

Early pleurodesis for malignant pleural effusion

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ABSTRACT

Background

Many cases of malignancy, either inside the thoracic cavity or from other body organs, accompanied by massive pleural effusion. The treatment for those cases is done by drainage and continued with pleurodesis after pleural fluid production <150 ml / day. This method takes long drainage duration and care, and the cost is enormous. To solve that problem we propose a way of management of malignant pleural effusion more efficiently.

Methods

From July 2008 to July 2009 there were 60 patients with pleural effusion due to malignancy. In the case group we performed pleurodesis early (pleural fluid production > 1000 / day), while in the control group pleurodesis performed if pleural fluid production <150 ml / day. Pleurodesis is succes if achieve pleural fluid production <100 ml/day before third days after procedure. Both groups used pleurodesis with chest tube (no.28-32).

Results

There were 60 patients which is eligible for this research. Allocation to groups were 30 patients performed early palliative therapy with talk and 30 patients performed conventional therapy (conventional pleurodesis). From the demographic depiction, tumor type, disease characteristic and length of stay both pleurodesis group result were no significant difference ($p > 0,05$). The duration of drainage and length of care was much shorter in group early pleurodesis ($p < 0.01$).

Conclusion

Early pleurodesis methods can shorten the drainage time and length of care without affecting the effectiveness of pleurodesis results

Keywords: massive pleural effusion, malignancy, pleurodesis, talc

Latar belakang

Banyak kasus-kasus keganasan, baik di rongga toraks maupun organ tubuh lainnya, dapat disertai dengan efusi pleura yang masif. Penanganan efusi pada kasus-kasus tersebut adalah drainase dan dilanjutkan dengan pleurodesis yang dilakukan setelah produksi cairan pleura <150 ml/hari. Cara ini membutuhkan waktu drainase dan waktu rawat yang lama, serta biaya yang tidak sedikit. Oleh karena itu diperlukan strategi penatalaksanaan efusi pleura pada keganasan yang lebih efisien.

Metode

Dari bulan Juli 2008 sampai Juni 2009 semua pasien yang dikonsultasikan ke divisi Bedah Toraks dan Kardiovaskular dengan efusi pleura karena keganasan direkrut untuk menjadi subjek penelitian. Pada kelompok kasus dilakukan pleurodesis secara dini (produksi cairan pleura > 1000 /hari), sedangkan pada kelompok kontrol dilakukan pleurodesis jika produksi cairan pleura < 150 ml/hari. Kedua kelompok dikatakan berhasil menggunakan pleurodesis jika produksi cairan pleura < 100 ml/hari dalam tiga hari setelah dilakukan pleurodesis. Kedua kelompok menggunakan pleurodesis dengan chest tube ukuran 28-32.

Hasil

Sebanyak 60 pasien memenuhi kriteria untuk dijadikan sampel penelitian. Sebanyak 30 pasien dilakukan terapi paliatif dini dengan talk dan 30 pasien dilakukan terapi konvensional (pleurodesis konvensional). Dari gambaran demografi, jenis tumor, karakteristik penyakit dan hasil pleurodesis kedua kelompok tidak ada perbedaan yang bermakna ($p > 0,05$). Lama drainase dan lama perawatan jauh lebih singkat pada kelompok pleurodesis dini ($p < 0,01$).

Kesimpulan

Metode pleurodesis dini dapat mempersingkat waktu drainase dan lama rawat pasien tanpa mempengaruhi efektifitas hasil pleurodesis

Kata kunci: efusi pleura masif, keganasan, pleurodesis, talk

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Background

Pleural effusion is an important complication in intrathoracic and extrathoracic malignancy patients. It was estimated that 150,000 new cases of pleural effusion in malignancy diagnosed each year.¹Based on study on 98 patient with malignant pleural effusion their median survival was 8,4 month.²Cases of pleural effusion in malignancy will increase as increasing number of malignancy patients. In Cipto Mangunkusumo Hospital itself there is no official data of pleural effusion cases in malignancy.

The types of malignancies that often cause pleural effusions include: lymphoma, mesothelioma, breast cancer, colon cancer, and ovaries. The most common cause of malignant pleural effusions are lung, breast, and ovarian cancers.²

In this study, we conduct new strategy therapy on malignant pleural effusion cases. Chemicals are introduced into the thoracic cavity with pleural fluid production more than 1000 ml per 24 hours after the insertion of chest tube (WSD). This procedure is not commonly done, usually the administration of these chemicals awaits the production of pleural fluid until less than 150 ml.

