Klinik Psikofarmakoloji Bülteni 1:3 1991

STRATEGIES IN ANXIETY AND PANIC: ACUTE INTERVENTION AND LONG TERM MANAGEMENT.

MYRIAM VAN MOFFAERT,M.D. PH.D.

Anxiety disorders have recently been recognized into a new classification scheme in the third edition of the American Psychiatric Association's Diagnostic and Statistical Manual (DSM III). The anxiety disorders are divided into four categories. The term neurosis is not used in DSM III: conditions characterized by hypochondriacal, hysterical, or depressive symptoms are placed under other categories. Namely axis II personality disorders.

Classification

1- Panic disorders

The central feature of panic disorder is a series of unprovoked anxiety attacks, involving an overwhelming subjective feeling of panic and terror. In adiction, several associated symptoms, mostly physical occur: dyspnea, palpitations, chest pain or unsteady feelings, feelings of unreality (derealization and/or depersonalization), paresthesias, hot and clod flashes, sweating, faintness, trembling and shaking, and a fear of dying, going crazy, or losing control of oneself.

2.- Phobic disorders

The phobic disorders are characterized by fear and avoidance of certain objects or situations with subsequent restriction of a person's normal acticvities. Agoraphobia is characterized by the fear of being alone or, paradoxically, of being in a public place. This disorder usually exists with panic attacks but can occur in their absence Social phobia differs from agoraphobia in that the patient has the specific thoug irrational, fear of behaving inan embarassing or humiliating manner in public. Simple phobias are associated with specific objects and tend to be less socially incapacitating than agoraphobia or social phobia. Such simple phobias are usually focused on patticular objects or animals such as snakes or spiders.

3- Post-traumatic stress disorders

Certain events such as accidents. Natural disasters, combat, and torture. are stressful to almost all persons. The post-traumatic stress disorders are pathologic reactions to these events and are characterized by reexperiencing the event through nightmares, intrusive recollections, or "flashbacks" in which the person vididly relives the trauma; "psychic numbing" with a constricted affect and emotional detachment: or autonomic overactivity with hypervigilance.insomnia , and an exaggerated startle response to minor stimuli. The onset of these symptoms can be acute or delayed for months to years. This disorder has been frequently seen among Vietnam war veterans.

4- Generalized anxiety disorder

This is the revised term for anxiety neurosis. is characterized by socially disabling anxiety without an identifiable cause that persists for at least 1 month. Increased psychomotor tension (shakiness, jitteriness, fidgeting), autonomic overactivity, apprehensiveness, and hypervigilance are common.

Other, less common, anxiety subtypes are Obsessive-compulsive disorder (characterized by recurrent ideas. thoughts, images, or impulses (obsessions) that incessantly invade the consciousness and seem senseless or repugnant to the person. These obsessions are usually accompanied by ritualistic stereotyped behaviours (compulsions) and Atypical anxiety disorder (a category reserved for patients who appear to have primary anxiety but do not meet the criteria for any fo the above conditions.

Epidemiology

According to the National Institute of Mental Health (NIMH) sponsored Epidemiologic Catchment Area (ECA) study, anxiety disorders are now recognized as the largest single psychiatric disorder group in the United States, with a one-month prevalence of 7.3 % of the population.Total anxiety disorder rates for women are higher in those between the ages of 18 and 44 years (10 % to 12%) than in those aged 45 years and older (7% to 8%).

Among men, rates for any anxiety disorder are in the 5% range between the ages of 18 and 64 years, with a significant drop to 3.6 %for those aged 65 years and older.

Specific aspects of panic disorder: the panic history Althought the first attack and most subsequent panic attacks are unprovoked, adverse life situations and events are often present in the background

(*) Professor of Psychiatry, Psychiatrische Kliniek Universitalr Ziekenhuis
De Pintelaan 185 9000 Gent. BELGIUM

when panic attacks first appear. Not uncommonly, the first panic attack occurs during a life-threatening illness. following an accident, or at the loss of a close interpersonal relationship.

Subsequent panic attacks

After the first panic attack, the patient usually forgets about the incident and anxiety returns to a normal level, without evidence of serious anxiety symptoms. A few days to weeks later, however, a second spontaneous panic attack occurs. Each panic attack tends to include the same cluster of symptoms for each specific patient.

Postatack events

In some patients the disorder becomes static at this stage; panick attacks continue, but patients return to normal between attacks. Although their ability to function is not seirously disrupted, such patients view the panic attacks as both painful and feared.

Most patients develop some degree of anticipatory anxiety after repetitive panic attacks; so, with each successive attack, rather than returning to a baseline state, the intermittent level of anxiety rises. Careful questioning of these patients reveals that this anxiety is generated by the fear of having another anxiety attack.

