CHAPTER

69

Practical Approach to Stress Related Disorders

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ABSTRACT

The high prevalence of stress related disorders and the magnitude of disability and distress have focused the efforts on managing them within the context of primary care physicians. Numerous studies from India have documented significant number of depression, anxiety, and common mental disorders cases in general hospital settings. Research has shown that there is robust neurotrophical basis of stress related disorders. The DSM-5 system of classification and the ICD-10 are supposedly a theoretical and not in same tuning. Physicians need a more practical classification which is at present lacking. At primary care level it will be sufficient to look for the following disorders: [1] Acute stress disorders (ASD) [2] Post-traumatic stress disorder(PTSD) [3] Anxiety disorders : Generalized anxiety disorder (GAD), Phobic anxiety, Panic disorders and some other similar disorders.

Successful treatment approaches generally involve medication combined with psychotherapy. Cognitive-behavioural therapy (CBT) has been proven superior. Combining CBT with medications is extremely helpful in resistant cases.

Stress (stressors and stress responses) plays a major role in immunological diseases and immune-related disease processes. There is a clear link between persistent stress and development of many diseases like cardio-vascular, diabetes, hypertension,asthma, headache, gastrointestinal disorders,obesity and dementia.

Stress related disorders are now posing heavy burden to a physician clinic. It has been estimated that 5 to 15 percent of consultations are sometimes due to continued stress related life situations in India. In busy clinic it is not easy to level the exact nature of such disorders according to criteria led in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition *(*DSM-5*)*, or International classification of diseases (ICD 10). Many physicians find the numerous case finding instruments and screening questionnaires to diagnose stress related disorders too cumbersome and time consuming for routine use. The many diagnostic criteria are elaborate and difficult to apply in routine medical practice. Studies have shown that focus on clinical presentations without diagnosis and the symptomatic management of people with emotional distress who present to primary care are complimentary and treatment guidelines do not seem to improve the situation.[1-2] The high prevalence of these disorders and the magnitude of disability and distress have focused the efforts on managing them within the context of primary care.

MAGNITUDE OF THE PROBLEM

Status of stress disorder research from India in relation to epidemiology, phenomenology, course, outcome and management are lacking. A meta-analysis of 15 epidemiological studies (on psychiatric disorders), by Ganguli in India, found the prevalence rate of anxiety neurosis to be 16.5/1000 population.[3] A meta-analysis by Reddy and Chandrashekhar yielded an estimated prevalence rate of 20.7% for all neurotic disorders, which was reported to be highest among all psychiatric disorders. The weighted prevalence rates of different anxiety disorders were 4.2% (Phobia), 5.8% (GAD), 3.1% (Obsession) and 4.5% (Hysteria).[4] Madhav in an analysis of ten Indian studies on psychiatric morbidity, concluded that prevalence rates for anxiety neurosis and hysteria were 18.5 and 4.1 per 1000 population respectively.[5] These are not the real picture as such studies were done in tertiary centers with limited sample size.[6]

WHAT IS STRESS

The concept of stress was developed by Hans Selye in th 1930s. Currently,stress usually refers to the consequence of the failure to respond appropriately to emotional or physical threats, whether actual signs of stress can be defined at a cognitive,emotional,physical or behavioral level. Although the stress response of the body functions to maintain stability or allostasis (process of achieving stability, or homeostasis), a long term activation of stress system can have serious negative consequences for the body.[7]

WHAT HAPPENS AT BIOCHEMICAL & NEUROTROPHIC LEVEL [FIGURE 1 AND FIGURE 2]

Latest studies have shown that stress decreases the expression of brain-derived neurotrophic factor (BDNF) in limbic structures that control mood and that antidepressant treatment reverses or blocks the effects of stress. Decreased levels of BDNF, as well as other neruotrophic factors, contribute to the atrophy of certain limbic structures, including the hippocampus and prefrontal cortex that has been observed in depressed subjects. Conversely, the neurotrophic actions of antidepressants could reverse neuronal atrophy and cell loss and thereby contribute to the therapeutic actions of these treatments.[8] Corticotropin-releasing hormone (CRH) initiates the cascade. One neural site linked to a sense of adversity is the amygdale. Glucocorticoids

