Characteristics of patients with soybean dust-induced acute severe asthma requiring mechanical ventilation


ABSTRACT: Patients presenting with acute severe asthma during the Barcelona's outbreaks caused by soybean dust inhalation from August, 1981, through September, 1987, characteristically showed an abrupt severe onset of each attack followed by a rapid relief of symptoms after treatment. To throw further light on clinical findings, pathophysiology and outcome in the most life-threatening episodes, we reviewed records of acute severe asthma patients treated by mechanical ventilation in one of the four main hospitals of the city. Twelve such patients (15 episodes) were compared to 24 non-epidemic asthmatic patients (25 episodes) also treated by mechanical ventilation in the same institution during the same period of time. There was a male predominance during outbreaks (p<0.03) and epidemic patients were ventilated fewer hours (12±8 h) (mean±SD), admitted fewer days to intensive care (1.6±0.7 days), and hospitalized fewer days (7.1±4.4 days) than non-epidemic patients (6±84 h, 4.6±3.8 days (p<0.001, each), and 16.0±13.2 days (p<0.004), respectively). These differences together with both the fulminating presentation of the episodes of epidemic asthma and the point-source origin of the asthma outbreaks previously shown are consistent with the unusual nature of the aetiologic agent, soybean dust.


From August, 1981, through September, 1987, 26 outbreaks of asthma have been detected in the city of Barcelona. These outbreaks affected a total of 687 patients and caused 1,155 emergency room admissions (mean admissions per epidemic, 44.4; range, 12-96) in the four largest urban hospitals which account for approximately 90% of the emergencies of the city [1-8]. Inhalation of soybean dust released during the unloading of soybeans at the city harbour was the cause of these epidemics [6, 7]. Once control measures on soybean unloading were implemented, epidemic asthma in the city of Barcelona seems to be at an end [7].

Anecdotal experience of physicians on attendance during the outbreaks consistently stated that the most striking clinical finding of these outbreaks was the sudden, severe onset of each attack and a rapid relief of symptoms after standardized treatment for acute severe asthma [1, 3]. This abrupt onset led the patients to the emergency room very rapidly, usually in less than one hour after the beginning of the attack, in a time-cluster presentation [4, 7]. Furthermore, the proportion of "epidemic patients" admitted to intensive care was substantially higher, regardless of whether they did or did not require mechanical ventilation, averaging 8.5% [1] and 11.9% [3] as opposed to 1.1% and 4.9% in non-epidemic asthma patients, respectively.

This dissociation between the degree of clinical severity of the epidemic attacks and the rapid resolution of the crisis following treatment in the majority of the patients is at variance with the usual evolution of non-epidemic patients with life-threatening acute severe asthma. We therefore reviewed records of both epidemic and non-epidemic asthmatic patients requiring mechanical ventilation to throw further light on clinical findings, pathophysiology, and outcome of patients suffering from the most life-threatening asthma attacks caused by soybean dust inhalation.

Material and methods

We reviewed all the available records of acute severe asthma patients treated by mechanical ventilation in Hospital Clinic (one of the four main hospitals of Barcelona) during the period of asthma outbreaks caused by soybean dust inhalation (from August, 1981, through September, 1987). The records of 12 epidemic asthmatic patients (attended in epidemic days),
admitted to the intensive care units and requiring mechanical ventilation on 15 different occasions were further reviewed. All were asthmatics who fulfilled the American Thoracic Society (ATS) criteria [9] and had been admitted to the emergency room because of their life-threatening clinical condition. Epidemic days were classified following epidemiological and statistical criteria described elsewhere [7].

A group of 24 non-epidemic asthmatic patients (attended in non-epidemic days) who were admitted on 25 occasions into the same hospital with life-threatening asthma, also needing ventilatory support over the same period of time, were included as controls. Five non-epidemic episodes of patients who were admitted on both epidemic and non-epidemic days were excluded from the analysis.

The criteria of inclusion for both groups of patients was the admission to the intensive care unit for ventilatory support due to the severity of their acute asthma attack without associated cardiorespiratory or systemic diseases. Patients who were intubated for less than one hour after the onset of artificial ventilation in the emergency room were not included.

