

CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF GENERALISED ANXIETY DISORDER (GAD) AND PANIC DISORDER (PD)

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IPS GUIDELINE COMMITTEE ON GENERALISED ANXIETY DISORDER (GAD) AND PANIC DISORDER (PD)

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REVIEW OF THE AVAILABLE GUIDELINES

Anxiety disorders are commonly seen in busy hospital settings. Such patients may not reach Psychiatric services at the outset, and may come after series of visits and treatment modalities from physicians, general practitioners, cardiologists, pulmonary physicians and others.

Generalized Anxiety Disorder (GAD) and Panic Disorder (PD) have a chronic course and are associated with significant morbidity.

GENERALIZED ANXIETY DISORDER

There are no definite guidelines available for GAD. Anxiety symptoms are prevalent in primary care settings. These symptoms are a source of considerable morbidity. The role of combined treatment is strongly felt in the management of GAD.

Benzodiazepines (BZDs) have been extensively used for the treatment of GAD and chronic anxiety symptoms. Although the BZDs are occasionally associated with abuse, more worrisome is their association with dependence (Hollister et al., 1981), even with the use of relatively low doses

After acute BZD treatment, symptoms relapse and /or rebound anxiety frequently occurs (Schweizer et al., 1995), BZDs cause attentional, psychomotor, cognitive and memory effects that may be associated with significant morbidity and even mortality (Thomas, 1998). The effectiveness of BZDs over the long term ultimately appears unclear (Schweizer et al., 1995).

Some patients may require long-term pharmacotherapy with these agents. Using gradual tapering regimens, switching to BZD's with a longer t_{1/2}, or using other interventions for the management of BZD withdrawal may ultimately be successful

With the exception of bupropion or desipramine, most agents approved as treatments for depression have shown efficacy as treatments for GAD or GAD- like symptoms (Rickels et al., 1990). A sub analysis of patients of GAD with more depressive symptoms found lowered efficacy for diazepam and increased efficacy for the antidepressants (Rickels et al., 1993). Venlafaxine has been used successfully in the treatment of GAD. It is important to understand that most of the disorders that are co morbid with GAD respond to antidepressants, some better than others, eg, OCD and major depression respond best to SSRIs.

Buspirone has been effective at doses of 20-40 mg in several clinical trials of GAD (Wheatley 1982). It is found to be comparable to BZDs in efficacy for GAD in head to head comparison studies (Cohn et al., 1989). Several negative trials of this agent also exist. More so, it has a slower onset of action than BZDs and some evidence indicates that patients who have received BZDs earlier believe that buspirone is less effective (Schweizer et al., 1986). Buspirone has no cognitive or psychomotor

impairment, has no alcohol potentiation and is well tolerated during maintenance treatment (Rakel, 1990). More so, those receiving buspirone do not experience abnormal anxiety or withdrawal symptoms. No study has examined the effect on GAD of combining CBT with either buspirone or a serotonergic antidepressant, so research in this area lags far behind clinical practice. Other drugs, which are also some times used for the treatment of anxiety and related disorders, are antipsychotics, Gabapentin and Hydroxyzine. Preliminary evidence for the use of antipsychotics (mainly SDAs) is in the cases of post combat PTSD and OCD as augmentation of the existing therapy in the doses sub therapeutic to those used in psychosis (Culpepper, 2003). Gabapentin has shown some potential for the treatment of GAD and also PD (Pollack et al., 1998). Hydroxyzine(antihistaminic drug) is used by primary care physicians in anxiety symptoms associated with organic disorders (Ontario guidelines, 2000).

PANIC DISORDER

Panic disorder with agoraphobia is the most frequent disorder examined in studies of combined treatment.

The preponderance of evidence favours the conclusion that imipramine has specific antipanic and antiphobic effects and that it acutely enhances the therapeutic effects of exposure (Mavissakalian, 1991) Imipramine produced statistically significant benefits beyond programmed practice, an effect accounted for by patients who had received higher doses of imipramine (150-200mg/D). The combination of imipramine with behavioural exposure may be superior to either treatment above reported in short-term treatment studies. (Telch et al., 1985; Zitrin et al.,1980).The long term follow-up of beneficial effects of imipramine is controversial. At six months follow-up, Zitrin et al., 1983, noted a higher rate of relapse among imipramine treated than among placebo treated patients.

Given the current predominant use of serotonergic antidepressants rather than TCAs or MAOI's, it is clear that further research on the combination of such drugs with CBT is greatly needed. De Beurs et al., 1995, reported beneficial effects of the combined treatment. (fluvoxamine and exposure) However, this study addressed only a short term follow-up.

Combination of CBT with a high potency BZD may expose the patient to an increased risk of relapse on discontinuation of the BZD and that perhaps the BZD detracts the patient's ability to make full use of the CBT. Otto et al., 1993 combined CBT with a moderately slow taper of BZD's (Alprazolam or clonazepam) medication. 76% of the CBT/ slow-taper patient but only 25% of the no CBT / slow taper patients were able to successfully discontinue medication. Most CBT patient remained BZD free at 3 months follow-up.