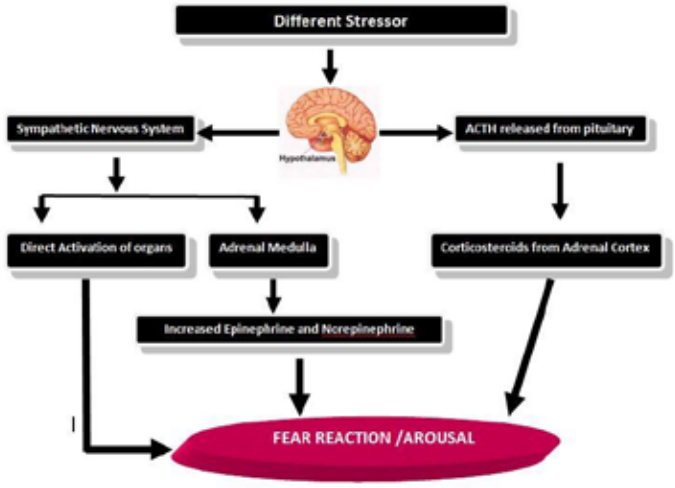

Fig. 1: What happens at Biochemical & Neurotrophic level

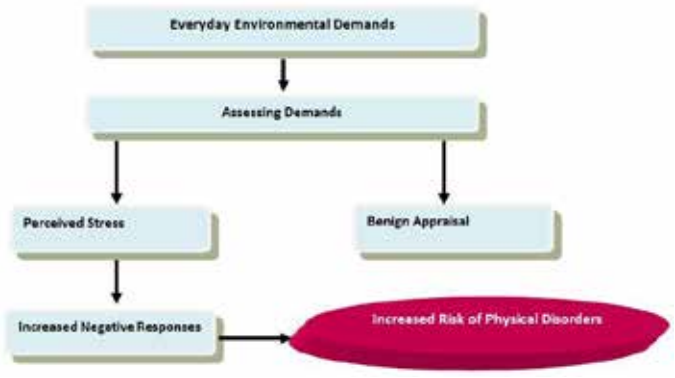

Fig. 2: What happens at Biochemical & Neurotrophic level

enhance the production of CRH in this region of the brain, resulting in increased attention to external events and, when sustained for longer periods of time, perhaps contributing to anxious depression.[9]

PRACTICAL APPROACHES

At first we need to know what are stress related disorders and how to differentiate them?

Worldwide DSM- 5 or ICD-10 are used by psychiatrists to pinpoint the diagnosis of stress related disorders. But it is not uniform in both guidelines. The DSM-5 chapter on anxiety disorder no longer includes obsessive-compulsive disorder. PTSD (Post-traumatic stress disorders) was also removed from anxiety disorders in DSM-5. In a simplified approach ICD -10 will be easy to follow. At primary care level it will be sufficient to look for the following disorders: [1] Acute stress disorder(ASD) [2] Post-traumatic stress disorder (PTSD) [3] Anxiety disorders : Generalized anxiety disorder (GAD),Phobic anxiety, Panic disorders.[5] Others like, Agoraphobia, Adjustment disorders, Dhat syndrome etc.

ANALYZING STRESS DISORDERS

1. Acute stress disorder (ASD) [Figure 3]

- A transient disorder (only between 2 days to 4 weeks) that develops in an individual without any other apparent mental disorder in response to exceptional physical and mental stress and that usually subsides within hours or days.

Differentiating Acute Stress Disorders (ASD) with PTSD		
Criteria	**ASD**	**PTSD**
Duration	Within 2 days to 4 weeks	Usually within 3 weeks
Symptoms	Mainly dissociative	Not a focus dissociative cluster
Resolution	Within 1 month	Persisting longer than 1 month

Fig. 3: Differentiating Acute Stress Disorders (ASD) with PTSD

- Autonomic signs of panic anxiety (tachycardia, sweating, flushing) are commonly present. The symptoms usually appear within minutes of the impact of the stressful stimulus or event, and disappear within two to three days (often within hours). Partial or complete amnesia for the episode may be present. If the symptoms persist, a change in diagnosis should be considered.

2. Post-traumatic stress disorder (PTSD)

- The DSM construct of PTSD, while legitimizing the longterm impact of trauma, does not clearly implicate the external event in causation.[10] Nowadays, the label PTSD seems to be employed in clinical psychiatric practice for patients who present with symptoms after a traumatic event.[10]
- The Indian Council of Medical Research collected data on psychiatric morbidity from clinics and from community surveys in Bhopal after Union Carbide disaster and described anxiety, depression, and adjustment reaction after the disaster, but made no mention of PTSD.[11-12] In Gujarat which was engulfed in communal riots in February 2002, the cardinal symptoms of PTSD (i.e., reexperience, avoidance, and arousal) and their relation to the trauma was documented.[13] Similarly, reports of PTSD have been described among Kashmiri Pundits forced to leave their homes and livelihoods.[14]
- PTSD is a diagnosis employed in clinical practice in India for people who present with the "classical" symptoms of the syndrome after a traumatic event (i.e., reexperience, avoidance, and arousal). PTSD arises as a delayed or protracted response to a stressful event or situation (of either brief or long duration) of an exceptionally threatening or catastrophic nature, which is likely to cause pervasive distress in almost anyone.
- Typical features include episodes of repeated reliving of the trauma in intrusive memories ("flashbacks"), dreams or nightmares, occurring against the persisting background of a sense of "numbness" and emotional blunting, detachment from other people, unresponsiveness

to surroundings, anhedonia, and avoidance of activities and situations reminiscent of the trauma.

