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ORIGINAL ARTICLE

Clinical observation of capecitabine monotherapy in elderly patients with advanced breast cancer*

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Abstract

Objective The aim of the study was to evaluate the safety and efficacy of capecitabine mono-chemotherapy in elderly patients with advanced breast cancer.

Methods The data from 36 cases of capecitabine monotherapy in elderly patients with advanced breast cancer were retrospectively analyzed. Oral administration of capecitabine 2000 mg/m^2 twice daily (D1–14) for 21 days constituted a cycle. The effect of the disease and main adverse reactions were evaluated every 2 cycles.

Results The data from 36 elderly patients were studied. The median number of chemotherapy cycles was 4. The total effective rate was 30.6% (11/36) and the disease control rate was 72.2% (26/36). The number of patients with clinical complete remission was 2, clinical partial response was 9, stable disease was 15, and progressive disease was 10. Where treatment was effective, the median time to progression was 6 months and the median overall survival was 9.5 months. The main adverse events were gastrointestinal reactions, bone marrow suppression, and oral mucositis; most of the reactions were grade 1 to 2. Grade 3 to 4 adverse reactions included granulocytopenia in 2 patients (12.5%) and hand-foot syndrome in 1 patient (6.7%).

Conclusion Capecitabine monotherapy was effective in controlling disease progression, and adverse reactions were tolerated by elderly patients with advanced breast cancer.

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Key words: capecitabine; elderly; advanced breast cancer; drug therapy

Breast cancer is one of the most common malignant tumors in women; its morbidity is an increasing trend. In developed countries, more than 60% of new breast cancer cases and more than 70% of breast cancer-related deaths occur in elderly patients [1–2]. Due to considerable individual differences in physical and psychological conditions, randomized clinical trials provide limited evidence. Personal factors play an important role in the decision-making process; therefore, the treatment of elderly breast cancer patients according to guidelines is difficult [3]. Therefore, understanding the characteristics of elderly breast cancer patients and formulating their chemotherapy regimens have important clinical significance. In order to avoid adverse reactions and have a higher disease control rate at the same time, we often choose monotherapy in elderly patients. Data from capecitabine monotherapy in 36 elderly patients with advanced breast cancer were retrospectively analyzed, and are reported herein.

Patients and methods

General information

Between November 1, 2011 and December 1, 2013, 36 elderly women with advanced breast cancer received treatment in our hospital (Oncology Department, General Hospital of Shenyang Military Region, Shenyang, China). The characteristics of the elderly breast cancer patients were as follows: (1) aged 65 years or more; (2) high estrogen receptor (ER)-positive rate and low or no human epidermal growth factor receptor 2 (HER2) expression; (3) most patients suffering from other diseases, such as diabetes and cardiovascular disease; and (4) greater inci-

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dence of bone metastases. All the pathological diagnoses showed invasive breast cancer. At the same time, the status of the ER, progesterone receptor, and HER2-related genes was determined in order to clarify the molecular classification. Most of the patients were hormone receptor-positive with low or no HER2 expression and aged 65 to 78 years with an average age of 71.5 years. Three patients received primary treatment, 9 patients progressed after anthracycline-based chemotherapy, 25 patients had recurrences after surgery, and all patients underwent endocrinotherapy after adjuvant chemotherapy. None of the patients received fluorouracil chemotherapy. All patients had measurable lesions (except for bone metastases), including lymph node, bone, lung, and liver metastases. All patients gave informed consent before chemotherapy. The effect of the disease was evaluated every 2 cycles; 2 to 8 chemotherapy cycles were administered with a follow-up review every 3 months. Before treatment, routine blood, liver, and kidney function tests and electrocardiograms were normal. The patients' expected survival was ≥ 3 months and the Karnofsky score was ≥ 60.

Treatment

Postprandial oral capecitabine (Shanghai Roche Pharmaceuticals Co. LTD., specifications: 1.5 g/piece) 2000 mg/m^2 twice daily (D1–14) for 3 weeks constituted a cycle. Two to 8 cycles were completed and the effect of the disease was evaluated every 2 cycles. During chemotherapy, all patients were given vitamin B6 and gastrointestinal mucosa protectors. Some patients received symptomatic treatment, such as hypotensive drugs, hypoglycemic drugs, and cardiotonic drugs.

Efficacy and adverse reaction evaluation

Following every 2 cycles of chemotherapy, computed tomography and medical resonance imaging were performed, and lesion sizes were measured and recorded to evaluate the effect of the disease. According to standard of Response Evaluation Criteria In Solid Tumors, outcomes were defined as follows: complete remission (CR), i.e., all the lesions had disappeared and this status was maintained for at least 4 weeks; partial response (PR), i.e., more than 30% of lesions were reduced in size and this status was maintained for at least 4 weeks; stable disease (SD), i.e., a status between PR and progressive disease (PD); PD, i.e., more than 20% of lesions had increased or new lesions had developed. CR + PR statistics indicate efficiency [total effective rate (OR)]. Disease control rate (DCR) was defined as CR + PR + SD. Time to progression (TTP) refers to the time from the initiation of chemotherapy to disease progression or death. Overall survival (OS) refers to the time from the start of chemotherapy to death or last follow-up. During chemotherapy, patients underwent routine blood, liver, and kidney function examinations, and were screened for drug-related adverse reactions. Evaluation of adverse reactions was in accordance with the United States National Cancer Institute adverse evaluation criteria.