Pollack et al., 1994, found that some panic patients resistant or only partially responsive to apparently adequate pharmacotherapy could be converted to treatment responders by adding CBT to their pharmacotherapy regimen.

SSRIs are the mainstay of pharmacotherapy. Convincing evidence is now available for fluvoxamine 150-300 mg/day (Black et al., 1993), paroxetine 40-60mg/day (Ballenger et al., 1998; Lydiard et al., 1991; Pollack et al., 1998; Rapaport et al., 1998); citalopram 20-40mg/ day (Lepola et al.,1998).

Individuals with PD are particularly sensitive to certain activating side effects of the SSRIs, such as insomnia, agitation and restlessness. Should these adverse effects occur without prior patient education, early treatment discontinuation may occur (Schneier et al.,1990) . As with TCAs, SSRIs should be started at lower doses eg 5-10 mg for paroxetine, 12.5-25mg for Sertraline, 25mg for fluvoxamine, 2.5-5mg for fluoxetine with gradual upward titration.

Amongst the BZDs, alprazolam and clonazepam have been used and studied. Anxiety that reappears during chronic treatment between doses of BZDs with short to medium t_{1/2} BZDs such as alprazolam or lorazepam has been referred to as inter-dose rebound anxiety. This is of clinical concern. Agents like clonazepam may be preferred because of the convenience of less frequent dosing and less frequent rebound anxiety, and being more user friendly during BZD tapering. Long term BZD

treatment may provide anxiolysis, but the possibility of emergence of depressive symptoms in some BZD treated patients may represent a relative disadvantage (Lydiard et al., 1987).

The response rates range from 50-70%. No data is available to guide treatment of PD with other psychiatric disorders. Thus, the management is largely speculative. The SSRIs have been very useful, because most conditions that occur in conjunction with PD appear to be responsive to these agents (eg social phobia & major depression).

Pharmacotherapy of PD during pregnancy is important area. If feasible, all medications should be avoided in the 1st trimester. CBT is a good alternative for women planning to be pregnant and for pregnant women who must discontinue medication, BZDs should be avoided; whenever drug treatment is necessary SSRIs appear safe and effective

Treatment with antidepressants may be restarted in the last trimester in women with a history of postpartum depression.

Overall the key on treatment of PD lies in combining treatments and systematically integrating them. The patients may have rapid relief when coordinated and integrated treatment is given (Otto et al., 1993; Spiegel et al., 1994).

STATUS REPORT OF INDIAN RESEARCH

There is scant literature regarding the studies on anxiety disorders.

Status of studies from India in relation to epidemiology, phenomenology, course, outcome and management of anxiety disorders, especially in relation to the generalized anxiety disorder and panic disorder is rather depressing.

In the understanding of an illness, epidemiological and community aspects are the major contributors. However, the relatively common occurrence of these illnesses is not backed strongly with the data-based studies.

EPIDEMIOLOGICAL AND CLINICAL STUDIES

- 1). In a meta-analysis by Reddy and Chandrashekhar (1998), 13 Psychiatric epidemiological studies assisting of 33572 persons in 6550 families were included. A prevalence rate of 20.7 for neurotic disorders was found.

The studies included in the meta-analysis were door-to-door enquiry of families as units and each individual member of the family separately. Severe psychiatric conditions were included and covered all age groups with availability of separate prevalence reports for rural and urban sectors and for males and females. The prevalence rates for generalized anxiety were different in studies done at different periods of time.

Sethi (1967)	-	17.9
Sethi (1972)	-	3.0
Nandi (1975)	-	12.3
Nandi (1977)	-	1.7
Nandi (1980a)	-	1.7
Nandi (1980b)	-	1.7
Sen (1984)	-	1.9
Nandi (1992)	-	1.4
Premaranjan (1993)	-	13.1

The weighted prevalence rate was found to be 5.8.

The estimated prevalence rate and their 95% confidence interval of generalized anxiety was 5.8 (4.7-7.9). Females (8.4:3.2) were more affected with anxiety disorders. The prevalence rate of generalized anxiety was 3.1 in rural and 11.6 in urban areas, which was statistically significant.

Interestingly in this Meta -analysis of neurotic disorders, panic disorder was missed out.

- 2). Prevalence rate of anxiety neurosis in India by Ganguli (2000) was 15/1000 in rural and 16/ 1000 in urban areas. 8 studies were included in reaching to the above figures. The rural -urban ratio was 100/106 for anxiety neurosis. The estimated prevalence rates of various anxiety disorders included in the anxiety neurosis were not separately assessed, thus leaving us blindfold in the overall affliction of the population from these individual disorders.
- 3). Srinivasan and Neerakal (2002) , studied 94 panic patients attending the OPD of psychiatry department . In agreement with earlier studies reported from the west, there is considerable comorbidity in the study conducted by Srinivasan and Neerakal 43 patients (45.7%) with panic attacks had co-morbid depression , which was severe enough to be diagnosed as major depression according to DSM-IV criteria. Majority of panic subjects had co-morbid primary depression (69.8%) and secondary depression was seen in only 30.2% which is in agreement with earlier studies (Noyes, 1987). More so , there was a greater prevalence of concurrent generalized anxiety disorder in panic patients with depression (both primary and secondary) as compared to panic patients without depression. This is in agreement with earlier reports (Cassano et al.,1989) . This being a cross-sectional study , limits its usefulness. A longitudinal study would more clearly identify relationship between panic disorder and depression. The phenomenology of panic disorder has been studied widely in the west but rarely done so in India. There is considerable co-morbidity between panic disorder and depression. Some suggest that about 40-60% of panic disorder patients in treatment settings have co-morbid depression The comorbidity of panic and depression results in a condition with greater symptom severity, inadequate treatment response and poorer outcome than pure panic disorder

