior to placebo in the treatment of acute mania in a meta-analysis of 12 trials. In this study, it was also found to be superior to chlorpromazine.

Three systematic reviews indicated that lithium therapy is effective at reducing relapse in patients with bipolar disorder. The effect of lithium is greater for prevention of manic and hypomanic episodes and marginal with respect to depressive episodes. Lithium is associated with an increased risk of manic relapse on discontinuation after less than 2 years on treatment.

ANTIDEPRESSANTS

Studies have shown that antidepressants offer minimal to no significant continuing clinical benefits to patients who have had 8-week post bipolar depressive episode remission. There are no robust effects on depressive episode prevention or enhanced remission rates with continued antidepressant use.

However, abrupt or rapid discontinuation or clinically effective antidepressant treatment was associated with a significantly shorter time to first new episode of major depression.

Selective serotonin reuptake inhibitors (SSRIs) have been associated with less "switching" compared with other antidepressants.

Hence, antidepressants should be used cautiously in patients with bipolar disorder and for the shortest period possible.

ANTIPSYCHOTICS

Antipsychotic drugs include typical antipsychotics, such as haloperidol, as well as atypical antipsychotics, such as olanzapine and quetiapine. As their name suggests, they are used in the treatment of psychosis. However, they have other indications as well.

Unfortunately, they may have side effects. Typical antipsychotics, such as haloperidol, are associated with extra-pyramidal side effects. Atypical antipsychotics, such as olanzapine, are associated with weight gain, hyperglycaemia and hypercholesterolemia.

Haloperidol, olanzapine and quetiapine were found to be effective in reducing agitation and aggression as shown in randomised controlled trials.

Recent randomised controlled trials have showed that olanzapine is effective at preventing relapse. Another trial showed that aripiprazole is effective as maintenance therapy in bipolar patients with recent manic or mixed episode. A randomised controlled trial also showed that quetiapine in combination with lithium or valproate is effective at preventing relapse in patients with bipolar I disorder.

BENZODIAZEPINES

Benzodiazepines are useful in treating anxiety, insomnia, agitation, seizures, muscle spasms and alcohol withdrawal. They are also useful in preparation for medical and dental procedures. Long-term use is discouraged due to possible adverse psychological and physical effects, including tolerance, physical dependence and withdrawal symptoms upon cessation of use.

In a meta-analysis, clonazepam and lorazepam, in both oral and intramuscular forms, have been shown to be effective in the acute treatment of agitation in mania. Advice should be given to the patient and caregivers with regards to its risk of tolerance as well as its role as a short-term acute treatment.

PSYCHOLOGICAL THERAPIES

Psychological interventions can help to improve the condition of a patient with bipolar disorder and the course of the illness, and maintain psychosocial functioning. In the studies evaluating the use of psychological interventions in patients with bipolar disorder, the majority has to do with treatment during the depressive episodes and as part of the maintenance treatments. Due to the nature of a patient in a manic phase, it is difficult to do psychological intervention during such times.

The aim of psychoeducational interventions is to provide patients (and sometimes family members and/or caregivers) with information about their illness and its treatment.

Psychological intervention should include training in recognizing early warning signs of relapse of depression or mania, in order to prevent recurrence of illness. Such early warning signs of depression or mania are often different for different people, suggesting that individuals have distinctive "relapse signatures".

Nevertheless, some common mania prodromes include:

- being more sociable.
- increased self-worth.
- racing thoughts.
- increased optimism.
- irritability.
- increased activities.
- decreased need for sleep.
- senses sharper.

Common depression prodromes include:

- loss of interest in activities or people.
- not being able to put worries aside.
- feeling sad.
- wanting to cry.
- interrupted sleep.

There is evidence for the effectiveness of the following forms of psychotherapy for bipolar depression:

- Family-focused therapy.
- Interpersonal and social rhythm therapy.
- Cognitive behaviour therapy.

Interpersonal social rhythms therapy was designed specifically for treating individuals with bipolar disorder. This approach evolved from Interpersonal Therapy (IPT). As with IPT, treatment focuses on four interpersonal problem areas (grief, interpersonal role transition, role dispute and interpersonal deficits). Issues in these areas are addressed by various strategies, which include eliciting and defining the salient problem area, followed by supported grieving/emotional processing and problem solving.

In addition to these traditional aspects of interpersonal therapy, interpersonal social rhythms therapy focuses on the regularity of daily activities. It prioritises the maintenance of structure and routine in these daily activities in spite of fluctuations in mood, for example those caused by life events.

Cognitive behavioural therapy aims to change dysfunctional cognitive styles and behaviour in order to improve emotional states.

Cognitive behavioural therapy focuses on helping patients detect early warning signs of depression and mania, and using cognitive behavioural strategies to improve mood when low, and reduce highs when manic.

As effective family functioning can maintain a person's psychological balance, family interventions may help relatives and caregivers to care for and support patients with bipolar disorder. Family therapy can include very different kinds of interventions from diverse theoretical backgrounds.

CONCLUSIONS

Bipolar disorder is a complex mental disorder requiring a holistic approach to treatment. Whilst medications do play a large role in the management, psychosocial interventions should not be neglected.

REFERENCES FOR FURTHER READING

1. MOH. CPG on Bipolar Disorder. MOH: Singapore 2011
2. MOH. Chronic Disease Management Programme: Dementia and Bipolar Disorder. Handbook for Healthcare Professionals. MOH: Singapore, 2011.

LEARNING POINTS

- **Bipolar disorder is a chronic relapsing and remitting disorder and poorly controlled bipolar disorder results in increased morbidity and increased suicide risk.**
 - **Long-term treatment and support are required to minimise the risk of recurrence and optimise quality of life, and social and personal functioning.**
 - **In the initial management of acute behavioural disturbance or agitation, the short-term use of a benzodiazepine (such as lorazepam) should be considered as an adjunct to the treatment.**
 - **If a patient develops acute mania, treatment options include starting an antipsychotic and/or mood stabilisers such as valproate or lithium.**
 - **Managing depressive symptoms in bipolar disorder has some similarities to managing unipolar depression but in bipolar disorder, antidepressants carry the risk of ‘switching’ or inducing a manic episode.**
 - **Electroconvulsive therapy (ECT) is recommended only to achieve rapid and short-term improvement of severe symptoms after an adequate trial of other treatment options has proven ineffective and/or when the condition is considered to be potentially life-threatening.**
 - **The management of disturbed behaviour in bipolar disorder should start with psychosocial and environmental interventions aiming to de-escalate any potential violent situations and an urgent referral to a psychiatrist or hospital is necessary.**
 - **The primary long-term treatments are pharmacological (mood stabilisers) and antiepileptics (sodium valproate, lamotrigine and carbamazepine) , are used as mood stabilisers in the treatment of bipolar disorder.**
 - **Antipsychotic drugs include typical antipsychotics, such as haloperidol, as well as atypical antipsychotics, such as olanzapine and quetiapine.**
 - **Psychological interventions can help to improve the condition of a patient with bipolar disorder and the course of the illness, and maintain psychosocial functioning.**
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