Results

Clinical efficacy

Thirty-six elderly breast cancer patients underwent 4 to 8 chemotherapy cycles (median, 6). One patient died after 4 cycles of chemotherapy because of disease progression. CR was observed in 2 cases; PR, in 9 cases; SD, in 15; and PD, in 10 cases. The OR was 30.6% (11/36), DCR was 72.2% (26/36), median TTP was 6 months, and median OS was 9.5 months.

Adverse events

In this study, the main adverse events were gastrointestinal reactions, bone marrow suppression, and oral mucositis. Most of the reactions were grade 1 to 2. Grade 3 to 4 adverse reactions included granulocytopenia in 2 patients (12.5%) and hand-foot syndrome in 1 patient (6.7%). Two patients' symptoms were relieved after 30% reduction in the capecitabine dose and continuation of chemotherapy (Table 1).

Table 1 Adverse events in 36 elderly breast cancer patients

Adverse reactions	Grade 0		Grade I		Grade II		Grade III		Grade IV	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Nausea & vomiting	26	72.2	7	19.5	3	8.3	0		0	
Granulocytopenia	20	55.5	8	22.2	6	16.7	1	2.8	1	2.8
Thrombocytopenia	26	72.2	8	22.2	2	5.6	0		0	
Hand-foot syndrome	21	58.3	8	22.2	6	16.7	1	2.8	0	
Anemia	25	69.4	9	25.0	2	5.6	0		0	
Liver damage	29	80.5	6	16.7	1	2.8	0		0	
Oral mucositis	26	72.2	6	16.7	4	11.1	0		0	
Diarrhea	31	86.1	3	8.3	2	5.6	0		0	

Discussion

The special physical conditions and higher hormone receptor-positive expression rate in elderly breast cancer patients advocate endocrine therapy; however, endocrine therapy may not be suitable for some patients, especially patients with hormone receptor-negative cancer [4]. According to guidelines, there is no evidence that combination chemotherapy is better than monotherapy. Due to age, fragility, and underlying disease, elderly women with advanced breast cancer cannot tolerate combination chemotherapy. There is no standard chemotherapy regimen for elderly patients with advanced breast cancer [5]. For advanced breast cancer, especially elderly women, the purpose is to prolong survival and improve the quality of life.

Capecitabine is a new oral drug of fluorouracil (FU), which is absorbed in the intestine. Its metabolites are converted into 5-fluorouracil by thymine phosphorylase, and thus have an antitumor effect [6]. As the concentration of the enzyme in tumor tissues is higher than in peripheral tissues, drug selectivity is better and adverse reactions are milder. This study shows that the effective rate of capecitabine monotherapy is high and the incidence of adverse reactions is low, making it suitable for elderly patients with advanced breast cancer. There are a number of clinical trials and case reports about single drug or combination capecitabine-based chemotherapy in advanced gastrointestinal cancer, breast cancer, and other tumors. Many studies show that the overall survival in breast cancer after combination chemotherapy is better than that with monotherapy, but monotherapy results in less severe adverse reactions and good tolerance [7–8]. Capecitabine monotherapy is good for the treatment of advanced breast cancer in elderly patients, because they often cannot tolerate combination chemotherapy. Cao *et al* [9] observed the difference in the curative effect and adverse reactions after capecitabine monotherapy and combination chemotherapy in elderly patients with breast cancer. The result showed that the ORs for the monotherapy group compared with the combination therapy group were 28.2% and 31.8%, respectively. The TTPs were (7.7 ± 2.1) months and (8.2 ± 1.8) months, respectively and the OSs were (13.7 ± 3.9) months and (15.0 ± 4.5) months, respectively. However, the grade 3 to 6 bone marrow suppression and gastrointestinal symptoms in the combination group were worse than in the monotherapy group ($P < 0.05$). The grade 3 hand-foot syndrome in the monotherapy group was worse than in the combination group ($P = 0.07$). Oshaughnessy *et al* [10] indicated that the capecitabine regimen compared with the cyclophosphamide, methotrexate, and fluorouracil regimen had a similar curative effect and was well tolerated. Phase II clinical trials showed that in patients who experienced taxane and anthracycline-based therapy failure, the OR for capecitabine was 20% [11]. Venturini *et al* [12] reported that in 631 advanced breast cancer cases with taxane and anthracycline-based drug resistance, the OR for capecitabine was 24%.

In this study, capecitabine monotherapy programs for the treatment of elderly patients with advanced breast cancer showed a good effect as follows: 2 cases of CR, 9 cases of PR, SD in 15 cases, and PD in 10 cases. The OR was 30.6% (11/36) and DCR was 72.2% (26/36); the median TTP was 6 months and the median OS was 9.5 months. The results were consistent with published literature. The main adverse events were gastrointestinal reactions, bone marrow suppression, and oral mucositis. Grade 3 to 4 adverse reactions were seen including granulocytopenia in 2 patients (12.5%) and hand-foot syndrome in 1 patient (6.7%). Other adverse events were grade 1 to 2. All adverse events could be tolerated and alleviated after symptomatic treatment and no patient had to stop treatment because of adverse reactions.

This study showed that the effective rate of the capecitabine regimen is high and this therapy is well tolerated in elderly patients with advanced breast cancer. Thus, it can be used in elderly patients or those in poor physical condition. However, the sample size is small in this study and for a further retrospective study. We look forward to the results of a prospective randomized clinical study with a larger sample size.

Conflicts of interest

The authors indicated no potential conflicts of interest.

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