Intrapleural Talc for the Prevention of Recurrence in Benign or Undiagnosed Pleural Effusions*

Francisco S. Vargas, M.D., F.C.C.P.; Jose Ribas C. Milanez, M.D.; Luiz Tarcisio B. Filomeno, M.D.; Angelo Fernandez, M.D.; Adib Jatene, M.D.; and Richard W. Light, M.D., F.C.C.P.

Chemical pleurodesis has become the preferred treatment for definitive management of malignant pleural effusions. The treatment of patients with recurrent benign or undiagnosed pleural effusions, however, remains a difficult clinical problem. Tetracycline has been widely used as a sclerosing agent, but parenteral tetracycline is no longer available. Therefore, alternative sclerosing agents are needed. Talc was used for the first time in 1935, and subsequently there have been several reports documenting its effectiveness in the treatment of malignant pleural effusion and pneumothorax. The objective of this study is to present our experience with a low dose of aerosolized talc for controlling nonmalignant pleural effusions. Between May 1985 and October 1992, twenty-two patients underwent talc pleurodesis at the time of thoracoscopy for control of a nonmalignant effusion. The cause of the effusion was cirrhosis in six patients, systemic lupus erythematous in two, chylothorax in five, and no diagnosis in nine patients. Follow-up has ranged from 18 days to 5 years. Only two patients (9 percent), one with cirrhosis and another with an undiagnosed pleural effusion, had a recurrence of the effusions. We conclude that the intrapleural administration of 2 g of aerosolized talc is an effective treatment for recurrent benign (including chylothorax) or undiagnosed pleural effusions.

(Chest 1994; 106:1771-75)

Key words: aerosolized talc; chylothorax; pleural effusion; pleurodesis

In recent years, chemical pleurodesis has become the preferred treatment for symptomatic malignant pleural effusions.1,2 The treatment of patients with recurrent nonmalignant pleural effusions, however, remains a difficult clinical problem.3 It is sometimes difficult to identify the precise cause of a recurrent pleural effusion, even after cytologic study, bacteriologic study, pleural biopsy, and thoracoscopy. These patients with recurrent benign or undiagnosed pleural effusions may benefit from chemical pleurodesis. A recent review of the literature between 1966 and 1992 revealed only 25 nonmalignant pleural effusions that had been treated with chemical pleurodesis.

For the last decade, tetracycline has been widely used for creating a pleurodesis. However, parenteral tetracycline is no longer available because of increasingly stringent manufacturing requirements. Therefore, alternative sclerosing agents are needed. Many agents, including antineoplastic drugs (thiotepa, nitrogen mustard, bleomycin, antimarial (quinacrine, mepracine), and antibiotics (minocycline, doxycycline) have been studied. Most of the studies have been performed on patients who had malignant pleural effusions.

Talc is an alternative to the agents listed above. Bethune2 in 1935 produced a pleurodesis via the insufflation of iodized talc into the pleural space. Since then there have been several reports documenting the efficacy of aerosolized talc13,14 or talc in a slurry15-17 in the treatment of pleural effusions, most of which had a malignant etiology. In addition, a recent study on animals documented that talc was as effective as mechanical abrasion in producing pleurodesis in animals.18

The objective of this study is to present our experience with a low dose of aerosolized talc for controlling recurrent benign or undiagnosed pleural effusions.

METHODS

This series consisted of 22 patients, 8 men and 14 women, mean age of 49.3 ± 18.0 (range, 5 to 80) years, who were admitted to the Department of Thoracic Surgery with recurrent apparently nonmalignant pleural effusion between May 1985 and October 1992 (Table 1). The cause of the effusion was cirrhosis in six patients, chylothorax in five, and systemic lupus erythematous in two. In nine patients we were unable to obtain a definite diagnosis after pleural fluid cytologic study, pleural biopsy, and thoracoscopy.

Selection of Patients

All patients who underwent pleurodesis were required to meet

*From the Instituto do Coração and the Hospital das Clínicas of the Faculty of Medicine of the University of Sao Paulo, Brazil, and the Department of Medicine of the Veterans Administration Medical Center, Long Beach, Calif, and the University of California Irvine.

