



## Panic disorder: Review of current status

Abdullah G. Mohammed, Abdulmuttalib Al-Fikki

Panic disorder (PD) is a common and typically disabling psychiatric condition that has a considerable impact on the quality of life. It impairs the social, family and working lives of sufferers at a time when they should make the greatest contribution to society. It leads to over-utilization of medical facilities in futile efforts to find physical causes for their symptoms. Frequent comorbid psychiatric conditions, most notably depression and other anxiety disorders complicate the clinical presentation, exacerbating

individual disability and increasing the economic burden to society. The development of antidepressants with specific serotonergic activity has facilitated effective drug treatment of the disorder. This article briefly reviews the etiology, diagnosis and pharmacotherapy of PD.

*Key words:* Panic, serotonin, comorbidity, antidepressants

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### Introduction

Panic disorder is a common psychiatric disorder. It is estimated to affect between 2% to 4% of the population at some time in their lives, and it affects almost 2% of primary care attendees.<sup>1-4</sup> It has a considerable impact on patients' lives as they tend to overutilize medical facilities in an attempt to find a medical explanation for their symptoms.<sup>5</sup>

A number of theories have been proposed to explain the etiology of panic disorder, including dysfunction of one or more neurotransmitters such as serotonin (5-HT), norepinephrine, gamma-aminobutyric acid (GABA), cholecystikinin, the 'false suffocation response' and cognitive and behavioral mechanisms.<sup>6-11</sup>

There is evidence to support a role for serotonin in the biology of panic disorder, but at present, the available evidence does not differentiate between the theories of 5-HT excess and deficit.<sup>12-16</sup>

The precise serotonergic dysfunction in panic disorder remains unclear, and it is likely that multiple brain regions and 5-HT receptors are involved.<sup>17</sup>

### Definitions

**PANIC ATTACK:** Is the hallmark of the panic disorder. It is a feeling of overwhelming fear that can be defined as a specific, discrete type of anxiety, characterized by an abrupt onset and rapid crescendo peak of prominent autonomic symptoms, often seeming to come 'out of the blue'. The attacks can occur in an attenuated form called *limited minor symptoms episodes* that cause substantial distress and impairment. The panic attack itself is sporadic and highly variable in its frequency.<sup>18</sup> A single simple attack is a powerful predictive marker for the presence of other psychiatric disorders, principally depression, panic disorder or other anxiety states.

A lifetime history of panic attack is also predictive of both future panic disorder and depression in the majority of cases.<sup>19</sup>

**PANIC DISORDER:** To describe the syndrome as panic disorder, it must include panic attacks, anticipatory anxiety about the possibility of having a panic attack, phobic symptoms and functional disability in daily life.

Psychiatrist, Psychological Medicine Hospital, Kuwait.

Correspondence: Dr. A.G. Mohammed, Psychiatrist, Psychological Medicine Hospital, P.O. Box 4081, Safat, Post Code 13041, Kuwait. Tel: 965 4843900 Ext. 3011; Fax: 965 4845578; Email: amohammed9@hotmail.com

**COMORBIDITY:** Comorbidity in psychiatric disorders is common. Depression is a common comorbidity in patients with panic attacks. Other anxiety disorders like phobias and social phobia are also common. Less common comorbid conditions include personality disorders and alcohol dependence.<sup>20-23</sup>

The presence of comorbidity results in more severe anxiety and depressive symptoms, a higher rate of suicide attempts, and a higher frequency of other comorbid conditions such as alcoholism. Patients with comorbidity have poorer response to medications and poor compliance with treatment, and consequently, higher rate of relapse with increased impairment of daily life activities.<sup>24-26</sup>

## Diagnosis

Key symptoms of panic disorder are those that comprise diagnostic criteria, i.e. recurrent unexpected panic attacks, inter-current anxiety or concern about attacks, implications or consequences of attacks or behavior changes to attacks (anticipatory anxiety), and for patients with agoraphobia, anxiety about

### DSM-IV criteria for panic attack

A discrete period of intense fear or discomfort, in which four (or more) of the following symptoms developed abruptly and reached a peak within ten minutes:

1. palpitations, pounding heart, or accelerated heart rate
2. sweating
3. trembling or shaking
4. sensation of shortness of breath or smothering
5. feeling of choking
6. chest pain or discomfort
7. nausea or abdominal distress
8. feeling dizzy, unsteady, lightheaded, or faint
9. derealization (feelings of unreality) or depersonalization (being detached from oneself)
10. fear of losing control or going crazy
11. fear of dying
12. paraesthesias (numbness or tingling sensation)
13. chills or hot flushes

having symptoms in situations where escape or getting help may be difficult. Phobic situations are avoided, or endured with marked distress. Thus panic disorder includes the following five domains:

1. Panic attacks, including limited symptom attacks;
2. Anticipatory anxiety;

3. Panic-related phobias (including agoraphobia and body sensation phobias);
4. Concern over wellbeing;
5. Disability in terms of work, social and family life.<sup>27</sup>

### DSM-IV diagnostic criteria for panic disorder

Both (1) and (2) below need to be satisfied:

1. Recurrent unexpected panic attacks
2. At least one of the attacks has been followed by a minimum of one month of the following:
  - a. persistent concern about having additional attacks
  - b. worry about the implications of the attack or its consequences (e.g. losing control, having a heart attack, 'going crazy')
  - c. a significant change in behavior related to the attacks

## Pharmacotherapy of Panic Disorder

Panic disorder can be treated by different modalities. This article focuses on pharmacological treatments. It should be stated, however, that non-pharmacological treatments such as cognitive behavioral psychotherapy are equally effective in treating panic disorder.

