The Utility of Daily Therapeutic Thoracentesis for the Treatment of Early Empyema*

Scott Sasse, MD, FCCP; Tan Nguyen, MD; Lisete R. Teixeira, MD; and Richard Light, MD, FCCP

Study objectives: To determine if therapeutic thoracentesis is as effective as early chest tube placement or no drainage procedure in the treatment of early empyema in rabbits. Design and interventions: An empyema, as evidenced by gross pleural pus and a decreased pleural fluid pH and glucose level, was induced in 49 rabbits. The rabbits were divided into three groups: 16 underwent daily therapeutic thoracentesis starting at 48 h, 14 underwent chest tube placement at 48 h, and 19 served as controls. Results: The mortality rate in the therapeutic thoracentesis group (0/16) did not differ significantly from that in the chest tube group (3/14) or that in the control group (6/19). At autopsy at 10 days, the gross empyema score in the therapeutic thoracentesis group (2.1 ± 0.3) was significantly lower (p < 0.05) than that in the chest tube group (2.8 ± 0.3) or the control group (3.5 ± 0.2). The mean pleural peel score of 5.8 ± 1.1 in the therapeutic thoracentesis group was significantly less (p < 0.05) than the score for the nonintervention control group (13.4 ± 1.6). Conclusions: From this study, we conclude that therapeutic thoracentesis is at least as effective as early chest tube placement for the treatment of early empyema using our rabbit model of empyema.

Key words: chest tubes; empyema; parapneumonic effusion; thoracentesis

Abbreviation: LDH = lactate dehydrogenase

Bacterial pneumonia has an associated pleural effusion (parapneumonic effusion) in approximately 40% of cases.1 A small percentage of these parapneumonic effusions evolve into complicated parapneumonic effusions or empyema and require drainage for their resolution. An empyema can also develop after chest trauma, surgical procedures, or from the spread of contiguous infection. There are several therapeutic options available for the drainage of these effusions. The therapeutic options (from the least invasive to the most invasive) include serial therapeutic thoracentesis, tube thoracostomy with a small chest tube, tube thoracostomy with a large chest tube, tube thoracostomy with intrapleural thrombolytics, thoracoscopy with the breakdown of adhesions, open surgical drainage, and surgical decortication.2

In the past few years, numerous articles have been published on the treatment of complicated parapneumonic effusions with thrombolytics3–7 or thoracoscopy.8–12 However, the role of therapeutic thoracentesis, a minimally invasive therapy for the treatment of complicated parapneumonic effusion or early empyema, has received little attention.13,14

The purpose of the present study was to evaluate the effectiveness of serial therapeutic thoracentesis for the treatment of early bacterial empyema. We have recently developed an experimental model of...
empyema in the rabbit. With this model, animals consistently develop an empyema after the intrapleural administration of Pasteurella multocida.\textsuperscript{15,16} We elected to study serial thoracentesis using this rabbit model for two reasons. First, controlled studies in humans are difficult to perform due to the heterogeneity of the patient population with complicated parapneumonic effusions and empyema.\textsuperscript{17} Second, it would be difficult to accrue significant numbers of patients due to the small number of patients with empyema seen at any one medical center during a 1-to-2-year time period. We hypothesized that therapeutic thoracentesis would be as effective as early chest tube placement for the treatment of early empyema.

**Materials and Methods**

This project was approved by the Animal Studies Committee at the Department of Veterans Affairs Medical Center, Long Beach, CA, prior to the start of the study. Forty-nine rabbits weighing from 2.0 to 3.0 kg were divided into three groups. The experimental group consisted of 16 rabbits that underwent daily therapeutic thoracentesis starting 24 h after empyema induction. A second group of 14 rabbits underwent chest tube placement at 24 h after empyema induction. A third group of 19 rabbits served as controls and had no chest tubes placed. There are different numbers of rabbits in the three groups, because our goal was to have at least 10 rabbits survive for 10 days in each group. The second and third groups of rabbits served as comparison groups and have been reported previously in a study involving the timing of chest tube placement.\textsuperscript{16}

**Empyema Induction:** An empyema was induced in the rabbits as previously described in our laboratory.\textsuperscript{15,16} In brief, the rabbits were first anesthetized with IM ketamine, 35 mg/kg, and IM xylazine, 5 mg/kg. The right chest wall of the rabbit was shaved, and 10\textsuperscript{8} P. multocida bacteria (in 2 mL of 0.5% brain heart infusion agar) were injected into the right pleural space. The position of the catheter in the pleural space was verified by observing a negative pressure deflection during inspiration using a pressure transducer. The rabbits were also given IM penicillin, 200,000 U once daily, starting at 24 h after empyema induction to prevent the death of the animals from sepsis. The narcotic buprenorphine, 0.05 mg/kg bid subcutaneously, was administered for analgesia until the animals were sacrificed.

