

Treatment of panic disorder

John W. G. Tiller, Associate Professor and Reader, Department of Psychiatry, University of Melbourne, Royal Melbourne Hospital, and Albert Road Clinic, Melbourne

SYNOPSIS

Panic disorder consists of recurrent, disabling attacks of panic. It is frequently complicated by agoraphobia and other anxiety disorders or depression. Panic disorder differs from an isolated panic attack, both clinically and in treatment. Many patients respond to a combination of lifestyle change, especially control of caffeine and alcohol use, and cognitive behaviour therapy. For panic disorder, high potency benzodiazepines are effective for acute and long-term treatment, but have the disadvantages of sedation, drug interactions and discontinuation problems. For long-term treatment, imipramine is effective, but a lack of tolerability substantially limits its use. Most new antidepressants are probably effective for panic disorder, but few have been approved for this indication.

Index words: cognitive behaviour therapy, benzodiazepines, antidepressants.

(Aust Prescr 2000;23:124-6)

Introduction

The separation of anxiety disorders into a number of discrete conditions has improved our understanding of these problems, and enabled better-focused treatment. Approximately one third of people will experience at least one panic attack in their life. This may typically occur after excessive caffeine or alcohol use, or when fatigued, or otherwise stressed. This is quite different from panic disorder in which there are recurrent and unexpected panic attacks and at least one of the attacks has been followed by a month or more of persistent concern about having additional attacks. There is also a significant change in behaviour related to the attacks. Panic disorder may occur with or without agoraphobia. Panic attack and panic disorder should be differentiated as they need different interventions.

Panic attack

A panic attack is a discrete period of intense fear or discomfort, in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes¹:

- palpitations, pounding heart, or accelerated heart rate
- sweating
- trembling or shaking
- sensations of shortness of breath or smothering
- feeling of choking
- chest pain or discomfort
- nausea or abdominal distress
- feeling dizzy, unsteady, light-headed, or faint

- derealisation (feelings of unreality) or depersonalisation (being detached from oneself)
- fear of losing control or going crazy
- fear of dying
- paraesthesias (numbness or tingling sensations)
- chills or hot flushes.

Panic disorder

The criteria for panic disorder¹ are the occurrence of recurrent and unexpected panic attacks with at least one of the attacks having been followed by a month or more of:

- persistent concern about having additional attacks
- worry about the implications of the attack or its consequences, for example, losing control, having a heart attack, or going crazy
- a significant change in behaviour related to the attacks.

Panic disorder may be spontaneous, or a reaction to certain situations. Spontaneous panic occurs in any circumstances, often seemingly 'out of the blue'. While it may be possible to identify pre-existing vulnerability such as fatigue, work or family stress, for many patients this is not the case. There may be a genetic factor which increases people's vulnerability to panic disorder.

Situational panic occurs when a patient is exposed to trigger events or circumstances. These may be when in a lift, car, bus, tunnel or on a bridge or in situations where the patient fears they will not be able to escape. The added fear of their situation, coupled with some pre-existing vulnerability, results in the panic occurring in that particular setting or settings.

Patients with panic disorder may present to doctors' surgeries or emergency departments. They may feel that they are having a 'heart-attack' or are about to die, or cannot get their breath or have 'air hunger', usually in the absence of any signs of respiratory disorder.

Agoraphobia

Panic disorder may occur with agoraphobia. The essential agoraphobic features are:

- anxiety about being in places or situations from which escape might be difficult (or embarrassing) or in which help may not be available in the event of having a panic attack
- avoidance behaviour.

Agoraphobic fears involve situations that include the following: being alone outside the home, or being home alone, being in a crowd, standing in a queue, being on a bridge, and travelling

in a bus, train or car. The patient avoids these (for example, travel is restricted) or else they are endured with marked distress or anxiety, or require the presence of a companion.¹

Differential diagnosis

All the above disorders require that the anxiety or phobic avoidance is not caused by other conditions, for example substance abuse, general medical conditions such as thyrotoxicosis, or another mental disorder such as the avoidance associated with social phobia (social anxiety disorder). Anxiety disorders may occur alone, together, or with other psychiatric illnesses, most commonly depression. The panic disorder commonly precedes the depression, but may follow it. If there are psychiatric comorbidities, treat each disorder.

