

MANIC DEPRESSIVE DISORDER

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Case Report



Javed, a 22 year old boy was brought to the hospital by his relatives as they noticed a change in his behaviour. According to them he was fine till about 15 days back when he started getting up early in the morning at around 5.00 a.m. He would also wake up the other members of his family and ask them to exercise. He would declare that he was feeling very energetic and was soon going to acquire some special powers by which he would be able to change the world. He would often go out for jogging and would run for about 2-3 hours. On the way he would gather a crowd of people and would start preaching them about religion. On his return he would demand heavy breakfast, a glass of milk, a glass of fruit juice and 5-6 bananas. He stopped going to his college as he thought that it was a mediocre task and he was blessed to do some extraordinary divine work.

He would repeatedly announce that he was feeling very happy and would start singing and dancing. He would prefer to talk in English rather than Hindi, his mother tongue, and coin funny new rhyming words which would make everyone laugh. Soon he started distributing household utensils and money to known as well as unknown people and if reprimanded or restrained would get angry and violent.

In view of his unusual behaviour, he was taken to their religious leader who directed them for a psychiatric consultation.

After hospitalization, in the ward, every morning he would greet all the doctors with a loud and cheerful 'good morning'. He would help the ward-boys and nursing staff in patient care and entertain patients with his witty talks, jokes and songs. He was the center of attention and the life of the ward. He was diagnosed to have a manic episode and was started on sodium valproate (500 mg) at bed-time, which was increased to 1000 mg in two divided doses after 2 days. He was also prescribed lorazepam (2 mg) at bed-time.

A gradual improvement was observed after about 8-10 days when he would feel embarrassed if he was asked to sing or when his jokes were repeated to him. He was discharged after 3 weeks and was asked to continue the medication for 6-8 months and maintain a regular follow up.

MANIC DEPRESSIVE DISORDER

Manic depressive disorder, as the name suggests, is a psychiatric disorder in which patients get recurrent episodes of mania and depression at an interval of few years to few months. The manic episodes are characterized by happy, euphoric, irritable or elated mood and increased psychomotor activity (psychomotor excitation) while the depressive episodes are characterized by sad or gloomy mood and decreased psychomotor activity (psychomotor retardation) or agitation.

It is also known as manic depressive psychosis, as patient often loses touch with reality during these episodes or bipolar mood disorder as mania and depression are considered as two polarities of disturbances in mood.

When patients get recurrent episodes of only depression, it is known as 'recurrent depression'. But interestingly when patients get recurrent episodes of only mania or even hypomania (less severe form of mania), it is still considered as bipolar mood disorder or manic depressive disorder though it should rather be called as 'recurrent mania'.

EPIDEMIOLOGY

About 1 in 100 individuals, irrespective of their gender, (male or female), have a risk of developing this disorder in their life time. Though in rare instances, the onset of the first episode of mania or depression has been reported during childhood, at the age of around 5-6 years or at the other extreme during the old age, in majority, the first episode occurs between the age of 20 to 40 years.

ETIOLOGY AND PATHOPHYSIOLOGY

There are a large number of studies implicating genetic factors, different neuroanatomical sites, neuroendocrine regulatory system, biogenic amines, psychodynamic factors and psychosocial factors in the understanding of etiology and pathophysiology of manic depressive disorder. But the overall picture is yet not very clear.

It seems that there may be genetic predisposition for the development of this disorder. Based on the therapeutic response to a various psychotropic agents, it seems that there might be an increase in the activity of noradrenergic and dopaminergic neurotransmitter systems during the manic episode; while decreased activity of the noradrenergic and serotonergic system may be associated with depression. Some of the recent studies have also indicated a decrease in GABA neurotransmitter system in mania as well as depression.

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CLINICAL FEATURES

MANIC OR HYPOMANIC EPISODE

The clinical features of manic and hypomanic episode are by and large the same but differ in severity. Unlike manic episodes, in hypomanic episodes the disturbances are not severe enough to cause impairment in social and occupational functioning and generally do not necessitate hospitalization.