**Diagnosis Thoracentesis:** A diagnostic thoracentesis was performed on all animals 24 h after bacterial injection to verify that an empyema was present. After the injection of 1% lidocaine locally into the subcutaneous tissues of the chest wall, a 21-gauge needle was inserted into the right fifth intercostal space, and a maximum of 2 mL of pleural fluid was removed for pleural fluid analysis. Pleural fluid specimens were analyzed for pH and glucose.

**Therapeutic Thoracentesis:** In the group of rabbits undergoing therapeutic thoracentesis, pleural fluid was aspirated once daily using a 19-gauge needle starting 24 h after bacterial injection. Thoracentesis was performed after the morning dose of buprenorphine, 0.05 mg/kg, and after the local injection of 1% lidocaine into the subcutaneous tissues of the chest wall at the puncture site. On each occasion, pleural fluid was aspirated until no more could be obtained. After a given rabbit had 3 days of consecutive thoracenteses without obtaining pleural fluid, no further thoracentesis attempts were undertaken.

**Early Chest Tube Group:** Chest tubes were placed as previously described.\textsuperscript{16} In brief, a 16F pediatric chest tube was inserted through the right fifth intercostal space after the rabbit had been anesthetized. The chest tube was sutured in place and protected from mastication with a molded aluminum chest tube protector. The chest tubes were allowed to drain spontaneously through a Heimlich valve. In addition, the chest tubes were aspirated bid using the three-way stopcock that had been attached to the chest tube proximal to the Heimlich valve.

**Evaluation on Sacrifice at 10 Days:** Nembutal, 60 mg, was injected through the marginal ear vein of the rabbit. The thorax was then dissected from the carcass, and the chest was bisected along a coronal plane from the diaphragm to the neck for examination. A gross score and a pleural peel score were then determined as follows.

**Gross Score:** A scoring system of 0 to 4 was used to grade the degree of pleural peel and empyema seen grossly at autopsy, where:

- 0 = normal pleural space and lung
- 1 = adhesions between the visceral and parietal pleura only
- 2 = minimal pleural peel without the presence of gross pus
- 3 = moderate pleural peel without gross pus; and
- 4 = pleural peel with gross pus.

Half integer values (i.e., 2.5, 3.5) were used if the appearance was intermediate between the above integer score descriptions.

**Pleural Peel Score:** The pleural peel score was obtained by measuring the thickness of the pleural peel (from the lung surface to the distal edge of the pleural peel) using a caliper at four different sites of the lung (inferiorly, superiorly, medially, and laterally). The thickness at each of the four sites (in millimeters) was summed to give the pleural peel score. At sites in which no pleural peel was present, an arbitrary score of 0.5 was assigned if adhesions alone were present. A score of 0 was given if the pleural surfaces appeared normal.

**Statistical Analysis:** All data were expressed as mean ± SEM. Mortality rates were compared between groups using chi-square analysis. One-way analysis of variance was used to compare the gross empyema score and the pleural peel score in the three different groups if the data met criteria for normality. If the data failed criteria for normality, the Kruskal-Wallis one-way analysis of variance on ranks was utilized (SAS Institute; Cary, NC). Pairwise comparisons of medians were carried out using Dunn’s method. Differences in the results were considered significant when p < 0.05.

**Results**

The initial diagnostic thoracentesis performed 24 h after bacterial injection revealed that the rabbits had pleural effusions with a mean pleural fluid pH < 7.10 and a mean pleural fluid glucose < 15 mg/dL (Table 1), consistent with empyema formation. There were no significant differences in the mean

| Table 1—Mean Pleural Fluid pH and Glucose Levels at 24 h in Three Different Groups |
|-----------------|-------|-----|-----|
| Group           | pH    | Glucose, mg/dL |
| Thoracentesis   | 7.03 ± 0.03 | 12 ± 0.5   |
| 24-h chest tube | 7.06 ± 0.04 | 11 ± 0.9   |
| Control (no treatment) | 6.97 ± 0.04 | 12 ± 0.8   |
pleural fluid pH and glucose values among the three different groups (Table 1).