Investigation

If there are concerns about the patient's physical health these should be investigated. Some patients present with respiratory symptoms such as a feeling of choking or having difficulty getting their breath. While they may clearly have a mental health problem a respiratory disorder should be excluded. Palpitations, tachycardia and chest pain may warrant an ECG. Difficulties in swallowing, a 'lump in the throat', gastrointestinal discomfort, constipation or diarrhoea may also require further investigation. Feelings of numbness with tingling and pins and needles may suggest a transient ischaemic attack, but bilateral symptoms, and the absence of focal signs normally point to a psychological cause.

The presence of symptoms which occur in multiple systems for brief periods of time without a change in consciousness, can usually suggest a panic attack or panic disorder rather than other disease. **These patients should not be over-investigated, or referred from specialist to specialist.** Recognise and diagnose panic disorder on its clinical criteria, not just as a diagnosis of exclusion.

Treatment of panic attacks

Any underlying problems should be treated. For example, if the patient has been drinking to excess and their panic attacks are triggered by either intoxication or withdrawal, reducing their intake of alcohol is central to treatment. Restricting caffeine intake or eliminating it from the diet may also help.

Spontaneous isolated panic attacks can be managed with simple lifestyle changes and stress management techniques. Education about the attack and the fact that it does not indicate a dire physical disease is important, as most isolated panic attacks will not recur. There is almost no role for pharmacotherapy in this case.

Treatment of panic disorder

Although there may be a slightly increased cardiovascular risk associated with panic disorder, for the vast majority of cases, the major disadvantages are the patient's emotional and behavioural responses to the symptoms. Cognitive behaviour therapy² is the treatment of choice, and helps many patients. It involves firstly educating the patient about panic disorder, its causes, outcome and management.

Teaching the patient relaxation techniques and how to deal with hyperventilation can help them to stop or control a panic attack. Rebreathing in a paper bag for someone who is hyperventilating, is rarely indicated in a general practice, or in emergency departments. The hyperventilation has usually settled by the time the patient presents. Encouragement to take slow deep measured breaths, using a watch or clock as a guide to respiratory rate, is a technique that patients can use anywhere. This is more socially acceptable than starting to breathe noisily into a paper bag when they fear an attack.

Cognitive behaviour therapy for panic disorder involves both cognitive and behavioural elements, but the cognitive elements may be more prominent. Behavioural elements may be more helpful with exposure and response prevention for situational panic. These behavioural treatments are useful in helping people gradually gain mastery of a feared situation and avoidance to dramatically free up their lives.

Drug treatment can be added to cognitive behaviour therapy. There is the suggestion that the response to this combined approach is better than either treatment alone and there may be a lower risk of relapse when medication is discontinued.

Pharmacotherapy³

Benzodiazepines

Alprazolam and clonazepam are effective for the acute therapy and the maintenance treatment of panic disorder. Effectiveness is probably not confined to these potent benzodiazepines and all benzodiazepines may be effective in high enough doses. They need to be taken continuously as the onset of panic is usually so fast that the worst of the panic attack is over before an acute dose of a benzodiazepine can be effective. As a result, there is the potential for problems with sedation, co-ordination, interaction with other sedatives and cognitive effects, which often impair the ability to benefit from psychological therapy. In part, the reduction in the effectiveness of psychological therapy caused by benzodiazepines, may be from a reduction in motivation. At the end of a course of therapy when the benzodiazepine is reduced, typically after some months of panic control, about a third of patients have difficulties in discontinuing the drugs. The dose should therefore be gradually tapered over a period as long as six months to a year. Despite the major limitations of benzodiazepines, they are uniquely effective for the acute control of panic disorder and agoraphobia.

The dose of a benzodiazepine to control agoraphobia is typically higher than that to control panic. Typical doses of alprazolam for controlling panic are 4 mg daily compared to 6 mg daily for agoraphobia.

Antidepressants

Several antidepressants have been used to treat panic disorder. As with depression, and unlike treatment with benzodiazepines, it is typically 2–4 weeks or even 6–8 weeks of treatment with an antidepressant before reduction in the frequency or severity of panic attacks is apparent. The response rate to antidepressants varies from 60–90%. Approximately 10–40% of patients (typically about 20–30%) will therefore need to be changed to another drug because of lack of benefit.⁴ If there is no response

to the medication after 6–8 weeks the dose should be slowly reduced, and an alternative drug prescribed.

If antidepressants work they should be continued for a minimum of six months. An extended panic-free period gives the patient the confidence to start new activities in their lives and return to a normal balance.

Antidepressants should be gradually reduced before stopping them. This typically takes 2–4 weeks, or occasionally longer if a more rapid reduction results in discontinuation effects.

