REVIEW ARTICLES

Fatal or Near-Fatal Asthma: Clinical Entity or Incorrect Management?

G.J. Rodrigo,[a] C. Rodrigo,[b] and L.J. Nannini[c]

[a]Departamento de Emergencia, Hospital Central de las Fuerzas Armadas, Montevideo, Uruguay.
[b]Unidad de Cuidado Intensivo, Asociación Española Primera de Socorros Mutuos, Montevideo, Uruguay.
[c]Sección de Neumología, Hospital G. Baigorria, Universidad Nacional de Rosario, Rosario, Santa Fe, Argentina.

Introduction

Asthma is a chronic inflammatory disease of the airways associated with hyperreactivity, airflow limitation, and respiratory symptoms.[1,2] It is a disease that occurs throughout the world regardless of the level of economic development. There is clear evidence that in the last 30 years the prevalence has increased considerably.[3-5] All asthma patients may develop exacerbations characterized by difficulty in breathing, cough, and wheezing, as well as a decrease in expiratory airflow that can be quantified by measuring lung function. To describe this condition, such terms as "asthma attack," "acute asthma," "asthmatic exacerbation," or "status asthmaticus" are used. The intensity of these acute episodes may vary from a mild attack to an extremely severe one, a condition called "near-fatal asthma" (defined by the appearance of various events such as cardiorespiratory arrest, hypercapnia, acidemia, the need for orotracheal intubation and mechanical ventilation, or admission to an intensive care unit [ICU]),[6-8] and sometimes the process culminates in death (fatal asthma). Near-fatal asthma affects a group of patients at risk for asthma death, and so its study can prove an important source of information on factors leading to a fatal outcome.[9] While acute episodes usually develop over a period of hours, days, or even weeks, in a minority of patients the onset of an attack may be rapid (a few hours or, rarely, minutes). Finally, although the overall mortality rate for asthma is relatively low compared to other diseases, asthma deaths have been associated with multiple, often contradictory, factors such as the use of asthma medication, a predisposition to rapidly developing extremely severe attacks,[10] errors in patient management, and delays in receiving medical attention.[11-17] The aim of this review is to analyze the phenomenon of fatal or near-fatal asthma in terms of recognition, pathophysiology, trigger and risk factors, and prevention and treatment in order to determine whether it constitutes a well-defined clinical entity with greater intrinsic severity, or is rather the result of a combination of factors present in a given patient and is therefore acquired and can be modified.

Correspondence: Dr. G. J. Rodrigo.
Departamento de Emergencia. Hospital Central de las FF.AA.
Avda. 8 de Octubre, 3020. 11600 Montevideo. Uruguay.
E-mail: gurodrig@adinet.com.uy

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Epidemiology

Acute asthma is a frequent cause of consultation in emergency departments, with adolescents and young adults requiring the most medical attention.[18] While the disease has been known since ancient times, it is only since the beginning of the twentieth century that asthma mortality has begun to receive attention from the scientific community.[19-22] In the 1960's there was a sharp "epidemic" increase among young asthmatics in the United Kingdom, New Zealand, and Australia.[23-28] In the United Kingdom the mortality rate for patients between the ages of 5 and 34 tripled between 1959 and 1966 (from 0.74 to 2.18 per 100 000). It is interesting to note that while during the 1970's asthma mortality rates in the United Kingdom and Australia declined, only in New Zealand was there another "epidemic" increase.[29,30] Although the 2 mortality peaks were related to the uncontrolled use of β agonists delivered by pressurized metered dose inhalers (isoprenaline and fenoterol, respectively), various studies have failed to rule out completely other causal factors (increased use of medication may reflect, for example, greater severity or insufficient control of the disease). While a decrease in mortality coincided with the withdrawal of fenoterol from the market in New Zealand, it was also accompanied by the introduction of inhaled corticosteroids.[31] Furthermore, in other countries no association could be found between the use of fenoterol and an increase in asthma mortality, and in still other countries where this β agonist was never used, higher

