Clinical Trial of Docetaxel Combined with Mitoxantrone for Advanced Breast Cancer

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Abstract **Objective** To evaluate the curative effect and toxicity of docetaxel plus mitoxantrone in the treatment of advanced breast cancer. **Methods** Fifty-two pathologically and cytologiclly proved cases of breast cancer with intravenous infusion of docetaxel 75mg/m2 on the first day, and oral dexamethasone 10mg was given on the day before docetaxel therapy for three days. Mitoxantrone was treated with intravenous infusion of Mitoxantrone 14mg/m2 on the first day. Each cycle was 21 to 30 days and the clinical response was assessed after two cycles. **Results** It showed that CR were 6 cases, PR 32 cases, NC 10 cases and PD 4 cases with an overall effective rate of 73.08% . The main side effects included neutropenia: in which grade III was 32.69 %, grade IV 25.00%, respectively; alopecia: grade II 44.23 %, grade III 21.15%. Diarrhea: grade II 32.69%, grade III 21.15%; **Conclusion** Docetaxel plus Mitoxantrone is effective for advanced breast cancer and toxicities are well tolerated.

Key Words Breast cancer; Chemotherapy; Docetaxel

Breast cancer is the main malignant tumor harmful to the women´s health and lives. Each year there are about 1.2 millions of women getting breast cancer and 500,000 women die of it all over the world. In recent years, the application of docetaxel has improved the treatment effectiveness of the advanced breast cancer. From March 1998 to August 2001, our hospital applied docetaxel combined with mitoxantrone in the treatment of 52 cases of advanced breast cancers and the recent treatment is reported as follows:

MATERIAL AND METHOD

Clinical Material

52 woman patients are pathologically diagnosed as breast cancer, the ages of the patients were from 39 to 73 years old, with the average age 55 years old. Initial treatment were 18 cases without any use of the anti-tumor chemotherapeutic medicines before and after the operation, and re-treatment were 34 cases without use of anti-tumor chemotherapeutic medicines before operation and all using the CAF option after the operation: i.e. no effects after treatment for two cycles with cyclophosphamide, adriamycin, and fluorouracial and it´s has been over one month after stopping the medicine treatment. Among the patients, there are infiltrating duct cancer 22 cases, pure cancer 16 cases, scirrhous cancer 8 cases, and pulpiform cancer 6 cases. According to the MRI, molybdenum target imaging inspection and visual check before the operation, this group of patients are clinically divided into III phase 16 cases and IV phase 36 cases. Karnofsky score at 60-90 before chemotherapy, both blood routine examination and KF are normal. The liver functions of six cases with liver transition are slightly abnormal while the others are normal.

Study method

Intravenous drip of docetaxel 75mg/m²dl for one hour. One day before application of docetaxel orally take dexamethasone 10mg.qd for three days running, intravenous drip of mitoxantrone 14mg/m²dl for 2 hours, 21-30 days as one cycle. Evaluate the treatment effects after two week´s treatment. Use ondasetron to stop the vomiting. The treatment effects are measured by CT chest imaging and B ultrasonic. By the WHO standard, it is classified as CR, PR, NC, and PD. Effective rate (RR) = CR+ PR. The bad reaction is judged as per WHO´s toxic and side reactions.

RESULTS

Clinical effects

All the 52 cases can be evaluated with treatment effects, in which CR were 6 cases, PR 32

cases, NC 10 cases, PD 4 cases. The results are shown in Table 1 and 2.

Toxic and side reactions the main toxic and side reactions of the chemotherapy by docetaxel combined with mitoxantrone are myelosuppression, leucopoenia and trombocytopenia. Besides, the frequent toxic and side reactions are baldness, diarrhea, nausea, vomiting and allergy. Only case 2 shows the difficulty in breathing and remission after expectant treatment and stop of chemotherapy (Table 3). No case dies of toxic and side reactions with only slight damage to liver function.

DISCUSSION

Docetaxel is a new kind of anti–cancer drug and can speed up the formation of micro–tube by the micro–tube protein and extend the length of the micro tube. Generally it can strengthen the polymerization and inhibit the depolymerization of the micro–tube protein to form the stable non–functional micro–tube bundle and inhibit the division and multiplication of the tumor cells. In addition, due to the distribution of docetaxel in higher concentration in the liver, this dynamic feature may

Table 1. Docetaxel Plus Mitoxantrone Presented the Effective of the Treatment (Case)

Item	Cases	CR	PR	NC	PD	CR+PR (%)
Clinical Stages						
III	16	6	8	2	0	87.50
IV	36	0	24	8	4	66.67
Pathological Gradin						
Infiltration	22	2	16	2	2	81.82
Duct Cancer						
Simple Cancer	16	2	10	4	0	75.00
Scirrhoma	8	0	4	2	2	50.00
Medullary	6	2	2	2	0	66.67
Carcinoma						
Primemival Cancer	18	6	8	4	0	77.78
Repetition Cancer	34	0	24	6	4	70.59

Table 2. On the Plae of theTransfer Presented the Effective ofTreatment(Case)

Placese of Metastasis	Cases	CR	PR	NC	PD	CR=PR(%)
Lung	16	2	10	4	0	75.00
Liver	12	2	6	4	0	66.67
Bone	20	0	6	8	6	33.33
Pleura	8	0	4	2	2	50.00
Lymph node	14	4	6	4	0	71.43
Kidney	6	2	2	2	0	66.67
Pericardium	4	0	2	2	0	50.00

Table 3. Docetaxel Plus Mitoxantrone Presented Adverse Effect for Treating the Breast Cancer [Case(%)]

Adverse Effect	Grade				
	0	Ⅰ	Ⅱ	Ⅲ	Ⅳ
Leukopenic	4(7.67)	5(9.62)	13(25.00)	17(32.69)	13(25.00)
Thrombocytopenia	38(73.08)	9(17.31)	5(9.62)	0(0.00)	0(0.00)
Baldness	3(5.77)	15(28.85)	23(44.23)	11(21.15)	0(0.00)
Nausea and Vomiting	37(72.15)	10(19.23)	4(7.69)	1(1.92)	0(0.00)
Dirrhea	13(25.00)	11(21.15)	17(32.69)	11(21.15)	0(0.00)

contribute to the higher treating rate in liver transfer.

The clinical observation of this group demonstrates that the effective rate of docetaxel combined with mitoxantrone in the treatment of advanced breast cancer is 73.08% without cardiac toxicity. Meanwhile, the effective rate of the docetaxel combined with the mitoanthrone on the cases with initial treatment is 77.78%, close to that on the re–treatment cases (70.59%). We think, first, this is due to the obviously higher inhibition of docetaxel on the breast cancer than cyclophosphamide and adriamycin; second, due to the good treatment effects of mitoanthrone on breast cancer and incomplete cross drug resistant with the adriamycin. The leucopoenia due to chemotherapy can be relieved by applying G–CSF and the trombocytopenia can be recovered automatically. The diarrhea can be treated by oral smecta. The pre–treatment with dexamethasone can greatly reduce the incidence of the allergy and dropsy and its side reaction can be endured.

To sum up, the docetaxel combined with mitoanthrone has obviously higher treatment effects in treatment of advanced cancer and the side reaction can be endured. We think it´s worthwhile to promote it.

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