Hyperventilation Syndrome and Asthma

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Hyperventilation syndrome is a common and often disabling condition. Traditional treatment consists of reassurance and anxiolytic drugs. Hyperventilation is known to precipitate an asthmatic reaction. A retrospective review of patients with hyperventilation syndrome was performed to ascertain the frequency of asthma as well as the response to bronchodilator medication. Forty-seven patients were seen. Thirty-eight were tested, and asthma was proved in 36. Two additional patients had positive clinical responses with bronchodilators. Thus, asthma was identified in 38 of 47 consecutive patients seen for hyperventilation syndrome (80 percent), and asthma was proved in 36 of 38 of patients tested (95 percent). Hyperventilation syndrome was eliminated in 29 of 35 patients (90 percent) treated with a combination of explanation and bronchodilator treatment.

Hyperventilation syndrome describes a symptom complex in which the diagnosis is made solely on clinical grounds. Psychiatric textbooks categorize it as an anxiety neurosis or a phobic response and recommend treatment with psychotherapy (i.e., reassurance) or minor tranquilizers. Asthma is also recognized as being under emotional control [1,2]. Few reports, however, have suggested any link between these two disorders [3–5]. Textbooks of pulmonary medicine list many causes for hyperventilation but clearly distinguish these from the hyperventilation syndrome [6–8]. Common causes of hyperventilation include exercise, primary central nervous system abnormalities (stroke, infections), salicylate poisoning, acidemia, hypoxemia, and fever. Hyperventilation, whether spontaneous or exercise-induced, is known to cause asthma. However, again, no mention is made of any link between the two syndromes.

In this retrospective review, a high proportion of patients with hyperventilation syndrome were found to have asthma. A combination of explanation and bronchodilator medication was found to be highly effective in either ameliorating or completely preventing symptoms of hyperventilation syndrome in these patients. The physiologic effects of hyperventilation syndrome are also discussed.

PATIENTS AND METHODS

All patients seen in a private practice of pulmonary medicine over a five-year period of time were reviewed. Hyperventilation syndrome was identified in 47 patients. The diagnosis was made by a history of episodic dyspnea associated with chest discomfort, palpitation, paresthesias, muscle spasms or cramps, visual disturbances, auditory disturbances, or near syncope, similar occurrences while asleep, and reproduction of these symptoms by voluntary hyperventilation. A diagnosis of asthma was suggested when a patient had symptoms of dyspnea, cough, or hyperventila-

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TABLE I Method of Diagnostic Asthma

Number of Patients	Test	Patients with Positive Test Result for Asthma	
		Number	Percent
12	Methacholine	10	83
19	Isoetharine	15	70
32	Serial spirometry	30	94
38	Any test	36	90

tion syndrome associated with factors known to be provocative for asthma other than anxiety. Asthma was confirmed by the following four methods: methacholine challenge, bronchodilator challenge, serial testing, or clinical follow-up.

The methacholine challenge and bronchodilator testings were performed at St. Thomas Hospital Medical Center by the Respiratory Therapy Department using a Pulmonary Function Laboratory, model 1000 IV (Gould-SRL Medical; Houston, Texas). The methacholine challenge test was performed after a baseline spirometric evaluation was performed and formal consent was obtained. The patient inhaled 2.5 mg of methacholine. The test result was considered positive if there was a 20 percent drop in the forced vital capacity, one-second forced expiratory volume, or forced mid-expiratory flow. If the test result was negative, the challenge was repeated using 10 mg of methacholine after a 20-minute interval. A bronchodilator test result was considered positive if the patient had a 20 percent improvement in the pre-testing one-second forced expiratory volume or forced mid-expiratory flow after the inhalation of 0.5 ml of isoetharine. Several patients underwent serial spirometric testing, performed with a Breon Spirometer, model 2400 (Breon Laboratories; New York, New York), to evaluate the response to bronchodilator therapy. This treatment was heterogenous and consisted of various combinations of theophyllines, inhaled steroids, inhaled or oral sympathomimetics, or inhaled cromolyn sodium. A positive response was considered to be a 20 percent improvement in the serial one-second forced expiratory volume values with bronchodilator therapy. An occasional patient was only examined for subjective and auscultatory changes only. A positive response was considered to be a decrease in symptoms or wheezing after the initiation of bronchodilator treatment.

