



REVIEW

Anxiety, panic and adult asthma: A cognitive-behavioral perspective

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Summary A review of previous research suggests increased probability of the prevalence of anxiety disorders, and particularly panic disorder and panic attacks in patients with asthma, as compared to a normal population. Research also indicates significant levels of co-morbidity between asthma and anxiety as measured on dimensional scales of anxiety and panic. Clinical anxiety and panic manifestations affect symptom perception and asthma management through the effects of anxiety symptoms such as hyperventilation, and indirectly through self-management behavior and physician response. However, there is limited data on the impact of anxiety co-morbidity on asthma quality of life. Some studies indicate that individuals with co-morbid asthma and anxiety or panic report worse asthma quality of life both in general and in relation to their symptomatology, being limited in their daily activities, in response to environmental stimuli and in regard to feelings of emotional distress. Cognitive-behavioral therapy (CBT) is an effective and empirically supported treatment of choice for anxiety disorders and panic attacks. However, standard CBT protocols for anxiety and panic may need to be specifically targeted at improving asthma outcomes. Also, asthma research literature is lacking in randomized controlled trials applying CBT to patients with co-morbid asthma and clinical anxiety manifestations. Trials evaluating CBT interventions in individuals with clinical anxiety manifestations and asthma may provide evidence of these interventions as an effective adjunct to improve asthma management and control. © 2006 Elsevier Ltd. All rights reserved.

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Introduction

Two recent reviews^{1,2} of the literature have described an increased rates of psychological co-morbidity ranging from anxiety and panic symptoms to anxiety disorders in adults with asthma. This psychological co-morbidity is likely to impact on asthma outcome and quality of life.² Innate biological factors may interact with psychological variables playing an important role in the way the patients adapt to or react to asthma symptoms.³

This review aims to take the reader through the published research in the area of co-morbid anxiety disorders and clinical manifestations of anxiety and panic symptoms in adult asthma, and the impact of this co-morbidity on asthma outcome and specifically asthma-related quality of life. Further, this review discusses current evidence and the theoretical possibilities that may explain this co-morbidity and explores treatment options using cognitive-behavioral interventions. The paper highlights these various aspects of research and suggests implications for policy and further research. It also identifies implications for the clinical practice of respiratory physicians, general practitioners, psychologists and allied health professionals, involved in the care of patients with asthma. The review advocates a holistic approach to the patient and emphasizes the treatment of "the patient with asthma" as opposed to treatment of "the asthma."

We completed a literature review using MEDLINE by pairing the word "asthma" with the following words: anxiety OR panic OR asthma quality-of-life OR cognitive behavioral interventions. Bibliographies of identified articles were hand searched for

additional references not identified through the search strategies. Key authors in the field were searched for additional references and similar articles were identified from the search functions of PUBMED. We limited the search strategy to include articles that (1) were English-language only (2) adult samples with a minimum age ≥ 18 years AND EITHER (a) assessed prevalence of anxiety disorders and symptoms in patients with asthma AND/OR (b) assessed the impact of anxiety and panic on various asthma outcome measures including asthma quality-of-life AND/OR (c) addressed the role of cognitive behavioral interventions in patients with co-morbid asthma and anxiety/panic.

We adopted a narrative format of presentation for this review, within a systematic framework, given the heterogeneity of anxiety constructs ranging from anxiety symptoms to anxiety disorders, as well as the multiple end points of asthma outcome, in the available literature.

Epidemiology of co-morbid asthma and anxiety/panic

Asthma and clinical anxiety disorders

Anxiety disorders are diagnosed clinically on a categorical scale (diagnosis/no diagnosis) based, for example, on the criteria of the Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition Text Revision (DSM-IV-TR).⁴ In this section, we review research relating asthma to anxiety disorders diagnosed categorically; in the next section we review the relationship between asthma and anxiety measured symptomatically.