Euphoria and Elation

Patients feel very happy. They exhibit good humour which is infectious in nature. They may express their happiness by singing popular hit numbers and dancing. A 70 year old patient was singing 'Tu chiz badi hai mast mast...' a hit Hindi film song, during his manic episode. During the episode he may be generally jovial and cheerful but when he is stopped from doing certain activity or is provoked he may become irritable, angry, abusive and violent. Another clinical manifestation of this euphoria is the over familiarity which many of the patients have during the manic episode. Sometimes the mood during the manic episode may be more irritable than euphoric (disphoric mania) due to which they make themselves a source of nuisance and annoyance.

Inflated self-esteem and grandiosity

He may appear to have an air of confidence. He may feel that he is very rich and famous. He may also think that he is blessed with some supernatural powers and can communicate with God. Many of the patients try to talk in English and put on expensive, fancy colorful clothes, ornaments and goggles, as these are supposed to be the symbols of higher status. Similarly they claim to have close contacts with famous people like the Prime Minister, Chief Minister or some famous film stars.

Increased energy and activity

Increased energy and activity may be creative and productive in hypomanic state. Many famous personalities had some of the most creative and productive years of their life during their hypomanic episodes. Theodore Roosevelt, during these episodes, worked very hard, for days together, talking, telephoning and writing thousands of letters! Similarly Robert Schumann gave the world his best musical pieces and Ernest Hemingway wrote extensive lectures during such periods.

The same increased energy and activity during manic episode no longer remains goal directed and so becomes non-productive. George-III of England, popularly called as the 'mad monarch' bolted his food and rode his horse to death during his manic episode. Some of the patients may make big business plans and borrow or invest a big amount during their manic episode and end up with heavy losses. Many patients get involved in excessive religious activities. Visiting temples, planning a pilgrimage, giving sermons and preaching about God and religion become their daily chores.

Pressure of speech and flight of ideas

A patient in a manic episode can be easily identified due to his peculiar way of talking. He starts talking spontaneously, even before any questions are asked to him. Once he starts, he keeps on talking and it is very difficult to interrupt him. He has lots of thoughts in his mind about which he wants to talk and he jumps from one topic to another. When asked about his morning breakfast a patient in his manic phase said "I had only bread; No butter; It is so expensive; Only politicians can afford it; They are responsible for the poverty; I will contest the next election and bring the reforms...." He may use rhyming words and poetic manners. One of the patients used to say "I am fine; I have no time; Let the sun shine; But I'll have my wine at nine".

Changes in Sleep, Appetite and Sexual Activities

Patients during their manic episodes have decreased need for sleep. These patients may sleep only for an hour or two. In spite of doing lots of activities throughout the day, they don't seem to get tired, fatigued or require rest.

They may develop a voracious appetite. The warning signal for one of the patients was an increase in her appetite which would herald the onset of the manic episode. The relatives would bring her to hospital as soon as she started demanding lots of fruits. She would eat a dozen bananas, few apples and other available fruits, at a time.

Increased sexual activities are frequently noticed in these patients. It may manifest in the form of eve teasing, promiscuous behavior, demanding more frequent sexual relations at odd times and places from the spouse, visiting commercial sex workers or putting up marriage proposals to any familiar or unfamiliar individuals.

Distributing and spending sprees

In a range of mania, it is not uncommon for the patients to distribute house hold articles, food, clothes and money. Frequently they also go on spending sprees. A patient during his manic phase purchased a couple of gold chains, bracelets, wrist watches and gifted some of these items to his friends. A lady was famous in her neighbourhood, as during her manic phases she would buy lots of vegetables and grocery items and distribute it to the poor people. The poor people in the neighbourhood would eagerly wait for her manic episodes.

Delusions and hallucinations

Apart from delusion of grandiosity, occasionally patients may harbour persecutory delusions which are secondary in nature. They may feel that because they are very rich some enemies may try to rob them of their wealth.