- There is usually a state of autonomic hyperarousal with hypervigilance, an enhanced startle reaction, and insomnia. The onset follows the trauma with a latency period that may range from a few weeks to months. The course is fluctuating but recovery can be expected in the majority of cases.

3. Adjustment disorders

- Adjustment disorder is a stress-related, short-term, nonpsychotic disturbance. The symptoms develop when the person is responding to a particular event or situation, for example a loss, a problem in a close relationship, an unwanted move, a disappointment, or a failure. No specific physical findings correlate with adjustment disorder, but people may consult a healthcare provider for poor sleep, aches and pains, indigestion, fatigue, and other typical symptoms.

4. Panic disorders

- An abrupt surge of intense fear or intense discomfort occurs that reaches a peak within minutes, and during which time four (or more) of the following symptoms occur: 1. Palpitations, pounding heart, or accelerated heart rate. 2. Sweating. 3. Trembling or shaking. 4. Sensations of shortness of breath or smothering. 5. Feelings of choking. 6. Chest pain or discomfort. 7. Nausea or abdominal distress. 8. Feeling dizzy, unsteady, light-headed, or faint. 9. Chilis or heat sensations. 10. Paresthesias (numbness or tingling sensations). 11. Derealization (feelings of unreality) or depersonalization (being detached from oneself). 12. Fear of losing**.** Diagnosis of panic attack needs to be considered after ruling out specific medical conditions.

5. Agoraphobia

- Patients having fearful and anxious about two or more of the following situations: using public transportation; being in open spaces; being in enclosed places; standing in line or being in a crowd; or being outside of the home alone in other situations can be diagnosed as agoraphobia.

6. Generalized anxiety disorder. (GAD)

- Patients having persistent and excessive anxiety and worry about various domains, including work and school performance, that the individual finds difficult to control should be leveled as GAD. Such persons also experience physical symptoms, including restlessness or feeling keyed up or on edge; being easily fatigued; difficulty concentrating or mind going blank; irritability; muscle tension; and sleep disturbance. Two main elements of the mental status examination should be assessed in generalized anxiety disorder, first involves asking about suicidal/homicidal ideation or plan and second involves formal testing of orientation/recall.

7. Specific phobias

- Individuals with specific phobias may fear embarrassment or humiliation (e.g., embarrassment about fainting when they have their blood drawn), but they do not generally fear negative evaluation in other social situations.

8. Situations which can mimic like stress induced disorders

- These have been not categorized. Dissociative [conversion] disorders have previously been classified as various types of "conversion hysteria". They are presumed to be psychogenic in origin, being associated closely in time with traumatic events, insoluble and intolerable problems, or disturbed relationships. The symptoms often represent the patient's concept of how a physical illness would be manifest. Medical examination and investigation do not reveal the presence of any known physical or neurological disorder.

9. Dhat syndrome

- Patients are diagnosed as Dhat syndrome if the physician is aware of the label and the explanation and the content is carefully focused. These patients could also receive a label of anxiety, depression, somatization, or neurasthenia if the physician emphasizes the form of the presentation. The patient perspective of "loss of semen" as cause of the symptoms is the hallmark of his illness.[15-17] Patients, relatives, and health workers often provide nonmedical explanations for the cause of illness. Many patients (and their relatives) simultaneously seek biomedical and nonbiomedical interventions.[18]

Essential to rule out medical disorders as they can mimic symptoms of stress disorders

Examples- hyperthyroidism, hyperparathyroidism, pheochromocytoma, vestibular dysfunctions, seizure disorders, and cardiopulmonary conditions (e.g., arrhythmias, supraventricular tachycardia, asthma, chronic obstructive pulmonary disease. Appropriate laboratory tests (e.g., serum calcium levels for hyperparathyroidism; Holter monitor for arrhythmias) or physical examinations (e.g., for cardiac conditions) are helpful in diagnosis. We should rule out CNS disorder by EEG, lumber puncture, CT scan,MRI or PET scan.