TREATMENT BASED STUDIES

- 1). Shah et al., 1990 conducted a controlled double blind trial of Buspirone and Diazepam in generalized anxiety disorder. Patients in both groups showed improvement on Hamilton Anxiety scale . However, in buspirone group, the improvement was seen in cardiovascular, somatic autonomic, anxious and mood symptoms ; while in the diazepam group, improvement was noticeable in anxious mood, tension, insomnia, cognitive symptoms, somatic and cardiovascular symptoms.
The mean total daily dosage required by the patient in buspirone group was 36.56 mg/day, which was more than reported elsewhere (Goldberg and Finnerty, 1982; Pecknold et al., 1985). More patients in the buspirone group dropped out midway in the trial compared to diazepam group . The lag time of anxiolytic efficacy of buspirone is longer and thus motivation for compliance is necessary.
- 2). Shah et al., 1991, evaluated alprazolam and diazepam in GAD. diagnosed by DSM III in a double blind multicentric study. Weekly evaluations were systematically carried out for a period of 4 weeks. 148 patients (79%) completed the trial. Results showed that alprazolam was as effective as diazepam as an anxiolytic. Drowsiness was less often reported with alprazolam. This was the short follow up study ; the efficacy of alprazolam in long term use needs to be evaluated.
- 3). Sahasi et al., 1991, ascertained the effectiveness of different relaxation techniques in the management of anxiety. Sahasi et al., (1989), found significant improvement among patients undergoing yoga therapy compared to those taking minor tranquilizer (Diazepam). In the 1991 study , psychological and self report data were obtained from the participants practicing progressive relaxation and yogic techniques of relaxation. Both techniques generated positive expectancies and produced a decrease in a variety of self-reported symptoms. Yogic techniques produced greater motivation to practice than progressive relaxation. The follow up rate was much better among the yoga group than those who were doing progressive relaxation. Yogic techniques are more readily acceptable by our population. Following yogic way of life acts probably as a psycho prophylactic against anxiety.

4. Vahia et al., 1993, conducted a study to compare the efficacy of meditation with that of imipramine and chlordiazepoxide in the treatment of GAD, diagnosed as per DSM III criteria. At the end of 5 weeks, meditation was found to be as effective as pharmacotherapy in controlling symptoms of anxiety . It was superior in altering trait anxiety. Meditation is an easy to learn and effective therapy. It has a distinct advantage over pharmacotherapy in that it does not have the associated problems of habit formation, withdrawal effects, overdosage or other undesirable effects.
5. Andrade et al.,2000 conducted a double blind controlled evaluation of the efficacy and adverse effect profile of sustained release Alprazolam .Disadvantage of Alprazolam is that its anxiolytic efficacy wears off much earlier than the drop in its blood levels. Therefore, thrice or even 4 times daily dosing may be necessary, despite which inter-dose anxiety is some times a clinical problem (Schweizer et al.,1993).In patients with panic disorder, sustained release alprazolam was found to be as effective as conventional alprazolam , the SR formulation was also well tolerated (Schwiezer et al.1993;), India, is probably the only country in which a sustained release preparation of alprazolam is commercially available . 40 patients with GAD, as per DSMIV diagnosis and stabilized on alprazolam therapy were randomized to receive first the same dose of either conventional or sustained release alprazolam for 2 weeks, followed by the other formulation of alprazolam in an identical dose for a further 2 weeks . No efficacy difference was observed between the two forms of alprazolam. Once daily SR formulation is as effective as the conventional form of the drug.The use in drug naïve patients and examining the long-term efficacy, compliance and withdrawal in naturalistic studies would be essential.

BIOCHEMICAL STUDIES

Understanding the biology of various psychiatric disorders has taken the front seat in psychiatric research. A number of studies provide considerable evidence for the role of anxiety and related emotional reactions in the development of coronary heart disease, seemingly more for angina pectoris than for Myocardial Infarction (Jenkins, 1976). Mishra et al., 1984, studied the lipid profile of patients of anxiety neurosis looking for the role of lipids in various stress conditions. Thirty six patients of anxiety neurosis diagnosed as per Feighner's diagnostic criteria (Feighner et al.,1972), attending the OPD were included with 24 control subjects. The patients were assessed on Hamilton anxiety scale. Seventeen patients had moderate anxiety score and 19 had mild anxiety score. The mean serum total cholesterol concentration of both subgroups in anxiety neurosis did not show any significant difference whereas their total glycerides showed highly significant increase with respect to controls. This may be due to increased activation of autonomic nervous system both in acute as well as in mild and prolonged stress situations.