Controlled efficacy data provide strong evidence for the clinical efficacy of agents in each of the 3 therapeutic classes:

1. Selective Serotonin Reuptake Inhibitors (SSRIs) e.g. paroxetine, fluvoxamine, citalopram;
2. Tricyclic Antidepressants (TCAs) e.g. clomipramine and imipramine;
3. Benzodiazepines (BDZs) e.g. Alprazolam & clonazepam in the treatment of panic disorder. The available evidence suggests that antidepressants such as SSRIs are a more effective therapeutic choice than benzodiazepines.<sup>28</sup>

**SSRIs:** A number of SSRIs is currently available for the treatment of PD. SSRIs are safe, well tolerated with fewer side effects, and can usually be given as a once daily dose. Therapeutic effects of medication do not appear until four to eight weeks. SSRIs offer sustained benefit over short or long term, and ease of dosing without problems associated with tolerability, safety or discontinuation.

**TCAs:** Considered the classic antidepressants, and have been used to effectively treat PD for many years. This class of medication, however, is associated with undesirable side effects, notably dry mouth and constipation.

Another disadvantage is that they are lethal in overdose.

**BDZs:** Classically termed *anxiolytics* because of their ability to calm down the autonomic hyperarousal manifested by the somatic symptoms of PD. Unlike antidepressants BDZs offer quick relief of the uncomfortable symptoms associated with PD. These medications are best used for a short time (2 to 4 weeks) until antidepressants take their effect. Prolonged use of BDZs should be avoided, to minimize the risk of dependence.<sup>29</sup>

Effective treatment of panic disorder clearly involves the recognition and appropriate treatment of the comorbid condition. Available data indicate that long term treatment of panic disorder is necessary, effective and well tolerated, and continuation of treatment for up to one year is essential in maintaining and extending short term improvements and in preventing relapse of panic disorder. Treatment should be continued in patients with substantial residual psychopathology of panic disorder, comorbid conditions especially phobic symptoms, a history of severe relapse or high levels of stress in their lives. If treatment of panic disorder is effective and full remission maintained, it should be stopped after 12 to 24 months, provided that the patient is not currently experiencing stressful life events. With all medications, withdrawal should be slow, planned and individualized.<sup>30</sup>

**Examples of different classes of medications used in the treatment of PD**

Class	Drug	Average daily dose
SSRI	Citalopram	10 - 60 mg
	Fluvoxamine	50 - 200 mg
	Paroxetine	20 - 40 mg
TCA	Clomipramine	75 - 300 mg
	Imipramine	75 - 300 mg
BDZ	Alprazolam	0.5 - 4 mg
	Bromazepam	3 - 9 mg
	Lorazepam	2 - 4 mg

### Clinical guidelines for primary care management of panic disorder

The following are clinical guidelines from the International Consensus Group on Depression and Anxiety:

1. Establish the diagnosis by conducting an appropriate, but limited, medical work up;

2. Educate patients about the disorder;
3. SSRI's are the drugs of first choice;
4. Start treatment with a low dose;
5. Manage side effects successfully to allow continuation of treatment;
6. The treatment goal is full remission across the syndrome: panic attacks, anxiety, phobias, well being and disability;
7. When panic is comorbid or response is incomplete, consider referral to a psychiatrist;
8. Continue effective treatment for 12 to 24 months, and consider stopping only when the patient is well and in a stable life situation;
9. Discontinue treatment slowly over 4 to 6 months;
10. Inform patients not to stop medication abruptly without consulting their physician.

### Conclusion

An important message for primary care physicians and their patients is that panic disorder is a chronic and disabling condition that often requires treatment over several years. Medical causes of panic attacks should be excluded.

Education about the nature of panic disorder and its associated comorbidity is essential. Clinicians should promptly initiate effective medication with exploration of life stressors and precipitating events. Moreover, the treatment should be started at low doses because patients with PD are particularly sensitive to physical symptoms and to medication side effects. Simple panic attacks can be managed adequately at a primary care level, but patients with a comorbid disorder require specialist care.

The first line of treatment for panic disorder is SSRI's. To ensure effective treatment of panic symptoms and to prevent future relapse, medications should be continued for a minimum of twelve months.

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### CME Questions

After you have completed reading the above article, take the test given below. Circle T (True) or F (False) in the answer sheet (page 50) to show the correct answer to each question. Questions 1 to 10 are related to the content in this article.

1. Panic disorder is one of the least common psychiatric disorders.
2. Patients with panic disorder often have comorbid psychiatric conditions.
3. Dopamine plays an important role in the etiology of panic disorder.
4. Panic symptoms occur exclusively in patients with panic disorder.
5. Symptoms of panic disorder include derealization and depersonalization.
6. SSRIs are the first line of choice in the treatment of panic disorder due to their favorable side effects.
7. Benzodiazepines should be used for a short term because of the risk of dependence.
8. Patients with panic disorder should be thoroughly investigated for medical conditions.
9. Paroxetine is used in the treatment of panic disorder.
10. Effective treatment of panic disorder should continue for 12-24 weeks.