Monitoring and referral

Physicians should closely monitor physical and psychological symptoms of all patients who have experienced trauma. Physicians should refer patients who have prolonged reactions that cause distress or affect interpersonal relationships and daily functioning.

Re-assessment

The difficulty in reaching a diagnosis at the time of the initial presentation is because it is often difficult to recognize the classic syndromes at the onset of the

Fig. 4: Treatment of Stress Disorders

illness. However, these can be identified over time as they develop the syndrome later.

OTHER COIN OF STRESS : STRESS-RELATED DISEASES

Stress (stressors and stress responses) plays a major role in immunological diseases and immune-related disease processes. Inflammation, infection, autoimmune processes, and perhaps even the onset and development of malignant tumors may occasionally be associated with the stress phenomenon. Stress has been shown to be important in vascular hypertension. It may serve as a risk factor,induce blood pressure spikes, or increase an already elevated blood pressure.

A stress-specific coronary syndrome, known as transient left ventricular apical ballooning cardiomyopathy or stress (Takotsubo) cardiomyopathy, also exists. Among patients with coronary heart disease, acute psychological stress has been shown to induce transient myocardial ischemia.[19]

Different forms of emotional stress are associated with an increased risk of development of type 2 diabetes, particularly depression, general emotional stress, anxiety, anger/hostility and sleeping problems.[20]

Exposure to stress (especially chronic stress) is a major risk factor in the pathogenesis of different diseases of gastrointestinal tract including gastroesophageal reflux disease (GERD), peptic ulcer, functional dyspepsia, inflammatory bowel disease (IBD), irritable bowel disease (IBS), and other functional disorders of GI tract.[21]

Development of psychological distress has been associated with asthma that is more difficult to manage, requiring higher doses of steroids,more frequent and prolonged admissions to hospital, and greater functional disability.[22]

TREATMENT PEARLS (FIGURES 4 & 5)

Which drugs to choose?

1. Selective serotonin reuptake inhibitors (SSRIs) are generally used as first-line agents, followed remotely by tricyclic antidepressants (TCAs). The SSRIs include paroxetine, escitalopram, sertraline, fluoxetine, fluvoxamine, and citalopram. SSRIs are helpful for generalized anxiety disorder, panic disorder, and social phobia. All SSRIs may be equal in the treatment of anxiety disorders.Paroxetine represents a partially sedating SSRI option that is also available in a controlled-release preparation which may improve tolerability.
2. Mirtazapine has a much more sedating effect, generally reducing its potential to aggravate initial anxiety. Mirtazapine acts distinctly as an alpha-2 antagonist, consequently increasing synaptic norepinephrine and serotonin, while also blocking some postsynaptic serotonergic receptors that conceptually mediate excessive anxiety when stimulated with serotonin.
3. Benzodiazepines act quickly but carry the liability of physiologic and psychologic dependence. They can be reasonably used as an initial adjunct while SSRIs are titrated to an effective dose, and they can then be tapered over 4-12 weeks while the SSRI is continued. This approach can improve short-term tolerability, although it may increase the risk of sedation.
4. Alprazolam has been widely used for panic disorder, but it is currently discouraged because of its higher dependence potential; alprazolam has a short half-life, which makes it particularly prone to rebound anxiety and psychological dependence. Clonazepam has become a favored replacement because it has a longer half-life and empirically elicits fewer withdrawal reactions upon discontinuation.
4. Buspirone is a nonsedating antipsychotic drug unrelated to benzodiazepines. It has been found to be comparable with benzodiazepines in reducing symptoms of anxiety and has fewer sedative or withdrawal adverse effects than benzodiazepines. Buspirone also has fewer cognitive and psychomotor adverse effects, which makes its use preferable in elderly patients. Buspirone is a novel antianxiety agent.
5. Trazodone is useful in the treatment of panic disorders. It is antagonist at the 5-HT2 receptor and inhibits the reuptake of 5-HT.
6. Serotonin And Norepinephrine Reuptake Inhibitors such as venlafaxine and duloxetine may be helpful in a variety of mood and anxiety disorder
7. The tricyclic antidepressants (TCAs) are a complex group of drugs that have central and peripheral anticholinergic effects, as well as sedative effects. They include imipramine and clomipramine. Caution is warranted in the use of TCAs because of their higher toxicity and potential lethality in overdose. Their use should be limited to cases in which SSRIs are ineffective or cannot be afforded.
8. Beta blockers such as propranolol are used to

