Chinese-German J Clin Oncol
DOI 10.1007/s10330-314-0006-8
November 2014, Vol. 13, No. 11, P515–P517

The clinical observation of neoadjuvant chemotherapy in locally advanced breast cancer with DX regimen*

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Received: 19 September 2014 / Revised: 9 October 2014 / Accepted: 25 October 2014

Abstract ***Objective:*** The recent clinical curative effect and adverse events of docetaxel and capecitabine (DX) of neoadjuvant chemotherapy in patients with locally advanced breast cancer was discussed. ***Methods:*** The data of 72 cases of neoadjuvant chemotherapy (DX) in locally advanced breast cancer after 4 cycles were retrospectively analyzed. Docetaxel 75 mg/m^2 by infusion 1 h on d1, capecitabine 2000 mg/m^2 by oral for twice daily on d1–14, 21 days was a cycle. ***Results:*** All 72 patients were assessed for efficacy and adverse events. The total effective rate was 80.5% (58/72), including pathological complete response (pCR) was 7 (9.7%), clinical complete remission (cCR) was 15(20.8%), clinical partial response (PR) was 43 (59.7%), stable disease (SD) was 8 (11.1%) and progressive disease (PD) was 6 (8.3%). The main adverse events were gastrointestinal reactions and bone marrow suppression. The 3 to 4 degrees of adverse reactions including granulocytopenia in 7 patients (20.6%), hand-foot syndrome in 6 patients (15.2%). ***Conclusion:*** The DX regimen provide a favorable efficacy and safety profile in patients with locally advanced breast cancer for neoadjuvant chemotherapy.

Key words breast cancer; neoadjuvant chemotherapy; docetaxel; capecitabine

Breast cancer is one of the common female malignant tumor, become to the first [1], and there is a trend of getting younger over [2]. Some literatures point out that on II, III period of patients with breast cancer could to neoadjuvant chemotherapy [3], but there is no standard treatment. Neoadjuvant chemotherapy of breast cancer (NACT) is a chemotherapy mode before local therapy (surgery and radiotherapy), also known as the preoperative chemotherapy [4]. The purpose of this study was to investigate the clinical efficacy and adverse reaction of DX regimen in patients with locally advanced breast cancer.

Materials and methods

General information

There were 72 women with locally advanced breast cancer, aged from 36 to 62 years, with an average age of 49 years. Including 15 IIb cases, 39 IIIa cases,18 IIIb cases; to evaluate tumor diameter 1.9 to 7.8 cm, with an average diameter of 4.45 cm; in 59 cases of lymph nodes can be touched with lateral alar. All patients underwent immunohistochemical in order to make clear the pathological diagnosis of invasive breast cancer and complete 4 cycles chemotherapy. Before treatment, patients without distant metastases, routine blood and liver and kidney function normal. The patients expected survival ≥ 3 months and Karnofsky score ≥ 70.

Treatment

Docetaxel (Shandong Qilu Pharmaceutical Co., Ltd., China; specifications: 20 mg/teams) 75 mg/m^2, intravenous infusion 1 h d1; capecitabine (Shanghai Roche Pharmaceuticals Co., Ltd., specifications: 1.5 g/piece) daily 2000 mg/m^2, 2 times postprandial oral, d1–14, 3 weeks for a cycle, completed 4 cycles. During chemotherapy patients were all given tropisetron hydrochloride, vitamin B6, dexamethasone and diphenhydramine. If necessary, given recombinant human granulocyte colony-stimulating factor, erythropoietin hormone or interlenkin-11 and other treatment.

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* Supported by grants from the Sub-Topics of Major Drug Discovery platform in the Twelfth-Five Year Research Program of China (No. 2012ZX09303016-002) and the Liaoning Province Science & Technology Development Funds (No. 2012225019).

Efficacy and adverse reactions evaluation

Palpation and ultrasound methods are used to test the lesions after 4 cycles chemotherapy. According to evaluation RECIST standard: complete remission (CR), partial response (PR), stable disease (SD) and progressive disease (PD). CR + PR statistics efficiency [response rate (RR)]. CR is divided into: pathological complete response (pCR) and clinical complete remission (cCR). During chemotherapy patients underwent routine blood, liver and kidney function examination, observing the drug related adverse reactions. Evaluation of adverse reactions was in accordance with the US. NCI developed adverse evaluation criteria.

