

A case series: Egyptian experience in using chemical pleurodesis as an alternative management in refractory hepatic hydrothorax

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Submitted: 17 January 2009

Accepted: 8 June 2009

Arch Med Sci 2010; 6, 3: 336-342
DOI: 10.5114/aoms.2010.14252
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Abstract

Introduction: Chemical pleurodesis is an effective treatment for malignant effusion and pneumothorax. Although this mode of therapy is less widely accepted in treatment of patients with hepatic hydrothorax, the need for palliative treatment in such patients encouraged us to do this work. The aim of study was analysing the outcome of chemical pleurodesis using bovoiodine, Vibramycin and talc slurry in treatment of hepatic hydrothorax.

Material and methods: A case series randomized study including 23 patients with symptomatic right side hepatic hydrothorax not responding to medical treatment and repeated thoracocentesis was conducted. From March 2007 to March 2008, 19 men and 4 women with a mean age of 54.3 ±8.1 years (range 42-70 years) underwent medical thoracoscopies to achieve pleurodesis by application of 3 sclerosing agents.

Results: Out of the 23 patients pleurodesis was repeated in 20 cases. Three cases did not attend their follow-up so their responses to pleurodesis are not known. The follow-up period of the study was 3 months. The procedure was effective in 15 of 20 patients (75%): 7/8 cases treated with bovoiodine (87.5%), and 4/6 cases with Vibramycin and talc slurry (66.7%) for each. There were 4 recurrences (20%) and a single case of mortality (5%) due to hepatic coma which can be attributed to the course of the disease. We detected minimal morbidity during the follow-up period of 3 months.

Conclusions: The procedure appears to be indicated for these fragile patients especially when medical therapy fails. Chemical pleurodesis deserves to be considered as an alterative therapy in such patients.

Key words: hepatic hydrothorax, pleurodesis, chemical sclerosing agents.

Introduction

Hepatic hydrothorax is defined as a pleural effusion usually > 500 ml, in patients with cirrhosis without cardiopulmonary disease [1]. A reasonable estimate is that it ranges from 4% to 6%, and even up to 10% with advanced disease [2]. In most cases (85%) hepatic hydrothorax develops on the right side, 13% of cases occurring on the left side and 2% being bilateral. Hepatic hydrothorax may develop even in the absence of ascites [3].

The exact mechanism of pleural effusion remains unknown, and a number of different mechanisms have been proposed to explain it [4].

However, several observations indicate that the most likely cause is passage of a large amount of ascites from the peritoneal to the pleural cavity through diaphragmatic defects [5, 6].

Traditional treatment of hepatic hydrothorax in a patient who fails to respond to aggressive medical management of ascites remains problematic and controversial. A review of the literature has revealed that no method is ideal yet [7, 8]. This study describes our experience in treating patients with refractory hepatic hydrothorax by chemical pleurodesis as an important palliative option using 3 sclerosing agents. The effect of pleurodesis will be evaluated with special focus on morbidity and mortality.

Material and methods

Study population

This case series randomized study consisted of 23 patients with clinical, laboratory and radiological evidence of liver cirrhosis, portal hypertension, and refractory right side symptomatic hepatic hydrothorax who were admitted to the chest and tropical departments of Cairo University Hospital from March 2007 to March 2008. The study was approved by the Human Ethics Committee of Cairo University and all subjects gave written informed consent before thoracoscopy and chemical pleurodesis. In this study all the 23 patients had refractory hepatic hydrothorax, i.e. multiple medical managements in the form of sodium and fluid restriction together with diuretic therapy and repeated therapeutic thoracentesis (2-5 times) failed to control moderate to massive transudative pleural effusions. Exclusion criteria were evidence of hepatic encephalopathy, massive ascites and recent or history of haematemesis.

Chemical pleurodesis

Medical thoracoscopy was performed under local anaesthesia on the 23 patients included in the study. After complete evacuation of the pleural fluid, a chest drain was introduced, followed by pleurodesis. In talc slurry, 2 to 3 g of asbestos-free talc were suspended in 50 ml of saline solution (0.9%), while with Vibramycin instillation of 1 g vibramycin in 50 ml of saline solution and in bovoiodine 20 ml of 10% bovoiodine in 80 ml of saline solution were used. An additional 20 ml of 1% lidocaine was added to all the sclerosing agents and the drain was flushed with 20 ml of saline. The drain was then clamped for 4 h after pleurodesis, and the patient was asked to change position every 15 min to allow adequate distribution of the sclerosing agent. Post procedure, medical therapy including albumin, plasma infusion and diuretics was maintained. If the trial of pleurodesis failed

another trial was done after 3-5 days according to the rate of fluid drainage, to a maximum of 3 times. Pleurodesis was repeated earlier in patients with a high rate of drainage. Chest tubes were removed when the volume collected remained < 100 ml in 24 h. Somatostatin was given to all the patients in a dose of 25-50 µg/h, 24 h before the procedure and continued until removal of the chest tube.