Previous research indicates an elevated prevalence of generalized anxiety disorder, panic disorder and elevated rates of panic attacks in clinical samples and community samples of patients with asthma.^{1,5–11} A recent comprehensive study in Germany determined the association between asthma and mental disorders in a large community sample ($N = 7124$) of adults aged 18–65.¹² The study systematically assessed participants with physician-diagnosed asthma, for anxiety disorders, using a structured interview. The study reported that asthma was associated with a significantly increased likelihood of any anxiety disorder, panic disorder and panic attacks (see Table 1).

Panic attacks are characterized by a period of intense fear, developing abruptly and reaching a peak within 10 min, with any four of the following symptoms: Shortness of breath, choking sensations, chest pain or discomfort, dizziness, abdominal distress or nausea, derealization or depersonalization, rapid heart rate, palpitations, sweating, hot flushes or chills, shaking or trembling, fear of losing control or going crazy, fear of dying. Panic disorder is characterized by recurrent panic attacks with at least a month of anticipatory anxiety of having a panic attack or change in behavior (e.g. avoidance) related to the attack.⁴

A higher prevalence of panic attacks has been reported in other clinical and community samples of individuals with a diagnosis asthma.^{6,8,9,11,13,14} Cross-sectional studies have found an association between self-reported asthma and panic attacks (OR = 5.88 (95% CI, 2.21, 15.62)), $N = 2768$.⁸ In a primary care sample of 998 adults, where 176 adults had physician-diagnosed asthma, the association between asthma and panic attacks remained significant (OR = 1.7 (95% CI, 1.1, 2.6)),

after controlling for sociodemographic factors and other mental disorders.¹⁰ Population studies based on self-reports have also found a significant association (OR = 1.7 (95% CI, 1.2, 2.4)), between respiratory disease and panic attacks after adjusting for demographic characteristics, comorbid disorders and physical co-morbidity.¹⁵ Other studies^{16–18} have also shown a higher prevalence of panic disorder in clinic samples of individuals with asthma and authors^{19,20} estimate that 6–38% of adults with asthma meet the diagnostic criteria for panic disorder as compared to 1–4% in the population at large.

Theoretical possibilities

Given the unpredictable and occasionally life-threatening nature of a disorder like asthma, the high prevalence of panic disorder and panic attacks in individuals with asthma over and above that in a population without asthma, is unsurprising. Some of the theories proposed to explain this comorbidity include the dyspnea-fear theory attributed to the somatic effects of hyperventilation,²¹ theory of abnormally sensitive carbon dioxide receptors in the central nervous system and abnormal "suffocation detectors".²² Other theories point to the fact that unpredictable and at times uncontrollable dyspnoea maybe a significant etiologic factor in panic disorder.^{23,24} Adrenergic-agonists, theophylline and other steroid medications, used in asthma management, have also been implicated in provoking anxiety.^{5,25,26}

Other authors have suggested common genetic influences and common environmental risk factors like cigarette smoking, low socioeconomic status or

Table 1 The prevalence of anxiety disorders in a community sample ($N = 7124$; Goodwin⁷).

	Current severe asthma (the past four weeks)	Lifetime non-severe asthma	Lifetime severe asthma
Any anxiety disorder	OR 2.65; 95% CI, 1.35–5.18	OR 1.51; 95% CI, 1.0–2.32	OR 2.09; 95% CI, 1.3–3.36
Panic disorder	OR 4.61; 95% CI, 1.09–9.4		OR 2.61; 95% CI, 1.29–5.25
Panic attacks	OR 4.12; 95% CI, 1.32–12.8		OR 2.84; 95% CI, 1.66–4.89
Generalized anxiety disorder			OR 5.51; 95% CI, 2.29–13.22
Specific phobia	OR 4.78; 95% CI, 2.35–4.05		OR 2.93; 95% CI, 1.71–5.0
Social phobia			OR 3.28; 95% CI, 1.42–7.59

Note: OR = odds ratio; CI = confidence interval.