death rates nonetheless were seen.[32] Finally, mortality rates remained stable or even decreased in various countries during the 1990's,[12,33,34] indicative, among other things, of improved treatment of the disease. Along the same lines, in the last decade there has been a decrease in the number of patients with acute asthma requiring ICU admission, as well as shorter hospital stays and a tendency to admit patients with less severe attacks.[35] While the frequency of life-threatening exacerbations depends on how such events are defined, it is estimated that 5 of every 100 000 asthma patients are affected annually.[36] At the present time, most deaths occur in the community (at home, at the work place, or on the way to hospital), with cerebral hypoxia resulting from cardiorespiratory arrest being the most frequently reported cause of death.[37]

Risk Factors

Multiple factors have been identified as increasing the probability of developing a fatal or near-fatal asthma attack (Table 1). However, not all patients have these characteristics, and many of those who do never develop this type of attack. The predictive value of these factors is therefore relatively small: their presence increases probability, while their absence is of little predictive value. For this reason, we should consider every asthma attack to be potentially fatal.[38]

The epidemiological marker most specifically associated with increased risk of death from asthma is probably hospitalization during the year preceding the event.[6-7,39-44] This is particularly true in cases of recurrent hospitalizations and patients requiring orotracheal intubation, mechanical ventilation, and ICU admission. In any event, such a history can only be found in a limited number of patients.

Numerous studies have found significant deficiencies in asthma management.[8,11-17,40-46] Thus, an insufficient number of asthma patients treated by specialists receive regular inhaled corticosteroid treatment or use peak flow meters or inhalation chambers, and adherence to therapy is often poor. Many patients lack a written action plan aimed at helping them to modify treatment in response to their own evaluation of the severity of their asthma. Studies show that death occurs typically in patients whose disease is not well controlled and whose condition deteriorates gradually over a period of days or weeks before the fatal or near-fatal episode. This observation suggests that both patients and doctors have sufficient time to recognize the seriousness of the asthma attack and reverse its progress. Errors committed particularly during the management of acute episodes, like misjudging the severity of the attack because of failure to use objective measurements of bronchial obstruction (peak expiratory flow [PEF] or forced expiratory volume in 1 second [FEV_1]) and undertreatment (administering insufficient doses of asthma medication) must also be mentioned.

TABLE 1
Risk Factors for Fatal or Near-Fatal Asthma

Previous episodes of near-fatal asthma
Hospitalization during the previous year
Intubation and mechanical ventilation previously required
Poor management of the disease
Increased use of β agonists
Low socioeconomic level
Psychiatric disease and psychosocial disorder
Atopy
Polymorphisms of β_2 receptors
Blunted perception of airway obstruction
Increased use of tranquilizers
Labile asthma

The increased risk of mortality associated with the use of β agonists has received considerable attention in the last few decades.[13,43,45-48] There is evidence that these drugs should be used as needed rather than on a regular schedule,[49] as the use of fast-acting β agonists increases noticeably the risk of a fatal or near-fatal attack. This does not mean, however, that a cause and effect relationship exists. Thus, in many patients, increased consumption is an indication of more severe and poorly controlled asthma. Tachyphylaxis to the bronchodilating action of fast-acting β agonists has not been demonstrated in asthma patients, with the exception of a subgroup (15% of the total) with the homozygous genotype containing the arginine-16 polymorphism, who do show desensitization to the bronchodilating action of agonists of β_2 receptors when treated with fixed doses.[50] Formoterol may be prescribed for as-needed relief,[51] but desensitization after 2 weeks of regular treatment has been described.[52]

Low socioeconomic level has also been linked to an increased risk of fatal or near-fatal asthma. This factor is thought to account for difficulties in access to health care systems, which would explain, for example, the ethnic differences referred to in the literature.[53] Special attention must be paid to the patient's personality traits and to psychological factors. Adverse psychological factors are more prevalent in patients hospitalized for acute asthma than in other asthma patients.[54,55] It has recently been shown that anxiety and depression increase the frequency of hospitalizations and recurrences.[56] Other risk factors include a history of atopy,[41,44] the presence of dysfunctional adrenergic β_2 receptors, or the use of major tranquilizers.[57,58]

