UPDATE ARTICLE

Diagnosing And Managing Panic Disorder In Primary Care

K Y Mak,* MBBS, DPM, MD, FRCPsych.
Department of Psychiatry
The University of Hong Kong

Summary

Panic disorder is a common and frightening disorder, but it is often under-diagnosed and under-treated. It has a high morbidity and mortality including suicide. The causes are multi-factorial, both biological and psychosocial. Co-morbidities include agoraphobia, other anxiety disorders, depressive disorder and substance abuse. A diagnosis checklist is suggested. Management using medications and/or cognitive-behavioural therapy is not difficult and relatively safe. Prompt recognition and treatment can have a gratifying response and good prognosis. (*HK Pract* 1999;21:417-424)

摘要

「恐懼症」(又名「驚恐障礙」)是一種常見而且令人恐懼的精神疾病。患者容易被漏診或是未能得到適當治療，病人自殺率和自殺死亡率都相當高。病因包括生理、心理、社會等多方面因素，病人可能同時伴有其他精神疾病，例如廣場恐懼症、焦慮症、憂鬱症、濫用藥物等等，所以要採用藥物或認知行為療法、或兩者結合全面治療。及時診治病人的反應和預後較好。本文建議使用檢查清單，以便簡單化診斷令治療更安全。

Introduction

Up to a third of people experience episodes of panic when under stress, such as being chased by a dog. This usually lasts less than 20 minutes, occurs mostly at day time, and when away from home. Up to 25% of sufferers also have 'nocturnal panics' and wake up with panicky feelings or thoughts, not related to bad dreams.[1] Such attack is similar to other anxiety states such as extreme stage fright, but it differs from anxiety in that a panic victim feels better when with other people and worse when left alone. Even then, isolated attack does not amount to a genuine panic disorder.

If the attacks occur frequently, it becomes a panic disorder, which is also fairly common. It is estimated that 7% of the population in the United States have recurrent panic attacks, and 3% of them have attacks frequently enough to be classified as suffering from panic disorder.

Panic disorder is often under-diagnosed by doctors in primary care. However, it is a distressing life-time disorder with recurrences. The sufferers may receive unnecessary medical tests and hospitalisations. If untreated, the disorder carries a significant morbidity (e.g. become home-bound) and mortality from suicide.[2]

Epidemiology

The life-time prevalence rate is 1-3%. The female to male ratio is 3 to 1 for those with co-existing agoraphobia (as the males may be forced to face the stressful situation), but this sex difference is less marked for those without agoraphobia. There is no ethnic or racial difference. The

* *Address for correspondence:* *Dr. K Y Mak, Hon. Clinical Associate Professor, Department of Psychiatry, The University of Hong Kong, Queen Mary Hospital, Pokfulam Road, Hong Kong.*

UPDATE ARTICLE

age of onset is usually in the mid-20s. It is uncommon after 40 and becomes rare after 60 years of age.

Clinical features

Firstly, panic attack is defined as "an unexpectedly, overwhelming anxiety, intense short episodes of fear of impending death or catastrophe, e.g. a heart attack, a stroke or going crazy".

For a panic disorder, there must be some distressing somatic and/or psychological symptoms (**Table 1**). During the attack, the ability to reason is disrupted, the urge to escape is overwhelming, and risky behaviour such as abruptly stopping the car and leaving the scene may result. In between attacks the sufferer often develops varying degrees of nervousness and apprehension, and becomes more irritable and restless and preoccupied about future attacks (fear of the panic). Some even develop an avoidant behaviour (**Table 2**) and they may finally become housebound.

There are often other co-morbidities which include the following:

1. Nearly three-quarter of patients suffering from agoraphobia (fear of being in a place from which escape might be difficult) have panic disorder.
2. About 50% of panic patients have other anxiety disorders, e.g. social phobias, obsessive-compulsive disorder, generalized anxiety disorder.

Table 1: Checklist for panic disorder

A. Have you unexpectedly (i.e. without any overt cause) experienced a recent attack of overwhelming anxiety, with the following features?

