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Clinical observation on pericardial effusion in patients with lung cancer treated by intrapericardial catheterization and infusion of highly agglutinative staphylococcin and cisplatin

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Abstract ***Objective:*** To evaluate the therapeutic efficacy of injecting highly agglutinative staphylococcin (HASL) and cisplatin into pericardial cavity of lung cancer patients with pericardial effusion. ***Methods:*** 81 patients were randomized into two groups: 45 in the experimental group (HASL and Cisplatin) and 36 in the control group (Cisplatin). At first pericardial effusion was drained out from a intrapericardial catheter and then different drugs were infused, respectively. 24 h after perfusion the draining continued again until drainage quantity was less than 30 mL every day. The draining lasted 10–15 days. ***Results:*** The response rate was 91.1% for the experimental group and 80.6% for the control group. There was no significant difference between the two groups ($P>0.05$). The complete remission was 77.8% for the experimental group and 52.8% for the control group, which was statistically significant difference ($P<0.05$). The adverse effects were myelosuppression and nausea and vomiting, which were 35.6% and 40.0% in the experimental group and 72.2% and 66.7% in the control group, respectively ($P<0.01$, $P<0.05$). ***Conclusion:*** Injecting HASL and cisplatin into pericardial cavity may be a better way to control pericardial effusion of lung cancer.

Key words pericardial effusion; lung cancer; highly agglutinative staphylococcin.

From March 1998 to June 2004, 81 malignant pericardial effusion of lung cancer patients were treated by injecting highly agglutinative staphylococcin (HASL) and cisplatin into pericardial cavity. The better therapeutic effects were obtained. The results were reported as below.

Materials and methods

Clinical data

From March 1998 to June 2004, 1622 patients with lung cancer were treated, of which 71 cases of stage I, 78 cases of II, 161 cases of IIIa, 769 cases of IIIb, 543 cases of IV. In these patients, 96 patients suffered from malignant pericardial effusion, of which 15 were concurrent pleural effusion. 81 malignant pericardial effusion alone were collected. There were 65 males and 16 females. The range of their ages was 49–65 with a median age of 60.5. 49 of them were adenocarcinoma and 26 were squamous cell carcinoma and 6 were unknown pathology. Lung cancer radical surgery was performed ever in 17 patients formerly. 26 patients ever were treated with radiotherapy and chemotherapy before. The thoracic computer tomography showed the quantity of pericardial effusion was large or middling, and width of effusion which was measured by B ultrasound ranged from 2 to 6.2 cm. Pericardial effusion of all patients were bloodred, of which 73 patients had malignant cell. No patients had heart disease history. They were randomly divided into two groups; the experimental group of 45 patients and the control group of 36 patients, the conditions of the two groups were comparable and had no statistical significant difference ($P>0.05$, Table 1).

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Therapy methods

The patients took semi-reclining position. The injecting spot was confirmed by B-type ultrasound at the most effusion area and then central venous catheter (CVC, 7F) was inserted into pericardial cavity. The effusion was drained into drainage pack from CVC persistently. When drainage quantity was less than 30–50 mL every day, pericardial cavity was perfused with HASL 20 mL (10 ng/mL), cisplatin 60 mg, dexamethasone 5 mg in the experimental group and cisplatin 60 mg, dexamethasone 5 mg in the control group and then CVC was enveloped with heparin cowl. For drug fluid can get in touch with pericardial wall sufficiently the patients were required to change body position repeatedly. The draining continued again 24 h after perfusion until drainage quantity was less than 30 mL every day which lasted 3 days and effusion depth less than

Table 1 The clinical data of the experimental and control groups (%)

Items	Experimental group (*n*=45)	Control group (*n*=36)	*P*
Sex			
Male	34 (75.6)	31 (86.1)	>0.05
Female	11 (24.4)	5 (13.9)	
Pathologic type			
Adenocarcinoma	27 (60.0)	22 (61.1)	>0.05
Squamous cell carcinoma	14 (31.1)	12 (33.3)	
Others	4 (8.9)	2 (5.6)	
Width of pericardial effusion			
≤2.5 cm	29 (64.4)	26 (72.2)	>0.05
>2.5 cm	16 (35.6)	10 (27.8)	

1 cm by B-type ultrasound confirmed. The draining lasted 10–15 days. Chemotherapy and radiotherapy were taken according to different patient's condition after treatment of pericardial effusion.

Evaluation of efficacy

The response to treatment were evaluated according to results of the chest x-ray and B-type ultrasound re-examination and symptom improvement and classified in accordance with JB Bluk's malignant pericardial effusion criteria. Complete response (CR) implied disappearance of the entire pericardial effusion and symptom and sign of pericardial tamponade, and no relapse for at least 4 weeks. Partial response (PR) implied reduction of more than 50% in the sum of pericardial effusion and clinical symptom partial remission for at least 4 weeks. No control (NC) was defined as not enough standard for a reduction of effusion and improvement of clinical symptom above mentioned.