Significant increase in VLDL concentration was seen in patients of anxiety neurosis. A significant rise in free cholesterol in mildly anxious patients and more significant reduction in esterified cholesterol was noted whereas moderate anxiety neurotics had only a significant reduction in esterified cholesterol fraction . No significant correlation was found between the different lipid parameters studied and anxiety score from Hamilton Anxiety Scale. This reflects that anxiety neurotics are at a greater risk for the development of atherosclerosis and its cardiovascular complications and that TGs , VLDL , cholesterol and esterified cholesterol are perhaps the biochemical variables mediating the cardiovascular psychosomatic response.

The assumptions are tentative , and regrettfully have never been studied again .

STUDIES ON LIFE EVENTS AFFECTING ANXIETY DISORDERS

Bhatti and Channabasavanna 1985, studied neurosis through stressful life events, personality dimensions, family interactional patterns and other sociological variables. They studied 60 neurotics and 60 controls, 92% respondents had stress in more than 1 area like work, education, family etc in

the experimental group. The mean number of stressful life events experienced by neurotics over a period of one year was around 5, which is much higher than the normal population. Only 40% respondents in the control group had stress in just one area.

Sharma and Ram(1988) carried out study on 84 patients of anxiety neurosis and 47 controls. On assessing the life events during life time and 6 months prior to the onset of illness by an open ended interview, using a scale suited for Indian population, frequency and stress scores experienced by patients and by controls was observed. It was observed that a variety of events were significantly more frequent in the patient group. Events related to personal, social , sexual , educational , occupational and financial areas were observed significantly more in patients during life time and six months prior to the onset of illness . Four events, namely, suspension from job, theft or robbery, broken engagement or love affair and conflict over dowry were found to be significantly more in patients during lifetime. Four other life events such as, major purchase or construction of house, failure in exam, appearing for interview and getting engaged or married were found to be significantly more in patients during the 6 months prior to the onset of the illness. Thus patients experience a variety of life events often more than the controls.

PROPOSED INDIAN GUIDELINES

GENERALIZED ANXIETY DISORDER (GAD)

DEFINTION : One of the anxiety disorders, where the primary symptoms of anxiety are present at most days for at least several weeks at a time, and usually for several months. The symptoms should usually involve elements of:

- a) Apprehension (worries about future misfortunes, feeling " on edge", etc)
- b) Motor tension (restlessness, inability to relax, trembling)
- c) Autonomic over activity (light-headedness, sweating, tachycardia, tachypnea, dry mouth etc)

The transient appearance of depressive symptoms, does not rule out the diagnosis of GAD as main diagnosis. The sufferer must not meet the full criteria for depressive episode, phobic disorder, panic disorder or OCD.

NATURAL HISTORY AND COURSE

The age of onset is difficult to specify, most have been anxious for long but report late. Nearly 1/3rd who have GAD seek psychiatric treatment. Many go to GPs, physicians, cardiologist, chest specialist for the somatic component of the disorder. Because of the high incidence of co-morbid mental disorders , the course and prognosis is difficult to predict. The occurrence of several negative life events greatly increases the likelihood that the disorder will develop. In all, it is a chronic condition that may be life long.

EPIDEMIOLOGY AND ASSOCIATED FEATURES

Reasonable estimates for 1 year prevalence range from 3-8%. The ratio of women to men is about 2:1 . Life time prevalence is about 5%. They occur in nearly 1/4th patients attending anxiety disorder clinics.

It usually co-exists with social phobia, specific phobia, panic disorder or a depressive disorder. Nearly 30-90 % patients have another mental disorder. A high percentage of patients develop depression and 25% develop panic disorder. Some may have dysthymia and substance use disorder.

TREATMENT PRINCIPLES AND ALTERNATIVES

1. PERFORMING A DIAGNOSTIC EVALUATION

Psychiatric evaluation and physical examination is necessary.

It includes history of present illness, current symptoms; past psychiatric history, general medical

history and history of substance use , personal history (eg. psychological development , life events and response to those events), social , occupational and family history; review of the patient's medications; physical and mental status examination and adequate diagnostic tool and criteria. Diagnose GAD according to ICD-10 (W.H.O, 1992)

Anxiety should not be due to the other Axis I disorder (eg. mood disorder, psychotic disorder, social phobia, OCD, somatization disorder, hypochondriasis, PTSD) or a general medical condition (eg. hyperthyroidism) or substance use disorder (intoxication or withdrawal). (see appendix-1 for flow chart)

2. EVALUATING PARTICULAR SYMPTOMS

Patients experience excessive anxiety but many of them experience panic attacks, which may worsen the clinical picture. The prolonged illness may cause depressive symptoms with emergence of suicidality and substance abuse.