Hallucinations are uncommon during manic episodes but once in a while, the patient may claim that he can communicate with God and can hear God's voice.

DEPRESSIVE EPISODE**Sadness, Apathy and Lethargy**

Pervasive sadness of mood is the hallmark of depressive episode. Patient just doesn't feel good even in the best of environment. It is qualitatively different from the feelings of unhappiness which one has after some unpleasant incident. It is associated with apathy and lethargy. They prefer to stay alone and there might be frequent crying spells either without any reason or over very trivial matters. Some patients may have more agitation and restlessness rather than classical sadness of mood

Loss of self esteem and confidence.

A bank officer refused promotion during one of his depressive episode as he thought that he would not be able to cope up with higher responsibilities. Along with loss of confidence, they also have difficulty in taking decision and as a result may continue to postpone the work.

Diminished interest and concentration

Patients don't feel like doing anything and they have to literally force themselves even to complete the daily routine. They do not enjoy activities they once enjoyed, any more, and so avoid participating in such activities. Quite often they complain of difficulty in concentration, forgetfulness and as a result make frequent mistakes in their work.

Hopelessness, Worthlessness, Helplessness and Suicidal ideation

Along with sadness of mood and other associated symptoms patients may start feeling that life is not worth living. He may see the situation as hopeless and may feel helpless to deal with it. Suicidal ideations are very common during depressive episodes and if not dealt with, in time, patient may attempt suicide.

Poverty of ideas and preoccupation with somatic symptoms

Like manic patients, even depressed patients have a typical manner of interacting. They speak in a very low and monotonous voice and prefer to answer in one or two words as far as possible. They may

complain that their mind is blank.

Psychomotor retardation and easy fatiguability

All the activities of a depressed patient go at a very slow pace. He may take more time than usual in taking bath, eating food or in completing a given task. He also gets tired and fatigued easily.

Sleep, Appetite and Sexual activities.

Insomnia and loss of appetite is reported almost by all the patients during their depressive episode though some patients may have hypersomnia and increased appetite. Patients wake up from sleep during the early hours of the day at around 4.00 a.m. or 5.00 a.m., but they just don't feel like getting out of bed. They don't feel fresh and energetic on waking. They may remain in bed just lying down for a couple of hours or wake up other members of the family when they are agitated. Along with loss of appetite some of the patients also complain that they do not relish good food during depressive phase. If the depression continues untreated for some length of time, patients may have substantial weight loss or rarely, weight gain, if there is an increase in appetite. Similarly they don't enjoy indulgence in sexual activities and frequency of such relationships markedly decreases. Some patients also complain of loss of erection or only partial erection.

Delusions and hallucinations

A 40 year old female attempted suicide as she felt that she had committed a great sin when she was 20 years old by refusing to visit the temple with her family members - a delusion of guilt. In rare cases, one may come across a depressed patient who has a delusion of poverty or nihilistic delusions. A 50 year old patient would not allow anyone to switch on lights or fans in the house, would insist on preparing only one item for lunch and dinner and would get angry if anything was bought for the house as he had developed a delusion of poverty.

In severe depression, patients may hear intermittent voices passing indecent comments about them and asking them to put an end to their lives.

COURSE

Manic depressive disorder is more identified by its longitudinal course than by the individual episodes.

As mentioned earlier, an individual may get his first episode between the age of 20 to 40 years. It may be an episode of mania or depression. The second episode may occur after 6-8 years. Gradually, as the disorder progresses, the interval between the two episodes decreases while severity and duration of each episode increases. Some patients may get mixed symptoms of mania and depression during the episode. When patients get four or more episodes in a year, it is considered as "rapid cycling". About 15 of patients develop rapid cycling. When the patient gets very frequent mood changes over a period of few days or even over a period of few hours in a day, it is called as "ultra-rapid cycling" and "ultradian mood alternations".