1. Shortness of breath or smothering	☐ Yes	☐ No
2. Dizziness, faintness, unsteadiness, or lightheadness	☐ Yes	☐ No
3. Increased heart rate or pounding heart	☐ Yes	☐ No
4. Trembling or shaking	☐ Yes	☐ No
5. Feeling of choking	☐ Yes	☐ No
6. Sweating	☐ Yes	☐ No
7. Abdominal distress or nausea	☐ Yes	☐ No
8. Feeling that one's surroundings are not quite real or feeling that oneself is not real	☐ Yes	☐ No
9. Feelings of numbness or tingling sensations	☐ Yes	☐ No
10. Hot flushes or chills	☐ Yes	☐ No
11. Chest pain or discomfort	☐ Yes	☐ No
12. Fear of dying	☐ Yes	☐ No
13. Fear of losing control or going crazy	☐ Yes	☐ No
Total	_____	_____

B. How often is your attack?

1. Once only	☐ Yes	☐ No
2. More than once	☐ Yes	☐ No
3. Approximately how many attacks in the past month?		

_____

C. Following the above attack(s), have you experienced (for a month or more) the following features?

1. Persistent concern about further attacks	☐ Yes	☐ No
2. Worry about the implications or consequences	☐ Yes	☐ No
3. A change in behaviour due to the attacks*	☐ Yes	☐ No

D. Have you any significant physical problems such as hyperthyroidism, addiction to coffee or strong tea etc.? ☐ Yes ☐ No

If yes, please specify the condition(s):

_____

* *Examples of change in behaviour: avoid or restrict going outside the home alone e.g. going to crowded places, standing in a line, travelling in a bus or a train etc. (agoraphobia)*

N.B.: *It needs a "yes" score of at least 4 items in A, a "yes" score for B-2, any "yes" score for C but a "no" for D to qualify for a panic disorder.*

UPDATE ARTICLE

3. About 50% of panic patients have an affective disorder such as depressive illness.
4. About 20% of panic patients have abuse of alcohol or drugs. Perhaps initially these are taken to calm the panics.
5. Some patients with somatoform disorder and hypochondriasis also have panic disorder.

Diagnosis

According to the DSM(IV) of the American Psychiatric Association, a panic disorder is diagnosed when there are recurrent unexpected attacks, and at least one of the following which lasts for 1 month or more:

a. persistent concern about further attacks
b. worry about the implications of the attack or its consequences (**Table 3**)
c. significant change in behaviour as a result of the attacks.

In addition, during the attack, at least four of the symptoms in the checklist (**Table 1**), must be present. Those with less than four symptoms are called 'limited symptoms' attacks. Furthermore, such distress must not be due to:

a. organic cause, e.g. hyperthyroidism, caffeine; or
b. overt cause, e.g. exposure to anxiety provoking situation.

Table 2: Some common forms of avoidant behaviour in panic disorder

1. Avoid travelling (especially by plane)
2. Avoid leaving home (or to places far from home)
3. Avoid lonely places (especially in tunnels)
4. Avoid driving on highways (especially to distant places)
5. Avoid going out alone (even to supermarkets)
6. Unease while waiting
7. Unease standing in queues

Table 3: Some common cognitive thoughts in panic disorder

1. I am going to die
2. I am going to have a heart attack or stroke
3. I am going to faint
4. I must have a brain tumour
5. I must have some incurable disease
6. I am going crazy
7. I will loose my self-control
8. I will act very foolishly
9. I will be paralysed
10. I am going to scream

Etiology

There are different etiological factors, viz.:

Biological factors

Panic disorder is caused by a super-sensitive suffocation alarm system[3] due to autonomic or adrenergic overactivity in the locus coruleus, the limbic system and the frontal cortex. The increased catecholamines produce excessive activity of the autonomic nervous system. This causes hyperventilation and alkalosis, which further aggravate the panic. Some postulate a genetic cause for this disorder, and some suggest the involvement of the neurotransmitter cholecystokinine 3.

Psychological factors

There are different psychological theories including Freud's unconscious sexual impulses threatening to burst into consciousness and the classical conditioning and learning theories. However, the current one is the cognitive-behavioural theory by Clark[4] who proposed that there is a cognitive misinterpretation of bodily sensations as signs of catastrophe or imminent danger (**Figure 1**). Such thoughts are often traceable to previous experiences such as asthma in childhood, or witnesses of death, etc.

Social factors

Panic disorder is often precipitated by stressors such as gains or losses in family, work or finance and health problem.

UPDATE ARTICLE

Perhaps it is a combination of various factors that produce the disorder. This means panic disorder is a bio-psycho-social disorder, and should be managed accordingly.

Management

General measures

Before treatment, the patient should be assessed objectively (see **Table 4**).

Some basic medical work-up should be done to rule out any organic causes such as hyperthyroidism and cardiovascular disease.

In treatment, the patient should be reassured of the relative benign nature of panic attacks. Secondly, there should be modification of any stressors (e.g. marital problem). Sometimes it is assuring to the patient if the panic attack can be demonstrated by the hyperventilation test, which can be relieved by controlled breathing exercises (8 slow breaths per minute either by abdominal breathing or by using a paper bag). In the past, panic disorder was induced by lactate infusion, but only about 50% of the patients showed a positive response.