Phobic avoidance behaviour

The development of phobias in patients with panic disorder is influenced by the number and severity of panic attacks, the treatment received, the attitudes of important people in the patient's life, and the patient's personality.

Patients with panic disorders are probably more prone to develop depression than are normal individuals. Because of this, the suicide rate of this group may be higher than normal.

A serious complicating factor in both panic disorder and agoraphobia is the development of drug and alcohol abuse.

A final common complication of panic disorder and agoraphobia is the development of pathological dependency.

Anxiety attacks presenting as a medical emergency

Psychiatrists see acute anxiety attacks with a considerable delay. as they remain longer in the care of primary physicians because of the dominant somatic presentation of the disorder. The diversity of somatization profiles allocates those patients to disparate medical specialies (pneumology. cardiology, emergency departments. neurology) where the physician tends to be more impressed by the symptom pattern that is specific for his particular field than by the psychological anxiety features. Psychiatrists working in institutions or in general psychiatric departments seldom see these patients in the early phases. Unless their disorder has lead to complications such as depression. hypochondriasis or agoraphobia. the patients are not routinely referred for psychiatric consultation.

The biology of panic attacks

The strongest argument for the biological basis of panic attacks is Pitts and McLure's finding (1967) which shows that sodium lactate infusion precipitates an anxiety attack with the same clinical sensations as the spontaneous panic or the phobic reaction in individuals with panic disorder, but generally fails to do so in non-panic patients. Drugs which block "natural" panic attacks also block the lactate-induced anxiety crises.

The mode of action of lactate is not established; it has been suggested that alterations Ca^{2+}, pH and redox reactions contribute to the anxiogenic effect. However, none of these hypotheses are as yet been confirmed.

Interestingly, treatment with antidepressants not only prevents spontaneous panic attacks but also panic induced by lactate.

Other stimuli that can induce anxiety in panic disorder patients are yohimbine (an alpha-adrenoceptor antagonist), caffeine and CO_2. Since all three treatments induce an increase in brain noradrenergic neurons originating in the locus coeruleus, these findings are compatible with the concept of an increased brain noradrenergic activity in panic. Also the beta-adrenoceptor antagonist isoproterenol is anxiogenic - the putative involvement of beta-adrenoceptors in the pathophysiology of panic attacks is, however, refuted by the lack of effect of beta-adrenoceptor antagonists in spontaneous as well as lactate-induced panic.

Strategics in the treatment of acute anxiety states

In treating anxiety, the physician must be prepared to (1) assess the efficacy of treatment over time; (2) determine when prolonged use is warranted; (3) discern if the patient is developing a tolerance to medication; (4) respond quickly and appropriately if a withdrawal syndrome become evident upon discontinuation of therapy

General principles of benzodiazepine anxiolytic efficacy

Benzodiazeines work by binding to specific CNS receptor sites, which are enriched in cortical and limbic-forebrain areas.c The net effect of the interaction of benzodiazepines with their receptors is to enhance the inhibitory properties of the neurotransmitter gammaaminobutyric acid (GABA).

GABA is the primary inhibitory neurotransmitter in the brain. GABA is known to increase the permeability of chloride ions through its receptor located on the chloride ion channel.

When a benzodiazepine binds to its receptor, GABA ergic neurotransmission is facilitated, and the rate of chloride ion transport accross the cell membrane is increased. The net effect is to hyperpolarize the cell andrender it less excitable.

Recent experiments with benzodiazepine receptor antagonists suggest that an alteration in the GABA/benzodiazepine receptor complex itself may underlie the development of tolerance and perhaps dependence.

Specific tactics in panic

Tricyclic antidepressants, monoamine oxidase inhibitors, and triazolobenzodiazepines. Exposure, cognitive, and behauiour therapies complete the adjunctive treatment regimen.

Advantages and disadvantages of tricyclic antidepressants are: delayed onset of action, exacerbation of anxiety symptoms, anticholinergic side effects, and other disadvantages are also discussed here.

Monoamine oxidase inhibitors are of questionable value in combating phobias. Dietary restrictions, delayed onset, weight gain, and other disadvantages outnumber the advantages.

Triazolobenzodiazepines have the advantage of rapid onset and are well tolerated. Some dependence/-withdrawal symptoms and sedation are among the disadvantages.

Triazolobenzodiazepines

Although classical benzodiazepines decrease the free-floating anxiety symptoms of panic attack patients, they have been reported as ineffective for treating the symptom cluster that is related to panic specifically. In a novel category of benzodiazepines. the triazolobenzodiazepines. Alprazolam has been extensively investigated and proven to be an effective anti-panic drug in world-wide trials. The efficacy of Alprazolam and its superiority over placebo especially for spontaneous panic attacks, is clear. However, it 15 not be forgotten thet Alprazolam doses between 2.5 to 6 mg are needed, with some patients needing up to 9 mg/day, which is higher than the average anxiolytic dose. A positive aspect of Alprazolam treatment is its quick onset of action, within the first week of treatment, and the low drop-out rate due to a particularly weel-tolerated drug regimen. The most frequently reported side effect is sedation, which, tends to diminish spontaneously or after dose reduction.