stressful life events¹⁰ as an explanation for this increased co-morbidity. Some authors have suggested a selection bias as an explanation for this high association between asthma and panic disorder. They indicate that comparable prevalence rates (16%) have been reported in hospitalized patients with chronic pain.²⁷ Other studies of patients with chronic illnesses like hypertension and diabetes mellitus have also found comparable prevalence rates of anxiety manifestations in their samples.²⁸ However, a recent prospective community study followed a cohort of 591 adults with asthma for 20 years. The results of the study indicate bidirectional longitudinal associations between panic and asthma and the authors suggest a dose response type of relationship¹¹ where active asthma predicted subsequent panic disorder (OR = 4.5 (95% CI, 1.1, 20.1)), and the presence of panic disorder predicted subsequent asthma activity (OR = 6.3 (95% CI, 2.8, 14.0)), even though gender, smoking and socioeconomic status were confounders. In conclusion, recent literature does suggest increased likelihood for anxiety disorders, and particularly panic disorder and panic attacks in patients with asthma, as compared to a normal population.

Asthma and other constructs of anxiety

Previous research also indicates significant levels of co-morbidity between asthma and anxiety as measured on dimensional scales of anxiety and panic.^{29,30} These measures include, among others, the Hospital Anxiety and Depression Inventory (HADS)³¹ and the Spielberg's State Trait Anxiety Inventory (STAI).³²

A study comparing psychological profiles of patients and healthy controls suggested that anxiety symptoms, as measured by the STAI, were more frequently associated with a diagnosis of asthma when compared to patients with chronic viral hepatitis or healthy controls.²⁹ Similarly, a large Australian population study³³ of 6609 adults suggested that patients with asthma ($n = 834$) demonstrated a higher prevalence of psychological distress (17.9%), as compared to individuals with no diagnosis of asthma (12.2%). Diagnosed mental health conditions were significantly more common in patients with asthma (16.2%) as compared to those individuals without asthma (10.8%). Another Australian study³⁴ found a prevalence of anxiety symptoms (a significant score of 8 or more than 8 on the HADS), in 40% of the clinic and research volunteer sample of patients with asthma.

However, in a Swedish population sample of 715 adults,³⁵ there was no evidence that those diagnosed with asthma had more anxiety or depression, than those individuals with no diagnosis of asthma. Despite this contradiction, individuals with asthma did demonstrate a significant association between reported respiratory symptoms and anxiety symptoms as measured by the HADS. Accordingly, anxiety and panic symptoms may exist, without being classified as a disorder and may influence the experience and behavior of an individual with asthma and affect symptom perception and asthma outcome.^{2,36} However, it cannot be suggested that asthma has a higher association with anxiety manifestations when compared to other chronic illnesses including diabetes mellitus and hypertension.³⁷⁻⁴⁴

The impact of anxiety and panic on asthma outcome

Anxiety compromises asthma outcome

Current evidence

The following research focuses on the role of anxiety symptoms and panic fears and anxiety disorders on various asthma outcomes. Some researchers⁴⁵ have reported an increased subjective perception of shortness of breath in anxious individuals with asthma even in the absence of any objectively measured change in airway obstruction. This may lead to an increased use of asthma medication for what may well be anxiety symptoms.⁴⁶ Moreover, the medications most often used to treat anxiety and panic (i.e., benzodiazepines) can affect respiratory symptoms and clinical findings.^{2,26,47}

The effects of panic-fear on the course of asthma are well documented. Important aspects of this research describes the subjective symptomatology of asthma, and defines a symptom category, delineated as panic-fear.⁴⁸ The reported frequency of panic-fear symptoms has been related to measures of medical intractability and "difficult asthma" such as: more intensive steroid regimen prescriptions⁴⁹; excessive use of as-needed medication⁵⁰; more frequent hospital readmissions⁵¹; and longer hospitalizations.⁵² These effects are often independent of objectively measured pulmonary impairment.^{50,53}

Two types of panic-fear have been delineated in the literature: panic-fear in response to the symptoms of asthma, termed illness-specific panic-fear and measured by the Asthma Symptom Checklist, and a more generalized panic-fear