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The requisite for the diagnosis of manic depressive disorder is the episodes of mania. During the first episode of mania one may have to keep in mind the differential diagnosis of acute psychotic episode or brief psychotic episode or schizophrenia. The longitudinal course of recurrent episodes of mania and/or depression at an interval of couple of years with more or less complete recovery between the episodes, will confirm the diagnosis of manic depressive disorder. Recurrent episodes of schizophrenia with some manic or depressive symptoms and episodes of schizoaffective disorder may be difficult to differentiate from manic depressive disorder.

Manic or depressive symptoms may be transiently seen in patients receiving certain drugs like steroids, contraceptive pills, anti-hypertensives etc. These symptoms are expected to remit once these drugs are discontinued.

Patients having organic mental disorders like neurosyphilis, cerebrovascular accident, space occupying lesion, dementia and hypothyroidism may also present with manic or depressive symptoms. In these conditions, other associated symptoms like memory impairment, and neurological deficits may help us to differentiate them from manic depressive disorders.

PHARMACOTHERAPY OF MANIC EPISODE

Lithium, Carbamazepine and Valproate

In the management of manic or hypomanic episode, lithium, carbamazepine or valproate can be used. As the therapeutic effect of these medicines is delayed by 8-10 days, most of the patients require either additional benzodiazepine or combination of lithium with carbamazepine or valproate, or an additional antipsychotic for the rapid control of symptoms.

It may be preferable to start lithium carbonate in the dose of 300 mg three times a day after two days in order to avoid nausea, vomiting or diarrhoea associated with high dose of lithium. Most of the adult patients (weight around 45-60 kg) require about 900 to 1200 mg of lithium per day in divided doses (i.e. about 20 mg/kg body weight). One may prefer to use a sustained release or controlled release preparation of lithium in order to reduce the gastrointestinal side effects and reduce the frequency of administration to once or twice a day.

In patients who do not tolerate lithium or in whom lithium is contraindicated due to some renal or cardiac problem, carbamazepine or valproate may be used. Similarly in a patient getting frequent episodes (4 or more per year rapid cycling) or those who have dysphoric mania, valproate may be preferable to lithium.

Carbamazepine may be started in the dose of 200 mg at bed time and gradually increased by 200 mg on alternate days to 600-1200 mg/day in divided doses. Controlled release and retard preparations are available, and may be preferable.

Sodium valproate may be started with 200-500 mg at bed time and increased to 1200-1500 mg/day. In severe cases a loading dose of 1000-1500 mg/day may be used on the very first day. Like lithium and carbamazepine, valproate is also available in a controlled release form. Valproate should be used with caution in patients with liver disease. When combined with antipsychotics it can result in increased sedation and severe extrapyramidal reaction. In some cases one may have to use a combination of lithium and carbamazepine or lithium and valproate.

After the remission of manic episode, the treatment may be discontinued after 6-8 months if the patient does not require maintenance therapy.

Antipsychotics and Benzodiazepines

As mentioned earlier, for rapid symptomatic control, along with these drugs one may have to add antipsychotics like haloperidol or chlorpromazine and/or benzodiazepines like clonazepam or lorazepam.

Some clinicians also use clozapine, due to its heavy sedative action, for control of manic episode. Clozapine should not be used along with carbamazepine as they both are known to cause agranulocytosis.

The addition of neuroleptics is not very much preferred by some clinicians as it carries an extra risk for adverse effects like extrapyramidal reactions, tardive dyskinesia and neuroleptic malignant syndrome.

Electroconvulsive Therapy

ECT may be used as a quick and effective treatment for the moderate to severe manic episode. While the patient is receiving ECT, it may be preferable to either discontinue or reduce the dose of these mood stabilizers. Valproate and carbamazepine increase the seizure threshold and thus the patient may not get seizure when administered ECT, while patients receiving lithium when treated concomitantly with ECT may develop confusion.

Newer Drugs

In recent years other anticonvulsants like lamotrigine and gabapentin, calcium channel blockers like nifedepine, amlodipine and nimodipine and other drugs like clonidine have been tried in the treatment of this disorder.

