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ORIGINAL ARTICLE

# Chemical pleurodesis by small bore catheter in hepatic hydrothorax: A feasibility study



Asem A. Hewidy<sup>a,\*</sup>, Nasef Abdelsalam A. Rezk<sup>a</sup>, Ahmed Abdel-Razik<sup>b</sup>

<sup>a</sup> Chest Medicine Department, Mansoura University, Egypt

<sup>b</sup> Tropical Medicine Department, Mansoura University, Egypt

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## KEYWORDS

Chemical pleurodesis;  
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**Abstract** *Background:* Hepatic hydrothorax treatment remains problematic, and chemical pleurodesis can be considered.

*Objectives:* The aim of this study is to compare the efficacy and safety of chemical pleurodesis by small bore catheter to tube drainage in hepatic hydrothorax.

*Methods:* A randomized clinical study included 30 patients with hepatic hydrothorax who were admitted to Chest Department, Mansoura University Hospital, Egypt from 2011 to 2014. Patients diagnosed with exudative effusion, renal impairment, hepatic encephalopathy were excluded. Patients were divided into 2 groups; group A (20 patients) managed by small catheter and group B (10 patients) managed by intercostal tube, chemical pleurodesis in both groups was done by Viscum. Clinical, radiological data and hospital stay duration were adopted for comparison between both groups.

*Results:* Pleurodesis was successful in group A 65% (13 patients) and in group B 70% (7 patients). Hospital stay duration was 10 days for group A and 11 days for group B. Post procedure chest pain score was less in group A than group B which was statistically significant. No serious complications and no mortality occurred.

*Conclusions:* Small bore catheter chemical pleurodesis has successful outcome, less post procedure chest pain and minimal complications in refractory hepatic hydrothorax.

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## Introduction

Hepatic hydrothorax is defined as pleural effusion (greater than 500 mL) in cirrhotic patients with no primary cardiac

or pulmonary diseases [1,2]. It is a manifestation of decompensated chronic liver disease, similar to the presence of ascites, hepatic encephalopathy, or variceal hemorrhage, the most likely mechanism is the passage of ascitic fluid from the peritoneal to the pleural cavity through diaphragmatic defects usually less than 1 cm, located in the tendinous portion of the diaphragm [3].

Hepatic hydrothorax is mostly right-sided (up to 85%) and is associated with ascites, initial treatment entails pleural space

\* Corresponding author.

E-mail address: [ahewidy@yahoo.com](mailto:ahewidy@yahoo.com) (A.A. Hewidy).

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drainage by thoracentesis for diagnostic evaluation and for therapeutic benefit. A sodium-restricted diet and judicious use of a loop diuretic with an aldosterone receptor antagonist (spironolactone, 100 mg/day) may provide initial ascites reduction and prevent hepatic hydrothorax development [4].

The usual treatment of hepatic hydrothorax in patients who fail to respond to aggressive medical management of ascites remains problematic and controversial. A review of the literature has revealed that no method is ideal at present [5]. This study is to compare the efficacy and safety of small bore catheter chemical pleurodesis and the conventional chemical pleurodesis by intercostal tube drainage.

### Study design

This prospective randomized controlled trial looked at two arms of treatment of refractory hepatic hydrothorax with chemical pleurodesis by small bore catheter (group A) and large bore catheter (group B). Clinical, radiological data and hospital stay duration were adopted for comparison between both groups. The patients were randomly selected using the closed envelop method.

### Patients and methods

This study included 30 patients with hepatic hydrothorax who were admitted to the Chest Department, Mansoura University Hospital, Egypt from January 2011 to August 2014. Ethical approval had been obtained from the local ethics committee. Patients signed their written consents after detailed explanation of the study protocol. Patients who had liver cirrhosis, portal hypertension, ascites and refractory hepatic hydrothorax were included in our study. In this study all patients had failed medical treatment with multiple medical managements in the form of sodium and fluid restriction, human albumin, diuretic therapy and repeated therapeutic thoracentesis. Patients who were diagnosed with exudative effusion, tuberculosis, bronchial carcinoma, malignant effusion, renal impairment, and hepatic encephalopathy were excluded from the study.