Tricyclic antidepressants

Imipramine and clomipramine have been widely studied in the treatment of panic disorder. Both are effective but poorly tolerated. This generally precludes their use in patients with panic disorder.

Monoamine oxidase inhibitors (MAOIs)

The irreversible non-selective inhibitors of monoamine oxidases A and B are effective, with phenelzine possibly being the most effective pharmacological treatment for panic disorder. Quite apart from the risk of dietary interactions, these medicines are not well tolerated when given in an effective dose. The recommended dose of phenelzine in the treatment of panic disorder is approximately 1 mg/kg/day, at which dose postural hypotension is a common disabling adverse event.

Newer antidepressants

All of the new antidepressants are probably effective in treating panic disorder. Their effectiveness seems to occur even in the absence of coexisting or comorbid depression. For some newer antidepressants there are extensive research data. Paroxetine has been approved for the treatment of panic disorder and the prevention of relapse. Sertraline is also approved in Australia for panic disorder. As with the tricyclics and MAOIs, the initial dose should be low and then gradually increased as these patients seem to experience more adverse effects when they start treatment. The final therapeutic dose which is required for the treatment of panic disorder is typically higher than the dose for the treatment of depression. For example, with paroxetine a common antidepressant dose is 20 mg/day while the dose is 40 mg/day or more for panic disorder. When treating agoraphobia with antidepressants, as with benzodiazepines, some patients need a higher dose than those with panic alone.

Summary

When a patient presents with panic disorder it is important to ascertain that this is not simply an isolated panic attack, or the consequences of maladaptive behaviours, or circumscribed stress. Brief counselling and some lifestyle changes could deal with such disorders. Panic disorder itself, with or without agoraphobia, can be usefully helped with cognitive behaviour therapy.

If symptoms are more marked, if the patient cannot relate to cognitive behaviour therapy, or if improvement is inadequate with the psychological approach alone, medications can be very helpful. Drugs can also be useful when there is not ready access to cognitive behaviour therapy. If immediate relief is essential, benzodiazepines may be uniquely effective, although

they have the potential for long-term adverse consequences. In general, one of the newer antidepressants is more appropriate. There is little merit in combining a benzodiazepine with an antidepressant for these patients. This is because the panic disorder has usually been long-standing, the time taken to respond to the antidepressant is relatively short, and the potential adverse consequences of benzodiazepines are substantial. After a response most patients on pharmacotherapy would be expected to continue treatment for 6–12 months usually in conjunction with cognitive behaviour therapy.

If a patient does not respond, their diagnosis should be reviewed, and consideration given to specialist referral. A specialist referral may also be indicated for those who are severely incapacitated by their panic disorder.

NOTE

The diagnostic features which are highlighted in this paper have been adapted from DSM-IV, the American Diagnostic and Statistical Manual of Mental Disorders, 4th Edition.¹ These are similar though not identical to diagnostic criteria for panic disorder in ICD-10 of the World Health Organization.⁵ DSM-IV Criteria have been referred to in this paper as they are the most commonly used by psychiatrists in Australia.

REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.
2. Tiller JWG. Cognitive behaviour therapy. Aust Prescr. In press 2001.
3. Writing Group for Therapeutic Guidelines: Psychotropic. Therapeutic Guidelines: Psychotropic. Version 4. Melbourne: Therapeutic Guidelines Limited; 2000.
4. Principles and practice of psychopharmacotherapy. Janicak PG, Davis JM, Preskorn SH, Ayd FJ. Baltimore: Williams and Wilkins; 1993. p. 449-64.
5. International statistical classification of diseases and related health problems: ICD-10. 10th revision. Geneva: World Health Organization; 1992.

FURTHER READING

- Andrews G, Crino R, Hunt C, Lampe L, Page A. The treatment of anxiety disorders: clinician's guide and patient manuals. Cambridge: Cambridge University Press; 1994.
- Hawton K, Salkovskis PM, Kirk J, Clark DM. Cognitive behaviour therapy for psychiatric problems: a practical guide. Oxford: Oxford Medical Publications; 1989.

Associate Professor Tiller has been a consultant to, or conducted medical research sponsored in whole or in part by, producers of all the new antidepressants, as well as producers of tricyclic antidepressants, monoamine oxidase inhibitors and benzodiazepines.

Self-test questions

The following statements are either true or false (answers on page 139)

5. Cognitive behaviour therapy is the treatment of choice for panic disorder.
6. New antidepressants usually need to be given in doses which are higher for panic disorder than the doses needed to treat depression.