Based on medical records data at RSUPNCM from 2008 - 2009, patients with pleural effusions which get chest tube inserted and pleurodesis done, the hospitalization duration were 20-30 days. This take a lot of time, effort, and cost. Until now, there have not been studies both domestically and abroad that examine palliative therapy (early pleurodesis) in cases of massive pleural effusion due to malignancy.

From past studies of pleurodesis which performed to massive pleural effusions cases, the use of talc chemicals has a high success rate about 90,6% at 30th days evaluation.³

Methods

All patient which consulted to Thoracic and Cardiovascular Surgery Division at Cipto Mangunkusumo Hospital from July 2008 to June 2009 were reviewed for eligibility as this research subjects. Patient then grouped as treatment (early pleurodesis) and control (conventional pleurodesis) by block randomization method. When a patient meet eligibility criteria consulted to Thoracic and Cardiovascular Surgery Division he/she then randomized to treatment or control group and the next patient which meet eligibility criteria consulted to Thoracic and Cardiovascular Surgery Division grouped as opposite group. After that the next patient get randomized again.

The inclusion criteria for this research was: (1) patient with malignant pleural effusion case (2) pleural fluid production from chest tube > 1000 ml/24 hours (3) Karnofski score of more than or equal to 60% (4) sign the informed consent to enroll the research.

The exclusion criteria included all cases with factors which affect pleural fluid production like hypoalbuminemia (blood albumin level < 2,5 mg/dl), chronic kidney failure (blood creatinine level > 2 mg/dl), chronic heart failure (NYHA functional class III and IV).

Drop out criteria were (1) missing data about duration of chest drainage, duration of hospitalization, time of complaint relief, blood albumin level, pleural fluid analysis (pH, LDH, glucose level), and Karnofski score (2) Patient want to stop treatment against doctor advice (3) patient died before discharged from hospital.

Pleurodesis Procedure

Pleurodesis was done via chest tube. In our hospital, we usually use chest tube with size of 28-32 Fr for adult patient with pleural effusion.

Before starting pleurodesis procedure we prepare sclerosing agent. Sclerosing agent

were combination of 5 gram of sterile talc powder, 50 ml of NaCl 0,9% solution, and 10 ml of lidocaine 2% solution. Talc were sterilized by 270°F autoclave.

Pleurodesis procedure were done by these consecutive step:

1. The procedure is done in the patient's ward
2. IV line with NaCl 0.9% fluid must be or have been established
3. Oxygen must be prepared
4. The patient's position is half-lateral decubitus on the contralateral side (the side of the chest tube is above), place the towel between the patient and the bed
5. Chest tube clamped with 2 clamps, then removed from WSD adapter
6. Clamps open for a moment, so that the lungs collapse in the pleural cavity
7. Syringe inserted to the chest tube both clamps are opened and the sclerosing material is injected through the chest tube
8. Patient is asked to breathe several times to get the solution spread across the pleural space
9. Chest tube then clamped again and the chest tube is connected to the WSD adapter
10. Avoid negative suction for two hours after pleurodesis. The patient's body position is altered (supine, decubitus lateral right-left) for 1 hour then the clamp is removed. After that chest tube can be connected to suction device of -20 mm H₂O

Pleurodesis procedure could be done three times. Pleurodesis is succes if pleural fluid production become less than 100 ml after 3 days. If the pleural fluid production > 100 ml after 3 days after third procedure was done then the procedure is failed.

Data analysis

Data which have been gathered were analyzed with IBM SPSS 17.0. The data analyzed with univariate analysis to define normality of data, bivariate analysis to define the correlation, and multivariate analysis to adjust correlation.