Tolerance for Alprazolam is very rare: patients are reported to be on Alprazolam for 6 to 7 months without developing tolerance. In fact, after this long treatment a dose decrease with the same effect is reported as possible. Dependence is an important issue. After 1 year of treatment dependence will have deleloped in 30% to 50% of all patients. So the tapering period must be particularly monitored with a lowering of the daily regimen by 0.5 mg every 4 days as a rule. The differential diagnosis between rebound, relapse or withdrawal is difficult. If symptoms start soon, withdrawal is the most plausible explanation, while in a relapse, symptoms, which will be known symptoms, will start later. For a differential diagnosis the symptoms should be observed during up to 3 weeks. If they remain, a relapse is probable; If they subside, they are withdrawel symptoms. tegretol and Clonidine have both been used to get through the withdrawal state rapidly,In the choice of drug regimen the associated symptomatology decisive. If obsessive-compulsive features are associated, the use of imipramine should be given priority because Alprazolam has no particular effect on obsessive-compulsive features. On the other hand, Alprazpolam is particularly effective on the somatization, and is consequently a first choice when multiple somatic anxiety symptoms are present.

The minimum treatment period is 6 months; triazolobenzodiazepines are the first choice of medications: the need for a slow taper period is indicated. Alprazolam and certain other benzodiazepines also have been found to be as effective as tricyclic antidepressants (TCAs) in the treatment of panic disorder. recent studies have demonstrated alprazolam's clinical efficacy across the full range of panic disorder symptoms, as well as an onset of action more rapid than that of imipramine, the TCA considered the "gold standard" for treatment of panic disorder.

Side effects

Clinical studies have shown that alprazolam has a side effect profile similar to that of other benzodiazepines. although drowsiness and lightheadedness occur less frequently than with diazepam. Experience with overdosage is limited but serious adverse events have not been reported to date. Side effects may be accentuated in the elderly or debilitated patient. As other benzodiazepines are known to reach the placenta and be excreted in breast milk, alprazolam should also be avoided in pregnancy, and in nursing mother until full human distribution data are available.

Dosage

Dosage should be individualised, starting at 0.25 mg to 0.5 mg thrice daily. In the elderly the starting dose is 0.25 mg twice daily. The dose is titrated upwards according to the needs of the patient to the recommended maximum of 4 mg/day in divided doses. Inital doses may be given at bedtime to minimise daytime lethargy. Abrupt withdrawal after longer term administration should be avoided.

Ease of administration, minimal side effects, rapid onset of action, and perceived ease of use of benzodiazepines as compared with TCAs make them acceptable to physicians who treat panic disorder.

Although beta-blocking agents may be helpful in reducing the cardiovascular symtoms such as palpitations and tachycardia, they do not on the whole provide comprehensive symptom relief. They may be indicated in the early phases of instauration of progressive doses of tricyclic antidepressants to patients who are oversensitive to symptoms such as tachycardia.

Combination of medicaton and behaviour strategies

The behavioral procedures classically used in panic disorder are systematic desensitization in vivo or in imagination, individually or in group and flooding, i.e. a sudden and complete exposure.

Most important is the fact that the type or recovery during behavioural treatment exclusively differs from that on Alprazolam treatment; while the latter are symptom-free during drug treatment, patients in a behavioural treatment still have some residual anxiety once the treatment is stopped.

Discontinuation of benzodiazepines

While withdrawal symptoms may occur with rapid discontinuation of benzodiazepines, gradual tapering of dosage may control the degree of the patient's discomfort.

In addition, if anxiety develops upon discontinuation of benzodiazepine therapy, the physician must distinguish between true withdrawal phanomena, short-term. rebound anxiety. and recurrence, and then plan apporopriate interventions.

REFERENCES

1- BALLENGER, J.C.: Biological aspects of panic disorder. Am. J.Psychiatry, 143: 4, 516-518.

2- KAHN, J.R.; STEVENSON, E.; TOPOL,P.; KLEIN D.F.: Agitated depression Alprazolam, and panic anxiety. Am.J.Psychiatry, 143: 9, 1172-1173.

3- KLERMAN, G.L.: Current trends in clinical research on panic attracks, agoraphobia, and related anxiety disorders. J. Clin Psychiatry, 47: 6 (suppl), 37-39.

4- SHEEHAN, D.V.: Current views on the treatment of panic and phobic disorders. Drug Therapy Hospital, 74-93.