3. EVALUATING SEVERITY OF FUNCTIONAL IMPAIRMENT

Many may continue to function in their social and occupational lives with some impairment, others may become severely incapacitated and give up their jobs and social duties. The impairment in different areas can be assessed self-administered visual analog scale.

4. ESTABLISHING AND MAINTAINING A THERAPEUTIC ALLIANCE

The treatment of GAD may be long lasting hence the alliance is crucial. Understanding the life events, the extent and severity of symptoms requires confiding and lasting therapeutic relationship. Attention to the patient's worries and fears are essential for long term gains

5. MONITORING THE PATIENT'S PSYCHIATRIC STATUS.

The symptomatic improvement in psychological and autonomic symptoms leads to greater confidence in the treating doctor. The anxiety goes slowly with treatment and bursts of severe symptoms during the treatment need constant monitoring.

6. PROVIDING EDUCATION TO THE PATIENT AND FAMILY

This seemingly unimportant aspect is most relevant to Indian settings where awareness of psychiatric illness and its realization and need for treatment with compliance is little. Many feel dejected, angry, isolated and may have suicidal ideas. Family and the patient need to be told that this is like any other illness that needs treatment and success depends on compliance.

7. ADDRESSING EARLY SIGNS OF RELAPSE

The education that the illness is a chronic relapsing illness is essential and emergence of anxiety with or without treatment should be promptly treated. Sudden discontinuation may lead to emergence of withdrawal symptoms thus early recognition by the patient and the family helps in prompt treatment.

MANAGEMENT

The aim of management is to provide relief in psychological and somatic symptoms and minimize the impairment. This can be addressed in following way.

1. PHARMACOTHERAPY

The drug treatment of GAD is some times is seen as a 6-12 month treatment, some evidence indicate that treatment should be long term (Rickels, 1990).

a). Goals

Reduce psychological and autonomic symptoms and other co morbid conditions. Improve occupational and social functioning.

b). Efficacy

Little Indian data to address the issue; mainly western data available.

c). Adverse effects

Different for different class of drugs.

BENZODIAZEPINES

Drugs of choice for GAD

Can be prescribed on as needed basis, so that patients take a rapidly acting BZD when they feel particularly anxious. Alternatively, BZDs prescribed for a limited period, during which psychosocial approaches are implemented. Some may fail to respond, and tolerance and dependence may occur.

Treatment for most anxiety conditions lasts for about 4 to 6 weeks, followed by 1 to 2 weeks of tapering drug use before it is discontinued.

Give low dosages initially and gradually achieve therapeutic response.

Intermediate t ½ BZD (8-15 hours) is preferred. Avoid adverse effects due to use of BZDs with long t ½

Use of divided doses prevents the development of adverse effects with high peak plasma levels.

Use medication in adequate dose, preferred molecules are Clonazepam, Chlordiazepoxide and Alprazolam, start with minimum effective dose and try to stop in next 6-8 week.

SSRIs

Effective in anxious patients with co morbid depression; also useful in anxious patients without depression, as they have strong anxiolytic effects, especially seen after 6-8 weeks of treatment.

Fluoxetine transiently increases anxiety; hence sertraline and paroxetine may be preferred.

Begin with SSRI's and BZDs and taper the latter after 2-3 weeks of use.

VENLAFAXINE

Works both on serotonin and norepinephrine.

Improves insomnia, poor concentration, restlessness, irritability and excessive muscle tension

BUSPIRONE

Takes 2 to 3 weeks for its action and patient may be lost for treatment .

Has been found to be useful in 60 to 80% patients with GAD

Evidences indicate that it improves cognitive symptoms.

OTHER DRUGS

Tricyclic and Tetra cyclic drugs

Anticholinergic and cardiovascular side effect profile is to be kept in mind. Avoid in suicidal patients.

BETA BLOCKERS

May be used in reducing the somatic manifestation of anxiety and in situational anxieties such as performance anxiety. Propranolol is often used for such effect.

2. PSYCHOTHERAPY

i. Cognitive behaviour therapy

Goals

--Psycho-education

Direct explanation of the symptoms and disorder to the patient and the family.

--Monitoring of anxiety

--Cognitive restructuring: Corrects the hypothesized cognitive distortions and helps to identify and counter fear of bodily sensations.

EFFICACY

It has been shown that yogic techniques produced greater motivation to practice than progressive relaxation (Sahasi et al., 1991). Meditation was found to be as effective as pharmacotherapy in controlling symptoms of anxiety (Vahia et al., 1993). The overall efficacy claims are backed by very few Indian studies, but are useful.

ADVERSE EFFECTS:

These are relatively benign. Some patients may develop dependence on the therapist and that needs cautious vigil.

It requires considerable time and discipline from the patients.

It addresses cognitive distortions and somatic symptoms

More effective with chronically anxious patients, may need 8-10 sessions

ii. Behavioural techniques

-Progressive Relaxation (Jacobson's)

-Meditation

-Yoga (sukhasna, tanasna, yoga nindra & savasna)

-Meditation

Patanjali advocated meditation to combat anxiety. According to him, an individual's thoughts and behaviour tend to depend on the environmental feedback.