Unfortunately, information to define atopic and non-atopic patients could not be obtained from the review of the clinical records. The medical treatment given to the patients was similar in both groups, including intravenous aminophylline at a constant rate (to maintain theophylline levels between 10–20 μg/ml), intravenous methylprednisolone (60 mg per 6 h), adrenergic agents (either epinephrine or terbutaline subcutaneously, or intravenous salbutamol, particularly during the first hours of admission to hospital) and rehydration. Mechanical ventilation was always accomplished with a volume-cycled machine (either Bennet MA-2B or Servo-Ventilator Siemens 900), being adjusted to obtain normal or near normal Paco₂ and arterial O₂ saturation above 90%. Data were reviewed regarding sex, age, smoking habits, duration and treatment of asthma, hours of mechanical ventilation, days of stay in intensive care, days of total hospitalization, arterial blood gases and intrathoracic pressures on admission, forced spirometry on discharge from hospital, and outcome. Patients were considered survivors if they lived to be discharged from the hospital following assisted ventilation.

Table 1. – Mean±so differences and ranges (in parentheses) between epidemic and non-epidemic patients

<table>
<thead>
<tr>
<th>Units</th>
<th>Epidemic group</th>
<th>p</th>
<th>Non-epidemic group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (patients)</td>
<td>12</td>
<td>&lt;0.03</td>
<td>24</td>
</tr>
<tr>
<td>Number of episodes</td>
<td>15</td>
<td></td>
<td>25</td>
</tr>
<tr>
<td>Sex</td>
<td>M/F</td>
<td>10 males/2 Females</td>
<td>9 males/15 females</td>
</tr>
<tr>
<td>Age</td>
<td>yrs</td>
<td>49±14 (23–79)</td>
<td>48±12 (21–69)</td>
</tr>
<tr>
<td>Duration of asthma</td>
<td>yrs</td>
<td>15±15 (1–45)</td>
<td>17±13 (3–50)</td>
</tr>
<tr>
<td>Duration of mechanical ventilation</td>
<td>h</td>
<td>12±8 (4–27)</td>
<td>&lt;0.001 65±84 (5–396)</td>
</tr>
<tr>
<td>Stay in IC *</td>
<td>days</td>
<td>1.6±0.7 (1–3)</td>
<td>&lt;0.001 4.6±3.8 (1–18)</td>
</tr>
<tr>
<td>Total hospitalisation *</td>
<td>days</td>
<td>7.1±4.4 (1–16)</td>
<td>&lt;0.004 16.0±13.2 (4–63)</td>
</tr>
<tr>
<td>Paco₂ (ER admission) *</td>
<td>kPa</td>
<td>17.7±16.0 (1.7–44.1)</td>
<td>NS 8.9±5.3 (1.6–24.1)</td>
</tr>
<tr>
<td>Paco₂ (ER admission) *</td>
<td>kPa</td>
<td>11.7±13.5 (6.6–17.2)</td>
<td>&lt;0.001 10.7±3.0 (4.9–15.5)</td>
</tr>
<tr>
<td>pH (ER admission)</td>
<td>units</td>
<td>6.99±0.10 (6.77–7.18)</td>
<td>&lt;0.001 7.03±0.16 (6.75–7.3)</td>
</tr>
<tr>
<td>Base excess (ER admission)</td>
<td>mM·l⁻¹</td>
<td>-11.8±5.0 (19–5)</td>
<td>NS -9.4±5.8 (20–1)</td>
</tr>
<tr>
<td>Airway pressures (IC admission)</td>
<td>cmH₂O</td>
<td>34±12 (16–50)</td>
<td>NS 41±16 (16–70)</td>
</tr>
<tr>
<td>% FEV₁ (on hospital discharge)</td>
<td>% pred</td>
<td>56±29 (15–90)</td>
<td>NS 61±20 (27–94)</td>
</tr>
<tr>
<td>FEV₁/FVC (on hospital discharge)</td>
<td>%</td>
<td>50±20 (18–74)</td>
<td>NS 57±13 (27–72)</td>
</tr>
</tbody>
</table>

*: Patients with brain death have been excluded; E: emergency room; IC: intensive care. **: O₂ supplied through bag-valve mask, intrathoracic tube or face mask; NS: not significant. Except for sex and age, means correspond to episodes. Conversion factor: 1 kPa=7.5 mmHg.