(derived from the Minnesota Multiphasic Personality Inventory), which is believed to reflect a stable personality trait.⁵ Extremely high illness-specific panic-fear leads to overuse of as needed medication, and is associated with maladaptive and disruptive anxiety during an asthma attack.⁵⁴ Also, as Kinsman and colleagues have pointed out, high illness specific panic-fear can lead to hyperventilation, potentially worsening asthma exacerbations through hyperventilation induced bronchoconstriction.⁵⁴

Specific psychological characteristics like illness specific panic-fear, as compared to more general asthma symptoms like breathlessness, characterized high emergency room attendees, in a sample of 30 adult patients with asthma.⁵⁵ All these patients had made two or more unscheduled emergency room visits for asthma exacerbations over the 1-year study period of an earlier study. Anxiety symptoms predicted high illness specific panic-fear suggesting an indirect effect with an increase in emergency room visits.

High generalized panic-fear can also impact negatively on the course of asthma and the potential benefits of self-management education. High generalized panic-fear is characterized by high anxiety, helplessness, and dependence in response to a variety of situations beyond those just related to breathing difficulties.⁵⁴ Furthermore, high generalized panic-fear is associated with worse medical outcome for asthmatics, including longer and more frequent hospitalizations. Generalized panic-fear scores are independent of objective medical indicators and highly stable across several months of intensive in-patient medical treatment.^{51,56}

In summary, the studies described here reflect how panic and anxiety adversely influences asthma directly through the effects of panic symptoms (e.g., hyperventilation), and indirectly through patient behavior (e.g., overuse of medications, self-management behavior) and physician response. Often studies have shown that these responses have been independent of the degree of objective pulmonary impairment or have been significant despite controlling for pulmonary impairment.^{5,55}

Theoretical possibilities

Patients with anxiety and panic symptoms can hyperventilate and this hyperventilatory response may trigger an asthma attack or worsen a current asthma attack. This could be related to cooling of the airways and related bronchoconstriction⁵⁷ or bronchoconstriction due to vagal mediation.⁵⁸ Anxiety symptoms characterized by prominent respiratory symptoms (breathlessness, choking or smothering sensations, and chest pain), may con-

fuse the patient appearing to be symptoms of an asthma attack, and may confuse the clinician when interpreting their cause. Further, the co-existence of asthma and anxiety/panic symptoms may make their discrimination challenging for both patients and their physicians.¹⁹

Anxiety and panic may also lead to phobic avoidance of situations which can lead to significant levels of personal handicap with social and functional restriction, much greater than the objectively measured physiologic level of impairment.³ Anxiety symptoms also influence preventative behavior and attitude towards the illness and its treatment and have been associated with poorly controlled asthma and non-adherence to steroids.⁵⁹

In conclusion, the relationship between respiratory symptoms and the state of an individual's asthma is complex and involves other psychosocial factors.⁶⁰ It is important for a treating physician who is trying to achieve asthma control to be aware that in some patients the answer may lie, not in stepping up asthma medication, but in considering the patient's psychological characteristics. However, the heterogeneity of the anxiety constructs ranging from anxiety and panic symptoms to anxiety disorders, in the literature, as well as the diversity of asthma outcome indicators does highlight the need for common constructs and outcome indicators, facilitating a more systematic review, analysis and assessment of the impact of anxiety manifestations.

The impact of anxiety and panic on asthma quality of life

Current evidence

There is limited data on the impact of anxiety comorbidity on functional status and asthma quality of life.¹ Quality of life remains an important outcome measure because well-controlled or stable asthma may not be equivalent to well-being of the patient.⁶¹

Quality of life can be assessed as two different constructs. Generic health-related quality of life focuses on an individual's subjective satisfaction and functioning and impairment across a number of life domains. Disease related quality of life; on the other hand, focuses directly on disease related symptoms and impairment.

An evaluation of generic health related quality of life measures in a large Australian population sample of 834 adults³³ suggests that asthma had a adverse impact on quality of life on the physical and mental health scale as measured by a generic health measure the SF-12. Anxiety disorders have a

significant impact on generic quality-of-life measures.⁶² However, very few studies have evaluated the impact of anxiety disorders and anxiety and panic symptoms on asthma specific quality of life measures in a systematic manner.