The mortality rate in the therapeutic thoracentesis group (0/16) did not differ significantly ($p = 0.155$) from that in the 24-h chest tube placement group (3/14; 21%) or that in the control group (6/19; 32%; Table 2).

The gross empyema score in the therapeutic thoracentesis group was significantly lower ($p < 0.05$) than the gross score from either of the other two groups (Fig 1). The mean ± SEM gross score was $2.1 ± 0.3$ in the therapeutic thoracentesis group compared to $2.8 ± 0.3$ in the 24-h chest tube group and $3.5 ± 0.2$ in the control group. In addition, the number of rabbits with a gross score of 4 at autopsy (indicating the presence of pus) was 3 of 16 (19%) in the therapeutic thoracentesis group, 3 of 11 (27%) in the 24-h chest tube group, and 6 of 15 (40%) in the control group. The numbers did not differ significantly in the three groups (Table 3).

The mean pleural peel score was also lower in the therapeutic thoracentesis group relative to either the 24-h chest tube group or the control group (Fig 2). The mean pleural peel score of $5.8 ± 1.1$ in the therapeutic thoracentesis group was significantly less ($p < 0.05$) than the mean pleural peel score in the control group ($13.4 ± 1.6$), although it did not differ significantly from the mean pleural peel score in the 24-h chest tube group ($7.8 ± 1.3$).

**Table 2—Mortality in Three Different Groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Rabbits, No.</th>
<th>Deaths, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracentesis</td>
<td>16</td>
<td>0 (0)</td>
</tr>
<tr>
<td>24-h chest group</td>
<td>14</td>
<td>3 (18)</td>
</tr>
<tr>
<td>Control (no treatment)</td>
<td>19</td>
<td>6 (32)</td>
</tr>
</tbody>
</table>

**Table 3—Gross Pus at Autopsy (Score of 4) in the Three Different Groups**

<table>
<thead>
<tr>
<th>Group</th>
<th>Rabbits, No.</th>
<th>Score of 4, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracentesis</td>
<td>16</td>
<td>3 (19)</td>
</tr>
<tr>
<td>24-h chest tube</td>
<td>11</td>
<td>3 (27)</td>
</tr>
<tr>
<td>Control (no treatment)</td>
<td>13</td>
<td>6 (46)</td>
</tr>
</tbody>
</table>

**Discussion**

The present study demonstrates that in our rabbit model of empyema, serial therapeutic thoracentesis is at least as effective as chest tube placement. Relative to the group of rabbits that were treated with chest tubes, the rabbits that received daily therapeutic thoracentesis had significantly lower gross empyema scores, and a trend toward a lower mortality rate. Pleural peel scores and the proportion of animals with pus at autopsy were comparable in the therapeutic thoracentesis group and the chest tube group. Both therapeutic thoracentesis and chest tube placement were more effective than no treatment.

The use of repeated therapeutic thoracenteses for the treatment of empyema has previously been advocated in selected cases as an initial therapeutic method that, if ineffective, would be followed by a more invasive drainage procedure. In 1962, the American Thoracic Society recommended repeated thoracenteses for nontuberculous empyemas that were in the early exudative phase.18 The exudative...
phase was defined as the stage of empyema in which the empyematous fluid is thin and contains few cellular elements. If fluid reaccumulated rapidly or if the patient remained toxic, a tube thoracostomy was recommended.

The effectiveness of therapeutic thoracentesis as a treatment for early empyema has been evaluated in several uncontrolled studies. In one recent study, 48 of 51 patients (94%) with empyema (purulent pleural fluid or positive microbiological studies on the pleural fluid) were successfully treated with daily thoracentesis. Some of these patients also received intrapleural injections of antibiotics. In another study, 28 of 111 patients (25%) with bacterial empyema (purulent exudate or positive culture) were successfully treated with antibiotics and thoracentesis alone. In a recent prospective study from the United Kingdom, 46 patients with empyema (opaque fluid in the pleural space, with the cloudiness due to neutrophils and/or organisms) were treated initially with therapeutic thoracentesis, and 19 of the patients (40%) required no further treatment. In general, therapeutic thoracentesis appears more likely to succeed when it is initiated prior to the formation of loculations.