Manuscript received November 29, 1993; revision accepted April 25, 1994.

Reprint requests: Dr. Light (111), VAMC Long Beach, 5901 East Seventh Street, Long Beach, CA 90822
Visits.

broad-spectrum
radiography
Chest
and
procedure
throughout
aerosolized by allowing
were
within
procedures
were
ventilated
(28F)
were
inserted
and
the
tumor
and
undergone
drainage;
the
treatment
premedicated before
(cephalosporin)
was
introduced, treatment
with
asbestos-free sterile
air
insufflator.

The
treatment
could be
this
tube
was
talc
could be
after
time.

the
patients
had
empyema 30
days
in
the
procedure.

Cardiovascular disease
hematemesis
and
two
other
disease.

Aerosolized
talc
was
very
effective
in
the
operation
of
myocardial infarction
at
18
days
(one
patient)
and
5
months
(two
patients).

The
intrapleural
insufflation
of
talc
was
associated
with
minimal
morbidity.
The
average
time
to
removal
of
the
chest
tubes
was 6.2
(range,
3
to
16)
days.

All
patients
complained
of
mild
pain
after
the
procedure
was
completed.

Four
of
the
22
patients
(18%
percent)
had
a
mild
temperature
elevation.
One
patient
with
systemic
lupus
erythematosus
developed
an
empyema 30
days
after
the
procedure.

No pathogen
was
isolated
from
her
empyema
fluid.

She
was
treated
with
decortication
and
made
an
uneventful
recovery
after
this.

No
episodes
of
respiratory
distress
syndrome
or
pneumonitis
were
observed
after
talc
pleurodesis.

Success
was
defined
as
a
continued
absence
of
pleural
fluid
on
all
follow-up
radiographs;
any
reaccumulation
was
regarded
as
a
treatment
failure.
Each
follow-up
chest
radiograph
was
obtained
in
the
upright
position.
Each
chest
film
was
compared
with
the
baseline
chest
film
after
the
initial
drainage.

RESULTS

Aerosolized
talc
was
very
effective
in
the
treatment
of
nonmalignant
pleural
effusion
(Table
2).
There
were
only
two
recurrences
(9 percent).
One
patient
with
cirrhosis
had
a
recurrence
after
4
months.
At
this
time,
he
was
retreated
with
talc
and
had
no
recurrence
during
the
next
2
months.
A
second
patient
with
an
undiagnosed
pleural
effusion
had
a
recurrence
at
30
days.
After
a
second
talc
insufflation,
there
was
no
recurrence
over
the
next
2
months.
The
follow-up
period
was
at
least
3
months
in
all
the
surviving
patients.
There
was
no
recurrence
in
five
of
six
patients
with
cirrhosis
and
in
none
of
the
five
patients
with
chyllothorax.

During
the
period
of
study,
6
of
the
22
patients
(27.3 percent)
included
in
the
study
died
because
of
another
disease.
Three
of
the
six
patients
(50 percent)
had
cirrhosis,
two
of
them
died
of
sepsis
(after
18
days
and
8
months),
and
one
had
hematemesis
1
month
after
pleurodesis.
The
other
three
patients,
one
with
chyllothorax
and
two
with
undiagnosed
pleural
effusion,
died
because
of
acute
cardiovascular
disease
(myocardial
infarction)
at
18
days
(one
patient)
and
5
months
(two
patients).

The
intrapleural
insufflation
of
talc
was
associated
with
minimal
morbidity.
The
average
time
to
removal
of
the
chest
tubes
was
6.2
(range,
3
to
16)
days.

All
patients
complained
of
mild
pain
after
the
procedure
was
completed.

Four
of
the
22
patients
(18 percent)
had
a
mild
temperature
elevation.
One
patient
with
systemic
lupus
erythematosus
developed
an
empyema
30
days
after
the
procedure.

No
pathogen
was
isolated
from
her
empyema
fluid.