Psycho-education on panic disorder using pamphlets is useful.

Figure 1: A cognitive model of panic attacks

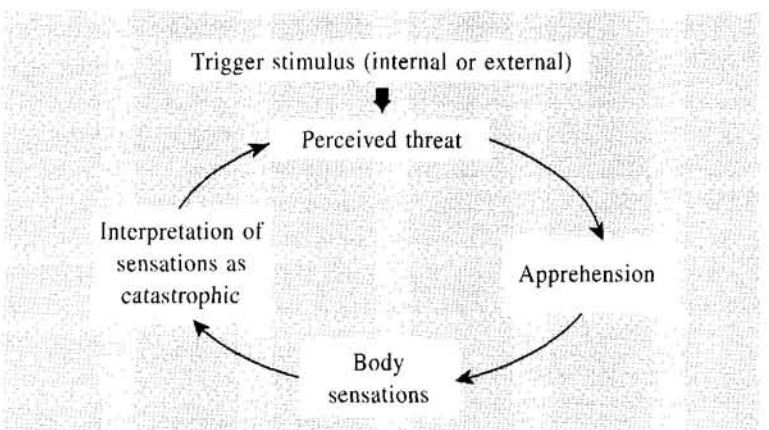

Table 4: Assessment of panic disorder

1. Date and time of the attacks.
2. Circumstances of the attacks – including places, whether alone or accompanied, and what sort of activity at that period, expected or unexpected.
3. Duration of the attack.
4. The physical sensations, the psychological feelings and thoughts, and the behaviour in response to the attack.
5. The outcome of the attack, especially any avoidant behaviour, both short term and long term.

This can instruct the patients how to stay calm using distraction, relaxation and rational thinking, and how to cope with stress with life-style adjustment, time management, adequate nutrition, exercise and rest.

Pharmacotherapy

Medications can be used to block the major or minor panic attacks (**Table 5**). Many conventional psychotropic drugs are useful. These include benzodiazepines (e.g. alprazolam, clonazepam), tricyclics (e.g. imipramine, clomipramine) and the monoamine oxidase inhibitors, (MAOIs) e.g. phenelzine. Occasionally, β-blockers (e.g. propranolol) and anticonvulsants (e.g. valproate, carbamazepine) have also been advocated. Most recently, the newer selective serotonin re-uptake inhibitors (SSRIs) have been advocated, including fluoxetine,[5] fluvoxamine,[6] paroxetine,[7] sertraline in either fixed dosage[8] or flexible dosage[9] and citalopram.[10] However, controlled trails of the third generation anti-depressants (such as nefazodone, venlafazine, mirtazapine) for panic disorder would soon be reported.

The recommended dosage for benzodiazepines appears alarming, but studies showed that cure, not just for symptomatic anxiety relief, is possible only at high doses.[11-12] However, the starting dose can be low to avoid the sedation. Likewise, when stopping the medication, the dosage should be tailed down gradually. Even then, many doctors are hesistant to scale up to a high

UPDATE ARTICLE

Table 5: Pharmacotherapy for panic disorder

Therapeutic agent	Brand name	Total daily dose
A. Benzodiazepines		
1. Alprazolam	Xanax	4 to 10 mg
2. Clonazepam	Rivotril	2 to 5 mg
B. Tricyclics		
1. Imipramine	Tofranil	150 to 250 mg
2. Clomipramine	Anafranil	150 to 250 mg
C. Monoamine oxidase inhibitors		
1. Phenelzine	Nardil	15 to 75 mg
2. Moclobemide	Aurorix	150 to 600 mg
D. Selective serotonin re-uptake inhibitors		
1. Fluoxetine	Prozac	20 mg
2. Fluvoxamine	Faverin	50 mg
3. Sertraline	Zoloft	50 mg
4. Paroxetine	Seroxat	20 mg
5. Citalopram	Cipram	20 mg

dosage and worry about the possibility of drug dependency. Therefore they can consider other types of medications. The effects of clomipramine seemed better than imipramine,[13] and the SSRIs seemed superior to the tricyclics because of less side-effects.[14] Anyway, whichever medication is used, the dosage should be titrated to a suitable level, maintained for a period and then tapered off; with the total duration usually lasting about a year. However, little is known about the long term efficacy of medications.