Table 01. Base characteristic of patients

	Case (%)	Control (%)	P value
Sex			
Female	25 (83.3)	28 (93.3)	0.424*
Male	5 (16.7)	2 (6.7)	
Shortness of breath			
Yes	30 (100.0)	30 (100.0)	NA
No	0 (0.0)	0 (0.0)	
Diagnosis			
Breast Cancer	13 (43.3)	18 (60.0)	0.321*
Ovarium Cancer	12 (40.0)	10 (33.3)	
Lung Cancer	5 (16.7)	2 (6.7)	
Age (years)	55.87 ± 6.31	54.03 ± 6.26	0.263 [€]
Leucocyte	7001.00 ± 1034.30	6626.67 ± 738,56	0.112 [€]
Albumin	2.71 ± 0.17	2.62 ± 0,07	0.060 [‡]
Pleural fluid Lymphocyte	91.53 ± 3.31	90.83 ± 1,49	0.206 [‡]
Pleural fluid glucose	59.90 ± 7.16	61.23 ± 4,96	0.245 [‡]
Pleural fluid LDH	51.83 ± 4.09	50.70 ± 4.61	0.318 [€]
Pleural Fluid pH	7.30 ± 0.05	7.26 ± 0.05	0.003 [€]

*Chi-Square test; [€]Unpaired T-test;

[‡]Mann-Whitney test; NA=Not Analyzed

Result

From July 2008 to June 2009, there were 60 patients which meet inclusion criteria and not meet exclusion criteria. There was no drop out patient. Basic data for the treatment group and control group were shown at table 01.

As seen in table 01, there are no statistically difference between treatment and control group except for pleural fluid pH which is more acidic for control group.

The result of pleurodesis were shown at table 02

Table 02. Pleurodesis outcome

	Pleurodesis Outcome		P value
	Succes (%)	Fail (%)	
Treatment	29 (96.67)	1 (3.33)	0.50
Control	30 (100.00)	0 (0.00)	

*Fisher exact test

As shown on table 02 pleurodesis outcome is better for control group but not statistically significant.

The duration of drainage and length of stay are shown on table 03. Both duration of drainage and length of stay are shorter for treatment group. Both parameter are significantly different between group.

Table 03. Comparison of duration of drainage and length of stay

	Treatment	Control	P value
Duration of drainage	5.8±1.4	16.2±2.0	<0,001
Length of stay	7.6±2.0	18.2±2.0	<0.001

*Mann-Whitney Test

Table 04. Corelation of basic data with duration of drainage and length of care

		Duration of drainage	Length of stay
Age	Corelation coefficient	-0.108	-0.108
	P value	0.412	0.411
Leukosit/ μ l	Corelation coefficient	-0.224	-0.228
	P value	0.085	0.079
Albumin	Corelation coefficient	-0.272	-0.277
	P value	0.036	0.032
Lymphocyte of Pleural fluid	Corelation coefficient	-0.075	-0.087
	P value	0.568	0.510
Pleural fluid glucose level	Corelation coefficient	0.101	0.107
	P value	0.444	0.415
Pleural fluid LDH	Corelation coefficient	-0.138	-0.156
	P value	0.291	0.233
Pleural fluid pH	Corelation coefficient	-0.417	-0.420
	P value	0.001	0.001
Sex			
	Female	Mean \pm SD	11.2 \pm 5.2
Male	Mean \pm SD	9.7 \pm 8.2	11.6 \pm 8.4
	P value	0.417*	0.292*

*Mann-Whitney Test. Corelations were calculated with Spearman Test

Corelation of basic data with drainage duration and length of stay are shown at table 04. The ages, leucocyte, lymphocyte, pleural glucose level, and pleural fluid LDH are not significantly corelated to duration of drainage and length of care. The corelated basic data to duration of drainage and length of stay are blood albumin and pleural fluid pH.

Multivariate analysis for drainage duration were shown at table 05.

Table 05. Multivariate analysis for drainage duration

	Coefficient	Correlation coefficient	P Value
Group (treatment=1,control=0)	-9.658	-0.878	0.000
Albumin	-1.484	-0.036	0.423
Leucocyte	0.000	-0.029	0.495
Pleural fluid LDH	0.071	0.056	0.238
Pleural fluid pH	-16.790	-0.160	0.002
Constanta	139.550		0.000
Linear regression			

Table 06. Multivariate analysis for length of stay

	Coefficient	Correlation coefficient	P Value
Group (treatment=1,control=0)	-9.860	-0.866	0.000
Albumin	-1.233	-0.029	0.574
Leucocyte	0.000	-0.019	0.702
Pleural fluid LDH	0.060	0.045	0.400
Pleural fluid pH	-17.538	-0.161	0.006
Constanta	146.493		0.002
Linear regression			

Multivariate analysis for duration of drainage and length of stay show only influenced by group they were assigned into and pleural fluid pH.

Shortness of breath complaint were still found after pleurodesis for 5 patients. The proportion and statistical analysis were shown at table 07.

