Noncardiac Pulmonary Edema Following Administration of Parenteral Paraldehyde*

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We report a nonfatal case of hemodynamically-documented noncardiac pulmonary edema following the parenteral administration of paraldehyde. Previous clinical and autopsy reports of pulmonary edema associated with paraldehyde are reviewed and the potential danger of this drug emphasized. We hypothesize that paraldehyde or its metabolites, as well as other low molecular weight organic compounds, can directly injure the alveolar-capillary membrane.

Numerous drugs have been associated with acute noncardiac pulmonary edema. These include sedatives and narcotics such as ethchlorvynol and heroin, as well as salicylates and thiazides. We report here the occurrence of hemodynamically-documented noncardiac pulmonary edema following the administration of intramuscular and intravenous paraldehyde. In addition, review of previous literature documents fatal pulmonary edema and hemorrhage following use of paraldehyde and emphasizes the narrow toxic-therapeutic range of this drug.

Case Report

A 65-year-old man was admitted with a six-month history of exertional calf claudication. Past medical history was remarkable for a long history of alcohol abuse with continued intake of up to one pint of hard liquor daily. Admission physical examination was unremarkable; initial arterial blood gas levels, drawn while breathing room air, showed pH, 7.42; Pco2, 34 mm Hg; Po2, 65 mm Hg. Serum albumin on admission was 4.3 g/dl. Admission chest x-ray film showed increased anteroposterior diameter, with flattening of the hemidiaphragms. Translumbar angiography showed extensive bilateral aorto-iliac peripheral vascular disease with occlusion of both superficial femoral arteries.

On the fourth hospital day, the patient underwent uncomplicated aorto-bifemoral vascular bypass with lumbar sympathectomy and required no perioperative blood transfusion. He was extubated shortly after the operation; levels of post-extubation arterial blood gas, drawn while breathing oxygen at 4 L/min by nasal prongs and at 40 percent mist mask, showed pH, 7.45; Pco2, 35 mm Hg; Po2, 105 mm Hg.

During the early morning of the sixth hospital day, the patient became disoriented and delirious with visual hallucinations, diaphoresis, and tachycardia. A presumptive diagnosis of alcohol withdrawal syndrome was made and the patient was treated with chlordiazepoxide, 25 mg intra-

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**Table:**

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<thead>
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<th>Time of Day</th>
<th>Dose of Paraldehyde</th>
<th>Route</th>
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<tbody>
<tr>
<td>0845</td>
<td>5 ml</td>
<td>IM</td>
</tr>
<tr>
<td>0900</td>
<td>5 ml</td>
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<tr>
<td>1000</td>
<td>3 ml</td>
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<td>1300</td>
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<td>1800</td>
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Intramuscular paraldehyde was administered in the lateral aspect of the gluteus maximus and intravenous paraldehyde was diluted with normal saline solution and administered slowly through a freely flowing peripheral intravenous line. Following the second intravenous dose of paraldehyde the patient developed respiratory difficulty and hypoxemia; arterial blood gas levels, drawn while breathing oxygen at 4 L/min by nasal prongs and 40 percent mist mask, showed pH, 7.47; Pco2, 67 mm Hg. Shortly after the third and final dose of intravenous paraldehyde, the patient became apneic, cyanotic, and hypotensive and required immediate endotracheal intubation. Physical examination at this time showed a normal temperature, systolic blood pressure of 80 mm Hg, no jugular venous distention, course crackles diffusely throughout both lungs, and normal cardiac findings. Chest x-ray film showed normal cardiac silhouette and diffuse bilateral alveolar infiltrates consistent with pulmonary edema (Fig 1). Continued hypotension required administration of norepinephrine and phentolamine intravenously. A triple-lumen Swan-Ganz catheter was inserted at the bedside and showed the following hemodynamic measurements: right atrial pressure, 5-9 mm Hg; right ventricular pressure, 25/12 mm Hg; pulmonary artery pressure, 25/13 mm Hg; pulmonary capillary wedge pressure, 10 mm Hg; cardiac index, 3.5 L/min/m². Arterial blood gas levels at this time, drawn while the patient was being mechanically ventilated with an Fio2 of .60, showed pH, 7.42; Pco2, 38 mm Hg; Po2, 78 mm Hg. Sputum and blood cultures were obtained and subsequently grew no pathogens.

The patient was treated conservatively with ventilator support and maintenance intravenous fluids. Gradual im-

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**Figure 1:** Chest x-ray film immediately following the insertion of Swan-Ganz catheter showing pulmonary edema with a normal cardiac silhouette.

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Noncardiac Pulmonary Edema (Mountain et al)

hemodynamic measurements were not available. Finally, Sinal and Crowe reported clinical and chest x-ray film evidence of pulmonary edema in a two-year-old child following administration of intravenous paraldehyde. Again, hemodynamic measurements were not available, but the authors felt cardiac causes could be excluded on clinical grounds.

The mechanism of noncardiac pulmonary edema associated with paraldehyde remains unknown. Of interest is that ethchlorvynol, another low molecular weight sedative, has been associated with noncardiac pulmonary edema. Glauser et al have performed studies in dogs that showed rapid excretion of ethchlorvynol by the lung. They suggested that ethchlorvynol or its metabolites may have a direct injurious effect on the alveolar-capillary membrane. Similarly, paraldehyde or its metabolites may directly produce lung injury and result in noncardiac pulmonary edema. Diabetic ketoacidosis and salicylate toxicity have also been associated with acute noncardiac pulmonary edema; both syndromes are associated with high levels of low molecular weight organic acids. One can speculate that a variety of low molecular weight organic compounds are potentially toxic to the alveolar-capillary membrane in the susceptible host.

In summary, we have presented a case of acute pulmonary edema with hemodynamically documented normal left ventricular filling pressure following the parenteral administration of paraldehyde. This report, as well as previous reports of fatalities, indicates that paraldehyde is a potentially lethal drug and should be used with extreme caution.

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