RESULTS

A total of 47 patients with hyperventilation syndrome were seen. Thirty-eight were tested as just outlined. Nine patients were lost to follow-up. Of these nine, three had positive results for asthma; the remaining six were not tested (**Tables I** and **II**).

Nine of the 47 patients were not thought to have asthma based on clinical findings. One patient was tested and found not to have asthma. All were given an explanation and reassurance concerning hyperventilation syndrome. Two returned for follow-up care and were able to completely control their symptoms.

A methacholine challenge test was performed in 12 patients; nine had positive results. Five patients had a positive response to 2.5 mg of methacholine and four had a positive response to 10 mg. Of the three patients without response, two had a positive response to bron-

TABLE II Clinical Characteristics and Results

Patient	Sex	Race	Age	Test	Response	Relief of Asthma	Relief of Hyperventilation Syndrome	Comment
1	F	W	46	PFT-BD	+	M	E	
				PFT-O	+			
2	M	W	37	PFT-M	+	E	E	
				PFT-O	+			
3	M		50					No test, no follow-up
4	M		25	PFT-M	+			No follow-up
5	M	W	43	PFT-BD	+	E	E	Later worse, litigation
				PFT-O	+			
6	F	W	61	PFT-BD	+	M	M	
7	M	W	28	PFT-BD	+	M	E	
				PFT-O	+			
8	M	W	24	PFT-BD	−	E	E	
				PFT-O	+			
9	F	W	31	PFT-O	+	E	E	
10	M	W	24	PFT-M	+			No follow-up
11	F		61					No test, no follow-up
12	M	W	32	PET-M	−			
				PFT-BD	+			
				PFT-O	+			

TABLE II (Cont'd) Clinical Characteristics and Results

Patient	Sex	Race	Age	Test	Response	Relief of Asthma	Relief of Hyperventilation Syndrome	Comment
13	F		49				E	No test, decrease with reassurance
14	M	W	52	PFT-BD	+	M	E	
				PFT-M	+			
				PFT-O	+			
15	M		31					No test, no follow-up
16	F	W	50	PFT-M	+	E	E	
				PFT-O	+			
17	M		30	PFT-BD	−		P	Referred to psychiatrist
18	F	W	21	PFT-O	+	E	E	
19	F	W	32	PFT-O	+	E	E	
20	M	W	31	PFT-O	+	E	E	
21	F	W	54	PFT-BD	+	E	E	
				PFT-O	+			
22	F	W	42	PFT-M	−	M	M	
				PFT-BD	+			
				PFT-O	+			
23	F	W	40	PFT-M	+	E	E	
				PFT-O	+			
24	F	W	34	PFT-O	−	M	M	Positive clinically
25	F	W	37	PFT-O	+	M	E	
26	F	W	34					No test, no follow-up
27	F	W	65	PFT-BD	+	M	M	
				PFT-O	+			
28	F	W	51	PFT-BD	+	E	E	
				PFT-O	+			
29	F	W	42	PFT-O	+	M	M	Litigation
30	F	W	38	PFT-O	+	E	E	
31	F	W	54	PFT-BD	+	E	E	
				PFT-O	+			
32	F	W	31			E	E	No test, positive clinically
33	F	B	26	PFT-BD	+	E	E	
				PFT-O	−			
34	F	W	63	PFT-BD	+			
35	F	W	43	PFT-M	+	E	E	
				PFT-O	+			
36	F		26	PFT-BD	+			No follow-up
37	F	W	30	PFT-M	+	M	E	
38	F	W	64	PFT-BD	−	E	E	
				PFT-O	+			
39	F	W	52					No follow-up
40	F	W	32	PFT-BD	+	E	E	
				PFT-O	+			
41	F	W	58	PFT-BD	−	E	E	
				PFT-O	+			
42	F	W	12				E	No test, decrease with reassurance
43	M		55	PFT-O	+	M	E	
44	F	B	55	PFT-M	+	P	E	
				PFT-O	+			
45	F	W	57	PFT-O	+	E	E	
46	F	B	55	PFT-M	−	E	E	
				PFT-O	+			
47	F	W	24					No test, no follow-up