Full laboratory work up was done, abdominal and trans-thoracic ultrasound chest to detect localizations and localization for the best site of drainage. Plain chest X-ray and CT chest scan were done before and after intervention. Aspiration of both pleural fluid and ascitic fluid was done and sent for biochemical analysis including pH, LDH, protein content and cellular pattern and also cytopathological examination, ZN stain, Gram stain and culture were done for aerobic and anaerobic organisms.

Patients were randomly divided into two groups; group A (20 patients) managed by small catheter insertion and group B (10 patients) managed by intercostal tube insertion. Chemical pleurodesis in both groups was done by using Viscum (Viscum Fraxini 2®; ABNOBA Helmittel GmbH-Germany) 5 ampoules diluted in 100 ml glucose 5%.

In group A, small bore catheter (Angiocath 12 gauge, Lenacath, Haidylena Co., 6th October, Egypt) was inserted in the pleural cavity under trans-thoracic ultrasound guidance, and under local anesthesia, pleural fluid drainage of 1.2–1.5 L per day was done till complete evacuation. The catheter was left until fluid drainage became less than 100 ml/day. After

**Table 1** The McGill Pain Questionnaire [8].

0	None
1	Mild, requiring no medications
2	Discomforting, requiring mild analgesics
3	Distressing, requiring strong analgesics
4	Horrible, requiring narcotic analgesics
5	Excruciating, not responding to narcotic analgesics

complete lung expansion the pleurodesis agent was injected. The valve of catheter was closed for 2 h with rotation of patient in all directions. Then catheter was opened to evacuate the remaining fluid. The catheter was removed after complete lung expansion.

In group B, intercostal tube (28F) was inserted in the pleural cavity under trans-thoracic ultrasound guidance, and under local anesthesia, pleural fluid drainage of 1.2–1.5 L per day was done until fluid drainage became less than 100 ml/day. After complete lung expansion the pleurodesis agent was then applied to the pleural surface and recesses. The tube was closed for 2 h then opened to remove the remaining fluid and was removed after complete lung expansion.

Successful pleurodesis was defined by a patient who no longer had dyspnea symptoms and had a chest roentgenogram that did not show pleural effusion 1 month after the chemical pleurodesis [6]. Dyspnea was evaluated according to American Thoracic Society (1999) before and after the intervention [7]. Post procedure chest pain scoring was done according to The McGill Pain Questionnaire [8] (see Table 1).

Clinical, laboratory, radiological and hospital stay duration end points were adopted for comparing the two interventions.

### Statistical methods

Data were analyzed using SPSS (Statistical Package for Social Sciences) version 15. Qualitative data were presented as number and percent. Comparison between groups was done by Chi-Square test. Quantitative data were presented as mean  $\pm$  S.D. Student *t*-test was used to compare between two groups.  $P < 0.05$  was considered to be statistically significant.

### Results

This study included 30 patients (19 male and 11 female) with hepatic hydrothorax who were randomly divided into two groups, group A treated by small bore catheter pleurodesis and group B treated by large bore catheter pleurodesis. Both groups were compared according to the clinical, radiological and hospital stay duration endpoints.

The mean age for group A was  $54.55 \pm 5.81$  and the mean age for group B was  $49.40 \pm 6.87$ . Group A included 20 patients, 13 male (65%) and 7 female (35%) while group B included 10 patients, 6 male (60%) and 4 female (40%). In group A, 8 patients (40%) were smokers, 8 patients (40%) were non-smokers and 4 patients (20%) were ex-smokers. In group B, 3 patients (30%) were smokers, 2 patients (20%) were non-smokers and 5 patients (50%) were ex-smokers (Table 2).

Dyspnea was present in all patients of both groups, chest pain was present in 2 patients of each group, productive cough was present in 11 patients (55%) of group A and in 4 patients

**Table 2** Clinical data of both groups.

	Group A (n = 20)		Group B (n = 10)		$\chi^2$	P
	No.	%	No.	%		
	Dyspnea	20	100	20		
Dry cough	9	45	6	60	0.600	0.439
Productive cough	11	55	4	40	0.600	0.439
Chest pain	2	10	2	20	0.577	0.448
Hemoptysis	3	15	0	00	1.667	0.197
Fever	1	5	0	00	0.517	0.472

(40%) of group B, dry cough was present in 9 patients (45%) of group A and in 6 patients (60%) of group B and hemoptysis was present in 3 patients (15%) of group A.

