Chinese Journal of Cancer Research 8(3):227–229,1996.

CLINICAL EFFICACY OF VINORELBINE PLUS CISPLATIN IN ADVANCED NON-SMALL CELL LUNG CANCER

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A clinical study of the efficacy of vinorelbine plus cisplatin regimen in the management of advanced NSCLC was performed in 35 patients. Five of the 35 patients failed to finish one cycle of chemotherapy with this regimen because of severe and intractable leukopenia or rapid progress of the disease. Tumor response and toxicity were evaluated in the remaining 30 cases. Results showed that, with this regimen, the objective response rate (CR+PR) was 46.7%. The most common toxicity was leukopenia; other side effects included alopecia, gastrointestinal reactions, slight and transient renal and hepatic impairment and peripheral neuropathy. It suggested that vinorelbine plus cisplatin is a safe and effective regimen in the management of advanced NSCLC.

Key words: Vinorelbine, Cisplatin, Non-small cell lung carcinoma, Management.

Non-small cell lung cancer (NSCLC) accounts for approximately 80% of the cases of lung cancer. Furthermore, 70% of patients are inoperable at the time of diagnosis because of regionally advanced or metastatic diseases. Therefore, chemotherapy of inoperable NSCLC is a topic deserving intense investigation. From Oct. 1994, we began to use vinorelbine plus cisplatin regimen to treat advanced NSCLC. In this paper, we report the results of our preliminary observation.

Accepted December 28, 1995

MATERIALS AND METHODS

Patient Selection

Inclusion criteria were: histologically proven NSCLC (inoperable or relapse after surgical resection), measurable disease, Karnofsky performance status of 50 or more, estimated life expectancy of more than 3 months, normal liver and renal functions, leukocyte count 4.0×10^9/L or greater, platelet count 100×10^9/L or greater and no peripheral neuropathy.

Altogether 35 patients were enrolled in the present study.

Treatment Protocol

Vinorelbine (Pierre Fabre Company, 10 mg/vial) was diluted with 100 ml of normal saline and intravenously infused at days 1, 8 and 15; dose for each separate infusion was 40 mg in all the cases except 4 patients, who received 50 mg of vinorelbine for each infusion. Cisplatin (Jinan Qilu Pharmaceutical Plant, 20 mg/vial) was diluted in 250 ml of normal saline and intravenously infused in day 1. To alleviate the gastrointestinal reactions, antiemtics were administered 2 hours prior to the infusion of cisplatin. Hydration was begun immediately after cisplatin infusion, including 500 ml of 5% dextrose, 250 ml of 20% mannitol and 500 ml of normal saline.

Response and Toxicity Evaluation

Pretreatment investigations included history-taking, physical examinations, complete blood cell counts, routine laboratory tests, chest radiograph and/or computed tomography scans. During chemotherapy, the patients were evaluated every other days for the hematologic toxicity and weekly for hepatic, renal and other side effects. World Health Organization (WHO) criteria were used to evaluate toxicity.

Tumor response was assessed by the WHO criteria. Complete response (CR) was defined as the complete disappearance of all measurable disease. Partial response (PR) required a greater than 50% reduction in the sum of the products of the two longest perpendicular diameters of all measurable lesions, without progression in any other sites. No change (NC) was defined as a less than 50% decrease or a less than 25% increase in the sum of the products of the two longest perpendicular diameters of all measurable lesions. Progressive disease (PD) corresponded to an increase of 25% or more in the sum of the products of two longest perpendicular diameters of all measurable lesions or appearance of any new lesion not identified previously. A response or stable disease had to be maintained for at least 4 weeks, with no new lesions appearing.

RESULTS

In five patients' treatment was discontinued before restaging (Four developed severe leukopenia after second infusion of vinorelbine and another refused chemotherapy after first infusion because of rapid progressive disease). The remaining 30 cases com-pleted at least one cycle of chemotherapy and were submitted to further evaluation. Patient characteristics and clinical response to therapy of the 30 cases were shown in Table 1 and 2 respectively.

Table 3 lists the toxicity of the chemotherapy. No treatment-related death occurred in this series. The most frequent hematologic toxicity was leukopenia, which occurred in 19 out of the 30 cases (63.3%). Of particular, leukopenia resulted in treatment delay in 3 patients. Slight thrombocytopenia was observed in 3 patients (10%). Infusionrelated side effects included grade I–II local skin reaction in 6 patients and local soft tissue necrosis due to extravasation of vinorelbine in 1 patient. Peripheral neuropathy manifesting as extremity numbness and paresthesia developed in 6 patients (20%).

Table 1. Patient characteristics (n 30)

Characteristic	
Sex (F/M)	8/22
Median age (yr.)	54
Stage	
III a	14 (46.7%
III b	12 (40%)
IV	4 (13.3%)
Previous local resection	9 (30%)
Histologic subtype	
Squamous cell carcinoma	17 (56.7%)
Adenocarcinoma	12 (40%)
Squamoadenocarcinoma	1 (3%)

Table 2. Tumor response (n· 30)

Histologic subtype	Number of cases	CR	PR	NC	PD	Objective response
Squamous cell carcinoma	17	2	6	7	2	8
Adenocarcinoma	12	1	4	7	0	5
Squamoadenocarcinoma	1·	0	1	0	0	1
Total	30	3	11	14	2	14

Objective response=CR+PR.

DISCUSSION

The prognosis of patients with inoperable NSCLC is ominous; long-term survival rate (more than 3 years) was reported to be as low as 5%. Furthermore, its response to chemotherapy is poor. Monochemotherapy generally produces response rates of approximately 15%[1] and combination chemo-

therapy less than 30%.[2] Vinorelbine, a semisynthetic vinca alkaloid, has resulted in an unusually high response rate (29%) as a single agent in advanced NSCLC. When used in combination with cisplatin, vinorelbine produced even higher response rates.[3,4] Our results showed that CR was 10%, PR 36.7% and objective response rate in our patients was 46.7%, very close to previous report.[3]

Table 3. Toxicity

Toxicity	Grading by WHO criteria				
	0	I	II	III	IV
Anemia	21	3	4	2	0
Leukopenia	11	5	9	4	1
Thrombocytopenia	27	3	0	0	0
Elevation of AST	29	1	0	0	0
Elevation of AKP	29	1	0	0	0
Elevation of BUN	27	3	0	0	0
Nausea/vomiting	12	8	5	4	1
Phlebitis	23	4	2	1	0
Alopecia	25	4	1	0	0
Neurologic	24	4	2	0	0

Leukopenia was the most common toxicity, and in some cases it was so severe and intractable that the therapy had to be discontinued or delayed. Close monitoring of hematologic toxicity during the therapy is imperative.

Another frequent side effect with this regimen was gastrointestinal reactions (60%), probably chiefly due to cisplatin infusion. In our practice, antiemetic treatment was listed as a routine premedication with this regimen. Peripheral phlebitis was a less common but troublesome side effect, which, in most cases, is avoidable if proper rinse with normal saline through the same vessel is given after vinorelbine infusion. In our series, other observed side effects included transient elevation of serum urea nitrogen, peripheral neuropathy, thrombocytopenia etc., but were generally slight and reversible.

In conclusion, our results suggest that vinorelbine plus cisplatin regimen is effective in some advanced NSCLC and can be well tolerated in most patients.

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