One such study⁶³ has reported a 21% prevalence of anxiety disorders in their sample of 136 adults with asthma. Participants were recruited from consecutive adult patients presenting to an asthma clinic with a primary clinical diagnosis of asthma. Patients with a psychiatric disorder had worse asthma control and reported greater bronchodilator use, independent of age, sex and asthma severity. These individuals also reported worse asthma quality of life both in general and in relation to their symptomatology, being limited in their daily activities, in response to environmental stimuli, and in regard to feelings of emotional distress. However, the psychiatric co-morbidity did not affect forced expiratory volume in 1 s (FEV₁) or forced vital capacity (FVC) or FEV₁/FVC % predicted values significantly. Another study⁶⁴ evaluated 101 patients with asthma in a clinic sample and concluded that in these patients both illness specific and generalized panic fears were significantly and negatively correlated with asthma quality of life, on an asthma specific measure, the Living with Asthma Questionnaire (LWAQ).

Some studies have identified the impact of anxiety symptoms on disease specific quality of life questionnaires. An evaluation of a clinical sample of 114 patients, with physician-diagnosed asthma and selected from a primary care situation⁶⁵ indicated that anxiety symptoms, as measured by the HADS anxiety scores correlated negatively with the Asthma Quality of Life Questionnaire (AQLQ) symptom score. There was no correlation with lung function measures. However, anxious individuals were more likely to report respiratory symptoms.⁶⁵ This could affect physician assessment of asthma control and may result in higher prescription of medication, some of which (short- and long-acting beta-agonists) could worsen anxiety and adversely influence perception of asthma symptoms. Similar results were seen in 113 adults enrolled from an outpatient clinic and with well-controlled asthma.⁶⁶ Anxiety symptoms as measured by the HADS accounted for significant variance, and were significantly and negatively correlated, with the constructs of the AQLQs (LWAQ and St. George's Respiratory Questionnaire).

Theoretical possibilities

In addition to the effect of asthma symptoms, and the physical limitations on quality of life, other factors may account for deterioration in the quality

of life. Phobic avoidance of feared situations or trigger factors and of course fear of the latter may be excessive and lead to a vicious cycle of fear, hyperventilation, panic and avoidance. This avoidant behavior may be severely disabling and isolating. It can become difficult for the patient and physician to determine if the feared objects or situations are being avoided for physiological or psychological reasons or both. This may lead to functional restriction much greater than objectively measured physiologic level of impairment.³ It may be speculated that this anxiety, panic and fear avoidance can further manifest with depressive symptoms leading to further deterioration in quality of life. Depressive symptoms are known to affect treatment adherence and lead to a vicious cycle of poorer asthma control and asthma quality of life.⁶⁷ Poor asthma quality of life may be further manifested in increased utilization of health resources, as suggested by a large prospective study of 1406 adult asthma patients in whom asthma quality of life significantly predicted subsequent Emergency Department utilization.⁶⁸ Thus, poor asthma quality of life has implications which reflect and impact not only on treatment and asthma control but also on many aspects of the individual's personal and social life.

It is reasonable to conclude that interventions aimed at anxiety management which include components targeting improved asthma quality of life and phobic avoidance may be an important adjunct to routine asthma management for many patients.

Treatment implications: Cognitive-behavioral therapy (CBT)

CBT interventions are based on the premise that the way you think affects the way you feel and the way you behave. CBT is an effective and empirically supported treatment of choice for anxiety disorders and panic attacks.⁶⁹ Anxiety-reducing medications may not be the preferred mode of dealing with comorbid anxiety in individuals with asthma because they do not address the root cause of the problem and many patients prefer the choice of a non-drug intervention. In addition some anxiolytic medications may affect ventilatory responses and interact with concomitant medication.^{26,36}

Some degree of anxiety about a serious illness like asthma is adaptive, bringing expeditious action to relieve distress.⁷⁰ Conversely, low illness focused anxiety may reduce symptom perception or interpretation, so that patients may minimize their

symptoms and be reluctant to use preventive medication or delay use of symptom relievers. A coping style associated with denial of the illness is unfavorable to good asthma management.

