AETIOLOGY AND MANAGEMENT OF MOOD DISORDERS

COURSE: PSYCHOPATHOLOGY
Paper III (PGDCP; SEM I); Unit 2

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AETIOLOGY AND MANAGEMENT OF MOOD DISORDERS

Over the years, a vast amount of literature has emerged probing the aetiology of mood dis orders. However, the aetiology of mood disorders is not known currently, despite several theories having been propounded.

Some of these include:

Biological Theories

The following findings (and theories) point towards a biological basis of mood disorders.

Genetic Hypothesis

The life-time risk for the first degree relatives of bipolar mood disorder patients is 25%, and of recurrent depressive disorder patients is 20%. The life-time risk for the children of one parent with bipolar mood disorder is 27% and of both parents with bipolar mood disorder is 74%. The concordance rate in *bipolar disorders* for mono zygotic twins is 65% and for dizygotic twins is 20%; the concordance rate in *unipolar depression* for monozygotic twins is 46% and for dizygotic twins is 20%.

Biochemical Theories

There are several biochemical hypotheses for the causation of mood disorders. The mono amine hypothesis suggests an abnormality in the monoamine [catecholamine (norepinephrine and dopamine) and serotonin] system in the central nervous system at one or more sites. Acetylcholine and GABA are also presumably involved.

The earlier models of a functional increase (in mania) or decrease (in depression) of amines at the synaptic cleft now appear simplistic, though urinary and CSF levels of amine metabolites indicate decreased norepinephrine and/or 5-HT function in depression, and increased nor epinephrine in mania.

The postsynaptic events involving the second messenger system, and alterations in the receptor number and function, are also important in addition to the synaptic and presynaptic events. The effects of antidepressants and mood stabilisers in mood disorders also provide additional evidence to the biochemical hypothesis of mood disorders.

Patients suffering from severe depression with suicidal intent/attempt appear to have a marked decrease in the serotonergic function, evidenced by decreased urinary and plasma 5-HIAA levels and the post mortem studies.

Neuroendocrine Theories

Mood symptoms are prominently present in many endocrine disorders, such as hypothyroidism, Cushing's disease, and Addison's disease. Endocrine function is often disturbed in depression, with cortisol hyper secretion, non-suppression with dexamethasone challenge (Dexamethasone suppression test or DST), blunted TSH response to TRH, and blunted growth hormone (GH) production during sleep.

The neuroendocrine and biochemical mechanisms are closely inter-related.

Sleep Studies

Sleep abnormalities are common in mood dis orders (e.g. decreased need for sleep in mania; insomnia and frequent awakenings in depression). In depression, the commonly observed abnormalities include decreased REM latency (i.e. the time between falling asleep and the first REM period is decreased), increased duration of the first REM period, and delayed sleep onset.

Brain Imaging

In mood disorders, brain imaging studies (CT scan/ MRI scan of brain, PET scan, and SPECT) have yielded inconsistent, yet suggestive findings. These findings include ventricular dilatation, white matter hyper intensities, and changes in the blood flow and metabolism in several parts of brain (such as prefrontal cortex, anterior cingulate cortex, and caudate).

Psychosocial Theories

Psychoanalytic Theories

In depression, loss of a libidinal object, *introjection* of the lost object, fixation in the oral sadistic phase of development, and intense craving for narcissism or self-love are some of the postulates of different psychodynamic theories. Mania represents a *reaction formation* to depression according to the psycho dynamic theory.

Stress

Increased number of stressful life events before the onset or relapse has a *formative* rather than a precipitating effect in depression though they can serve a precipitant role in mania. Increased stressors in the early period of development are probably more important in depression.

Cognitive and Behavioural Theories

The mechanisms of causation of depression, according to these theories, include depressive negative cognition (cognitive theory), learned helplessness (animal model), and anger directed inwards. These concepts are useful in the psy cho logical treat ment of mild (to moderate) depression. Several other theories have also been pro pounded but are currently considered to be of doubtful value as theories of causation of depression.

MANAGEMENT

Somatic Treatment

Antidepressants

Antidepressants are the treatment of choice for a vast majority of depressive episodes. The usual starting dose is about 75-150 mg of imipramine equivalent. The clinical improvement is assessed after about two weeks. In case of non improvement, the dose can usually be increased up to 300 mg of imipramine equivalent.

A variety of antidepressants are now available in the market. Since almost all antidepressants are equal in antidepressant efficacy and there is no single antidepressant effective for all depressed patients, the choice of antidepressant is often dictated by other factors. These factors include cost and ease of availability of the drug, the side-effect profile of the drug, past history of response and (any) co-morbid medical or psychiatric disorders.

The newer antidepressants such as *selective serotonin reuptake inhibitors* (*SSRIs)* (e.g. fluoxetine, sertraline, citalopram), mirtazapine, and *serotonin norepinephrine reuptake inhibitors* (*SNRIs)* (e.g. venlafaxine, duloxetine) have very little anti cholinergic side effects and, hence, are generally safer drugs to use in elderly patients with benign hyper trophy of prostate.

Both venlafaxine and duloxetine have been associated with hypertension and should be used with care in those with a history of cardiac illness.

The antidepressant dosage is monitored on the basis of clinical improvement. Routine monitoring of blood levels is not usually indicated.

For the first, uncomplicated, depressive episode, the patient should receive full therapeutic dose of the chosen antidepressant for a period of 6-9 months, after achieving full remission. It is wise to taper the antidepressant medication, when the treatment is to be stopped after the continuation phase.

There are three main phases of treatment

i. *Acute treatment* (till remission occurs),

ii. *Continuation treatment* (from remission till end of treatment), and

iii. *Maintenance treatment* (to prevent further recurrences).