After the acute period, continued therapy may be necessary, and acute withdrawal of the medications may be harmful. Continued treatment with clonazepam,[15] alprazolam[16] or imipramine[17] seemed to show continued efficacy, but these studies were uncontrolled and retrospective. Judge *et al*[18] found a high relapse rate among patients switched to placebo compared with continued paroxetine; and recently, Michelson *et al*[19] found that continuing treatment for 24 weeks with fluoxetine is better than placebo.

Psychotherapy

Various psychological measures have been advocated such as psychoanalysis or psycho-dynamic psychotherapy. However, in recent years, the most successful paradigm is the use of cognitive-behavioural therapy (CBT). Using this method, the therapist together with the patient try to identify the circumstances and the common bodily sensations and associated thoughts, and the previous coping strategies (**Table 6**). The definitive therapy consists of firstly to replace faulty thinking with adaptive ones or alternative explanations, e.g. I will never faint, my heart is normal, I can overcome this panic attack, etc. Next, the patient has to test them out by facing the panicky situations (called exposure, either by graded/systematic desensitization, or by flooding) and to overcome the faulty avoidant behaviour with more appropriate response, e.g. stay in the place and breathe slowly. Finally, there should also be relapse prevention by recognizing the early signs and restarting the cognitive therapy again. Such therapy could be conducted individually or in a group.

Drugs or psychotherapy

Whether drug therapy or psychotherapy is superior in treating panic disorder is controversial.[20-22] It has been suggested that a combination of drug therapy with psychotherapy is superior (**Table 7**). Studies so far included imipramine,[23] phenelzine,[24] fluvoxamine,[25] paroxetine[7] and busipirone.[26] On the other hand, Loerch *et al*[27] had recently found that CBT was highly effective either in combination with moclobemide (the new reversible MAOI) or with placebo.

Miscellaneous measures

Others measures have been tried with occasional success. One method is the use of the biofeedback machine. There is hypnosis therapy which induces a trance-like state by suggestion, and the patients are then

(Continued on page 423)

UPDATE ARTICLE

Table 6: The construction of a dysfunctional thought diary

Date	Situation	Emotions (severity)	Thoughts	Outcome
1 Jan 99	Crossing the road	Anxious (moderate)	Fear of collapse	Panic and faint
2 Feb 99	Restaurant	Sadness (severe)	I'll lose control	Panic and leave

Table 7: Comparing various treatment methods for panic disorder

Treatment	Effectiveness	Side-effects	Drop-outs	Onset	Cost
Pharmacotherapy					
1. Tricyclics	High	Moderate	Moderate	Fair	Low
2. Benzodiazepines	High	Mild	Low	Fast	Fair
3. SSRIs*	High	Mild	Low	Fair	High
4. Beta-blockers	Mild	Low	Moderate	Fast	Low
5. Short-term placebo	Fair	Nil	Low	Varies	Nil?
6. Long-term placebo	Low	Nil	High	Varies	Nil?
Psychotherapy					
1. Cognitive-behavioural	High	Nil	Low	Slow	High
2. Psychoanalysis	Low	Nil	High	Very slow	Very high
3. Biofeedback	Mild	Nil	Moderate	Fair	Fair

** SSRIs = selective serotonic re-uptake inhibitors*

told that there will be no more panic attacks. However, its benefit is usually short lasting.

Prognosis

About 50% of the patients show recurrent or mild symptoms, with 30% recovering from the disorder. However, 20% of the patients run a chronic, severe course. In fact, those with severe, prolonged periods of the disorder, and continued avoidant or other maladaptive behaviour, require long-term management. ■

References

1. Rachman S, de Silva P. *Panic Disorder – the facts*. Oxford: Oxford University Press. 1996.
2. Clayton PI. Suicide in panic disorder and depression. Current therapeutic research 1993; 54(6):825-831.
3. Klein DF. False suffocation alarms, spontaneous panics, and related conditions: an integrative hypothesis. *Arch Gen Psychiatry* 1993;50:306-316.
4. Clark DM. A cognitive approach to panic. *Behav Res Ther* 1986;24:561-570.
5. Michelson D, Lydiard RB, Pollack M, *et al.* Outcome assessment and clinical improvement in panic disorder: evidence from a randomized controlled trial of fluoxetine and placebo. *Am J Psychiatry* 1998;155:1570-1577.
6. Hoehn-Saric R, McLeod DR, Hipsley PA. Effect of fluvoxamine on paci disorder. *J Clin Psychopharmacol* 1993;13:321-326.
7. Oehrberg S, Christiansen PE, Behnke K, *et al.* Paroxetine in the treatment of panic disorder: a randomised, double-blind, placebo-controlled study. *Br J Psychiatry* 1995;167:374-379.
8. Longberg PD, Wolkow R, Smith WT, *et al.* Sertraline in the treatment of panic disorder. *Br J Psychiatry* 1998;173:54-60.
9. Pollack MH, Otto MW, Worthington JJ, *et al.* Sertraline in the treatment of panic disorder. A flexible-dose multicenter trial. *Arch Gen Psychiatry* 1998;55:1010-1016.
10. Wade AG, Lepola U, Koponen HJ, *et al.* The effect of citalopram in panic disorder. *Br J Psychiatry* 1997;1170:549-554.
11. Spier S, Esar G, Rosenbaum J, *et al.* Clonazepam in the treatment of panic disorder and agoraphobia. *J Clin Psychiatry* 1986;47: 238-242.
12. Kahn RS, van Praag HM. Panic disorder: a biological perspective. *Eur Neuropsychopharmacol* 1992;2:1-20.

