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A retrospective clinical study of safety and efficacy of vinorelbine/epirubicin/fluorouracil (NEF) regimen as a postoperative chemotherapy for breast cancer

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Abstract ***Objective:*** We aimed to investigate the safety and efficiency of vinorelbine/epirubicin/fluorouracil (NEF) regimen as adjuvant chemotherapy for breast cancer. ***Methods:*** From 2005 to 2008, 227 female breast cancer patients were treated with the NEF regimen: vinorelbine 25 mg/m^2 iv on days 1 and 8; epirubicin 60 mg/m^2 iv gtt on day 1; 5-Fu 500 mg/m^2 iv gtt on day 1. Chemotherapy was repeated every 21–28 days for a total of 6 cycles. ***Results:*** The major side effects were neutropenia and gastrointestinal syndrome, with a 5-year survival rate of 85.4%. ***Conclusion:*** NEF regimen is safe and guarantees a high survival rate which could be recommended as a adjuvant chemotherapy regimen for breast cancer.

Key words vinorelbine/epirubicin/fluorouracil; breast cancer; adjuvant chemotherapy

In late 1970's, based on the result that response rate of anthracycline was higher than that of cyclophosphamide/methotrexate/5-fluorouracil (CMF) regimen, anthracycline was approved in adjuvant chemotherapy for breast cancer [1]. In recent years, several regimen have shown effective outcomes [2], such as taxol/epirubicin/cisplatin (TEC) regimen and epirubicin-cyclophosphamide followed by docetaxel (EC-T) regimen. But before chemotherapy, the side effects of different regimens needs to be taken into account. According to some research and its results, as first-line single agent therapy, vinorelbine is a efficient and well tolerated agent in the treatment of advanced breast cancer, with response rate of 40% [3]. But whether NEF is efficient as adjuvant chemotherapy for breast cancer is still unknown. The combination of vinorelbine/epirubicin/fluorouracil (NEF) regimen is not included in standard adjuvant chemotherapy regimens for breast cancer yet. So we retrospective analyzed 227 female breast cancer patients in our hospital who had therapy with NEF regimen as adjuvant chemotherapy to observe the safety and survival rate of NEF regimen.

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Patients and methods

Patients

A total of 227 female pathologically diagnosed breast cancer patients were enrolled, with Karnofsky performance status ≥ 70. Other eligibility criteria included: adequate bone marrow (white blood cell count > 3.0 × 10^9 and platelet count > 150 × 10^9), liver function (bilirubin and transaminases < 2.5 times the upper limit of normal) and renal function (creatinine < 2.5 upper limit of normal); and no evidence of metastatic disease; age < 70 years. Patients with active cardiac disease, significant arrhythmia, any serious medical or psychiatric condition, pregnant condition or lactating period were excluded from the study.

Treatment

Patients were treated with NEF as follows: vinorelbine 25 mg/m^2 into normal saline by 100 mL intravenous bolus infusion in 20–30 min on days 1 and 8, epirubicin 60 mg/m^2 into normal saline by 100 mL intravenous bolus infusion on day 1, fluorouracil 500 mg/m^2 into 5% glucose by 500 mL intravenous bolus infusion on day 1, every 3 weeks for six cycles.

Four mg navoban was injected as intravenous bolus before chemotherapy. Routine blood test, blood biochemistry and tumor markers were reviewed during and after

Table 1 Characteristics of 227 breast cancer patients treated with NEF as postoperative adjuvant chemotherapy

Characteristics	No. of patients
Age (years)	
Median	58
Range	40–67
Menopausal status	
Pre	127
Post	100
Pathology	
Infiltrating ductal	215
Infiltrating lobular	12
Grade	
I	16
II	99
III	112
Nodal status	
Positive	158
Negative	69

chemotherapy weekly.

Follow-up

The aim of this study is to study overall survival. Survival data were obtained from the follow-up visit.

Statistical analysis

The study data were analyzed through the STATA 8.0 software. The Kaplan-Meier method was used for plotting survival curves.