Data were collected retrospectively for the period 1981–1984, whereas they were collected prospectively since 1985, when the Emergency Room Admission Monitoring System [4] was implemented. During the period 1985–86, there were 18 epidemic and 12 non-epidemic episodes requiring intensive care in our hospital. Seven out of the 18 epidemic episodes (all but one included in the present report) and 8 out of the 12 non-epidemic episodes (6 of them included as controls) required mechanical ventilation. One or two patients in each group, respectively, are not included because of incomplete clinical records.
Results

Table 1 summarizes the principal findings for each group. Duration of asthma and maintenance treatment were similar in the two groups. All the patients admitted to the emergency room were in both severe acute respiratory failure and mixed respiratory and metabolic acidosis. The epidemic patients had developed fulminating acute asthma and were in a moribund condition on arrival, or had cardiorespiratory arrests shortly before or after admission, requiring intubation and institution of mechanical ventilation at once. By contrast, in the non-epidemic patients the rate of evolution of the attacks was more variable, ranging from a few hours to many days before their arrival at the hospital. Three patients in each group were admitted to the emergency room in cardiorespiratory arrest which led to brain death. Typical signs for the assessment of acute severe asthma, namely pulsum paradoxus, respiratory accessory muscle use, or low peak flow rate, were not recorded because of the very severe clinical condition of the epidemic patients, and overload of patients during the outbreaks.

There was a male predominance in the epidemic group (10 males and 2 females), a finding that was significantly different from the sex ratio in non-epidemic subjects, which included 15 females and 9 males (p<0.03). Seven of the twelve epidemic patients and eight of the twenty-four non-epidemic ones were either regular smokers or ex-smokers. Moreover, epidemic patients required a shorter period of mechanical ventilation (12±8 hours; range, 4–27; median, 9.5) than non-epidemic individuals (65±84 hours; range, 5–396; median, 40) (p<0.001) and fewer days of intensive care stay (1.6±0.7 days (range, 1–3; median, 1.5) versus 4.6±3.8 days (range, 1–18; median, 3.0), (p<0.001). The days of total hospitalization were also significantly lower in the former group (7.1±4.4 days (range, 1–18; median, 6.5) versus 16.0±13.2 days (range, 4–65; median, 13.0), p<0.004).

There were no significant differences in arterial blood gases and acid-base status on admission, peak airway pressures generated by the ventilator within the first hours of mechanical ventilation, spirometry on discharge, nor in final outcome. Except for the 6 patients who died of brain death, all epidemic and non-epidemic patients survived.

Discussion

Those patients who suffered from acute severe asthma due to soybean dust inhalation and needed mechanical support for their life-threatening respiratory failure, exhibited some particular clinical findings not previously reported in other epidemics [10–17].

First the abrupt onset of the acute attacks together with the point-source type of the outbreaks. The most severe cases who developed a fulminating attack were in a moribund status on arrival at the hospital and/or had cardiorespiratory arrest early after admission, needing immediate and aggressive intensive care [1, 3, 4]. Another strong sign of the severity of the epidemic asthma attacks was the elevated proportion of epidemic episodes that needed intensive care, whether or not they required assisted ventilation. According to the Emergency Room Admissions Monitoring System designed to detect patients with epidemic acute severe asthma admitted to the main hospitals of Barcelona during the period 1985–86 [4], 25 out of 326 epidemic episodes (7.7%) and 38 out of 3,624 non-epidemic episodes (1.1%) needed intensive care (Antó JM and Sunyer J, unpublished data). These violent and severe clinical features have been previously reported in endemic or epidemic castor-bean asthma [13], but not in other epidemics. However, the aetiologic role of inhaled soybean in Barcelona's asthma outbreaks has been reported elsewhere [6, 7]. On the other hand, anaphylactic reactions after the ingestion of soybean had been previously described [18].

Second, the duration of mechanical ventilation was substantially shorter for the epidemic episodes than for the non-epidemic ones in spite of similar levels of arterial blood gases and mean peak airway pressures generated by the ventilator. A review of the published studies of asthmatic patients needing ventilatory support [19–27] (table 2) shows that while our epidemic patients had a shorter duration of mechanical ventilation, none of them was ventilated for more than 27 h. Our non-epidemic patients showed durations of artificial ventilation very similar to all the other reports. In addition, epidemic patients required fewer days of both intensive care and total hospitalization stays than non-epidemic patients. This issue was specifically addressed only in the studies of Dandoli and Perret [24] and Mountain and Sahn [27], which showed a mean duration of total hospitalization of 12 days (range, 2–43 days) and 8.1 days (range, 4–15 days), respectively. The finding that epidemic patients needed fewer hours of mechanical ventilation and were discharged earlier from both the intensive care setting and the hospital strongly suggests that soybean dust provoked the massive attacks of severe asthma through a short-acting, but powerful, airborne allergic mechanism.