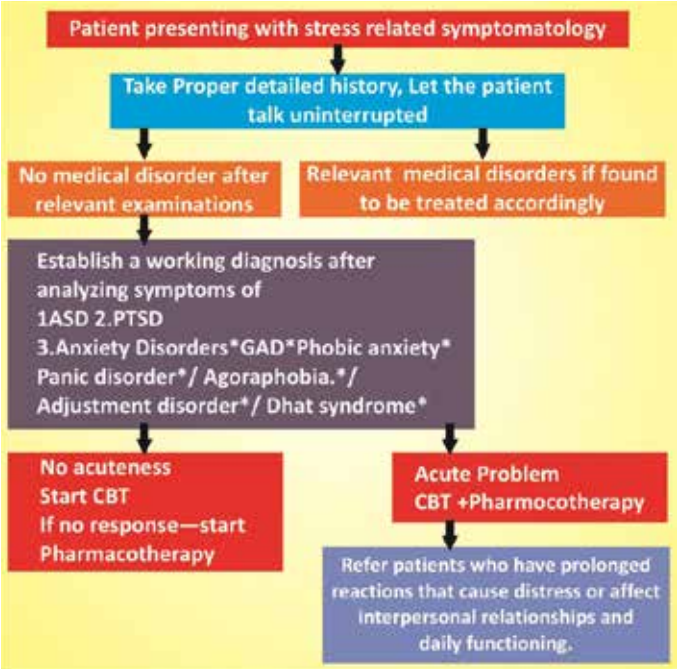

Fig. 5: Algorithm for Management of Stress Disroders

control autonomic symptoms (eg. Tachycardia) in anxiety disorders.

DRUGS AND OTHER INTERVENTIONS IN SPECIFIC SITUATIONS

Treatment usually consists of a combination of pharmacotherapy and/or psychotherapy.Deciding which treatment or combination of treatments to prescribe depends on a careful interview and assessment of the patient's goals and level of pathology.

For Generalised Anxiety Disorders successful treatment approaches generally involve medication combined with psychotherapy. However, cognitive-behavioral therapy (CBT) has been proven superior in placebo-controlled trials. CBT generally includes self-reward as well as problem solving and can be as effective as medications, especially for children with mild generalized anxiety disorder. Combining CBT with medications is extremely helpful in resistant cases Other psychotherapies, such as relaxation therapy, supportive psychotherapy, or mindfulness therapy, have been used if CBT is not appropriate.[23-24]

For panic attacks pharmacotherapy, cognitive and behavioral psychotherapy, and other psychological treatment modalities are all used to treat panic disorder. Untreated panic attacks can subside spontaneously within 20-30 minutes, especially with reassurance and a calming environment.[25]

Agoraphobia (specifically, the panic symptoms) most often responds to treatment with an SSRI. Benzodiazepines can be used either as an adjunct or as primary treatment; however, benzodiazepines are usually not chosen as a first-line treatment because of the potential for abuse. If the patient has frequent panic attacks and no history of substance abuse, a benzodiazepine can be considered until the SSRI takes effect.

PTSD treatment is often best accomplished with a combination of pharmacologic and non-pharmacologic therapies. Medications may be required to control the physiological symptoms, which can enable the patient to tolerate and work through the highly emotional material in psychotherapy. A meta-analysis of studies in adults with PTSD indicated that trauma-focused cognitive-behavior treatment (CBT) and Eye Movement Desensitization and Reprocessing (EMDR) should be first-line non-pharmacologic therapies for PTSD.[25]

Social phobia typically responds to either an SSRI or a monoamine oxidase inhibitor (MAOI). Initiate treatment with an SSRI and titrate to the minimum effective dose. SSRIs approved for social phobia include paroxetin including SR form and sertraline, but other SSRIs have also been shown to be effective (eg, fluvoxamine).

Non-western psychological interventions like yoga and meditation, which are employed across diverse clinical problems and are popular across cultures. These are useful in the management of a range of contents in dissimilar contexts, regions, and cultures.[15]

Interpersonal Psychotherapy (IPT) may also be effective in the treatment of eating disorders and anxiety disorders.[26]

FINAL POINT

All physicians working in general medical settings find difficulty in separating anxiety, depression, and somatic presentations because of milder, less distinct syndromes and overlapping symptoms. It is difficult to employ the more complex classification. It would be time consuming and impractical in primary care. The psychiatric classifications for use in primary care should consider the different context. There should be increased efforts to assess and manage issues related to context and cultures, meaning and idioms of distress, and coping and stress. Do not ignore the patient version of illness and never say he or she has hysteria. Psychological factors present before exposure to stress also have an impact on responses to stress and its assessment is equally important.

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