Follow-up

Serial chest radiographs were performed 2 h after pleurodesis, on the second post-procedure day and at subsequent follow-up visits every month for 3 months' follow-up. The procedure was considered successful if there was absence of pleural fluid on the follow-up chest radiographs; any re-accumulation was regarded as a recurrence.

Statistical analysis

Quantitative data were presented as minimum, maximum, means and standard deviation (SD) values. Qualitative data were presented as frequencies and percentages. Statistical analysis was performed with SPSS (Statistical Package for the Social Sciences Inc., Chicago, IL, USA) version 13 for Microsoft Windows.

Results

Characteristics of subjects

The 23 patients were 19 men (82.6%) and 4 women (17.4%). Their age ranged from 42 to 70 years (mean 54.3 ±8.1 years). They all had clinical, laboratory and radiological evidence of liver cirrhosis, portal hypertension, and refractory right side symptomatic hepatic hydrothorax, i.e. they had undergone multiple medical managements that failed to control moderate to massive pleural effusions. All had Child Pugh B score and the chemical analysis of their pleural effusion showed evidence of transudative effusion. All underwent therapeutic thoracoscopy with pleurodesis using bovoiodine in 9 cases, Vibramycin (doxycycline) in 7 cases, and talc slurry in 7 cases. The selection of the sclerosing agent to be used was randomized. During the study period, 3 patients did not attend their follow-up visits so their response to chemical pleurodesis is not known. These 3 cases were 1 case from each of the 3 sclerosing agents used. The rest of the 20 patients were followed up for 3 months. Using the same agent, a second retrieval of pleurodesis was done in 16 cases, while it was repeated 3 times in 4 cases (Table I).

Outcome of chemical pleurodesis

The outcome of the present work revealed that chemical pleurodesis was effective in treatment of

hepatic hydrothorax in 15/20 patients (75%); they were 7/8 cases (87.5%) treated with bovoidine, 4/6 cases (66.7%) with Vibramycin and 4/6 cases (66.7%) with talc slurry. However, a single case treated with talc slurry died of hepatocellular insufficiency (5%) after 14 days following the procedure; this patient failed to respond to thoracocentesis repeated 5 times and also needed

pleurodesis to be repeated 3 times due to a high rate of chest tube fluid drainage. In addition, recurrence of pleural effusion occurred in 4 cases (20%); they were 2 cases (50%) with encysted effusion and another 2 cases (50%) with minimal right side pleural effusion. Cases with pleurodesis repeated 3 times showed more possibility of recurrence and complications (Table II).

Table I. Frequency, percentages and results of the 3 pleurodesis materials

No. of followed up cases = 20		Povo-iodine		Vibramycin		Talc slurry	
		Frequency	%	Frequency	%	Frequency	%
Ascites	No	1	12.5	0	0	0	0
	Mild	3	37.5	2	33.3	2	33.3
	Moderate	4	50	4	66.7	4	66.7
Previous thoracocentesis	2 times	1	12.5	0	0	0	0
	3 times	5	62.5	4	66.7	3	50
	4 times	2	25	2	33.3	2	33.3
	5 times	0	0	0	0	1	16.7
Number of pleurodesis sessions	1 time	1	12.5	1	16.7	0	0
	2 times	7	87.5	6	75	3	50
	3 times	0	0	1	16.7	3	50
Recurrence	Yes	1	12.5	2	33.3	2	33.3
	No	7	87.5	4	66.7	4	66.7
Complications	Yes	6	75	4	66.7	5	83.3
	No	2	25	2	33.3	1	16.7
Severity of pleural effusion	Moderate	2	25	1	16.7	3	50
	Massive	6	75	5	83.3	3	50

Table II. Frequency and percentages in cases with and without recurrence

No. of followed up cases = 20		Recurrence		No recurrence	
		Frequency	%	Frequency	%
Gender	Male	5	100	11	73.3
	Female	0	0	4	26.7
Previous thoracocentesis	2 times	0	0	1	6.7
	3 times	4	80	8	53.3
	4 times	0	0	6	40
	5 times	1	20	0	0
Number of pleurodesis sessions	1 time	0	0	2	13.3
	2 times	2	40	12	80
	3 times	3	60	1	6.7
Complications	Yes	5	100	8	53.3
	No	0	0	7	46.7
Severity of pleural effusion	Moderate	0	0	6	40
	Massive	5	100	9	60

The time needed to remove the chest tube ranged from 4 to 17 days with a mean of 9.8 ± 2.3 days (in bovoiodine the range was 5-9 days with a mean of 8.1 ± 2 days, in Vibramycin the range was 6-15 days with a mean of 9.4 ± 4.3 days and in talc slurry the range was 4-17 days with a mean of 10.3 ± 3.6 days). Post-procedure hospital stay ranged from 5 to 18 days.