In group A 17 patients (85%) had clear fluid, 3 patients (15%) had yellowish fluid, in group B 7 patients (70%) had clear fluid, 3 patients (30%) had yellowish fluid of both ascetic fluid and pleural effusion gross picture examination. Direct Gram stain of ascetic fluid and pleural effusion in both groups showed no organisms, and ZN stain for all patients was negative (Table 3).

There was no significant difference between biochemical analysis of both ascetic fluid and pleural fluid (Table 4).

There was statistically significant difference in group A in improvement of dyspnea, dry cough and productive cough after pleurodesis and in group B there was statistically significant difference in group B in improvement of dyspnea after pleurodesis (Table 5).

In group A, 13 patients (65%) had successful pleurodesis and 7 patients (35%) had recurrent effusion after 1 month, in group B 7 patients (70%) had successful pleurodesis and 3 patients (30%) had recurrent effusion after 1 month (Table 6).

The duration of hospital stay was 10.05 ± 2.48 days in group A and 11.70 ± 2.36 days in group B which was not statistically significant (Table 7).

Post procedure chest pain score showed that in group A 5 patients (25%) had no chest pain, 13 patients (65%) had mild pain and did not need any analgesia, one patient had discomforting pain that improved with mild analgesia paracetamol 500 mg tablet and one patient had distressing pain and needed strong analgesia (Ketorolac injection). In group B one patients (10%) had no chest pain, 3 patients (30%) had mild pain and did not need any analgesia, 4 patient (40%) had discomforting pain that improved with mild analgesia paracetamol 500 mg tablet and 2 patients had distressing pain and needed strong analgesia (Ketorolac injection). Post procedure chest pain score was less in group A than in group B which was statistically significant (Table 8).

**Table 4** The clinical endpoints in both groups.

	Group A (n = 20)		P	Group B (n = 10)		P
	No. before	No. after		No. before	No. after	
	Dyspnea	20		0	<0.001*	
Dry cough	9	0	0.003*	6	3	0.083
Prod. cough	11	2	0.003*	4	3	0.317
Chest pain	2	0	0.157	2	0	0.157
Hemoptysis	3	0	0.083	0	1	0.317
Fever	1	0	0.317	0	1	0.317

**Table 5** The success rate in both groups.

	Group A (n = 20)		Group B (n = 10)		$\chi^2$	P
	No.	%	No.	%		
	Success	13	65	7		
Recurrent	7	35	3	30		

**Table 6** The hospital stay in both groups.

	Group A (n = 20)	Group B (n = 10)	t	P
Hospital stay	10.05 ± 2.48	11.70 ± 2.36	1.744	0.092

**Table 7** Post procedure chest pain score.

Pain score	Group A (n = 20)		Group B (n = 10)		$\chi^2$	P
	No.	%	No.	%		
	0	5	25	1		
1	13	65	3	30		
2	1	5	4	40		
3	1	5	2	20		
4	0	0	0	0		
5	0	0	0	0		

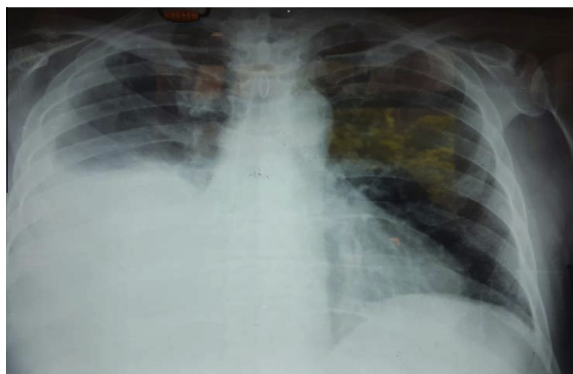
In group A one patient had empyema, 2 patients had mild bleeding controlled by hemostatics, 2 patients had hydropneumothorax that was resolved spontaneously, 2 patients had sur-