She
was
treated
with
decortication
and
made
an
uneventful
recovery
after
this.
No
episodes
of
respiratory
distress
syndrome
or
pneumonitis
were
observed
after
talc
pleurodesis.

DISCUSSION

In
this
prospective
study,
the
intrapleural
administration
of
2
g
of
aerosolized
talc
at
the
time
of
thoracoscopy
was
an
effective
treatment
for
nonmalignant
pleural
effusions,
including
those
secondary
to
chyllothorax
and
those
secondary
to
cirrhosis.
The
recurrence
rate
in
the
present
series
was
only
9
percent.

In
previous
studies,
aerosolized
talc
has
been
very
effective
in
treating
malignant
pleural
effusions.
Aelony
and
coworkers\textsuperscript{13}
reported
that
2.5
g
of
aerosolized
talc
controlled
the
effusion
in
23
of
28
patients.
Table 2—Duration of Drainage and Results of the Intrapleural Insufflation of Talc

<table>
<thead>
<tr>
<th>No.</th>
<th>Chest Tubes</th>
<th>Duration Days</th>
<th>Recurrence</th>
<th>Follow-up, mo</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ant</td>
<td>Post</td>
<td>Cirrhosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>7</td>
<td>8</td>
<td>No</td>
<td>8</td>
<td>Death after 8 mo: sepsis</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td></td>
<td>No</td>
<td>1</td>
<td>Death after 1 mo: hematemesis</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td></td>
<td>No</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td></td>
<td>No</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td></td>
<td>No</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td></td>
<td>Yes</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>6</td>
<td>No</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td>5.3</td>
<td>No</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>10</td>
<td>No</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>3</td>
<td>No</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>4</td>
<td>No</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>8</td>
<td>No</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>5</td>
<td>No</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>6</td>
<td>No</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td></td>
<td>11</td>
<td>No</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td></td>
<td>11</td>
<td>No</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td></td>
<td>4</td>
<td>No</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td></td>
<td>6</td>
<td>No</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td></td>
<td>3.3</td>
<td>No</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td></td>
<td>7</td>
<td>Yes</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td></td>
<td>4</td>
<td>No</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td></td>
<td>4</td>
<td>No</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

(82 percent) with malignant pleural effusions. Hartman and associates reported that the intrapleural administration of 3 to 6 g of aerosolized talc controlled the pleural effusion for 90 days in 95 percent of 39 patients with malignant effusions. It should be noted that the thorascopy in both the aforementioned studies was performed under local anesthesia and intravenous sedation while the thorascopy in the present series was performed under general anesthesia. Comparable results have also been reported with talc in slurry. Adler and Sayek treated 44 hemithoraces with malignant pleural effusion with 10 g of talc in 250 ml of saline solution and reported control of the effusion in 41 (93 percent). Webb and coworkers reported a 100 percent success rate in 28 patients with malignant effusions who were given 5 g of talc and 3 g of thymol iodine in 50 ml of saline solution. However, these researchers did not count patients whose lungs did not completely expand after the procedure and therefore the reported results may be somewhat misleading.

Talc has been used less frequently for the treatment of benign effusions. Aelony and associates did treat 11 patients with benign effusions with aerosolized talc and reported that the effusions were controlled in all. In the series of Webb et al., six patients had benign effusions and there was no recurrence after talc in any of these patients.

In the present series, all five patients with chylothorax were treated successfully with the aerosolized talc. In general, it appears that it is difficult to create a pleurodesis in patients with chylothorax. Robinson reported that pleurodesis was unsatisfactory when he used nitrogen mustard, tetracycline, or quinacrine. Le Coultre and associates reported that pleurodesis with quinacrine was unsuccessful in two of four patients. Meurer and Cohen concluded that the intrapleural administration of tetracycline did not help in the management of chylothorax. Previous reports on the intrapleural instillation of talc have been favorable. Weissberg reported that instilled talc successfully controlled the pleural fluid in seven patients with chylothorax while Adler and Levin reported the successful treatment of one patient each with aerosolized talc and talc in slurry. In view of the excellent results in the present series and the two aforementioned series with talc, it must be considered the preferred agent for creating a pleurodesis in patients with chylothorax.