Early post-procedure results

Post-procedure results showed that 7 out of the 22 cases reported absence of any complications and were not associated with recurrence of hepatic hydrothorax. The remaining cases (15 patients) showed early and mostly minimal and limited morbidity. There were 4/22 patients (18.2%) who suffered from surgical emphysema, 2 patients (9.1%) with minimal left side pleural effusion which disappeared spontaneously after a few days, 2 patients (9.1%) with superficial wound infection, 1 patient (4.5%) with mild thoracic pain, another single patient (4.5%) who complained of failure of the lung to expand immediately after the procedure and was treated by negative suction with complete lung expansion, and a single patient (4.5%) who developed pre-hepatic coma 4 days after the procedure, cured by medical therapy and associated with no recurrence of hepatic hydrothorax.

Late post-procedure results

However, during the follow-up period 2 out of 19 patients (10.5%) developed late complications. A patient treated with bovoiodine suffered from tense ascites 2 months after the procedure (3 l were tapped) but with no associated recurrence of hepatic hydrothorax. The second patient treated with talc slurry developed tense ascites and hepatic coma at the end of the follow-up period (3 months), recovered with medical therapy and was associated with recurrence of encysted right side pleural effusion. There were no reported episodes of respiratory distress syndrome, pneumonitis or empyema in our cases (Table III).

Discussion

Despite numerous reports describing clinical features, pathogenesis and treatment for hepatic hydrothorax, the optimal or standard therapy has not been established [8]. The term refractory hepatic hydrothorax is used when medical treatment with salt restriction and diuretics is ineffective, as prolonged diuretic treatment may result in depletion of the intravascular volume and impaired renal function. Medical therapy has proved to be effective in just one third of the reported patients, but the effect has been chiefly temporary. Many authors also consider that clinical

management of hepatic hydrothorax is usually difficult and ineffective and can result in deterioration of the clinical status [2, 5, 8].

In contrast to ascites, which becomes massive (< 10 l) while presenting mild symptoms in most patients, relatively small volumes of fluid (< 1 l) within the chest cavity cause significant symptoms and occasionally need urgent rapid removal [9]. Although thoracentesis is the most effective method for rapid relief of dyspnoea secondary to massive pleural effusion associated with hepatic hydrothorax, it carries the risk of substantial protein depletion without preventing fluid re-accumulation, especially if repeated thoracentesis is required [7]. Pleural drainage by chest tube thoracotomy can be very dangerous in patients with massive ascites and pleural effusion. Runyon *et al.* [10] reported 2 deaths resulting from associated massive protein and electrolyte depletion. Also prolonged drainage through the chest tube may cause renal failure, impaired immunological functions and iatrogenic infection as common sequelae [11].

Out of the 20 cases that have been followed up during this work we used Vibramycin in 6 cases, with no recurrence in 4 cases (66.7%). The reported adverse effects are pain and fever with tetracycline and pain with doxycycline [12]. In our work the number of patients was small. Pain and fever were not reported with the use of Vibramycin. However, recurrence occurred in 2 patients; 1 suffered from encysted effusion and the other from minimal right side pleural effusion. Also, surgical emphysema, left side pleural effusion and hepatic precoma were each found in a single case.

In our study we selected asbestos-free talc slurry to be used in 6 patients to avoid the claims associated with the hazards of asbestos. We reported no recurrence in 4 patients (66.7%). The reported complications with talc pleurodesis include fever, chest pain, empyema, incomplete expansion of the lung, pneumonia, wound infection [7, 13-16] and ARDS [17]. In our cases recurrence occurred in a single case and complications in the form of chest pain, surgical emphysema, left mild pleural effusion, tense ascites and hepatic coma were each noticed in 1 patient. Also, the only mortality in our work was in a patient treated with talc slurry; it occurred 14 days after the procedure due to rapid increase of bilirubin and creatinine followed by hepatic coma and death, and this can be attributable to the course of the disease since the patient's medical status necessitated thoracentesis 5 times before our procedure.