However, as already indicated, research supports the view that asthma is associated with an increased prevalence of anxiety disorders; particularly panic disorder and panic attacks, and also anxiety symptoms and panic fears. Co-morbid anxiety results in poorer asthma outcome on various measures including asthma quality of life.^{18,30} Therefore, anxiety management with due consideration to the above-mentioned caveats, could be an essential component of asthma management, in patients where anxiety is a co-morbidity and where it significantly impacts asthma outcome.

A Cochrane review⁷¹ of psychological interventions for adults with asthma has evaluated 14 randomized controlled trials of varied psychological interventions for adults with asthma. These reviewers highlighted the poor methodological quality and the poor sample size as also the diversity of interventions and outcomes. Only three of these studies^{20,72,73} used a comprehensive CBT intervention. A meta-analysis of two^{20,73} of these studies indicated an improvement in asthma quality of life. The intervention group also demonstrated a reduction in anxiety traits or symptoms. Another case control trial⁷⁴ that used a comprehensive CBT intervention also reported a significant decrease in anxiety and improvement in asthma quality of life. However, none of these studies except the most recent by Ross et al.²⁰ has evaluated a sample of participants with co-morbid asthma and clinical anxiety manifestations. Given the dearth of research and the limited number of rigorous CBT trials as well as the diversity of asthma outcomes, we echo the concerns of the Cochrane reviewers for larger RCTs with common interventions, taxonomy and outcome indicators.

Implications for future research: can CBT interventions targeting co-morbid clinical anxiety manifestations and asthma improve asthma quality of life?

Rigorous CBT trials that involve participants with comorbid clinical anxiety manifestations and asthma are urgently needed. However, it is possible that standard CBT protocols for anxiety and panic should be specifically tailored and modified for patients with asthma and²⁶ and targeted at improving asthma quality of life.

Phobic avoidance of feared situations or trigger factors, and of course fear of the latter, may lead to a vicious cycle of fear, hyperventilation, panic and avoidance. This avoidant behavior can affect asthma quality of life and asthma control.

Standard anxiety reduction techniques depend on gradual or graded exposure to external anxiety causing stimuli. The anxiety stimuli are gradually increased in intensity in a hierarchical order (systematic desensitization and graded exposure). However, in patients with asthma the external anxiety-causing stimuli may include asthma triggers, which have both the potential to cause anxiety and directly cause real asthma worsening.

Patients with asthma may or may not benefit from behavioral components like systematic sensitization or graded exposure to asthma triggers. How should asthma triggers be used to help reduce panic? Is exposure to asthma triggers necessary?⁵ It may be important for standard anxiety reducing CBT interventions to be modified to target asthma related avoidance behaviors and fear of asthma triggers through a problem solving module and appropriate use of asthma medication and the Asthma Action Plan. This could have a positive impact on asthma specific quality-of-life measures but has never been adequately tested.

Secondly, the central component in the standard CBT treatment of panic attacks is exposure to internal physiological sensations (interoceptive exposure) that are associated with anxiety and panic. Fear of dyspnea may be central to panic attacks in patients with asthma. Interoceptive exposure habituating patients to dyspnea symptoms may have to be substituted by objective monitoring and strategies like the Asthma Action Plan, to deal with an asthma attack. Anxiety reduction techniques in individuals with asthma would have to be necessarily associated with appropriate asthma monitoring and with focus on symptom perception. Skills differentiating asthma and anxiety symptoms may remain an important component of the intervention.

Conclusions

Asthma research literature is lacking in controlled treatment outcome studies applying CBT to patients with co-morbid asthma and clinical anxiety manifestations.⁷⁵ Randomized controlled trials evaluating CBT interventions, in individuals with co-morbid asthma and clinical anxiety manifestations or a diagnosed anxiety disorder, may provide evidence of these interventions as an effective adjunct to improve asthma quality of life.

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