PFT = pulmonary function test (spirometry); BD = bronchodilator; O = office; M = methacholine challenge.
+ = positive response; − = negative response; E = excellent improvement; M = moderate improvement; P = poor improvement.

TABLE III Patients' Improvement

	Excellent	Moderate	Poor
Asthma	23	11	1
Hyperventilation syndrome	31	5	1

chodilator challenge, and all three had positive responses on serial spirometric testing in the office.

A bronchodilator test was performed in 19 patients: 15 had positive results. Two of the four patients without response were already receiving treatment at the time of testing. Three of the four had significant changes in response to bronchodilator treatment on serial spirometric testing in the office. The only patient with no response at all was never thought to have asthma and was referred back to his psychiatrist.

Serial spirometric testing was performed in 30 of 32 patients. Two patients did not show a change in their spirometric values in response to medication changes, but both had a positive clinical response. One had a positive response to isoetharine. Neither underwent office spirometric testing before the use of bronchodilators.

Of the patients, nine were not tested. Eight were not thought to have a clinical syndrome compatible with asthma and have been described. One was treated with bronchodilators and had prompt resolution of her symptoms.

Thus, 38 patients were tested and only two had a negative response to all tests (95 percent). One patient was not thought to have asthma, had no clinical response to bronchodilators, had poor results with reassurance, and was referred back to his psychiatrist. The other patient had a negative result with serial spirometric testing but had a positive clinical response. She did not undergo office spirometric testing before the use of bronchodilators. One other patient was never tested but also had a clinical response to bronchodilators. The latter two patients were considered asthmatic with good responses but with insufficient testing to allow a firm diagnosis.

Thus, methacholine challenge gave positive results in nine of 12 patients tested (75 percent), bronchodilator challenge gave positive results in 15 of 19 (70 percent), and serial spirometric testing gave positive results in 30 of 32 (94 percent). Thirty-eight patients had either a positive diagnostic result for asthma (36) or a positive clinical response to asthma treatment (two). Therefore, asthma was diagnosed in 38 of 47 consecutive patients seen for hyperventilation syndrome (38 of 47, or 80 percent).

Improvement in the asthma as well as the hyperventilation syndrome occurred over time (**Table III**). The hyperventilation syndrome responded better than the asthma in terms of completeness (31 of 37 excellent, five of 37 moderate, and one of 37 poor responses as compared with 23 of 35 excellent, 11 of 35 moderate, and one of 35 poor responses, respectively). The hyperventilation syndrome responses were graded as excellent if all symptoms were controlled or completely ameliorated, moderate if the hyperventilation syndrome occasionally bothered the patient, or poor if no change was observable. A similar scoring system was used for the asthma. The two patients who were given reassurance only were both listed as having excellent responses in the hyperventilation syndrome group.

COMMENTS

Hyperventilation syndrome is a clinical disorder consisting of a stereotyped set of symptoms in a compatible clinical setting. Laboratory tests have not proved useful in the diagnosis of hyperventilation syndrome, which is made solely on the basis of history and clinical challenge. Occasionally, blood gas determination shows hypocapnea and respiratory alkalosis during an attack, but this is considered to be only confirmatory.