It has also been suggested that blunted perception of dyspnea in the presence of airway obstruction constitutes a risk factor.[59] This characteristic is found predominantly in patients who are female, older, with longer duration of disease, a lower daily consumption of β agonists, and a greater number of emergency department visits, hospitalizations, and episodes of fatal or near-fatal asthma.[60] Although the factors that affect the perception of dyspnea (changes in lung volume parameters, speed of bronchoconstriction, anxiety level, duration of asthma, age, and airway inflammation) are

not fully understood, blunted perception is probably not an inborn defect, but rather an acquired one susceptible to modification.[61,62] However, through the use of the evoked potential technique, a difference in the mechanisms of perception of respiratory effort has been found between subjects with and without asthma.[63] Finally, cases of extreme diurnal variation in PEF (labile asthma) have been described, and while patients experiencing such variation may have normal values during the periods between attacks, fluctuations can contribute to the development of fatal or near-fatal asthma episodes.[64]

Pathophysiology

Table 2 shows the multiple factors that can trigger a fatal or near-fatal asthma attack through airway inflammation, spasm of airway smooth muscle, or both. These are the same factors that trigger any asthma exacerbation. Exposure to allergens, particularly *Alternaria alternata* spores,[65] air pollution (both indoor and outdoor), and respiratory infections (frequently viral) are the main triggers that have been clinically identified. Other known factors are emotional upset,[62] food preservatives like sodium metabisulfite,[66] and drugs like β blockers, aspirin, and nonsteroidal anti-inflammatory drugs.[67] The use of illegal drugs and alcohol also appears to be a precipitating factor.[68-70] Finally, so-called "epidemic" asthma, defined as the clustering in space and time of an abnormally high number of patients with asthma attacks reported in at least a dozen places around the world, is probably linked to a combination of factors like environmental pollution and weather changes.[71] However, only on rare occasions do studies on near-fatal asthma describe the possible causes of a potentially fatal attack. A previously published review article found that only in 7% of more than 1000 episodes was the cause discovered.[72]

TABLE 2
Triggers of Fatal or Near-Fatal Asthma

Allergens
Respiratory infections
Emotional upset
Exercise
Air pollution
Food and preservatives/coloring agents
Drugs
Weather changes

The progressive narrowing of the airway due to inflammation and/or increase in smooth muscle tone of the respiratory bronchioles is a fundamental factor in the exacerbation of asthma leading to: *a)* an increase in airflow resistance, *b)* lung hyperinflation, and *c)* a decrease in the ventilation-perfusion ratio ($\dot{V}/\dot{Q}$). Thus, respiratory insufficiency is the consequence of increased work of breathing, inefficient gas exchange, and muscle fatigue.

Onset of Asthma Attacks

There are 2 different pathogenic scenarios for the onset of asthma exacerbations (Table 3). When the predominant factor is airway inflammation, patients show slow clinical and functional deterioration (measured in hours, days, or even weeks), which characterizes the first type—the slow-onset asthma attack. Information from various cohort studies shows that the prevalence of this kind of attack is about 80% to 90% among adults presenting to an emergency department with acute asthma.[73-76] The most frequent triggers are upper respiratory infections, and such patients show a slow response to therapy (Figure 1). In the second scenario, in which bronchospasm is the predominant mechanism, the attack develops rapidly, has a sudden onset, and may be asphyxiating. This type of attack develops in less than 3 to 6 hours after the first symptoms, and in rare instances in only minutes. Respiratory allergens, exercise, and psychological or social stress are the most frequent triggers. Although the severity of this type of attack is initially greater, patients show a more rapid response to treatment and are hospitalized less frequently.