Positive feedback is reassuring, while negative feedback induces anxiety and inadequacy.

Meditation is defined as " a family of techniques which have in common a conscious attempt to focus attention in a non-analytical way, and attempt not to dwell on discussive ruminating thoughts".

Patients are asked to assume a comfortable, supine posture and concentrate on the chosen imagery while regulating breathing.

With practice, ability to discard discussive thoughts and retain concentration on the chosen imagery improves.

It is easy and cost effective

Non-habit forming and no withdrawal effects or over dosages.

iii. Supportive Psychotherapy

Offers reassurance and comfort

No Indian data on its usefulness exist.

iv. Insight oriented Psychotherapy

Identifies ego strengths and uncovers the unconscious conflicts

No Indian data on its usefulness exists

3. COMBINED PHARMACOLOGICAL AND PSYCHOTHERAPEUTIC

Long-term outcome is better when they are used in combination

PANIC DISORDER (PD)

Definition : There are recurrent attacks of severe anxiety (panic) which are not restricted to any

particular situation or set of circumstances, and which are therefore unpredictable.

Several attacks of autonomic anxiety should have occurred within a period of 1 month .

- a) In circumstances when there is no objective danger
- b) Without being confined to unknown or predictable situations and
- c) With comparative freedom from anxiety symptoms between attacks (although anticipatory anxiety is common).

Panic disorder must be distinguished from panic attacks occurring as part of established phobic disorders.

If the criteria for a depressive disorder are fulfilled at the same time, the panic disorder should not be given as the main diagnosis.

NATURAL HISTORY AND OUTCOME

Several types of panic attacks may occur, most commonly is the unexpected attack. Some may also experience situationally predisposed panic attacks or situationally bound attacks.

Many may have agoraphobia, in which they experience anxiety and avoidance of places or situations where escape or help may be unavailable. Panic attacks may vary in their frequency and intensity. It leads to disruption of interpersonal relationships and social functioning. There are no naturalistic Indian studies, but follow-up study of patients suggests that at 4-6 years post-treatment about 30% of individuals are well, 40-50 % are improved but symptomatic, and remaining 20-30 % have symptoms that are same or slightly more.

EPIDEMIOLOGY

Lifetime prevalence 1.6 to 2.2%

Nearly 1/3rd-1/2 have agoraphobia. The lifetime prevalence of major depression may be high in patients with PD.

Many of them report in the medical emergencies in state of panic attacks.

TREATMENT PRINCIPLES

1. Performing a diagnostic evaluation

Detailed psychiatric history, including family, social and occupational history.

Diagnostic evaluation and evaluating the symptoms.

Presence of any other Axis I Disorder, general medical condition or substance use disorder should be looked for.

2. Evaluating Particular symptoms

Frequency of panic attacks may vary in the individuals; anticipatory anxiety and the degree of phobic avoidance varies from patient to patient.

Treatment may be influenced by the particular constellation of symptoms.

3. Evaluating types and severity of functional impairment

Loss of occupational and social functioning may be severe. The patient may be encouraged to define a desirable level of functioning for him or herself.

4. Establishing and maintaining a therapeutic alliance

This is important, for Indians as this will help in improving the compliance and greater involvement and understanding of the treatment.

5. Monitoring the patient's psychiatric status

Usually, panic attacks are controlled first but sub-threshold panic attacks may linger and require further treatment.

Many illnesses eg depression, substance use disorders co-occur with PD and need for recognition of these disorders is essential.

6. Educating the patient and the family

This is very important for Indian populace. They may believe that they have heart or lung disease and may undergo extensive medical evaluation.

Telling the patient that panic attacks are not life threatening helps in long-term treatment.

7. Enhancing treatment compliance

Educating, ensuring therapeutic alliance helps in improving treatment compliance, so necessary to treat the disorder.

8. Addressing early signs of relapse

Reassuring the patient and evaluating regularly the patient help in relapse identification.

MANAGEMENT

Like GAD the aim of management is to provide relief in psychological and somatic symptoms and minimize the impairment. This can be addressed in the following way (also see appendix flow chart 2).

1) PHARMACOTHERAPY

Effective pharmacological treatment for panic disorders should generally continue for 8-12 months (Levitt et al., 2001).

i. SSRIs

Goals

Reduce the intensity and frequency of panic attacks, anticipatory anxiety and associated depression.

Efficacy

-No Indian studies available

-However, Fluoxetine, Sertraline, Paroxetine, Fluvoxamine used

Side Effects

Safe; headaches, irritability nausea, GI complaints, increased anxiety reported.

Dose

Initial dose should be lower than that usually prescribed to patients with depression.

Fluoxetine 10mg/ day (10-80 mg/D)

Paroxetine 10 mg/ day (upto 40 mg/D)

Sertraline 25mg/D (50-200mg/D)

Fluvoxamine 50mg/D (50-300 mg/D)

No studies in India on doses and length of treatment available.

Length of treatment should be guided by the overall psychopathology, side effect profile, and patient and family demands.

ii. TCAs

Goals- Reduce the intensity and frequency of panic attacks, anxiety and depression.