Symptoms of hyperventilation syndrome include chest tightness, dyspnea, palpitations, dizziness, syncope, ocular and auditory changes, paresthesias, muscle spasms, and similar nocturnal symptoms. These symptoms appear to be the result of the hyperventilation syndrome rather than its cause. In an excellent early review of the physiologic changes caused by hyperventilation, Brown [9] noted that hypocapnea and the ensuing respiratory alkalosis may produce central nervous system, circulatory, and electrolyte changes. Central nervous system changes include a predisposition to seizures, which may be produced by impaired glucose or oxygen delivery or cerebral vasoconstriction. In addition, prolonged hyperventilation (for more than 24 hours) seems to sensitize the brain, leading to more prolonged hyperventilation. The effects on peripheral nerves or nerve muscle units were also thought to be due to such factors as hypoglycemia, vasoconstriction, or alkalemia, with resultant shifts in electrolyte concentrations.

Hyperventilation is known to cause vascular spasm in certain arterial beds. Neill [10] noted that there was an increased resistance and diminished coronary artery blood flow with a widened coronary (atrioventricular) oxygen difference. Because of the Bohr effect, diminished oxygen is available for myocardial cells. Thus, it is conceivable that hyperventilation alone could cause significant myocardial ischemia in a patient with coronary artery disease. Whether this is the cause of the palpitations in hyperventilation syndrome or whether they are due to the nonspecific effect of circulating catecholamines during these episodes is unknown. Hyperventilation also affects the electrocardiographic findings by flattening or inverting the T waves or causing arrhythmias or RST segment depression [10]. Similar changes are seen in blood flow to the brain, forearm, and hands during hyperventilation.

Changes in nerve function are common accompaniments of hyperventilation syndrome and include paresthesias (they are usually described as circumoral or in the hands, but they can actually be almost anywhere; in our patients, the hands and arms were the most frequently affected sites, followed by the perioral regions, feet and legs, and face, and the paresthesias occasionally were unilateral, most generally on the left side), muscle spasm and cramps (generally, they involve the hands, arms, and feet and legs, and, again, sometimes are unilateral), visual disturbances (these are described as blurring of the vision, the presence of "floaters," or generalized "blackening" of the vision), and auditory changes (there may be generalized "muffling" of the hearing or tinnitus). In alkalemic-induced changes in the concentration of ionized calcium or magnesium, the usual explanation for these symptoms is acute alkalemia, whether metabolic or respiratory in origin, which caused a shift in ionized electrolyte concentrations with greater protein binding. Infusion of an acid substance will reverse these changes and symptoms. Acidemia also causes alterations in ionized electrolyte concentrations and can produce similar changes in nerve conduction with tetanic symptoms. Vasoconstriction and the Bohr effect would be expected to lead to localized acidemia. Thus, it is unclear whether the peripheral nerve symptoms during hyperventilation syndrome are caused by vasoconstrictive-acidemic or hypocapneic-alkalemic effects. The dizziness and syncope are believed to be due to cerebral vasoconstriction.

The etiologic factors behind chest pain and dyspnea are more difficult to explain. Three different types of chest pain were described by Wheatley [11] in 1975. The first type is sharp, fleeting, and periodic, originating in the hypochondrium or left anterior chest with radiation into the neck, left scapula, or inferior rib margins. It can be accentuated by muscular motion of the chest. The second type is a persistent localized ache, lasting hours to days, associated with chest wall tenderness. This is similar to a fibrositic pain and can be relieved with local injections of anesthetics. The third type is a diffuse, dull aching, heavy-pressure sensation over the entire precordium or substernum. In our patients, the latter form was the most common and was described as a heavy weight ("an elephant sitting on my chest") or a squeezing ("a tight belt around my chest"). It is the most difficult to differentiate from coronary artery pain. Several of our patients underwent stress testing and cardiac catheterization or had been receiving disability payments because of the chest pain despite their young age or the unusual finding of chest pain lasting hours to days.