UPDATE ARTICLE

Key messages

1. Panic disorder is not uncommon, and is often a life-time disorder with recurrences.
2. It is often under-diagnosed and unnecessary medical investigations are done.
3. If untreated, there is a significant morbidity and sometimes mortality by suicide.
4. The causes are often bio-psycho-social, and treatment is effective using a similar bio-psycho-social approach.
5. At present, the selective serotonin re-uptake inhibitors are relatively safe and effective; while cognitive-behavioural psychotherapy is the method of choice.

13. Modign K, Westberg P, Erikkson E. Superiority of clomipramine over imipramine in the treatment of panic disorder: a placebo controlled trial. *J Clin Psychopharmacol* 1992; 12:251-261.
14. Nutt D. The role of SSRIs in anxiety disorders. *Eur Neuropsychopharmacology* 1995;5:260-261.
15. Pollack MH, Tesar GE, Rosenbaum JR, *et al.* Clonazepam in the treatment of panic disorder and agoraphobia: a one-year follow-up. *J Clin Psychopharmacol* 1986;6:302-304.
16. Nagy LM, Krystal JH, Woods SW, *et al.* Clinical and medication outcome after short-term alprazolam and behavioral group treatment in panic disorder: 2.5 year naturalistic follow-up study. *Arch Gen Psychiatry* 1989;46:993-999.
17. Aronson TA. A naturalistic study of imipramine in panic disorder and agoraphobia. *Am J Psychiatry* 1987;144:1014-1019.
18. Judge R, Burnham DB, Steiner MX, *et al.* Paroxetine long-term safety and efficacy in panic disorder and prevention of relapse: a double-blind study. In *Xth World Congress of Psychiatry, Madrid, vol.2*. New York: World Psychiatric Association. 1996.
19. Michelson D, Pollack M, Lydiard RB, *et al.* Continuing treatment of panic disorder after acute response: randomised, placebo-controlled trial with fluoxetine. *Br J Psychiatry* 1999;174: 213-218.
20. Black DW, Wesner R, Bowers W, *et al.* A comparison of fluvoxamine, cognitive therapy, and placebo in the treatment of panic disorder. *Arch Gen Psychiatry* 1993;50:44-50.
21. Marks I, Swinson RP, Basoglu M, *et al.* Alprazolam and exposure alone and combined in panic disorder with agoraphobia: a controlled study in London and Toronto. *Br J Psychiatry* 1993;162:776-787.
22. Clark DM, Salkovskis PM, Hackmann A, *et al.* A comparison of cognitive therapy, applied relaxation and imipramine in the treatment of panic disorder. *Br J Psychiatry* 1994;164:759-769.
23. Mavissakalian M, Michelson L. Self-directed in vivo exposure practice in behavioral and pharmacological treatment of agoraphobia. *Behav Therapy* 1983;14:506-519.
24. Sheehan DV, Ballenger J, Jacobsen G. Treatment of endogenous anxiety with phobic, hysterical and hypochondriacal symptoms. *Arch Gen Psychiatry* 1980;37:51-59.
25. Cottraux J, Note LD, Cungi C, *et al.* A controlled study of cognitive behaviour therapy with busipirone or placebo in panic disorder with agoraphobia. *Br J Psychiatry* 1995;167: 635-641.
26. De Beurs E, van Dyck R, van Balkom AJLM, *et al.* Assessing the clinical significance of outcome in agoraphobia research: a comparison of two approaches. *Behav Therapy* 1994;25: 147-158.
27. Loerch B, Graf-Morgenstern M, Hautzinger M, *et al.* Randomised placebo-controlled trial of moclobemide, cognitive-behavioural therapy and their combination in panic disorder with agoraphobia. *Br J Psychiatry* 1999;174:205-212.