Death in Status Asthmaticus*

ROLE OF SEDATION

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The recent alarming increase in deaths from bronchial asthma has led to major attempts to resolve the problem, including the current study of factors in air pollution by groups at Tulane University and elsewhere. Necropsy studies by Unger, Bullen, Walker and Frost, Cardell and Pearson, and Earle, have underscored chronic bronchial alterations in asthmatic persons in whom there were superimposed changes brought about by infection.

Why do most patients with status asthmaticus survive the attack and more importantly, why do some fail to do so? In an attempt to answer this question, we reviewed the records of patients who died during a five-year period at Charity Hospital in New Orleans, and compared them with an equal number of records, randomly selected, of similar patients who survived. Particular attention was paid to the amount and type of medication administered since it was felt from our own experience, as well as that of others, that this might be of crucial importance.

Method of Study and Results

There were 109 patients who died with a diagnosis of "asthma." After studying the charts, 80 were excluded, as these patients did not die of bronchial asthma, but of such conditions as myocardial infarction, tuberculosis, cerebrovascular accident, and the like. The necropsy slides of the residual 29 patients were reviewed by a pathologist. Other diseases were found to have contributed substantially to exitus in 14 persons.

There remained 15 case records of individuals whose death could be ascribed unequivocally to bronchial asthma. In these cases, we calculated the amount of sedative medication that the patient had received 36 hours prior to death (Table 1). Sedative medication is here taken to include not only barbiturates, chloral hydrate and opiates, but also ether, and sedative antihistaminic drugs. The comparative sedative effect of the drugs used was determined by reference to tables in Drill's Pharmacology in Medicine text. Since we were unable to find information directly comparing the sedative action of antihistamines, barbiturates, and opiates, we indirectly estimated equivalent doses from the above mentioned tables. The direct effect of the drugs on the respiratory center was also taken into consideration in calculating the equivalent doses.

It is realized that equating 75 mg. of diphenhydramine (Benadryl), 120 mg. of phenobarbital, 7½ mg. of morphine, 50 mg. of meperidine hydrochloride (Demerol), and 60 mg. of codeine is somewhat arbitrary. Blood levels of these drugs, if available, would have been useful in this comparison, but no definite equivalents for human beings are available in the literature. We therefore chose the usual amounts that are said to produce sedation, as one "unit." Oxygen, injudiciously administered to patients with CO₂ retention may produce sedation by precipitating CO₂ narcosis. In those cases in which oxygen inhalation therapy was used, the oxygen was given at the rate of 7 liters per minute and not at 1 liter per minute with gradual increase in the flow rate as recommended by Barach.*

Diphenhydramine, the antihistaminic used in almost every instance in these patients, is unique in producing sedation in

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a much higher percentage of patients than other antihistaminics.18

Table 1 and Table 2 summarize the amount of sedative medication administered to those patients who died during an attack of status asthmaticus (Group 1) and to those who survived (Group 2), respectively. Figure 1 graphically compares the two groups with relation to the amount of medication received.

Ten patients received 4 or more units of sedative medication (defined under Fig. 1). Only one of these survived. Patient No. 5 in Group 1 received less than 4 units; however, she received 3 grains of phenobarbital intravenously one and a half hours prior to her death. Patient No. 11 in the death group received less than 4 units of sedative medication, but had chronic pulmonary insufficiency and received oxygen therapy prior to death, a procedure known to be fraught with hazard under such circumstances. It is well known that patients with chronic pulmonary disease and resultant CO₂ retention may die very quietly and pink as a result of too vigorous oxygen therapy. The remaining four patients in Group 1 died almost immediately on arrival at the hospital. Two of these died during the administration of intravenous aminophylline, and perhaps some causal relationship exists.11,18 Because the amount of sedation, if any, received prior to death is not known, these cases are not included in Fig. 1.

We feel that the severity of the asthmatic attack in the two groups is comparable. The reason for this has to do with the general criteria for admissions of an asthmatic to the hospital. They must have failed to respond to a vigorous therapeutic regimen in the emergency room. It is not unusual for an asthmatic patient to be managed in the emergency room for 12 to 24 hours before being admitted to the hospital.