TABLE 3
Predominant Characteristics of Patients with Acute, Slow- or Rapid-Onset Attacks

Type 1: Slow Progression	Type 2: Rapid Onset
Acute attacks following gradually increasing symptoms	Acute attack that develops quickly, has a sudden onset, or is asphyxiating
Progressive deterioration (>6 h; often days or weeks)	Rapid deterioration (<3-6 h)
From 80% to 90% of patients	From 10% to 20% of patients
Mostly female	Mostly male
Upper respiratory infection as most frequent trigger	Respiratory allergens, exercise, and psychosocial stress as most frequent triggers
Less severe airway obstruction	More severe airway obstruction
Slow response to treatment and more frequent hospitalizations	Rapid response to treatment and less frequent hospitalizations
Predominant mechanism: airway inflammation	Predominant mechanism: smooth muscle spasm

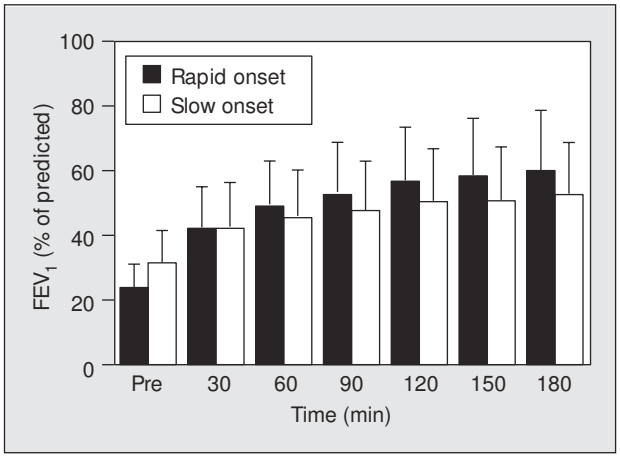

Figure 1. Mean values for forced expiratory volume in 1 second (FEV_1) in patients with rapid- and slow-onset asthma treated with high repeated doses of salbutamol inhaled over a 3-hour period. There are significant differences between the 2 groups (*P*<.05), pretreatment (pre) and at 120, 150, and 180 minutes of treatment (Reproduced with the permission of Rodrigo and Rodrigo.[76])

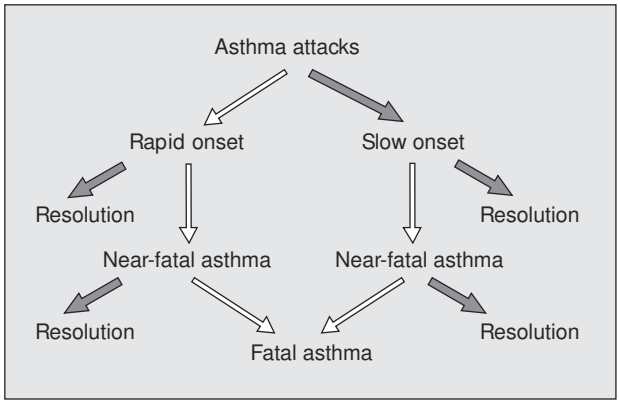

Figure 2. Natural history of fatal or near-fatal asthma. The thickness of the lines represents the frequency of each event (not proportional).

Other studies have evaluated the progression of specific cases of fatal or near-fatal asthma (Table 4).[7-8,10,41,43,46,77] It can be observed from the data that between 10% and 60% of patients with near-fatal asthma had rapid-onset (<3-6 h) attacks. The study showing the highest percentage, a survey of specialists of whom barely 11% responded,[41] was probably subject to considerable bias, and an examination of the remaining studies indicates that, on average, no more than one third of the patients had rapid onset attacks, a proportion slightly higher than the one found in severe acute asthma patients. It must be pointed out that these studies included small samples of patients with fatal or near-fatal asthma and were therefore potentially subject to considerable bias. It has also been shown that the duration of symptoms can be underestimated and may therefore be longer than reported.[73] In general terms, the duration of fatal or near-fatal asthma attacks may be similar to that of severe exacerbations requiring emergency department treatment. It has also been suggested that these 2 types of progression are characterized by different tissue substrates, with a predominance of neutrophils in the infiltrate of the bronchial submucosa in patients with rapid-onset fatal asthma, and of eosinophils in patients in whom onset is slow.[78] However, these results are based on the evaluation of only a few patients. Finally, consistent with such observations, it is possible to describe a natural history of fatal or near-fatal asthma that would have as its starting point an asthmatic crisis whose progression might vary depending on the presence or absence of a combination of factors (Figure 2) and that might in certain instances be life threatening.