**Table 3** Comparison between biochemical analysis of ascetic fluid and pleural effusion.

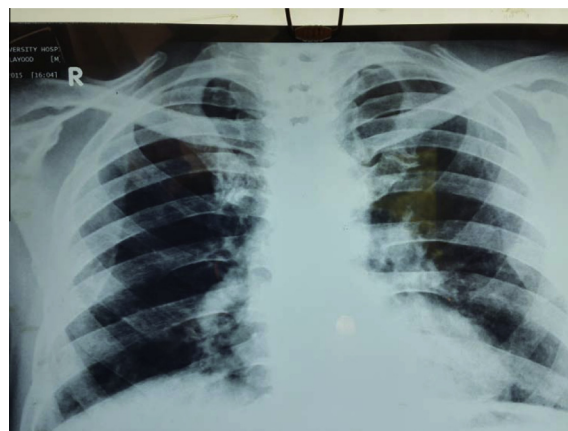
	Group A (n = 20)		P	Group B (n = 10)		P
	Pleural effusion	Ascetic fluid		Pleural effusion	Ascetic fluid	
	pH	7.62 ± 0.40		7.48 ± 0.62	0.269	
Protein	842.50 ± 247.38	839.00 ± 188.76	0.925	861.00 ± 157.93	1595.00 ± 2151.99	0.317
LDH	166.80 ± 36.71	166.50 ± 35.14	0.863	169.00 ± 36.35	174.00 ± 41.42	0.544
Glucose	92.15 ± 22.39	91.60 ± 19.81	0.935	94.30 ± 12.20	93.50 ± 21.99	0.871

**Table 8** Complications in both groups.

	Group A (n = 20)		Group B (n = 10)		$\chi^2$	P
	No.	%	No.	%		
	Empyema	1	5	1		
Mild bleeding	2	10	3	30	1.920	0.166
SC emphysema	2	10	3	30	1.920	0.166
Hydropneumothorax	2	10	0	0	1.071	0.301
Encephalopathy	1	5	3	30	3.606	0.058
Mortality	0	0	0	0	–	–

**Figure 1** Pleural effusion before procedure.**Figure 2** Drained effusion with small bore catheter.

gical emphysema that was resolved with oxygen therapy and one patient had hepatic encephalopathy that improved with medical treatment and there was no procedure related mortality. In group B one patient had empyema, 3 patients had mild bleeding controlled by hemostatics, 3 patients had surgical emphysema that was resolved with oxygen therapy and 3 patients had hepatic encephalopathy that improved with medical treatment and there was no procedure related mortality (Figs. 1–3).

**Figure 3** Successful pleurodesis after 1 month.

## Discussion

The patients with advanced liver cirrhosis with unilateral pleural effusion, mostly in the right side, usually presented with shortness of breath, cough, hypoxemia and/or chest discomfort. Relief of symptoms and prevention of pulmonary complications and infections are critical for the patients with refractory hepatic hydrothorax [6].

Conventional treatment methods for hepatic hydrothorax such as sodium restriction and diuretics, and repeated thoracentesis cannot give the treatment target in many patients. Increasing the doses of diuretics to achieve the negative sodium balance may precipitate hepatic encephalopathy and may increase the serum creatinine level, which indicates a decrease in the glomerular filtration rate. Although, thoracentesis for hepatic hydrothorax is both useful and safe, thoracentesis dependence may be associated with deteriorating clinical status and impaired quality of life. Actually, when thoracentesis is required every 2–3 weeks, alternative strategies must be considered [9].

The term refractory hepatic hydrothorax is used when medical treatment with salt restriction and diuretics are ineffective, as prolonged diuretic treatment may result in depletion of the intravascular volume and impaired renal function. Many authors also consider that clinical management of hepatic hydrothorax is usually difficult and ineffective and can result in deterioration of the clinical status. There have been a variety of mechanisms to explain the shift of ascitic fluid into the pleural space, including hypoalbuminemia, azygos vein hypertension, leakage from the thoracic duct, transdiaphragmatic lymphatic migration and most important, the pressure – gradient – directed flow through diaphragmatic defects [5].

Pleural drainage by chest tube thoracostomy can be very dangerous in patients with massive ascites and pleural effusion. Runyon et al. [10] reported two deaths resulting from associated massive electrolyte and protein depletion. Also, prolonged drainage through the chest tube may cause renal failure, impaired immunological functions and iatrogenic infection as common complications [11].

Pleural drainage by chest tube thoracostomy and chemical pleurodesis was attempted by using tetracycline in 1977 by Falchuk et al. [12].



In our study, all included patients had transudative pleural effusion and ascites with no significant difference between biochemical analysis of both ascitic fluid and pleural fluid, direct Gram stain of ascitic fluid and pleural effusion in both groups showed no organisms, ZN stain for all patients was negative and the cytopathological examination was free from malignant cells.