DISCUSSION

According to Hilding,19 the most important change in status asthmaticus is the metamorphosis of ciliated epithelium to mucus-producing goblet cells. In consequence, focal areas of atelectasis result due to mucus plugs which are not adequately removed. There is no question that mucus

![Figure 1: The dosages listed are equivalent to one unit of sedative medication: 75 mg. diphenhydramine; 120 mg. phenobarbital; 7½ mg. morphine; 50 mg. meperidine hydrochloride; 60 mg. codeine; 60 ml. ether.](image-url)
### Table 1—Patients Who Died During an Attack of Status Asthmaticus

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Antihistamine</th>
<th>Opiate</th>
<th>Barbiturate</th>
<th>Miscellaneous</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 30</td>
<td>F</td>
<td>W</td>
<td>Diphenhydramine 100 mg.</td>
<td>Meperidine Hydrochloride 50 mg.</td>
<td>Phenobarbital 450 mg.</td>
<td>Patient was treated elsewhere with unknown amount of sedation. On arrival at Charity Hospital, patient was given nalorphine hydrochloride.</td>
</tr>
<tr>
<td>2. 65</td>
<td>M</td>
<td>C</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Patient died immediately on arrival at hospital. Not known whether patient received prior sedative medication.</td>
</tr>
<tr>
<td>3. 33</td>
<td>F</td>
<td>C</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Died 15 minutes after arrival at hospital and also 10 minutes after injection of aminophylline.</td>
</tr>
<tr>
<td>4. 51</td>
<td>M</td>
<td>C</td>
<td>Diphenhydramine 50 mg.</td>
<td>Meperidine Hydrochloride 250 mg.</td>
<td>Phenobarbital 240 mg.</td>
<td>50 mg. of meperidine hydrochloride given 4 hours before death.</td>
</tr>
<tr>
<td>5. 46</td>
<td>F</td>
<td>W</td>
<td>0</td>
<td>0</td>
<td>Amobarbital 450 mg.</td>
<td>Patient was given 300 mg. of amobarbital 1½ hours before death, 180 mg. of which was intravenous.</td>
</tr>
<tr>
<td>6. 36</td>
<td>F</td>
<td>C</td>
<td>Diphenhydramine 200 mg.</td>
<td>Meperidine Hydrochloride 75 mg.</td>
<td>Phenobarbital 360 mg.</td>
<td>Patient was given an intravenous infusion 4 hours before death which contained 75 mg. of meperidine hydrochloride, 100 mg. diphenhydramine and 225 mg. amobarbital.</td>
</tr>
<tr>
<td>7. 20</td>
<td>F</td>
<td>C</td>
<td>Diphenhydramine 100 mg.</td>
<td>Meperidine Hydrochloride 100 mg.</td>
<td>At least 360 mg.</td>
<td>Patient with a history of iodide sensitivity who was given iodides 12 hours prior to death.</td>
</tr>
<tr>
<td>8. 58</td>
<td>M</td>
<td>W</td>
<td>Diphenhydramine 250 mg.</td>
<td>0</td>
<td>Phenobarbital 120 mg.</td>
<td>Patient had been in status for at least a week. Died in the accident room. Was said to have &quot;chronic lung disease.&quot; Was given oxygen by nasal catheter.</td>
</tr>
<tr>
<td>9. 34</td>
<td>F</td>
<td>C</td>
<td>0</td>
<td>Meperidine Hydrochloride 250 mg.</td>
<td>Phenobarbital 480 mg.</td>
<td>Gravida 4, Para 4, with uncomplicated prenatal course who developed hypertension and asthma the day following delivery. The patient was given heavy sedation for hypertension and this depressed respiration. Patient became comatose and died.</td>
</tr>
<tr>
<td>10. 53</td>
<td>M</td>
<td>C</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Patient died 10 minutes after arriving at the hospital.</td>
</tr>
<tr>
<td>11. 57</td>
<td>F</td>
<td>C</td>
<td>0</td>
<td>0</td>
<td>Phenobarbital 120 mg.</td>
<td>Patient with chronic pulmonary insufficiency who received oxygen.</td>
</tr>
<tr>
<td>12. 22</td>
<td>F</td>
<td>W</td>
<td>Diphenhydramine 150 mg.</td>
<td>Meperidine Hydrochloride 150 mg.</td>
<td>Phenobarbital 300 mg.</td>
<td>Patient received 150 mg. of diphenhydramine, 25 mg. promethazine, and 120 mg. phenobarbital 4 hours before death.</td>
</tr>
<tr>
<td>13. 22</td>
<td>F</td>
<td>C</td>
<td>Diphenhydramine 300 mg.</td>
<td>Meperidine Hydrochloride 50 mg.</td>
<td>Phenobarbital 180 mg.</td>
<td>Patient received 450 mg. amobarbital in intravenous infusion containing 100 mg. diphenhydramine 35 minutes before the death. Died during administration of intravenous aminophylline.</td>
</tr>
<tr>
<td>14. 60</td>
<td>M</td>
<td>C</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Patient received 180 mg. phenobarbital, 60 ml. ether 4 hours before death.</td>
</tr>
<tr>
<td>15. 37</td>
<td>F</td>
<td>C</td>
<td>Diphenhydramine 350 mg.</td>
<td>0</td>
<td>Phenobarbital 360 mg.</td>
<td>Patient received 180 mg. phenobarbital, 60 ml. ether 4 hours before death.</td>
</tr>
</tbody>
</table>

**Code:** C=colored; W=white.
plugging is a consistent finding in patients who die in status asthmaticus. Moreover, Bullen found that asthmatic patients who died of intercurrent disease or injury, with no asthma at the time, had larger quantities of mucoid secretion in the bronchi than is commonly found in nonasthmatics. We also noted this in our original group of 109 patients.