TABLE 4
Onset of Asthma Exacerbations in Cases of Fatal or Near-Fatal Attacks*

Study	Design	Asthma Assessed	Rapid-Onsed Near Fatal Asthma (%)	Fatal Asthma Rapid-Onset (%)
Wasserfalen et al[10]	Descriptive Retrospective	Near-fatal asthma (mechanical ventilation) in ICU	29	
Kallenbach et al[77]	Case–control Retrospective	Near-fatal asthma (mechanical ventilation) in ICU	28	25
Turner et al[7]	Case–control Prospective	Near-fatal asthma in hospitalized patients	<10	
Hessel et al[46]	Case–control Retrospective Multicenter	Fatal asthma		38
Hannaway[41]	Descriptive Survey of specialists (11% response)	Fatal and near-fatal asthma	60	80
Moore et al[43]	Descriptive Retrospective	Near-fatal asthma in hospitalized patients	38	
Plaza et al[8]	Descriptive Prospective Multicenter	Fatal and near-fatal asthma in hospitalized patients	20	9

*ICU indicates intensive care unit.

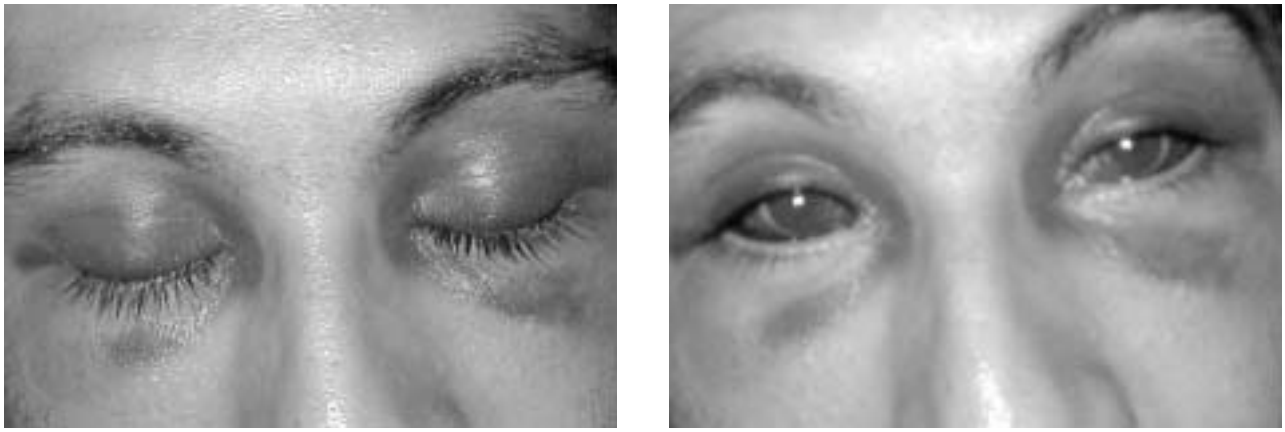

Figure 3. Thirty-five-year old male patient with a severe asthma attack that developed over a 1-week period. Treated at home by a mobile emergency unit physician with high doses of inhaled β agonists, he quickly improved (intubation not required). He was later taken to an intensive care unit to continue treatment and on admission hematomas on the upper and lower eyelids (left) together with conjunctival hemorrhages (right) were observed.

