Phenobarbital or Diazepam Therapy and Plasma Pseudocholinesterase Activity

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Plasma pseudocholinesterase activity is the strongest single determinant of intensity and duration of action of succinylcholine. For example, a cholinesterase inhibitor (phospholine iodide) produced a measured decrease in plasma pseudocholinesterase activity and prolonged succinylcholine-induced neuromuscular blockade. Based on visual observations of twitch response and return of sustained tetanus in response to ulnar-nerve stimulation using a peripheral nerve stimulator, we suspected decreased intensity and duration of succinylcholine-induced neuromuscular blockade in four patients receiving chronic phenobarbital therapy. The possibility of increased serum pseudocholinesterase activity in patients receiving phenobarbital was considered.

METHODS

Venous blood was obtained from these four patients and eight additional patients receiving phenobarbital for determination of serum pseudocholinesterase activity. Plasma phenobarbital concentrations and dibucaine numbers were also determined. In addition, plasma pseudocholinesterase activities and dibucaine numbers were measured in patients taking diazepam chronically and in patients not taking any medication. Those patients receiving phenobarbital or diazepam had been taking these drugs for ten consecutive days or longer.

RESULTS

Plasma pseudocholinesterase activities and dibucaine numbers were similar for all three patient groups (table 1). Differences between groups were not statistically significant (P > 0.05). Pseudocholinesterase activity was greater than normal, but less than 14 units/ml, in five patients not taking any medication, one patient receiving diazepam, and no patient receiving phenobarbital.

DISCUSSION

Phenobarbital and benzodiazepines (diazepam) increase the amount of drug-metabolizing enzymes in liver microsomes (enzymatic induction). Pseudocholinesterase is a non-microsomal enzyme, and increased enzyme activity secondary to microsomal

<table>
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<tr>
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<th>Phenobarbital (12 Patients)</th>
<th>Diazepam (6 Patients)</th>
<th>No Medication (30 Patients)</th>
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</thead>
<tbody>
<tr>
<td>Serum pseudocholinesterase activity (normal 3–8 units/ml)*</td>
<td>6.2 ± 0.4</td>
<td>7.0 ± 0.7</td>
<td>5.8 ± 0.5</td>
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<tr>
<td>Dibucaine number (normal 77–83)*</td>
<td>80 ± 0.4</td>
<td>80 ± 0.8</td>
<td>80 ± 0.4</td>
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<tr>
<td>Serum phenobarbital (therapeutic level 20–30 µg/100 ml, E. B. Solow)</td>
<td>22.2 ± 3</td>
<td>39 ± 4</td>
<td>50 ± 15</td>
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<tr>
<td>Age (years)</td>
<td>72 ± 7</td>
<td>74 ± 6</td>
<td>70 ± 3</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72 ± 7</td>
<td>74 ± 6</td>
<td>70 ± 3</td>
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enzyme induction resulting from either phenobarbital or diazepam seemed unlikely. Indeed, our clinical impression that succinylcholine-induced neuromuscular blockade was less in the presence of chronic phenobarbital therapy was not supported by increased plasma pseudocholinesterase activity.

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Malignant Acanthosis Nigricans and Anesthesia

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Acanthosis nigricans is characterized by symmetric, verrucose hyperplasia of the skin, with hyperpigmentation.1-4 When the condition is severe, the skin develops a papillary quality. The distribution is predominantly in the body folds. If extensive involvement occurs, lesions may be seen on the lips, palate and buccal mucosa. This disease may be benign or malignant, the latter form being associated with a variety of malignant neoplasms, usually of the gastrointestinal tract. Since 1889, about 500 cases of acanthosis nigricans have been reported.5 Thus, although well known, it is still a rare syndrome, especially if only the cases with extensive oral mucous membrane involvement6 are considered. The following report describes a patient with the malignant form of the disease that posed a problem during induction of general anesthesia.

REPORT OF A CASE

A 74-year-old man had been in good health until a year before admission to the hospital, when he had noticed warty, dark, thick folds over the wrists, groin, and neck. These accentuated skin markings had increased during the six months prior to admission. At the same time he had had a significant weight loss and difficulty in swallowing, and lesions of the oral mucosa had developed.

On admission, the patient weighed 45 kg. He had classic cutaneous changes of acanthosis nigricans; the diagnosis was confirmed by histologic examination of a biopsy specimen. Most striking were the papillomatous lesions involving the gums, buccal mucosa, tongue, palate, and lips. The lesions caused difficulty and pain in swallowing, associated with accumulation and frequent expectoration of blood-tinted salivary secretions. The patient had not experienced significant coughing or difficulty in breathing, however. Complete blood count, roentgenogram of the chest, EKG, sigmoidoscopy, liver biopsy, bone roentgenographic survey and barium-enema studies disclosed no abnormality. Also, studies for endocrinopathy and blood chemistry were negative except for an abnormally high value for lactic dehydrogenase. Roentgenograms of the upper gastrointestinal tract were normal except for innumerable papillary masses in the mucosa of the pharynx and esophagus. When the biopsy specimen of a supraclavicular lymph node showed a mucin-producing adenocarcinoma, the diagnosis was changed to malignant acanthosis nigricans. The patient was scheduled for elective exploratory laparotomy to search for a resectable primary tumor.

On the morning of the operation, after premedication with diazepam, 10 mg, and atropine, 0.4 mg, im, anesthesia was induced with thiamylal, 200 mg. The patient began to cough, and succinylcholine, 60 mg, was given to facilitate ventilation and orotracheal intubation. An oropharyngeal airway was inserted and the lungs were ventilated with pure oxygen. On removal of the anesthetic mask and oral airway, the lips, gums, tongue, and palate were found to be significantly bloody from sloughing of the papillomatous mucosa that had been in contact with the mask and airway (fig. 1). Attempted laryngoscopy revealed an unusual amount of secretions in the hypopharynx despite

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REFERENCES