There was statistically significant difference in group A in improvement of dyspnea, dry cough and productive cough after pleurodesis and in group B there was statistically significant difference in improvement of dyspnea after pleurodesis.

In group A, 13 patients (65%) had successful pleurodesis and 7 patients (35%) had recurrent effusion after 1 month. In group B, 7 patients (70%) had successful pleurodesis and 3 patients (30%) had recurrent effusion after 1 month. These results were comparable to those reported by Woo et al. [6] who used Viscum album and found that refractory hepatic hydrothorax can be controlled with chemical pleurodesis via chest tube with or without VATS in as many as 72.7% of patients. It is also comparable to those reported by Kaddah et al. [13] who revealed that chemical pleurodesis was effective in the treatment of hepatic hydrothorax in 15/20 patients (75%), there were 7/8 cases (87.5%) treated by bovoidine, 4/6 cases (66.7%) with vibramycin and 4/6 cases (66.7%) with talc slurry. The success rate in patients subjected to Viscum pleurodesis was less than that obtained by El-Morsy et al. [14] (87.9%) who used SBC in malignant pleural effusion and this is accepted as the success rate in malignant effusion was more than that in hepatic hydrothorax.

The duration of hospital stay was  $10.05 \pm 2.48$  days in group A and  $11.70 \pm 2.36$  days in group B which was not statistically significant. This was comparable to Kaddah et al. [13] in which the time needed to remove the chest tube was  $9.8 \pm 2.3$  days, but it was more than that reported by El-Morsy et al. [14] pleurodesis via SBC (6.5 days) regardless the agent used and it can be explained as they used it malignant pleural effusion.

Post procedure chest pain score showed that in group A 5 patients (25%) had no chest pain, 13 patients (65%) had mild pain and did not need any analgesia, one patient had discomforting pain that improved by mild analgesia paracetamol 500 mg tablet and one patient had distressing pain and needed strong analgesia (Ketorolac injection). In group B one patient (10%) had no chest pain, 3 patients (30%) had mild pain and did not need any analgesia, 4 patient (40%) had discomforting pain that improved by mild analgesia paracetamol 500 mg tablet and 2 patients had distressing pain and needed strong analgesia (Ketorolac injection). Post procedure chest pain score was less in group A than in group B which was statistically significant so that small bore catheter pleurodesis is more comfortable to the patients than large bore catheter.

In group A one patient had empyema, 2 patients had mild bleeding controlled by hemostatics, 2 patients had hydropneumothorax and resolved spontaneously, 2 patients had surgical emphysema that resolved with oxygen therapy and one patient had hepatic encephalopathy that improved with medical treatment and there was no procedure related mortality, in group B one patient had empyema, 3 patients had mild bleeding controlled by hemostatics, 3 patients had surgical emphysema that resolved with oxygen therapy and 3 patients had hepatic encephalopathy that improved with medical treatment and there was no procedure related. These complications were less than those reported by Woo et al. [6] who reported

complications occurred were low grade fever/leukocytosis (100.0%), pneumonia (9.1%), pneumothorax (36.4%), azotemia/acute renal failure (54.6%) and hepatic encephalopathy (36.4%). Chest pain and percutaneous drainage (PCD) site pain and chest pain occurred in all the 11 patients during the chemical pleurodesis. Five patients (45.5%) were suspected to have procedure-related mortality due to the occurrence of acute renal failure. This difference was due to good selection of our patients and less invasive procedures in our study. Our results were comparable to those of Kaddah et al. [13] who showed that 7 out of the 22 cases reported absence of any complications. The remaining cases (15 patients) showed early and mostly minimal and limited morbidity. There were 4/22 patients (18.2%) suffering from surgical emphysema, 2 cases (9.1%) with minimal left side pleural effusion, 2 cases (9.1%) with superficial wound infection, one case (4.5%) with mild thoracic pain and a single case (4.5%) developed prehepatic coma 4 days after the procedure, who was cured by medical therapy and had no recurrence of hepatic hydrothorax.

## Conclusion

Small bore catheter chemical pleurodesis is not inferior to large bore tube chemical pleurodesis in management of refractory hepatic hydrothorax with successful outcome, less post procedure chest pain and minimal complications.

## Conflict of interest

There is no conflict of interest.

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