Pulmonary Mechanics and Cardiopulmonary Interactions

As has already been established, airway obstruction is the most important pathophysiological factor in acute asthma, causing a decrease in airflow that can be quantified by measuring lung function (PEF, FEV_1).[79] When expiratory flow limitation is sufficiently severe, dynamic hyperinflation develops. This phenomenon can be discerned in a chest x-ray by observing the increase in pulmonary diameters and the flattening of the diaphragmatic domes. Dynamic hyperinflation, together with the increase in respiratory muscle activity and extreme variations in intrathoracic pressure (due to the effort of the inspiratory and expiratory muscles), affects cardiovascular activity.[80] During forced expiration intrathoracic pressure increases and both venous return and right ventricular filling decrease. Conversely, increased inspiration effort caused by airway obstruction leads to an increase in venous return and right ventricular filling. The extreme changes in negative pleural pressure can also affect left ventricular function by increasing the afterload. Thus, the effect of these 2 cyclical events is to increase systolic volume during inspiration and reduce it during expiration. This can be measured as an increase in paradoxic pulse, the difference between maximum and minimum systolic blood pressure during the respiratory cycle.

Gas Exchange

The most common arterial blood gas abnormality occurring in patients with asthma exacerbations is hypoxemia accompanied by hypocapnia and respiratory alkalosis.[81-83] If airway obstruction is considerable and persists, there may be an increase in hypoxemia together with hypercapnia and metabolic (lactic) acidosis, in addition to respiratory acidosis, due to muscle fatigue and inability to maintain adequate alveolar ventilation. Studies of patients with respiratory insufficiency secondary to a severe asthma attack assessed by the inert gas elimination technique have shown the existence of a bimodal $\dot{V}/\dot{Q}$ distribution with slight shunting.[84-86] These studies indicate that a substantial proportion of blood flow perfuses lung units with low $\dot{V}/\dot{Q}$ ratios. This regional $\dot{V}/\dot{Q}$ mismatch constitutes the most important mechanism of hypoxemia. Carbon dioxide retention during asthma exacerbations may also be associated with a $\dot{V}/\dot{Q}$ imbalance, as well as with alveolar hypoventilation due to muscle fatigue. These observations have important therapeutic implications: given that the predominant disorder is a $\dot{V}/\dot{Q}$ ratio imbalance, hypoxemia can be quickly corrected by administering moderate concentrations of oxygen (25%-40%).

The combination of hypercapnia and an increase in intrathoracic pressure can produce a considerable increase in intracranial pressure. Various clinical reports have described asthma patients with neurological signs such as pupil dilation in 1 or both eyes,[87-88] quadriparesis,[89] as well as subarachnoid[90] and subconjunctival bleeding (Figure 3)[91] developing during an acute episode.

Pathophysiological Events in Fatal Asthma

The 2 most important pathophysiological events directly implicated in fatal asthma are cardiac arrhythmias and asphyxia. The first is linked to the adverse effects of bronchodilators. It goes without saying that this association has generated an intense fear in both patients and doctors of using β agonists, especially those administered through pressurized metered dose inhalers, and this situation has led to undertreatment. Thus, cardiac arrhythmias could be responsible for a considerable proportion of the asthma deaths observed. Theoretically, risk increases with the use of high doses of β agonists in the presence of hypoxia, hypopotassemia, and QTc

interval prolongation.[92,93] Various studies have shown a connection between bronchodilator aerosols and the increased mortality seen in the 1960's in particular,[94,95] finding a positive correlation between sales of these drugs and asthma deaths. However, epidemiological evidence has also shown important discrepancies between these 2 factors in various countries.[96] Similarly, it is unlikely that the second "epidemic" beginning in New Zealand in 1975 can be attributed to the use of bronchodilators, as mortality began to decline in 1979, while sales of bronchodilators continued to rise steadily until well into the 1980's.[97] More recent studies of cases and controls have confirmed that excessive use of short-acting β agonists together with underuse of inhaled corticosteroids is associated with fatal or near-fatal asthma.[7,13,46,47,98,99] However, this association can be explained by the fact that the more severe the asthma, the more medication is required and the greater the mortality rate.[100] In these studies no association of arrhythmias with episodes of fatal or near-fatal asthma was observed,[7,41,77,100] nor was the use of high doses of β agonists in the treatment of patients with severe asthma attacks accompanied by arrythmias.[101,102]