PHARMACOTHERAPY OF DEPRESSIVE EPISODE

While using antidepressants in the treatment of a depressive episode in patients suffering from manic depressive disorder, a major concern is about the increased risk of developing an antidepressant induced manic episode during the course of the treatment and more frequent episodes when antidepressants are used during the depressive episode. Development of rapid cycling in these patients has also been associated with use of tricyclic antidepressants. Thus the mainstay of the treatment of manic as well as depressive disorder remains mood stabilizers like lithium, carbamazepine and valproate.

Lithium, Carbamazepine and Valproate

Lithium is still the standard and widely used treatment of the depressive episode though some of the therapists may prefer to use carbamazepine or valproate as a first line of treatment depending on their personal experience. Valproate and carbamazepine may also be used as an alternative when the patients do not tolerate the adverse effects of lithium or as an adjuvant to lithium when patients do not show adequate response.

A significant number of patients seem to tolerate valproate better than they tolerate lithium or carbamazepine.

The initial dosage and the dose titration of these mood stabilizers for depressive episodes is similar to its use in the manic episode.

If the patient develops depressive episode when he is already receiving any of the prophylactic mood stabilizers, it is desirable to check the adequacy of the dosage and patient's compliance to these medicines. Increasing the dose to achieve higher blood level may be considered if it is tolerated.

One should also look out for other causes for the symptoms of depression like exposure to a psychologically stressful event, hypothyroidism, use of alcohol or other drugs etc.

Electroconvulsive Therapy (ECT)

When the depressive episode is very severe, patient has active suicidal ideation, or patient has delusions and hallucinations or when patients do not show adequate response to mood stabilizers, one may consider the use of ECT in the treatment of depressive episode in patients suffering from manic depressive disorder.

As mentioned earlier, while a patient is receiving ECT, it may be preferable to either discontinue or reduce the dose of mood stabilizers. Valproate and carbamazepine increase the seizure threshold and thus the patient may not get a seizure when administered ECT, while patients receiving lithium when treated concomitantly with ECT may develop confusion.

ECT is one of the very quick and effective treatments for the depressive episodes of manic depressive disorders.

Antidepressants

As mentioned earlier, use of antidepressants should be avoided as far as possible, in the treatment of

depressive episode of manic depressive disorder.

Yet, occasionally, when the patient does not show adequate improvement with mood stabilizers, one may be forced to add antidepressants in these patients.

Specific serotonin re-uptake inhibitors (SSRIs) like fluoxetine or sertraline may be preferable over tricyclic antidepressants (TCA's) like imipramine or amitriptyline as the risk of developing antidepressant induced manic episode seems to be minimal with the use of SSRIs

The use of antidepressants should be restricted to the minimum duration of about 4-6 weeks. It should not be continued for 6-8 months after the improvement as it is usually done in case of major depression or recurrent depression. It should be gradually reduced and discontinued as soon as there is a symptomatic improvement in order to avoid drug-induced manic episode and rapid cycling.

Thyroxine

Apart from its use in cases of hypothyroidism, thyroxine may also be used to potentiate the effect of antidepressants, even when there is no clinical or laboratory evidence of hypothyroidism.

MAINTENANCE THERAPY

As in manic depressive disorder, patients are at a risk of recurrent episodes of mania or depression, a prophylactic treatment with lithium, carbamazepine or valproate may be considered.

Though it is recommended that in general, prophylactic maintenance therapy is indicated in any patient who has more than one episode, many clinicians may not feel very comfortable putting the patient on long term or probably life time maintenance therapy immediately after the second episode.

If the interval between the first and second episode is quite long of about 8-10 years, it is likely that the third episode may occur after another 6-8 years. Under such circumstances, taking into consideration patient's compliance, cost of the therapy etc. one may not prefer to put the patient on maintenance therapy immediately after the second episode.

For the decision of maintenance therapy, one should take into consideration many factors like the severity of the episodes response to treatment, number of episodes, interval between the episodes, risk of adverse effects and cost of the therapy.