Results

The recent efficacy

All the 72 cases could evaluated efficacy after 4 cycles. The RR was 80.5% (58/72), including 7 pCR cases (9.7%), 15 cCR cases (20.8%), 43 PR cases (59.7%), SD patients 8 (11.1%) and PD patients 6 (8.3%). A total of 59.7% (43/72) of patients with stage reduced, including: 18 cases with IIIb period, 6 cases fell to IIIa, 4 cases fell to IIb, 2 cases dropped to IIa; 39 cases with IIIa period, 13 cases dropped to IIb, 8 cases fell to IIa, 2 cases dropped to zero; 15 cases with IIb period, 3 cases dropped to IIa and 5 cases dropped to zero.

Tumor size and lymph node metastasis

Seven patients with breast lump and axillary lymph nodes are negative in 72 patients with breast cancer. In cCR, 2 cases of axillary lymph node negative and breast lumps positive, 5 cases of axillary lymph node positive and breast lumps negative; Axillary lymph nodes and breast lumps are positive of PR.

Adverse events

In this study, the major adverse events were gastrointestinal reactions and bone marrow suppression. The 3 to 4 degrees of adverse reactions include: granulocytopenia in 7 patients (20.6%),hand-foot syndrome in 6 patients (15.2%). The data were shown in Table 1.

Discussion

Breast cancer is the most common malignancy in women, it is reported that each year about 1.3 million women suffer from breast cancer worldwide [5]. Many studies show that neoadjuvant chemotherapy can reduce the primary tumor volume, reduce tumor load, reduce the clinical staging and improve the RR, pCR in locally advanced breast cancer [6]. The observation of tumor size and related biological index changes after neoadjuvant chemotherapy, the sensitivity of chemotherapy related indicators are discussed [7].

Docetaxel [8] is a new kind of antineoplastic with resistance to microtubules belong to paclitaxel. It can be combined with free tubulin, form stable microtubule polymers, thus inhibiting cell mitosis, so due to cell death. Capecitabine [9] is a new type of fluorouracil ammonia formic acid esters antitumor medicine by oral. It converted into 5-Fu by thymine phosphorylase (TP) catalysis in tumor cells, and thus play a role of antitumor. Many studies show that docetaxel combined with capecitabine regimen provide synergistic antitumor [10], and the main applications are the two medicine joint major toxic effects did not increase [11].

In this study, docetaxel + capecitabine recombination chemotherapy programs in the treatment of patients with locally advanced breast cancer show good effect: pCR 9.7%, cCR 20.8%, PR 59.7%, SD 11.1%, PD 8.3%. Many studies have shown that neoadjuvant chemotherapy can reduce the primary tumor volume in patients with locally advanced breast cancer, increase cancer resection rate, its efficiency can reach more than 80% [12]. This study shows that RR 80.5%, in line with most of the literature. All patients can complete 4 cycles of neoadjuvant chemotherapy and have well tolerated. The main adverse reactions are bone marrow suppression, gastrointestinal reactions and hand-foot syndrome. The 3 to 4 degrees of adverse reac-

Table 1 The adverse reactions of the 72 patients (*n*)

Adverse reactions	Degree 0	Degree I	Degree II	Degree III	Degree IV	Incidence (%)
Nausea & vomiting	30	29	13	0	0	58.3
Granulocytopenia	38	15	12	5	2	47.2
Thrombocytopenia	48	19	5	0	0	33.3
Hand-foot syndrome	39	22	6	4	1	45.8
Anemia	45	22	5	0	0	37.5
Fatigue	52	16	4	0	0	27.7
Alopecia	55	15	2	0	0	23.6
Liver damage	63	6	3	0	0	12.5
Renal damage	67	5	0	0	0	6.9
Stomatitis	68	4	0	0	0	5.6

tions including granulocytopenia in 7 patients (20.6%), hand-foot syndrome in 6 patients (15.2%). Other adverse events for 1 to 2 degrees, all adverse events can tolerate and alleviate after give symptomatic treatment. It indicating that there are lower incidence of adverse reaction of this combination neoadjuvant chemotherapy regimen, and do not affect the effect of chemotherapy. In a phase II study about the regimen in the treatment for patients with locally advanced breast cancer, Lebowitz *et al* [13] have reported effective rate was 90%, the pCR was 10%, the CR was 31%, the PR was 59%. This regimen have higher efficacy in patients with locally advanced breast cancer and be well tolerated.