A more likely hypothesis is that death occurs as a result of asphyxia due to extreme airflow limitation and resulting hypoxia. Thus, it has been shown that episodes of near-fatal asthma are associated with respiratory insufficiency and hypoxemia.[103] The data have shown that despite the presence of severe hypercapnia, patients can recover rapidly once effective treatment is begun and hypoxemia corrected. Despite the marked respiratory acidosis found in such patients and the hypopotassemia found in some of them, no arrhythmias have been detected. Moreover, this hypothesis is supported by pathology, which has revealed that the most probable cause of death in patients with fatal asthma is almost invariably significant airway obstruction.[104]

Recognizing the Severe Asthma Attack

It is relatively easy to recognize a severe asthmatic crisis. In a patient who is able to stand, a combination of difficulty in speaking, accessory muscle use, and mental confusion indicates the imminence of a severe life-threatening asthma attack. However, with the exception of a subgroup in whom the attack may come on very rapidly, in the vast majority of patients this clinical picture is the final result of a long process developing over many hours, days, or even weeks. Therefore, the different signs and symptoms usually cited as indicators of severity occur late and are not very reliable.[11]

Probably the most useful of the clinical signs of severity is the use of accessory muscles, often in a way that results in suprasternal retractions, the presence of which is indicative of marked airway obstruction.[105] Other signs of severity usually mentioned include a respiratory rate more than 30 breaths per minute, heart rate more than 120 beats per minute, and paradoxic pulse more than 12 mm Hg. However, evidence from several clinical studies indicates that more than 50% of adult patients with acute severe asthma have a heart rate between 90 and 120 beats per minute, and that only 15% of them are above this range.[105,106] Generally, success of bronchodilator therapy is accompanied by a decrease in heart rate, although some patients, especially older ones, may still experience tachycardia due to the chronotropic effects of β agonists.[107] The respiratory rate in patients with severe asthma is usually between 20 and 30 breaths per minute, and only 20% of them are above this range.[108] Paradoxic pulse values are reliable indicators of severe exacerbation only if they are more than 25 mm Hg. This limitation, coupled with the practical difficulty of obtaining the measurement, makes the use of paradoxic pulse inadvisable.[109] Finally, both wheezing and dyspnea are found in almost all severe exacerbations and show a poor correlation with the degree of obstruction.

In view of the fact that one of the major causes of fatal or near-fatal asthma is underestimation of the severity of the attack, it is essential that airway obstruction in such patients be measured objectively by PEF or FEV_1, either to determine the initial severity of the attack (static assessment) or to evaluate response to treatment (dynamic assessment).[110] Furthermore, in all patients oxygen saturation should be measured by pulse oximetry on a continuous basis in order to assess and correct hypoxemia.[111] On the other hand, blood gas analyses will only be necessary in patients who do not respond to correct treatment. In summary, while the patient's clinical signs and symptoms must be considered, repeated assessment of PEF or FEV_1 along with continuous measurement of oxygen saturation by pulse oximetry, is a critical element in assessing the degree of airway obstruction, gas exchange, and response to treatment.

Treatment and Prevention

Given the multifactorial nature of fatal and near-fatal asthma, treatment and prevention should be multidimensional. Identifying patients at high risk is difficult, since risk factors, though clearly identified, are not very specific and are therefore of little predictive value. Reducing trigger and precipitating factors is also an important objective, but one that is difficult to achieve, as such stimuli are often not clearly identified. Perception of dyspnea should be measured at least once in most patients in order to identify those at greatest risk. However, the test of increasing inspiratory load is not readily available and requires special equipment. The use of the Borg scale during a bronchial provocation test is an alternative, not only because a fall of 20% in FEV_1 after a histamine challenge under 0.25 mg/L is an indicator of severity and the need for anti-

inflammatory treatment,[112] but also because it permits simultaneous assessment of any alteration in the perception of dyspnea.[113] Another finding in asthmatics with frequent exacerbations has been an increase in closing volume and closing capacity in comparison with stable subjects.[114] The lack of a residual bronchodilatory effect of deep inspiration is another phenomenon associated only with the most severe forms of asthma.[115]