Efficacy- No Indian studies available

Started at lower doses, as some may have super sensitivity initially.

Side effects

Anticholinergic side effects; sleep disturbances, orthostatic hypotension

Cognitive disturbances

Weight gain

Cardiovascular side effects

Dose

Started at lower doses, as some may have super sensitivity initially.

Imipramine 50-200mg/D

Clomipramine 25-150mg/D

No studies on doses and length of treatment available

Western data indicates that maintenance treatment is beneficial for at least a year after a patient has achieved a response to the tricyclic.

iii. Benzodiazepines

Goals- Same as SSRIs

Efficacy

Studied by Andrade et al. 2000 in the use of SR Alprazolam;

Western data indicate the usefulness of Alprazolam, clonazepam, lorazepam, and diazepam

Dose

Alprazolam - Upto 5-6 mg/day

Clonazepam - Upto 4 mg /day

Diazepam - Upto 5-40 mg/Day

Side effects

Withdrawal anxiety, seizures

Tolerance, Dependence

Length of treatment needs to be studied but should be preferably tapered after 4-8 weeks.

iv. Venlafaxine

Mean dose 150mg/Day.

v. Beta Blockers

Alleviates anxiety and autonomic over activity.

Sole use not very effective

Useful when combined with BZDs due to additive effects.

Propranolol is often used for such effect.

2 PSYCHOTHERAPY

i. Cognitive Behaviour Therapy

a) Goals

-Psycho education

-Continuous panic monitoring

Keeping a daily diary

-Cognitive restructuring

Correction of catastrophic misinterpretation of bodily sensations

-Exposure to fear cues

Hierarchy of fear evoking situations is made and patient experiences situations at the lower end, gradually moving to the higher level.

b) Efficacy

-No Indian studies to evaluate the efficacy

-Difficult to conduct considering the lack of proper training facilities and the poor degree of motivation amongst Indian patients.

c) Adverse Effects

-Benign and safe but carries higher risk of patient dropouts for Indian Populace.

-Psychological dependency needs to be checked

ii. Psychodynamic Psychotherapy.

a) Goals

-Identifies core conflicts and reduces panic

b) Efficacy

-No published Indian reports of evaluating the efficacy.

c) Adverse Effects

-Benign but psychological dependency needs to be checked.

iii. Group Therapy

-No studies available

-A greater proportion of panic free subjects among those who had been given group CBT than among delayed treatment control subjects.

3. COMBINED PHARMACOLOGICAL AND PSYCHOTHERAPEUTIC

Long-term outcome is better when they are used in combination.

SPECIAL POPULATIONS

Child and Adolescent population

Literature little in West and India

PD occurs in children and, more commonly in adolescents; it often is preceded by or co-occurs with seasonal affective disorder.

PD is accompanied by a variety of specific phobias eg of animals, height, darkness etc.

Medication management strategies that are effective for adults with PD have received anecdotal support for use with children and adolescents but no conclusive support exists.

SSRI's, BZD's (clonazepam, alprazolam), TCA's may be useful.

GERIATRIC POPULATION

Search for co morbid diagnosis especially general medical conditions should be undertaken.

If medication is used, the required dose may be lower than that for younger patients. It is useful to

remember the following:

- Lower initial dose
- Gradual Escalation
- Lower Target Dose

SUICIDAL PATIENTS

Adequate dosages should be used.

Comorbid depression is common

Suicidal ideas and past suicidal attempts should be recorded in patients with panic attacks.

SUBSTANCE USE DISORDERS

May worsen panic attacks and interfere with treatment response.

Treatment of substance use disorder is essential.

Other Anxiety Disorders

Comorbidity is common with patients of PD.

Pharmacotherapeutic consideration remains the same. But tailor made treatment to the comorbidity will greatly help in overall recovery.