Dyspnea is a constant finding in hyperventilation syndrome. In 1953, Brown [9] suggested that prolonged hyperventilation begets hyperventilation. A change in the sensitivity for carbon dioxide in the respiratory center or carotid bodies was thought to be the possible cause.

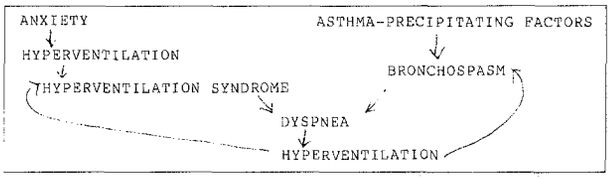

Figure 1. *Whatever the stimulus, both hyperventilation syndrome and asthma cause dyspnea, creating a mutual feedback disorder.*

Dyspnea, however, is also a frequent if not constant feature of an asthmatic attack. The finding of asthma in so many patients in this report and the disappearance or diminution in the frequency or severity of hyperventilation syndrome points to asthma as a cause of the dyspnea in some patients with this syndrome.

Hyperventilation is known to cause asthma. The best known example is exercise-induced asthma. McFadden [12] performed many experiments in cold- and exercise-induced asthma and concluded that energy loss by the tracheobronchial tree is the common pathway behind the precipitation of an asthmatic attack. It appears to be under vagal control. The lost energy is spent in either heating or humidifying the air, and it appears to make little difference whether the hyperventilation is spontaneous or exercise-induced.

There appears to be a dual response to the symptom of dyspnea in a patient with hyperventilation syndrome (**Figure 1**) and asthma. The sensation of shortness of breath may be the result of an anxiety response, which causes hyperventilation, producing the symptoms of hyperventilation syndrome. Conversely, it may be a manifestation of bronchospasm-induced ventilatory abnormalities. Hyperventilation is the common response to this feeling of shortness of breath. This hyperventilation may then be a stimulus for more asthma or further reinforce the symptoms of hyperventilation syndrome. Thus, both the hyperventilation syndrome and asthma feed back upon themselves.

The proper testing for asthma in a patient with hyperventilation syndrome is probably not exercise testing. Exercise-induced hyperventilation may cause chest discomfort in patients with hyperventilation syndrome, leading to voluntary reductions in flow rates with false-positive results. Even methacholine challenge produced symptoms of hyperventilation syndrome in some of the patients tested in this study; treatment with bronchodilators and clinical follow-up or serial spirometric testing may prove to be the most sensitive way of making the diagnosis of asthma in a patient with hyperventilation syndrome.

In the present series, 39 of 47 consecutive patients with hyperventilation syndrome had either spirometrically proved or clinically responsive asthma. Excellent improvement in hyperventilation syndrome was seen in 29

of 35 of these patients using a combination of explanation and bronchodilator medications. Two other patients had excellent responses to explanation and reassurance only. Anxiolytic agents were used in only three patients, but they did not seem to affect the course of either the asthma or the hyperventilation syndrome. The one patient with no response was referred back to his psychiatrist. In contrast, the asthma proved more difficult to treat with only 23 excellent responses, 11 moderate responses, and one poor response. No significant association was found between the degree of control of the asthma and the severity of the spirometric abnormality or the degree of hyperventilation syndrome symptoms.

In summary, a high proportion of patients with classic symptoms of hyperventilation syndrome were found to have asthma. This diagnosis was substantiated by laboratory testing or a clinical course compatible with a diagnosis of asthma. Whether this represents a skewed sample due to the nature of the patient population, or is a frequent underlying feature in patients with hyperventilation syndrome, is a question that should be answered by prospective studies of patients with hyperventilation syndrome. We should point out that eight patients were not tested for asthma because they lacked a suggestive history. Whether these eight patients also had asthma is a question that remains unanswered due to the limitations inherent in a retrospective analysis.

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