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PACLITAXEL PLUS CISPLATIN IN THE TREATMENT OF ADVANCED NON-SMALL CELL LUNG CANCER

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Management of advanced non-small-cell-lung-cancer (NSCLC) is still a challenge to clinicians, with poor response rate to chemotherapy and ominous prognosis. Many antineoplastic agents, including ifosfamide, navelbine, docetaxel and paclitaxel etc. have been demonstrated to be clinically active,[1] and some of which have been put into clinical use in our country recently. Among these drugs, paclitaxel is thought to be one of the most promising agents in this category.[2] Its price, however, is now hardly acceptable in China and severely hinders its wide use. From Feb. 1994 through Jan 1996, we applied paclitaxel plus cisplatin regimen to four patients with advanced NSCLC, and following is a report of our preliminary experience.

TREATMENT PROTOCOL

Before therapy, all the four patients had a complete history and physical examinations, complete blood count, electrolytes, hepatic and renal biochemical tests, urinalysis, chest roentgenogram, computed tomographic scans of the thorax and electrocardiogram.

Paclitaxel was a concentrated sterile solution (30mg/5ml/vial). Diluted in 250 ml of 5% dextrose and intravenously infused over 8 hours. During every infusion of paclitaxel, a physician was present for the initial 1 hour. Electrocardiogram and blood pressure was continuously monitored during and 30 min after the infusion (Sirecust 960, Siemens). Cisplatin was then infused at the dose of 60 mg.

To prevent allergic reactions, the following premedications were delivered: 1. dexamethasone 10 mg iv, 12 hours before paclitaxel; 2. diphenhydramine 50 mg iv, 30 min prior to paclitaxel and 3. ranitidine 50 mg iv, 1 hour before paclitaxel.

Paclitaxel and cisplatin were administered every 21 days. During every cycle of treatment, patients were evaluated every other days for the hematologic toxicity, weekly for hepatic toxicity and other side effects. Computed tomographic scans of the thorax were obtained and tumor response assessment was made every 43 weeks. Fiberoptic bronchoscope examination was repeated if necessary.

CASE REPORTS

The patient characteristics and clinical data were summarized in Table 1, and the management and side effects in Table 2 and 3 respectively. Generally, the chemotherapy was well tolerated; no infusion-related death or severe reactions were observed. No interruption of the infusion, treatment delay, dose reduction were required.

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Table 1. Patient characteristics and clinical data

	case 1	Case 2	Case 3	Case 4
Sex	Female	Female	Male	Male
Age (yrs)	54	48	52	60
BSA (m^2)	1.57	1.70	1.80	1.95
Karnof sky Performance Status	80	90	70	80
Present Symptoms	cough, chest pain, dyspnea	No	cough, malaise low-grade fever	No
CT of the chest	left side pleural effusion; bilateral interstitial lesions	Multiple lung nodules	Atelectasis of the right upper lobe and multiple mediastinal lymphadenopthies	A mass in the left upper lobe
Extrathoracic metastasis	No	No	L1 and L2 vertebrae	Liver
Diagnostic approach	FB biopsy	FB biopsy	FB biopsy	FB biopsy
Cell types	*Adenocarcinoma*	Adenocarcinoma	Squamous cell carcinoma	Squamous cell carcinoma
Stage	IIIb	IIIa	IV	IV

FB : Fiberoptic bronchoscope.

Table 2. Management And Outcome

	Case 1	Case 2	Case 3	Case 4
Prior treatment	No	No	No	No
Cycles of chemotherapy with paclitaxel	4	3	2	3
Doses of paclitaxel	150 mg 240 mg 240 mg 240 mg	240 mg 240 mg 270 mg	240 mg 270	210 mg 240 mg 240 mg
Outcome	Complete remission	Partial remission	Worse	No change

Table 3. Side effects

	Case 1	Case 2	Case 3	Case 4
Alopecia	+	+	+	+
Nausea/vomitting	+	+	+	+
Myalgia	–	–	–	+
Hypotension/ bradycarida	–	–	Transient during infusion of taxol	Transient during infusion of taxol
Neutropenia	+	+	+	+
Thrombocytopenia	+	+	+	+
Liver and renal	Slight and transient	Slight and transient	–	–

DISCUSSIONS

The mechanism of therapeutic effects of paclitaxel is through its profound disruption of the tubulin-microtubular system. It is known to bind to the microtubule polymer and thus imparts exceptional stability to this system, which depresses the effects of essential intracellular regulatory elements on this system, thereby altering microtubulin dynamics and depriving the cell of its ability to control and organize the cytoskeleton.[3]

Paclitaxel has demonstrated to have impressive clinical antitumor activity in patients with breast, lung, head and neck, and advanced platinum -refractory ovarian carcinomas. In fact, it is reported that paclitaxel resulted in the best response rate and the highest 1 year survival rate in NSCLC.[4] From the 4 cases reported herewith, our primary impression is that paclitaxel plus cisplatin may be a effective regimen for advanced NSCLC; certain cases, however, may not be sensitive to this management. Since paclitaxel is very expensive and has some potentially severe adverse reactions, close observation and evaluation of treatment response are imperative, in order to make timely adjustment on the chemotherapy regimen.

According to the literatures, the most severe side effect of paclitaxel is hypersensitivity reactions and severe symptoms such as dyspnea and hypotension usually develop within the first hour of paclitaxel infusion. Therefore, premedications (see Treatment protocol) are of extremely importance and should be strictly followed. In addition, bedside observation by a physician during the first hour of infusion is also indicated to find severe adverse effects early and to give timely treatment. In our practice, we monitored the ECG and BP continuously during and 30 min after the paclitaxel infusion, which, we believe that it is important for the detection of cardiovascular accidents. One of our patients experienced transient bradycardia during the first infusion of paclitaxel and decrease in the infusion speed was required to alleviate the symptoms. Cardiovascular accidents are reported to be another potentially life-threatening adverse effects apart from allergic reactions.[5]

Another point worthy to be mentioned is that it has been shown that meylosuppression was more profound when paclitaxel was given after cisplatin than with the alternate sequence. Therefore, we delivered paclitaxel before cisplatin in our patients.

As we mentioned above, paclitaxel may be one of the most important agents in the management of NSCLC. Our experience, however, is quite limited and further observations and studies are needed before we can form an conclusive opinion.

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