APPENDIX-FLOWCHART -2

**PANIC DISORDER
Diagnosed by ICD10**

Acute Attack

**Psycho pharmacological
Treatment**

- i. SSRI-
Fluoxetine
Paroxetine
Sertraline
Fluvoxamine
Citalopram

- ii. BZDS
Alprazolam
Clonazepam
Diazepam

- iii. SNRI
Venlafaxine

- iv. NaSSA

- v. Beta Blockers : Propanolol
Useful when combined
with BZDs

- vi. TCAs
Imipramine
Clomipramine

Long Term Care

**Psycho pharmacological
Treatment**

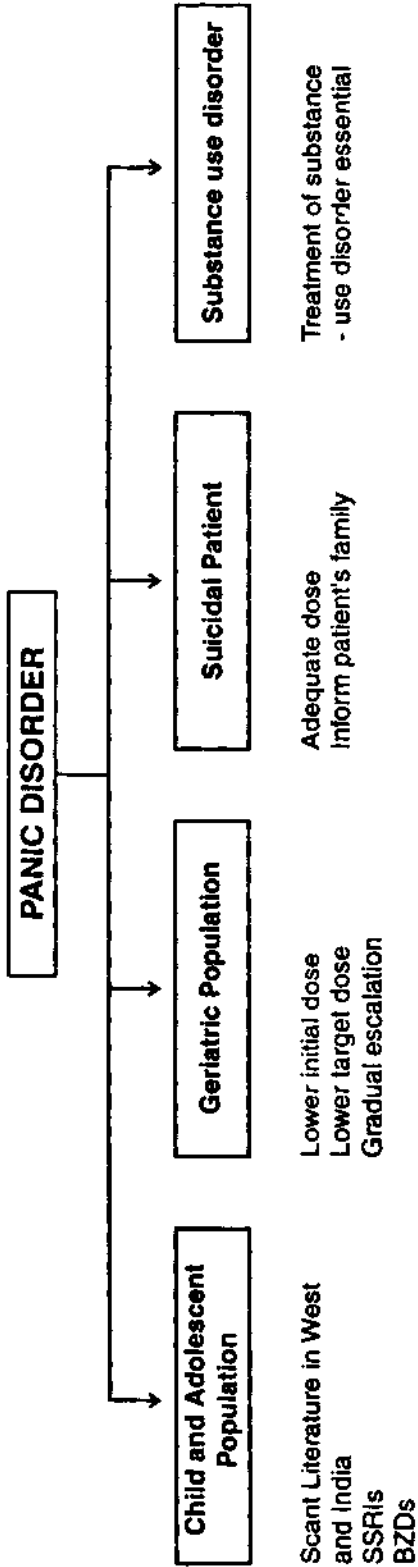
- i. BZDs
- ii. SSRIs
- iii. TCAs
- iv. Venlafaxine
- v. NaSSA
- vi. Beta Blockers
(Propanolol)

Ravi Kiran Mathur

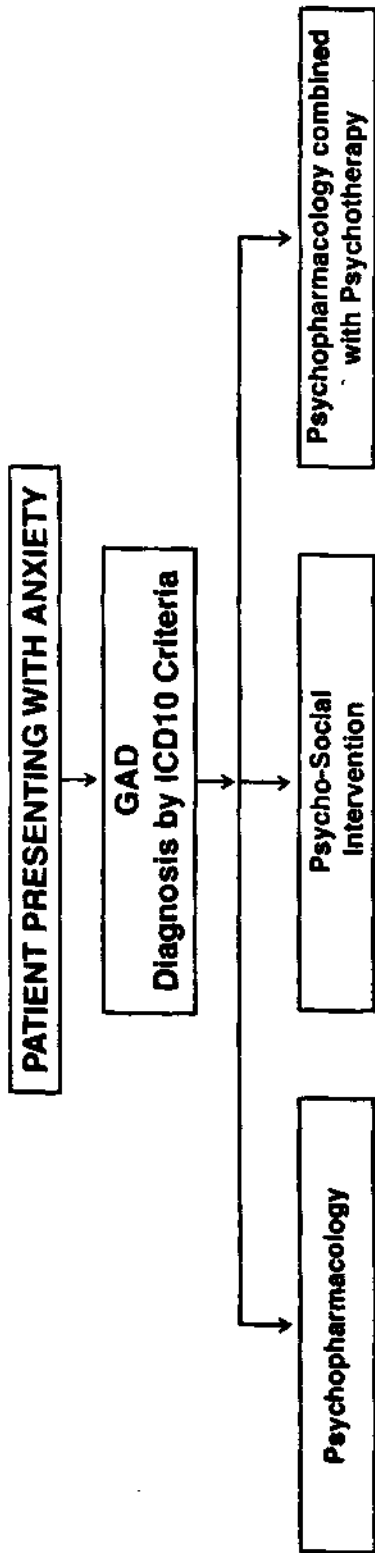
Psychotherapy

- CBT
- Psychodynamic
- Psychotherapy
- Group therapy

APPENDIX-FLOWCHART -2 (Contd..)



APPENDIX-FLOWCHART -1 (Contd..)



Psycho-pharmacology

Benzodiazepines

Clonazepam
 Chlordiazepoxide
 Diazepam
 Alprazolam
 Initiate from minimum adequate dose /prescribed for a limited period(6-8 weeks) / use with caution for dependence

Psycho-Social Intervention

Cognitive -behaviour therapy
 Relaxation therapy
 Yoga & Meditation
 Supportive Psychotherapy
 Insight Therapy
 Family Therapy
 Psycho education

Psycho-pharmacology combined with Psychotherapy

Long term outcome is better when they are used in combination.

- SSRIs
- SNRI
- NaSSA
- Other
- TCA
- Beta Blockers
- Paroxetine; Sertraline ; Fluoxetine
- Venlafaxine
- Mirtazapine
- Buspirone
- Tricyclic & Tetra cyclic
- Propranolol

APPENDIX-FLOWCHART -1 GAD

THINGS TO REMEMBER FOR GAD :

1. Anticholinergic and cardiovascular side effects to be kept in mind when using Tricyclic & Tetra cyclic for side effects . Precaution in suicidal patients.
2. Long term treatment may be required
3. Psycho-pharmacological therapy combined with psychotherapy works better.

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