Table 07. Shortness of breath complaint after pleurodesis

	Shortness of breath		P value
	Yes(%)	No (%)	
Treatment	5 (16.7)	25 (83.3)	0.052
Control	0 (0.0)	30 (100)	

*Fisher's exact test

Discussion

From the results of this study it was shown that early palliative therapy (early

pleurodesis) gave satisfactory results for patients with massive pleural effusion in malignancy. Although this method is still new and no publication about it, the results of this study was quite satisfactory.

Methods of research conducted is early palliative therapy (early pleurodesis) on massive pleural effusion due to malignancy. The procedure is to inject chemicals into the pleural space through the chest tube at the time of fluid production > 1000 ml / 24 h. This procedure is indeed different from conventional procedure which usually done by other researchers, which pleurodesis was done after the production of pleural fluid <150 ml / 24 hours. However, this new procedure was satisfactory from 30 patients on treatment group 29 patients (96.7%) successfully treated and only 1 patient (3.33%) failed.

Other procedure was studied by Yildirim et al's from turkey which periodical pleurodesis (with interval of 6 hours after pleural fluid aspiration) is compared with conventional pleurodesis / standard. The results obtained quite well, the length of chest tube drainage and duration of hospitalization were shorter and specially lower costs.⁴

The chemicals used are 5 gram of sterile talc, based on many research talc was shown good results for pleurodesis. Success rate of talc as chemicals based pleurodesis on reports from the japan is 90.6%.³ From the study of Shaw PHS and colleagues comparing some chemicals as sclerosant, talc was shown as the most effective material.⁵ In accordance with the principle that the chemicals used for pleurodesis should be chemicals which are effective, easy to obtain, cheap, and do not cause serious side effects. Talc has the above mentioned criteria so that talc is recommended as one of the chemicals for pleurodesis. The common side effect of talc include fever and chest pain which

occur only on 10.5% and 14.0% respectively.³

The method to administer talc to pleural space is entirely through the chest tube which has been inserted prior to pleurodesis. Some researchers do pleurodesis with thoracoscopy. A study to compare thoracoscopic pleurodesis to conventional chest tube pleurodesis has shown that thoracoscopic pleurodesis is not statistically different to chest tube pleurodesis.⁶

Side effects which commonly complained after pleurodesis with talc are pain and fever. From research by Inoue et al incidence of chest pain about 14% and fever occur to 10.5% patient.³ While in this research got side effect of pain as much 13 people (21,6%) and no fever. To reduce chest pain side effect, analgesia could be given prior to procedure. NSAID or opioid can be used. Data from Rahman NM research found that NSAID was not inferior to opioid to relief the pain but need significantly more rescue medication.⁷

The most serious side effects of pleurodesis procedure is ARDS (acute respiratory distress syndrome), especially if talc was used as sclerosant. ARDS after pleurodesis though to be happen by three mechanism, migration of talc particle from pleural space to systemic circulation, inflammation from talc (including contamination), and release of inflammation cytokin to systemic circulation.⁸

Based on the results of the this study the insertion of chest tube (drainage) duration on treatment group is 5, 8 days and length of patient care is 7.6 days. While the control group drainage duration is 16.2 days and length of stay 18.2 days (table 3). Based on Yildirim et al the duration of drainage of patients undertaken a new procedure of pleurodesis (rapid pleurodesis) is 1.87 days and the average patient length of stay is 2.33 days. While control group duration of drainage is 7.00 days and length of stay is 8.33 days.⁴

After the procedure, shortness of breath complain was greatly reduced, only 5 (16.67%) patients who still complain shortness of breath after the procedure. There are persistent complains of shortness of breath but it usually from patients with lung malignancy.

Age of patients ranged from 45 years to 65 years and most patients are women, this is in accordance with the malignancy of the female organs. In this paper the most common cause of malignancy is breast cancer, which is 13 people in the case group and 18 people in the control group. Previous study is differ from one another about the most common cause of malignant pleural effusion. Previous study shown that the breast cancer is the most common cause of malignant pleural effusion^{3,4} while another study show that lung cancer is the most common cause of malignant pleural effusion² and yet another study show mesotelioma as the most common cause of pleural effusion.⁶

Conclusion

Early pleurodesis outcome is not statistically different from conventional pleurodesis but has statistically significant shorter duration of drainage and length of stay.

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