With regard to the proper use of asthma medication, probably the most important single factor in the treatment of chronic asthma is the use of inhaled corticosteroids. It has been shown that the regular use of low doses of these drugs is associated with a decreased risk of death from asthma.[116] The treatment of exacerbations, as has been previously indicated, includes an accurate assessment of severity and response to treatment. This implies in particular the generalized use of peak flow meters, both by medical staff and patients. Therapy must be adjusted according to the initial severity of the attack and to response to treatment. The objectives of therapy are to maintain adequate oxygen saturation through the administration of oxygen, to relieve airway obstruction by repeatedly administering high doses of inhaled bronchodilators, to reduce inflammation, and to prevent relapses through the use of systemic corticosteroids. As we have also mentioned, hypoxemia is produced by regional $\dot{V}/\dot{Q}$ mismatches, for which reason it can be corrected by administering moderate concentrations of oxygen. It must be noted that oxygen therapy at high concentrations may be associated with gas exchange deterioration in patients with the most severe airway obstructions.[117,118] It must be stressed, therefore, that the aim of oxygen therapy should be to achieve an adequate saturation (>92%) rather than to use predetermined concentrations. Selective short acting β_2 agonists, administered by inhalation, constitute the first line of drug treatment for an asthma attack. The combined use of β agonists and anticholinergics (ipratropium bromide) is indicated in severe crises.[119-122] Finally, the use of systemic corticosteroids is the most effective way to act against inflammation and to reduce relapses.[123-125] Lung function measurements should be taken into account in deciding whether to hospitalize or discharge patients.

An area of particular importance is asthma education. A large part of the morbidity and mortality of this disease is due to such factors as denial, delays in seeking medical attention, and insufficient treatment, aspects that can be modified through education. Education is considered fundamental in helping patients increase their motivation, confidence, and skills in managing the disease. Asthma education may take various forms, from promoting knowledge of the disease to more complex interventions, such as developing self-management skills. Education based on offering information is generally easy to implement and can be readily adapted to different contexts and situations. Furthermore, it is less costly than other modalities and seems to cover the needs of patients with respect to knowledge of their disease. However, there is no evidence to suggest that education limited to information alone can affect such variables as hospitalizations, visits to specialists or emergency departments, lung function, or use of medication.[126] On the other hand, the use of self-management plans, the process by which patients modify their treatment in response to their own evaluation of the severity of their disease according to predetermined criteria, has shown a beneficial effect on the principle variables studied, including mortality.[13,127]

Finally, patients who have experienced a near-fatal attack should receive particular attention, given their poor long-term prognosis.[128,129] The creation of asthma centers with open programs, treatment available free of charge, and special attention to educational and socioeconomic aspects can have a positive effect on the rate of asthma hospitalizations despite the poor prognosis.[130] Patients at greatest risk should be followed up regularly by asthma center staff.[12]

Conclusion

Fatal or near-fatal asthma is an infrequent event in the natural history of the disease. Although fatal or near-fatal asthma has been set forth as a well-defined clinical entity characterized by sudden onset and absence of warning signs, evidence shows that is in fact an event that usually has been developing for some time, and that it occurs as a consequence of a combination of variable factors in each patient, with a final, shared outcome of asphyxia due to severe airflow limitation. As it is difficult to identify such patients, a good strategy would be to treat every asthma attack as a potentially fatal one, and to act accordingly. The key to management lies fundamentally in the objective assessment of severity together with treatment suited to the patient's situation, in which the regular use of inhaled corticosteroids plays an important part. Finally, education in the form of self-management plans has a beneficial effect on the principal variables, including mortality.

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