

Perception, personality, and respiratory control in life-threatening asthma

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Introductory article

Chemosensitivity and perception of dyspnea in patients with a history of near-fatal asthma

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Background. Many deaths from attacks of asthma may be preventable. However, the difficulty in preventing fatal attacks is that not all the pathophysiologic risk factors have been identified. **Methods.** To examine whether dyspnea and chemosensitivity to hypoxia and hypercapnia are factors in fatal asthma attacks, we studied 11 patients with asthma who had had near-fatal attacks, 11 patients with asthma who had not had near-fatal attacks and 16 normal subjects. Their respiratory responses to hypoxia and hypercapnia, determined by the standard rebreathing technique while the patients were in remission, were assessed in terms of the slopes of ventilation and airway occlusion pressure as a function of the percentage of arterial oxygen saturation and end-tidal carbon dioxide tension, respectively. The perception of dyspnea was scored on the Borg scale during breathing through inspiratory resistances ranging from 0 to 30.9 cm of water per liter per second. **Results.** The mean (\pm SD) hypoxic ventilatory response (0.14 ± 0.12 liter per minute per percent of arterial oxygen saturation) and airway occlusion pressure (0.05 ± 0.05 cm of water per percent of arterial oxygen saturation) were significantly lower in the patients with near-fatal asthma than in the normal subjects (0.60 ± 0.35 , $P < 0.01$, and 0.16 ± 0.08 , $P < 0.01$, respectively) and the patients with asthma who had not had near-fatal attacks (0.46 ± 0.29 , $P = 0.003$, and 0.15 ± 0.09 , $P = 0.004$). The Borg score was also significantly lower in the patients with near-fatal asthma than in the normal subjects, and their lower hypoxic response was coupled with a blunted perception of dyspnea. **Conclusions.** Reduced chemosensitivity to hypoxia and blunted perception of dyspnea may predispose patients to fatal asthma attacks. (*N Engl J Med* 1994;330:1329-34)

Pattern of life-threatening asthma

In most cases of severe life-threatening asthma the attack develops against a background of poorly controlled disease. However, in 10-20% of cases of fatal or near-fatal asthma the onset appears to be sudden and unexpected, with death sometimes occurring within a couple of hours. Such episodes have been termed "sudden asphyxic asthma"¹ and are accompanied pathologically by only mild inflammatory changes and little mucous plugging of the airways.² A noteworthy feature of near-fatal asthma is that attacks are often recurrent and a previous life-threatening episode represents one of the most important factors predicting asthmatic death.³ Acute severe asthma runs "true to type" in that, if hypercapnia develops during one severe attack, it is likely to recur in a subsequent episode.⁴ Since fatal and near-fatal asthmatic attacks have similar features,⁵ study of the latter should improve un-

derstanding of the nature of fatal attacks and might direct attention to possible ways of reducing asthma mortality.

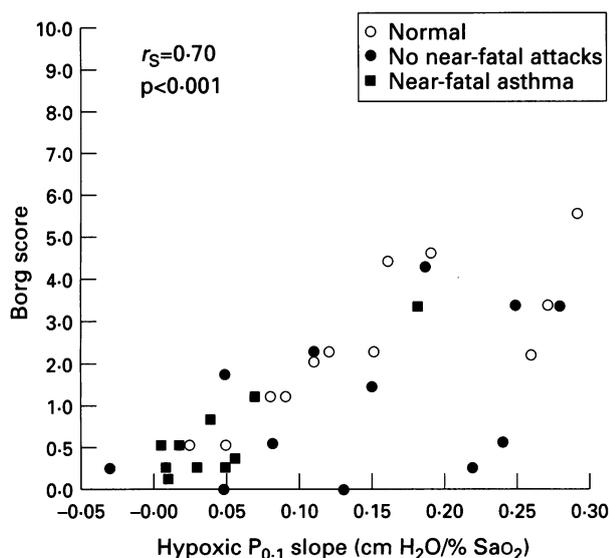
Perception and respiratory control

Retrospective analyses of asthma deaths have emphasised failure to appreciate the severity of the final episode, suggesting that poor perception may be a contributory factor. Various studies over the past 20 years have examined variability of both the ventilatory drive and the perception of asthma in different patients. Several recently published papers have added to the information available on the interrelations between, on the one hand, respiratory chemosensitivity and drive to the respiratory muscles and, on the other hand, the perception of symptoms, personality, and psychological profile of asthmatic patients. The results focus attention

on some of the factors which may contribute to fatal and near-fatal asthma.

Two classic papers published in the 1970s showed that some patients with asthma have blunted chemosensitivity or impaired perception of the severity of narrowing of the airways. Firstly, Rebeck and Read,⁶ studying a group of adults during recovery from severe asthma, showed that those who had developed hypercapnia during the acute attack, failed to show the anticipated increase in ventilatory response to carbon dioxide when in remission. Secondly, Rubinfeld and Pain⁷ asked unselected asthmatic subjects to grade the severity of chest tightness accompanying methacholine induced bronchoconstriction; considerable variation was seen in the perception of severity, and the correlation between symptoms and objective assessment was only weak. Importantly, 15% of the patients were shown to be "poor perceivers".