In summary, this study shows that the effective rate of docetaxel + capecitabine regimen is high, and the incidences of adverse reactions are low in patients with locally advanced breast cancer. This recombination chemotherapy program can reduce the primary tumor volume, reduce tumor staging, increases the chances of patients with surgical resection. DX regimen for locally advanced breast cancer patients is effective and well tolerated. It is expected to become the neoadjuvant chemotherapy for locally advanced breast cancer. But this study sample size is less and for retrospective study, we looking forward to have a larger sample size of prospective randomized clinical study results.

Conflicts of interest

The authors indicated no potential conflicts of interest.

References

1. Jemal A, Bray F, Center MM, *et al*. Global cancer statistics. CA Cancer Clin, 2011, 61: 69–90.
2. Bleyer A. Young adult oncology: the patients and their survival challenges. CA Cancer J Clin, 2007, 57: 242–255.
3. Crozier JA, Swaika A, Moreno-Aspitia A, *et al*. Adjuvant chemotherapy in breast cancer: To use or not to use, the anthracyclines. World J Clin Oncol, 2014, 5: 529–538.
4. Doval DC, Dutta K, Batra U, *et al.* Neoadjuvant chemotherapy in breast cancer: review of literature. J Indian Med Assoc, 2013, 111: 629–631.
5. Yalcin B. Overview on locally advanced breast cancer: defining, epidemiology, and overview onneoadjuvant therapy. Exp Oncol, 2013, 35: 250–252.
6. Straver ME, van Adrichem JC, Rutgers EJ, *et al.* Neoadjuvant systemic therapy in patients with operable primary breast cancer: more benefits than breast-conserving therapy. Ned Tijdschr Geneeskd, 2008, 152: 2519–2525.
7. Shien T, Akashi-Tanaka S, Miyakawa K, *et al.* Clinicpathological features of tumors aspredictors of the eficacy of primary neoadjuvant chemotherapy for operable breast cancer. World J Surg, 2009, 33: 44–51.
8. Moon YW, Lee S, Park BW, *et al*. S-1 combined with docetaxel following doxorubicin plus cyclophosphamide as neoadjuvant therapy in breast cancer: phase II trial. BMC Cancer, 2013, 13: 583.
9. Kamal AH, Camacho F, Anderson R, *et al.* Similar survival with single-agent capecitabine or taxane in first-line therapy for metastatic breast cancer. Breast Cancer Res Treat, 2012, 134: 371–378.
10. Venturini M, Del Mastrol L, Garrone O, *et al.* Phase I, dose-finding study of capecitabine in combination with docetaxel and epirubicin as first-line chemotherapy for advanced breast cancer. Ann Oncol, 2012, 13: 546–552.
11. Pronk LC, Vasey P, Sparreboom A, *et al.* A Phase I and pharmacokinetic study of the combination of capecitabine and docetaxel in patients with advanced solid tumours. Br J Cancer, 2013, 83: 22–29.
12. Taguchi T. The development of neoadjuvant chemotherapy in breast cancer. Gan To Kagaku Ryoho, 2012, 39: 876–881.
13. Lebowitz PF, Eng-Wong J, Swain SM, *et al.* A phase II trial of neoadjuvant docetaxel and capecitabine for locally advanced breast cancer. Clin Cancer Res, 2004, 10: 6764–6769.

DOI 10.1007/s10330-314-0006-8
Cite this article as: Zhang M, Qiu JN, Qu SX, *et al*. The clinical observation of neoadjuvant chemotherapy in locally advanced breast cancer with DX regimen. Chinese-German J Clin Oncol, 2014, 13: 515–517.