Pleurodesis With Polidocanol in Pigs*
An Experimental Study

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Polidocanol was instilled in five pleural cavities of three pigs. Adhesions formed in all. Adhesion distribution varied from covering a minor part to most of the lung, depending on the amount of polidocanol. One control cavity treated with sodium chloride was unaffected. Microscopy showed fibrous bridges between the pleural layers and mild submesothelial fibrosis and inflammation.

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**Materials and Methods**

Three female pigs (Danish landrace/Yorkshire) from a production herd, weighing between 42 and 55 kg, were subjects of this study. They were treated under general anesthesia and assisted ventilation after intubation. The protocol was approved by the Danish Inspection for Animal Experiments.

**Surgical Procedure**

The first two pigs underwent bilateral pleurocentesis with a trocar and pigtail catheter. When pneumothorax was obtained, 10 ml of 3 percent polidocanol (polidocanol 3 percent; 3 g 1-hydroxypropylthiododecanol and 5 g absolute alcohol diluted with sterile water to 100 ml) was instilled into each pleural cavity. The lung was reexpanded and the air exsufflated through the catheter, which was then removed. To obtain larger pneumothorax and better distribution of the sclerosant, pig 3 had a 2-cm incision and a balloon catheter was inserted in the pleural cavity. Twenty milliliters of polidocanol 3 percent was instilled, air was exsufflated, and the catheter was removed. As control, the same procedure was carried out on the opposite side with instillation of 20 ml of 0.9 percent sodium chloride.

**Examination Procedure**

At autopsy, after 33 days in pigs 1 and 2 and 40 days in pig 3, the thorax was opened by a sternal split, and the pleural cavities with the lungs and the pericardial sac were examined. The distribution and degree of adhesions were examined. Representative biopsy specimens were taken. The biopsy specimens were fixed in formaldehyde, embedded in paraffin, cut, and stained with van Gieson-Hansen, hematoxylin-eosin, and chromotrope aniline blue for microscopic examination.

**Results**

Five pleural cavities were treated and one served as control. All the treated cavities were affected by polidocanol, but not to the same extent.

The pigs were observed postoperatively in case relief of pain was necessary, but no additional drug was needed. The animals behaved and ate normally, showing no signs of pain or respiratory distress.

**Macroscopic Findings**

In pig 1, the dorsal quarter of the lung was adherent on the right side; on the left side, dispersed areas up to the size of a hand were adherent to the chest wall. When the pleura was opened, the right lung collapsed almost completely, whereas the left lung collapsed only partially. In pigs 2 and 3, adhesions were more widely distributed, involving about 50 percent of the surface on both sides in pig 2 and 80 to 90 percent on the treated side in pig 3 (Table 1), and in these pigs the lungs did not collapse when the pleura was opened. The control pleura was unaffected with total lung collapse. Adhesions were not broken when the pleural cavities were opened. The collapse of the lungs varied inversely with the degree and distribution of adhesions.

It was possible to separate the lung from the chest.
Table 1—Short Review of Surgical Circumstances and Clinical Findings

<table>
<thead>
<tr>
<th></th>
<th>Pig 1</th>
<th>Pig 2</th>
<th>Pig 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>55</td>
<td>42</td>
<td>43</td>
</tr>
<tr>
<td>Amount of polidocanol 3%, ml*</td>
<td>10</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Dosage, mg/kg</td>
<td>5.5</td>
<td>7.5</td>
<td>15</td>
</tr>
<tr>
<td>Procedure</td>
<td>Pleurocentesis</td>
<td>Pleurocentesis</td>
<td>Minithoracotomy</td>
</tr>
<tr>
<td>Catheter</td>
<td>Pigtail catheter 8</td>
<td>Pigtail catheter 8</td>
<td>Balloon (Foley 16)</td>
</tr>
<tr>
<td>No. of pleura treated</td>
<td>2</td>
<td>2</td>
<td>1</td>
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<tr>
<td>Pleura(e) affected</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>Adhesion formation, %</td>
<td>&lt;25</td>
<td>50</td>
<td>80-90</td>
</tr>
</tbody>
</table>

*In each pleural cavity treated.

wall with blunt digital dissection in all five treated cavities. Examination of the pericardial cavities showed no overt changes.

Microscopic Findings

In all three pigs, there was a general picture of mild submesothelial fibrosis, and a slight inflammatory reaction with scattered lymphocytes and histiocytes in the lung parenchyma. The mesothelial lining was intact in pig 1, whereas there were many areas of mesothelial destruction in pig 2, and pig 3 in addition showed bridges of fibrosis connective tissue (Fig 1). The pericardial sacs were not affected. The control pleura showed no microscopic changes.

**Figure 1.** Photomicrograph showing fibrous adhesions between visceral and parietal pleura (arrows) (hematoxylin-eosin, original magnification ×40).

**Discussion**

In the field of spontaneous pneumothorax, many substances are known to produce adhesions, but the mechanism is uncertain since acidity alone is not responsible. Furthermore, though widely accepted, sclerosant therapy is still discredited by some because of the pain that often accompanies the treatment. Addition of local anesthetics has been suggested. However, systemic absorption of both tetracycline and lidocaine has been reported following intrapleural instillation. In dogs, intrapleural and intravenous injection of polidocanol in doses of 10 mg/kg caused no systemic effects apart from drowsiness, but the pleural absorption as such was not examined. We
used up to 15 mg/kg and saw no effects that could not be explained by the general anesthesia.

Originally developed as a long-acting local anesthetic, the detergent polidocanol, a polyethylene-oxide-derivate (1-hydroxypolyethoxydodecane), has a thrombogenic and/or sclerosant effect in varicose veins, but has been thought not to affect an intact endothelial venous lining.7 Due to its anesthetic effects, polidocanol might overcome the above mentioned obstacles of sclerotherapy. Yet, no experiments have previously been carried out to investigate the possible sclerosant effect on the pleura.

The present study showed that polidocanol had a sclerosant capability on the intact mesothelium of the porcine pleura. The effect was localized, and mild general fibrosis took place. Adhesions with fibrous bridges of connective tissue between the pleural layers were demonstrated microscopically.

The pathologic picture of the mesothelial linings was consistent with the findings in other studies.15 It seems that when a drug affects the mesothelium of the pleura, the principal pathologic picture will always be the same, with variation only in the degree of mesothelial destruction and underlying fibrosis.5,15

There are two possible explanations for there being relatively few adhesions in the pleura of one of the pigs. First, the pig in question was somewhat heavier (55 kg) than the others and the dosage therefore was relatively lower. A dose-dependent response has also been reported with tetracycline.9 Second, a small pneumothorax or exudation of liquid may have prevented full lung expansion and thus the two sides from adhering all over.

We conclude that polidocanol (Aethoxysklerol) has a potent sclerosing effect on the mesothelial linings of the pleura of the pig. Further studies are needed to determine the future role of polidocanol in the treatment of spontaneous pneumothorax and hydrothorax.

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