The study by Kikuchi *et al*⁸ suggests an association between reduced chemosensitivity and impaired perception of a respiratory load. They concentrated on 11 patients who had survived near-fatal asthma (five had had recurrent attacks) and compared these with a group with similar very mild airways obstruction at the time of study but with no history of severe attacks. Reductions in both the ventilatory and mouth occlusion pressure responses to hypoxia were seen in the patients who had survived a near-fatal asthma attack, while the other asthmatic subjects had responses which were similar to normal. Differences in response to carbon dioxide were less marked. The subjects were also asked to score the sensation of dyspnoea while breathing via an artificial external resistance. Again, the dyspnoea score during resistance breathing was less in the group who had had a near-fatal asthma attack. Moreover, there was a correlation between the dyspnoea score during resistance breathing and the magnitude of the hypoxic response (figure). The authors point out that resection of the carotid bodies is reported to result in both abolition of the ventilatory response to



Relation between perception of dyspnoea during breathing via an increased resistance and the mouth occlusion pressure response to hypoxia in normal subjects (○) and asthmatic patients who either had (■) or had not (●) suffered a near-fatal attack. Note that patients in the former group have lower hypoxic responses and lower perception of dyspnoea than the other groups. Reproduced from Kikuchi *et al*⁸ with permission.

hypoxia and lack of perception of dyspnoea; they therefore suggest that their results may be attributable to dysfunction of the carotid chemoreceptors and that this may predispose some individuals to fatal asthma.

It is well recognised that the sensation of dyspnoea or breathlessness depends on activation of, and afferent information from, the respiratory muscles. In healthy subjects the score of "breathlessness" when ventilation is stimulated – for example, by carbon dioxide or exercise – is closely related to the ventilation achieved. In this context it seems a missed opportunity that Kikuchi *et al* reported neither the dyspnoea rating during hypoxic stimulation nor ventilation during loaded breathing. It is therefore unclear whether the poor perception of dyspnoea during resistance breathing by patients with near-fatal asthma reflects a lower level of ventilation or impaired perception. It should also be noted that the sensation associated with external loading is different from, and not necessarily closely related to, that accompanying spontaneous or induced bronchoconstriction.

In a study by Boulet and colleagues⁹ patients with asthma were subjected to methacholine challenge and asked separately to score their perceptions of airways obstruction, breathlessness, and any associated anxiety. As shown earlier by Rubinfeld and Pain,⁷ there was considerable variation between individuals in perception of both narrowing of the airways and breathlessness. Although there was a correlation between the two types of sensation, the subjects were capable of distinguishing between them. Overall, for a given reduction in the forced expiratory volume in one second the perception of symptoms was actually greater in the asthmatic subjects than in controls, and the authors suggested that the enhanced perception might reflect greater familiarity with the symptoms in the patient group. In this paper the asthmatic subjects were unselected, but in an earlier study¹⁰ concentrating on patients with near-fatal asthma the same group showed that perception of induced asthma was similar when compared with a group of asthmatic subjects with no history of severe attacks. However, perception of the severity of *spontaneous* asthma appeared to be less good in the group who had had a near-fatal asthma attack. These apparently paradoxical findings might be reconciled by the observation that perception of bronchoconstriction by subjects with previous near-fatal asthma is more likely to be blunted at a time when bronchial hyperresponsiveness is more pronounced.¹¹

Personality and psychopathology

Boulet *et al*⁹ found that the anxiety level scored by unselected asthmatic patients during induced bronchoconstriction was similar to that reported by a non-asthmatic control group. In their earlier study,¹⁰ however, they had shown that the personality profiles of patients with near-fatal asthma showed higher scores suggesting psychological disturbance, although no specific psychological pattern was evident. An important role for psychological factors in fatal or near-fatal asthma is also suggested by the frequent recognition that denial and consequent non-compliance with treatment or follow up are contributory aetiological factors.^{11,12} These conclusions are supported by a further recent survey of the psychiatric features of patients with life-threatening asthma. Campbell *et al*¹³ assessed 77 consecutive

LEARNING POINTS

- * Near-fatal asthma attacks usually occur against a background of poor control.
- * A minority are apparently “sudden” and unexpected.
- * A near-fatal asthma attack is a strong predictor of a subsequent fatal attack.
- * Contributory factors may include: poor perception of severity; low chemosensitivity; denial; unrecognised psychopathology.

patients who had presented with near-fatal asthma attacks using standard questionnaires to detect psychiatric morbidity. They showed that 43% of the subjects gave responses consistent with psychiatric “caseness” and 20% had previously had a formal psychiatric consultation. More specifically, significant denial was shown by 57% of the subjects and a high denial score was related to the mode of presentation with the acute attack, in that those scoring higher on the denial scale were more likely to report presentation with “sudden” collapse rather than with progressive respiratory distress.