We used bovoiodine in 8 cases with complete control of the effusion in 7 cases (87.5%). Recurrence in the form of encysted pleural effusion was noted in 1 patient (12.5%). There were complications in the form of surgical emphysema

Table III. Characteristics and outcome of our case series

No. of cases	Age [year]	Sex	Ascites	Pleural effusion	Previous thoracentesis	Sclerosing agent	No. of sessions	Length of stay	Complications	Follow-up/3 months
1	50	F	Moderate	Rt Massive	2	Boviodine	1	7	–	No recurrence
2	53	M	Mild	Rt Massive	3	Boviodine	2	14	Wound infection	Recurrence with encysted effusion
3	62	F	Moderate	Rt Moderate	4	Vibramycin	2	12	–	No recurrence
4	70	M	Mild	Rt Massive	3	Vibramycin	1	4	–	No recurrence
5	51	F	Moderate	Rt Moderate	3	Talc	2	11	–	No recurrence
6	63	M	Moderate	Rt Massive	3	Talc	3	15	Pain	Recurrence of minimal effusion
7	68	M	Mild	Rt Massive	4	Vibramycin	2	13	Hepatic precoma (4 days after thoracoscopy)	No recurrence
8	65	M	Moderate	Rt Massive	3	Vibramycin	2	9	Minimal left pleural effusion	Recurrence of minimal effusion
9	57	M	Mild	Rt Massive	5	Talc	3	16	Patient had rapid increase of bilirubin and creatinine and patient had hepatic coma and died 14 days after thoracoscopy	
10	50	M	Mild	Rt Massive	4	Boviodine	2	11	–	No recurrence
11	52	M	Mild	Rt Moderate	3	Boviodine	2	11	Failure of the lung to expand and lung expanded by –ve suction	No recurrence
12	43	M	Moderate	Rt Massive	5	Talc	1	7	–	Follow-up of patient failed
13	56	M	Moderate	Rt Massive	3	Boviodine	2	10	Wound infection	No recurrence
14	51	M	Moderate	Rt Massive	3	Boviodine	2	8	*Surgical emphysema *Tense ascites 2 months after procedure (tapping of 3 l)	No recurrence
15	68	M	–	Rt Massive	4	Boviodine	2	10	–	No recurrence

Table III. Characteristics and outcome of our case series – cont

No. of cases	Age [year]	Sex	Ascites	Pleural effusion	Previous thoracentesis	Sclerosing agent	No. of sessions	Length of stay	Complications	Follow-up/3 months
16	45	M	Moderate	Rt Massive	3	Vibramycin	2	13	*Surgical emphysema *Minimal left pleural effusion	Follow-up of patient failed
17	50	F	Moderate	Rt Massive	3	Vibramycin	2	8	–	No recurrence
18	54	M	Moderate	Rt Moderate	3	Talc	2	14	Surgical emphysema	No recurrence
19	45	M	Moderate	Rt Massive	4	Talc	3	15	–	No recurrence
20	52	M	Moderate	Rt Moderate	3	Boviodine	2	9	Surgical emphysema	No recurrence
21	53	M	Moderate	Rt Massive	3	Boviodine	2	11	–	Follow-up of patient failed
22	42	M	Moderate	Rt Massive	3	Vibramycin	3	18	*Tense ascites *Hepatic coma 3 months later	Recurrence with encysted effusion
23	48	M	Mild	Rt Moderate	4	Talc	2	8	Left minimal pleural effusion disappeared after tube removal	No recurrence

in 2 patients (25%), wound infection in 2 patients (25%), failure of the lung to expand which was treated by negative suction with complete expansion of the lung in 1 case (12.5%) and tense ascites in another single case (12.5%), but there was no pleuritic pain or hypotension seen in any of our patients treated with bovioidine, although these 2 complications were the most reported in the literature [18, 19]. The argument about the use of iodopovidone because of these 2 complications can be explained by the fact that the use of any effective pleural irritant, including talc [20], can and will produce intense pleuritic pain and a vasovagal reaction if analgesia and anaesthesia are inadequate, and the control of pain should be individualized.

We used somatostatin in all of our patients to reduce the drainage volume and shorten the duration of chest tube removal. Somatostatin reduces splanchnic and hepatic blood flow as well as the portosystemic pressure gradient. Therefore, we used it in our patient instead of TIPS, as in contrast to TIPS, somatostatin has few, mostly minor side effects [21, 22]. The only drawback is that it is expensive. Our data revealed that using the 3 sclerosing agents there was no recurrence in 15 patients (75%) (bovioidine 87.5%, Vibramycin and talc slurry 66.7% each) and the rates of recurrence and complications of the 3 sclerosing agents used were almost comparable.

In conclusion, in our case series, we used 3 sclerosing agents with a convenient outcome and minimal complications. The medical decision in such patients should be individualized and the balance between treating hepatic hydrothorax and the deterioration of the hepatic condition and ascites should be weighed.

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