It seems apparent that anything that decreases the ability of the patient to oxygenate himself, decreases his chances of survival. One need only note the frequent pathologic findings compatible with anoxia, such as widespread petechial hemorrhages, which are found in patients dying of asthma, to be convinced that anoxia is the crucial pathophysiologic event leading to death. Sedation seems to have done this in at least nine of our patients who died. The importance of morphine in contributing to death from asthma has been emphasized repeatedly. We do not feel that morphine is unique in this property. The individual in status asthmaticus depends in large part on his accessory muscles of respiration for breathing. This requires voluntary effort, which the patient is unable to perform if he is oversedated. In addition, the cough reflex is depressed with resultant failure to remove mucus plugs. Finally, there is a direct and indirect effect on the respiratory centers leading to decreased involuntary ventilation. The conscious hypoxic patient is very anxious, and a tense physician, in an attempt to allay the patient’s anxiety, may inadvertently depress his ventilation.

It might be well to mention that most of the clinical-pathologic studies which have been done on patients who died during an attack of status asthmaticus, fail to give any detailed information concerning the type and amount of medication received prior to death. From our above experience, these studies might well be reevaluated in terms of sedative medication received by the patient.
SUMMARY AND CONCLUSIONS

Thirty patients with status asthmaticus were studied and divided into two groups based on survival. The sedative medication received by those patients who survived and those who succumbed was compared. In those patients who died and in whom the amount of sedation received prior to death was known, there existed a high degree of correlation between death and the amount of sedation received. Although the two groups may not be strictly comparable, it seems clear that the more sedation that was given, the greater the hazard to life.

RESUMEN

Se estudiaron 30 enfermos con estado de mal asmático y se dividieron en dos grupos, basándose en la sobrevida. La medicación sedante que recibieron los enfermos que sobrevivieron y los que fallecieron se comparó. En los que fallecieron y en los que la cantidad de sedantes se conocía antes de la muerte existía una elevada correlación entre la muerte y la cantidad de sedante administrado. Aunque los dos grupos no sean estrictamente comparables parece claro a mayor sedación mayor peligro para la vida.

RESUMÉ

Trente malades atteints d’asthme furent étudiées et divisées en deux groupes selon leur survie. L’auteur a comparé la médication sédatrice reçue par les malades qui survécurent et celle reçue par ceux qui succombèrent. Chez ceux qui moururent et chez lesquels la quantité de sédatif reçu avant la mort était connue, il y avait un haut degré de corrélation entre la mort et la quantité de sédatif reçu. Bien que les deux groupes ne soient pas strictement comparables, il semble clair que plus la dose de sédatif donnée est élevée, plus le danger s’accroît.

ZUSAMMENFASSUNG

Es wurden 30 Patienten mit einem Status asthmaticus untersucht und auf der Basis der Überlebenszeit in zwei Gruppen geteilt. Die sedative Medikation, die diejenigen Patienten erhalten hatten, die am Leben blieben, wurde mit derjenigen verglichen, die bei den tödlich ablaufenden Formen angewandt worden waren. Es erwies sich nun ein hoher Grad von Korrelation zwischen tödlichem Ablauf und Ausmaß der vorgeommenen Sedierung bei denjenigen Fällen, die zum Tode kamen und bei denen das Ausmaß der Sedierung vor dem Tode bekannt war. Obwohl beide Gruppen nicht im genauen Wortsinn vergleichbar sind, liegt es doch nahe anzunehmen, daß, je stärker man sedierend vorgeht, umso größer die Lebensgefahr ist.

REFERENCES


For reprints, please write Dr. V. J. Derbes at 1430 Tulane Avenue, New Orleans 18, Louisiana.

PECTUS EXCAVATUM

Pectus excavatum is an uncommon deformity whose etiology is not clear. The great majority of patients are without symptoms except for cosmetic aspects. In view of this, surgical correction seldom should be performed on women. It seems worthwhile to have the patient undertake exercises to promote the development of muscles and the expansion of lungs during the period of observation.

The optimal age for operation is between three and five years. Subperichondral stripping of all deformed rib cartilages and rib ends, removal of the xiphoid process, and osteotomy of the upper part of the sternum without fixation prostheses seem adequate. The results appear gratifying out of proportion to the skeletal correction obtained.