To our knowledge, randomized controlled prospective studies in humans have not been completed comparing repeated therapeutic thoracentesis to alternative techniques. The heterogeneity of complicated parapneumonic effusions and empyema in humans, the high costs of such a study, and the long time periods that are required to accrue adequate numbers of patients make such a study difficult. There have been no previous animal studies addressing this issue.

Can the results of the present study be extrapolated to humans? Our rabbit model of empyema and our treatment methods differ from the human model in several ways. First, there is no pneumonia in our model, so the effusion cannot be classified as a parapneumonic effusion (the most common etiology of empyema in humans). This difference is probably relatively unimportant, because the study was designed to evaluate the effectiveness of two different methods for the treatment of empyema, not the treatment of the underlying pneumonitis. Second, the chest tubes placed at 24 h were not attached to continuous suction; instead, they were allowed to drain continuously through the Heimlich valve and were subjected to aspiration only bid. The lack of continuous suction could have led to the chest tubes being less effective. Nevertheless, the present study demonstrates that serial therapeutic thoracentesis can be curative. Third, the present study was done in rabbits rather than humans, and it is unknown if this species difference is important in determining the outcome of treatment.

The use of therapeutic thoracentesis has some advantages over tube thoracostomy in the management of patients with parapneumonic effusion. First, some patients could possibly be treated as outpatients if therapeutic thoracentesis rather than tube thoracostomy was utilized. Second, although tube thoracostomy is usually a relatively benign procedure when performed by an experienced operator, the procedure can be associated with serious complications, which include intercostal arterial bleeding, perforation of the pulmonary artery or the heart, perforation of an abdominal organ, infection of the pleural space, as well as pain. Third, the mobility of patients treated with tube thoracostomy is markedly compromised due to the need for a pleural drainage system.

What should be the place for serial therapeutic thoracentesis in the management of complicated parapneumonic effusions or early empyema? Based on our review of the literature and the results of the present study, we propose the strategy outlined in Figure 3 for the management of patients with pneumonia and pleural effusion or early empyema. Additional studies will be necessary to verify the utility of our suggested approach. Since thoracentesis is indicated to classify the effusion in these patients, we suggest that the initial thoracentesis be a therapeutic rather than a diagnostic thoracentesis. Fluid obtained at this therapeutic thoracentesis should be analyzed for glucose, pH, lactate dehydrogenase (LDH), WBC, and differential as well as Gram’s stained and cultured. If the fluid is completely evacuated with this therapeutic thoracentesis and never recurs, no additional invasive treatment need be directed toward the pleural space. If the fluid is loculated, then a chest tube should be inserted and thrombolytics should be considered.

If the pleural fluid is completely evacuated but subsequently recurs, the results of the initial thoracentesis should guide the therapy. If the initial pleural fluid glucose was > 60 mg/dL, the pH > 7.20, the LDH less than three times the upper normal limit for serum, and the Gram’s stain and culture negative, the patient can be treated with antibiotics alone as long as the patient is doing well clinically. If one or more of the above criteria are not met, a second therapeutic thoracentesis should be performed with repeat diagnostic evaluation of the pleural fluid.

If the fluid recurs after the second therapeutic thoracentesis, a small chest tube should be placed if the pleural fluid glucose was < 60 mg/dL, the pH < 7.20, the LDH more than three times the upper
normal limit for serum, and the Gram’s stain positive or the culture positive at the time of the second therapeutic thoracentesis. If none of these criteria are met and the patient is clinically improving, then the patient can be treated with antibiotics alone. If loculation should occur at any time, consideration should be given to administering intrapleural thrombolytics or performing thoracoscopy to break down the loculations.

In conclusion, the present article demonstrates that early empyema in rabbits can be managed with serial therapeutic thoracentesis. Based on the present animal study and previous uncontrolled studies in humans, we suggest that the initial thoracentesis in all patients with pneumonia and pleural effusion or early nonloculated empyemas be a therapeutic thoracentesis. If the pleural effusion subsequently recurs, therapeutic thoracentesis can be utilized in the management of those patients whose effusions are not loculated and whose pleural fluid biochemical parameters are improving.

REFERENCES

Figure 3. Management of patient with pneumonia and pleural effusion of empyema.