The treatment of patients with cirrhosis and large
pleural effusions is difficult.24 In the present series, aerosolized talc was effective in controlling the pleural effusion secondary to cirrhosis. Previous reports on attempts at pleurodesis in patients with pleural effusions secondary to cirrhosis have used tetracycline for the most part and the results have been mixed. Falchuk et al25 reported successful pleurodesis in two patients treated with tetracycline while Ikard and Sawyers26 reported two failures with tetracycline. It is important to realize that tube thoracostomy can be very dangerous in patients with massive ascites and pleural effusion. Runyon and associates27 reported two deaths that resulted from massive protein and electrolyte depletion. All of our patients with cirrhosis were maintained in the intensive care unit for at least 24 h after the procedure. Based on the present series, aerosolized talc appears to be the preferred agent if pleurodesis is attempted in patients with pleural effusions secondary to ascites. However, if this procedure is attempted, the patient should be placed in the intensive care unit before the chest tube is placed and monitored closely for fluid depletion and electrolyte disturbance after the chest tube is placed.

It appears that the intrapleural insufflation of talc is associated with relatively few side effects. The intrapleural administration of talc has been reported to cause acute pneumonitis29 and the adult respiratory distress syndrome.29 Both of these reports involved patients who had received talc in a slurry, and in retrospect, we speculate that the acute respiratory distress was possibly due to re-expansion pulmonary edema rather than an adverse reaction to talc. We have observed several patients who developed acute respiratory distress after the intrapleural administration of tetracycline, which we believed represented re-expansion pulmonary edema. In the past, there was concern about the possibility that the asbestos in talc could lead to the development of malignant mesothelioma and other asbestos-related diseases. However, Lange and coworkers30 studied 114 patients 22 to 35 years after talc pleurodesis for spontaneous pneumothorax and found no patients with mesothelioma. Additionally, asbestos-free talc is now available. There has also been concern that the intrapleural administration to young individuals could lead to progressive pleural thickening. Again the results of the study by Lange and coworkers30 tend to discount this since the mean total lung capacity of patients who had received talc many years previously was 89 percent of predicted.

What dose of talc should be insufflated? In the present study, only 2 g of talc was insufflated while other studies have used up to 10 g.15 The recurrence rate in the present study using 2 g of talc was only 9 percent. Since the lower dose appears to be effective, we recommend a dose of 2 g for the treatment of benign effusions. It remains to be seen whether 2 g of talc is sufficient for patients with mesothelioma or malignant pleural effusion. The pleura in these patients is less normal and a higher dose of talc may be necessary for the treatment of these conditions.

In conclusion, we believe that therapy is indicated for patients who are symptomatic with recurrent nonmalignant pleural effusions. The present study shows that the intrapleural insufflation of 2 g of talc at the time of thoracostomy is an effective treatment for nonmalignant pleural effusions, including those due to chylothorax and cirrhosis with ascites. If thoracostomy is not performed or if it is not available, we suggest that talc in slurry may be an effective alternative since it has been shown to be very effective for creating pleurodesis in patients with malignant pleural effusions17 and in normal rabbits.31 However, to our knowledge, there have been no randomized controlled clinical trials comparing talc slurry vs intrasulfated talc.

REFERENCES
5 Anderson CB, Philpott GW, Ferguson TB. The treatment of malignant pleural effusions. Cancer 1974; 33:916-22
9 Hatta T, Tsubota N, Yoshimura S, Yanagawa M. Effect of intrapleural administration of minocycline on postoperative air leakage and malignant pleural effusion. Kyobu Geka 1990; 43:253-86
22 Weissberg D. Pleurectomy for chylothorax associated with intestinal lymphangiectasia. Thorax 1987; 42:901-02
24 Light RW. Pleural Diseases. Dis Month 1992; 28:266-331
27 Runyon BA, Greenblatt M, Ming RHC. Hepatic hydrothorax is a relative contraindication to chest tube insertion. Am J Gastroenterol 1986; 81:566-67