Maintenance treatment may be indicated in the following patients:
i. Partial response to acute treatment.
ii. Poor symptom control during the continuation treatment.
iii. More than 3 episodes (90% chances of recurrence).
iv. More than 2 episodes with early age of onset, or recurrence within 2 years of stopping antidepressants, or severe and/or life-threatening depression, or family history of mood disorder.
v. Chronic depression (> 2 years) or double depression.

About 20-35% of depressed patients are *refractory* to antidepressant medication. The management of a treatment refractory depressed patient is best done by a psychiatrist, often at a tertiary care centre. These patients may require one of the following alternatives:

i. A change of antidepressant (*Switch*),
ii. Combination of two types of antidepressants,
iii. Augmentation with lithium,
iv. Augmentation with T3 or T4,
v. Augmentation with antipsychotics,
vi. Electroconvulsive therapy, or
vii. Use of newer and experimental techniques.

One type of depression, namely delusional depression (depression with *psychotic* features), is usually refractory to antidepressants alone. The treatments of choice in this condition include:
i. An antidepressant with ECT, or
ii. An antidepressant with antipsychotics, or
iii. An antidepressant with lithium.

Electroconvulsive Therapy (ECT)
The indications for ECT in depression include:
i. Severe depression with suicidal risk
ii. Severe depression with stupor, severe psychomotor retardation, or somatic syndrome.
iii. Severe treatment refractory depression.
iv. Delusional depression (psychotic features).
v. Presence of significant antidepressant side effects or intolerance to drugs.

Severe depression with suicidal risk is the first and foremost indication for use of ECT. The prompt use of ECT can be life-saving in such a situation.

The response is usually rapid, resulting in a marked improvement. In most clinical situations, usually 6-8 ECTs are needed, given three times a week. When six ECTs are administered, the usual pattern is three ECTs in the first week, two in the second week and one in the third week. However, improvement is not sustained after stopping the ECTs. Therefore, antidepressants are often needed along with ECTs, in order to maintain the improvement achieved. The safety of the ECT procedure has now been well-established.

ECT can also be used for acute manic excitement, if it is not adequately responding to anti psychotics and mood stabilisers.

Lithium (Li)

Lithium has traditionally been the drug of choice for the treatment of manic episode (acute phase) as well as for prevention of further episodes in bipolar mood disorder. It has also been used in treatment of depression with less success. There is usually a 1-2 week lag period before any appreciable response is observed. So, for treatment of acute manic episode, antipsychotics are usually administered along with lithium, in order to provide cover for the first few weeks. The usual therapeutic dose range is 900-1500 mg of lithium carbonate per day.

Antipsychotics

Antipsychotics are an important adjunct in the treatment of mood disorder. The commonly used drugs include risperidone, olanzapine, quetiapine, haloperidol, and aripiprazole.

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Other Mood Stabilisers

The other mood stabilisers which are used in the treatment of bipolar mood disorders include:

1. Sodium valproate

2. Carbamazepine and Oxcarbazepine

3. Benzodiazepines

Other Treatments

Psychosurgery is an extremely rarely used method of treatment and is resorted to only in exceptional circumstances.

In depressive episode, which is either chronic or persistently recurrent with a limited or absent response to other modes of treatment, one of the following procedures may very rarely be performed:

i. Stereotactic subcaudate tractotomy, or
ii. Stereotactic limbic leucotomy.
In carefully selected patients, the results are reported to be satisfactory. However, in the current day and age, psychosurgery is hardly ever considered in routine clinical practice.

Psychosocial Treatment

Although somatic treatment appears to be the primary mode of management in major mood disorders, psychosocial treatment is often helpful. These indications include:

i. As an adjunct to somatic treatment.
ii. In mild to moderate cases of depression.
iii. Certain selected cases.

These methods include

Cognitive Behaviour Therapy

Cognitive behaviour therapy (CBT) aims at correcting depressive negative cognitions (ideations) such as hopelessness, worthlessness, helplessness and pessimistic ideas, and replacing them by new cognitive and behavioural responses. CBT is useful in mild to moderate, non-bipolar depression and can be used with or without somatic treatment.

Interpersonal Therapy

Interpersonal therapy (IPT) attempts to recognise and explore interpersonal stressors, role disputes and transitions, social isolation, or social skills deficits, which act as precipitants for depression. It is useful in the treatment of mild to moderate unipolar depression, with or without antidepressants.

Psychoanalytic Psychotherapy

The short-term psychoanalytic psychotherapies aim at changing the personality itself rather than just ameliorating the symptoms. Their usefulness is uncertain, particularly in florid depressive or manic episode. These techniques are however helpful in the treatment of selected patients (such as dysthymic disorder, depression co-morbid with personality disorders, or depression with history of childhood loss/child abuse).

Behaviour Therapy

This includes the various short-term modalities such as social skills training; problem solving techniques, assertiveness training, self-control therapy, activity scheduling and decision-making techniques. It can be useful in mild cases of depression or as an adjunct to antidepressants in moderate depression.

Group Therapy

Group psychotherapy can be useful in mild cases of depression. It is a very useful method of psycho education in both recurrent depressive disorder and bipolar disorder.

Family and Marital Therapy

Apart from educating the family about the nature of illness and the usefulness of somatic treatment, family therapy has not been found very useful in treatment of mood disorders per se. These therapies can however help decrease the intra familial and inter personal difficulties, and to reduce or modify stressors, which may help in a faster and more complete recovery. Their most common use in clinical practice is to ensure continuity of treatment (such as lithium prevention in patients with bipolar disorder) and adequate drug concordance.


Thank
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