Results

All 227 patients who were involved in this study were diagnosed as breast cancer and received operation between 2005 and 2008. All pathologic type were invasive ductal carcinoma or lobular carcinoma. Patient characteristics are presented in Table 1.

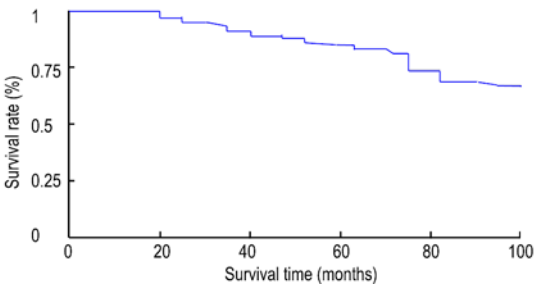

Fig. 1 Survival curve of 227 breast cancer patients treated with NEF as postoperative adjuvant chemotherapy by Log-rank test

Toxicity

All patients' toxicity were assessed. Treatment related side effects were reversible, and there was no termination of chemotherapy due to the toxicity or death caused by adverse events. Leukopenia rate was 81%, 42% of them with grade III–IV and none with infection. There were 29% patients with grade I–II thrombocytopenia and 2% with grade IV thrombocytopenia. Grade I–II gastrointestinal toxicity rate was 49%, and grade III–IV gastrointestinal toxicity rate was 16%, mainly manifested as nausea and vomiting. Other side effects also included alopecia elevated aminotransferases, no treatment-related death occurred. Treatment related adverse events are shown in Table 2.

Survival time

After following up for 96 months, 5-year survival rate was 85.4%; survival curves was checked by Log-rank test (Fig. 1).

Discussion

5-fluorouracil/epirubicin/cyclophosphamide (FEC), TEC, taxol/cyclophosphamide (TC) are considered as standard adjuvant chemotherapy regimens for breast

Table 2 Toxicity by 227 breast cancer patients treated with NEF as postoperative adjuvant chemotherapy

Toxicities	Grade							
	I		II		III		IV	
	No. of patients	%	No. of patients	%	No. of patients	%	No. of patients	%
Leukopenia	34	15	39	17	45	20	50	22
Thrombocytopenia	54	24	11	5	13	6	5	2
Nausea, vomiting	49	22	25	11	20	9	15	7
Diarrhea	34	15	9	4	11	5	0	0
Constipation	52	23	23	10	0	0	0	0
Oral ulcer	34	15	40	18	5	2	0	0
Elevated ALT	57	25	11	5	11	5	7	3
Elevated AST	61	27	18	8	0	0	0	0

ALT: alanine aminotransferase; AST: aspartate aminotransferase

cancer patients. However, the side effects of different regimens needs to be considered before chemotherapy. For instance, before the injection of docetaxel, a big dose of glucocorticoid should be used as premedication, therefore regimens involves docetaxel should not be chosen to patients with diabetes, gastritis or gastric ulcers [4]. On this background, it is crucial for us to design a clinical research and continuously explore new adjuvant chemotherapeutic combinations for breast cancer patients with special clinical conditions. Vinorelbine is a semi-synthetic vinca-alkaloid, can inhibit tubulin polymerization to form microtubules and induce microtubule depolymerization, which is the mechanism that the proliferation of tumor cell division could be stopped at the metaphase [5]. The combination of vinorelbine and epirubicin (NE) was tested in treating breast cancer patients in 1990, the response rate was 60%, 3-year disease-free survival was 68% and overall survival was 81% [6]. So the regimen include NE can be regarded as a good choice for breast cancer patients as adjuvant chemotherapy. In this report, we observed 227 breast cancer patients who had therapy with NEF regimen to understand the safety and efficacy of NEF as adjuvant chemotherapeutic. The 5-year survival rate of our study is 85.4% with tolerant side effects. Its known that the 5-year survival rate of CEF regimen is 70%–80%, the 5-year survival rate of TEC regimen is 75%–86%. As a conclusion, NEF regimen can be recommended as a reasonable option for breast cancer patients as and this conclusion deserves to be further investigated by randomized comparison clinical studies.

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