Respiratory muscle activity

The paper by Allen *et al*¹⁴ compares the ability of asthmatic and control subjects to produce maximum voluntary activation of the diaphragm and follows from an earlier study¹⁵ in which the same group postulated that patients with asthma have an impaired ability to activate the respiratory muscles by voluntary mechanisms. In their earlier study they examined the effect of phrenic nerve stimulation superimposed on a maximal voluntary inspiratory manoeuvre in order to assess how completely the diaphragm could be activated voluntarily. Although the extra transdiaphragmatic pressure generated by such a superimposed “twitch” was relatively small (adding only 10–20% to that obtained voluntarily), this was greater in asthmatic patients than in controls. The authors pointed out that these findings might be of relevance to the phenomenon of “central” fatigue in which it becomes increasingly difficult to maintain voluntary activation during extreme loading of a muscle even though non-voluntary stimulation shows that contractile force is preserved. The relevance of these findings to spontaneous breathing may be questionable since it is well recognised that the voluntary neural pathway of respiratory muscle activation is separate from the involuntary or “automatic” pathway which dominates control during spontaneous breathing. It is, however, possible that voluntary drive becomes important with extreme loading and consequently the authors speculated that the apparently impaired voluntary activation of the diaphragm in subjects with asthma might be relevant to progressive central fatigue during severe attacks, and might be one of the factors that determine the development of ventilatory failure. In their recent study¹³ the authors have compared the ability to produce maximal voluntary activation of the diaphragm with the psychological state of a group of asthmatic subjects and have shown that features of depression correlate with reduced ability to produce complete activation. Clearly,

it is important to extend these observations by focusing specifically on patients who have shown that they are prone to severe attacks.

Conclusions

The factors contributing to fatal or near-fatal asthma are complex and likely to be both multiple within an individual and variable between individuals. A common thread in the papers summarised here is the important influence of psychological factors, both in terms of innate personality and unrecognised psychopathology. Psychological factors and personality may, for instance, determine the level of perception and awareness of the severity of asthma, as well as physiological responses to chemical and mechanical stimuli and the ability during a severe attack to achieve and maintain adequate contraction of the respiratory muscles. Psychological factors may also have more mundane, but no less important, implications for compliance with medical advice and the general approach to self-management of asthma. These in turn may influence the likelihood of developing, and the ability to survive, a life-threatening attack.

- 1 Wasserfallen J-B, Schaller M-D, Feihl F, Perret C. Sudden asphyxic asthma: a distinct entity? *Am Rev Respir Dis* 1990;142:108–11.
- 2 Sur S, Crotty TB, Kephart GM, Hyma BA, Colby TV, Reed CE, *et al*. Sudden-onset fatal asthma: a distinct entity with few eosinophils and relatively more neutrophils in the airway submucosa? *Am Rev Respir Dis* 1993;148:713–9.
- 3 Rea HH, Scragg R, Jackson R, Beaglehole R, Fenwick J, Sutherland DC. A case-control study of deaths from asthma. *Thorax* 1986;41:833–9.
- 4 Mountain RD, Sahn SA. Clinical features and outcome in patients with acute asthma presenting with hypercapnia. *Am Rev Respir Dis* 1988;138:535–9.
- 5 Campbell DA, McLennan G, Coates JR, *et al*. A comparison of asthma deaths and near-fatal asthma attacks in South Australia. *Eur Respir J* 1994;7:490–7.
- 6 Rebuck AS, Read J. Patterns of ventilatory response to carbon dioxide during recovery from severe asthma. *Clin Sci* 1971;41:13–21.
- 7 Rubinfeld AR, Pain MCF. Perception of asthma. *Lancet* 1976;i:882–4.
- 8 Kikuchi Y, Okabe S, Tamura G, Hida W, Homma M, Shirato K, *et al*. Chemosensitivity and perception of dyspnea in patients with a history of near-fatal asthma. *N Engl J Med* 1994;330:1329–34.
- 9 Boulet L-P, Courmoyer I, Deschesnes F, Leblanc P, Nouwen A. Perception of airflow obstruction and associated breathlessness in normal and asthmatic subjects: correlation with anxiety and bronchodilator needs. *Thorax* 1994;49:965–70.
- 10 Boulet L-P, Deschesnes F, Turcotte H, Gignac F. Near fatal asthma: clinical and physiologic features, perception of bronchoconstriction and psychogenic profile. *J Allergy Clin Immunol* 1991;88:838–46.
- 11 Ruffin RE, Latimer KM, Schembri DA. Longitudinal study of near fatal asthma. *Chest* 1991;99:77–83.
- 12 Yellowlees PM, Ruffin RE. Psychological defences and coping styles in patients following a life threatening attack of asthma. *Chest* 1989;95:1298–303.
- 13 Campbell DA, Yellowlees PM, McLennan G, Coates JR, Frith PA, Gluyas PA, *et al*. Psychiatric and medical features of near fatal asthma. *Thorax* 1995;50:254–9.
- 14 Allen GM, Hickie I, Gandevia SC, McKenzie DK. Impaired voluntary drive to breathe: a possible link between depression and unexplained ventilatory failure in asthmatic patients. *Thorax* 1994;49:881–4.
- 15 Allen GM, McKenzie DK, Gandevia SC, Bass S. Reduced voluntary drive to breathe in asthmatic subjects. *Respir Physiol* 1993;93:29–40.