Third, there was an elevated predominance of males among epidemic patients. Although the sex prevalence for all the Barcelona's outbreaks was 53% for females and 47% for males, there was a male predominance (79%) among epidemic patients who required intensive care during the period 1985–86 (Antó JM and Sunyer J, unpublished data). Although we do not have an adequate explanation for this finding, it is of note that most of the studies of non-epidemic asthmatic patients treated by mechanical ventilation have always included a larger number of females [19, 21–26]. It is also of interest to recall that, in the recent work of Mountain and Sahn [27], one of the most provocative clinical findings was precisely the significant predominance of men with acute severe asthma episodes presenting with hypercapnia.

There were no differences in age, nor in duration or treatment of asthma. Although the retrospective nature of the present study does not show the precise proportion of extrinsic and intrinsic asthmatics in each group of patients, there is enough epidemiologic and immunologic evidence of the extrinsic nature of epidemic patients.
Furthermore, when patients were discharged from hospital they showed the same degree of moderate to very severe airflow obstruction. Interestingly, arterial blood gases on admission and peak airway pressures generated by the ventilator during the first hours of mechanical ventilation were similarly altered in each group, suggesting the same degree of severity in both gas exchange abnormalities and lung mechanics impairment.

Our group [28] set out a recent study to assess the mechanisms of abnormal gas exchange in 8 patients with status asthmaticus requiring mechanical ventilation, including 3 epidemic subjects reported in the present study (patients 4, 6 and 7, in [28]). This failed to show differences between epidemic and non-epidemic individuals in both the degree of severity and extent of ventilation-perfusion (VA/Q) mismatch, the fundamental mechanism underlying abnormal gas exchange in acute severe asthma [28, 29].

The clinical and functional findings of the present report, together with the epidemiological and immunological data revealing that the point-source asthma outbreaks of Barcelona were caused by the inhalation of soybean dust released during the unloading of soybean at the city harbour, reinforce the view of a severe, short acting bronchial challenge provoked by soybean dust inhalation which appears to be an uncommon, albeit very powerful, airborne allergic agent.

Acknowledgements: To Prof T.J.H. Clark (London, England) for his critical review and comments, and to Dr M. Mahalich (Service d’Anestesiologia, Hospital Clinic) for his help in collecting part of the data.

References


RÉSUMÉ: Les patients développant un asthme aigu sévère au cours des épidémies de Barcelone, provoquées par l'inhalation de poussière de soya, ont montré de façon caractéristique un début aigu et sévère de chaque crise, suivi d'un soulagement rapide des symptômes après traitement. Afin d'élaborer davantage les manifestations cliniques, la physiopathologie et l'évolution des épisodes les plus sévères, nous avons repris les dossiers des patients atteints d'asthme aigu sévère traités par ventilation mécanique, dans un des quatre hôpitaux principaux de la ville. Douze de ces patients (15 épisodes) ont été comparés à 24 patients asthmatiques non épidémiques (25 épisodes) traités eux aussi par ventilation mécanique dans la même institution, pendant la même période. L'on a noté une prédilection masculine pendant les épidémies et une durée de ventilation plus courte chez les patients épidémiques (12±8 h) (moyenne±DS), un séjour plus bref dans l'unité de soins intensifs (1.6±0.7), et une hospitalisation plus courte (7.1±4.4 jours), que chez les patients non épidémiques (65±84 h, 4.6±3.8 jours (p<0.01) pour les deux premiers et 16.0±13 jours (p<0.004), d'hospitalisation). Ces différences, ainsi que le début fulminant des épisodes d'asthme épidémique, et l'origine ponctuelle des crises asthmatiques démontrées antérieurement, sont en rapport avec la nature inhabituelle de l'agent étiologique, la poussière de soya. Eur Respir J., 1990, 3, 429-433.