Follow-up

Therapeutic effect was evaluated by B-type ultrasound rechecking 4 weeks after treatment. The time of follow-up lasted 6 months and all of the patients were followed up and no patients suffered constrictive pericarditis. Implantation metastasis along pricking path happened on one patient.

Results

Response to treatment

Response to treatment for two group patients has been listed at Table 2.

Toxicity

Toxicity was classified as 0–IV according to WHO criteria for clinical toxicity (Table 3). The major toxicity was nausea, vomiting, fever and bone marrow depression. All symptoms were controlled by symptomatic treatment. No patients happened severe lesions of renal function, arrhythmia, heart failure, and pulmonary edema. No secondary infection occurred in the course of indwelling catheter.

Discussion

Malignant pericardial effusion is one of common complications of advanced lung cancer. Severe effusion have risk of life because pericardial tamponade. Draining out entire effusion as far as possible is a key way of controlling pericardial effusion[1]. To drain continuously and slowly with CVC into pericardial cavity can avoid pulmonary edema and acute cardiectasis induced by quick draining so effusion may be drained out thoroughly, and actor with drug into pericardial cavity and new effusion may be drained out continuously. CVC can be remained in pericardial cavity for longer time which avoid lesion of needlepoint to heart because conventional nyxis at less effusion and complaint of secondary infection made by repeating paracentesis.

Cisplatin is a broad-spectrum and better effectiveness anti-tumor drug which can kill the tumor cell directly but need not be transformed in body. After cisplatin is perfused into cavity its concentration peak value and area under curve (AUC) are 20 and 12 times of which in plasma respectively and which can generate powerful destroying

Table 2 The recent effect for the experimental and control groups

Groups	*n*	CR (%)	*P*	χ^2	PR (%)	NC (%)	RR (%)	*P*	χ^2
Experimental	45	35 (77.8)	<0.05	5.63	6 (13.3)	4 (8.9)	41 (91.1)	>0.05	1.10
Control	36	19 (52.8)			10 (27.8)	7 (19.4)	29 (80.6)		

Table 3 Toxicity in the experimental and control groups

Toxicity	Experimental group (*n* = 45)					Control group (*n* = 36)					*P*
	0	I	II	III	IV	0	I	II	III	IV	
Myelosuppression	29	12	4	0	0	10	7	15	4	0	<0.01
Fever	7	13	25	0	0	24	9	3	0	0	<0.001
Nausea / Vomiting	27	11	7	0	0	12	9	11	4	0	<0.05

to tumor in terms of the principles of concentration and time dependent of anti-tumor drug[2] and which can make pericardium chemical phlogosis followed by pericardiosymphysis and sequentially restrain recurrence of pericardial effusion.

HASL is a biological response modifier of combined therapy for malignant tumor and which is extracted from the metabolite of eutherapaputic and lower toxicity staphylococcus variant. Due to extensive pharmaco-activity HASL can increase markedly immune function of patients and a count of leukocyte in peripheral blood, repair the organism cell to be harmed, restrain directly tumor growth also, increase effectiveness of radiochemotherapy and decrease toxicity of radiochemotherapy[3-9]. HASL is better drug which may be used as injecting into cavity and its mechanism is it may not only induce pericardium phlogosis and pericardiosymphysis but also produce biological response modulation effect through multiple modality to control pericardial effusion. The combined therapy of HASL and chemotherapy drug (cisplatin) can increase further effect of killing the tumor cell and decrease toxicity of chemotherapy drug[10]. There have been recently many reports about treatment of pericardial effusion in patients with lung cancer with injecting chemotherapy drug and immunomodulator into pericardial cavity and these studies all showed there were not notable toxic effect to be observed. Its mechanism is that immunomodulator activate leukomonocyte of the pericardial cavity to form LAK cell and increase activity of NK and TC cell while the chemotherapeutic drug produce cytotoxic effect to the tumor which have invaded or metastasized on pericardium, thereby producing double effect of killing the tumor cell[11]. The present study showed that The RR was 91.1% for experimental group and 80.6% for control group. There were no significant differences between two groups (P>0.05). The CR was 77.8% for experimental group and 52.8% for control group, which were statistically significant differences (P<0.05). Though RR had no significant differences, experimental group was superior in absolute numbers to control group. So combined therapy of injecting HASL and chemotherapy into pericardial cavity had synergistic effect. The incidence of myelosuppression was markedly lower in the experimental group than that in the control group (35.6% versus 72.2%, P>0.01, Table 3). The nausea and vomiting were much less happened in the experimental group compared with the control group (40.0% versus 66.7%, P<0.01, Table 3). So combined therapy of HASL and local chemotherapy can decrease markedly toxicity of radiochemotherapy .

In summary, combined therapy of HASL and chemotherapy has synergistic effect on the treatment of malignant tumor, and can increase the cellular immune function of patients and the numbers of the white blood cell and decrease the adverse reactions of chemotherapy. To drain continuously and slowly with CVC into pericardial cavity has better compliance, and may drain out effusion thoroughly and which avoid repeating paracentesis, consequence may decrease incidence of the lethal complication with the secondary infection and so on.

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