ORIGINAL RESEARCH ARTICLE

Clinical application of trastuzumab and docetaxel in the chemotherapy of human epidermal growth factor receptor 2 positive breast cancer patients

DOI: 10.29063/ajrh2025/v29i5s.12

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Abstract

This study was designed to investigate the effects of trastuzumab combined with docetaxel in the treatment of human epidermal growth factor receptor 2-positive breast cancer patients. Fifty-two human epidermal growth factor receptor 2-positive breast cancer patients accepted chemotherapy at the Hangzhou Linping District Maternal & Child Health Care Hospital from January 2018 to January 2023. They were randomly separated into a control group and a research group. The control group was given docetaxel injection, while in addition to docetaxel injection, the research group was given trastuzumab. The results showed that relative to the control group, the research group had higher objective response rate, higher disease control rate, lower levels of tumor makers and inflammatory cytokines, lower occurrence of adverse events, higher quality of life scores, as well as longer survival time. We conclude that docetaxel plus trastuzumab chemotherapy can promote the clinical efficacy, reduce the levels of tumor markers as well as inflammatory cytokines, lessen the adverse reactions, and promote quality of life and survival time in human epidermal growth factor receptor 2-positive breast cancer patients. *(Afr J Reprod Health 2025; 29 [5s]: 97-104).*

Keywords: Human epidermal growth factor receptor 2, breast cancer, docetaxel, trastuzumab, chemotherapy, quality of life

Résumé

Cette étude visait à évaluer les effets du trastuzumab associé au docétaxel dans le traitement du cancer du sein exprimant le récepteur 2 du facteur de croissance épidermique humain (FCEH). Cinquante-deux patientes atteintes d'un cancer du sein exprimant le FCEH ont suivi une chimiothérapie à l'hôpital de soins maternels et infantiles du district de Linping à Hangzhou de janvier 2018 à janvier 2023. Elles ont été réparties aléatoirement en un groupe témoin et un groupe de recherche. Le groupe témoin a reçu une injection de docétaxel, tandis que le groupe de recherche a reçu du trastuzumab en complément. Les résultats ont montré que, par rapport au groupe témoin, le groupe de recherche présentait un taux de réponse objective plus élevé, un taux de contrôle de la maladie plus élevé, des taux plus faibles de facteurs tumoraux et de cytokines inflammatoires, une incidence plus faible d'événements indésirables, des scores de qualité de vie plus élevés et une survie plus longue. Nous concluons que la chimiothérapie par docétaxel et trastuzumab peut améliorer l'efficacité clinique, réduire les taux de marqueurs tumoraux et de cytokines inflammatoires, atténuer les effets indésirables et améliorer la qualité de vie et la survie des patientes atteintes d'un cancer du sein positif au récepteur 2 du facteur de croissance épidermique humain. *(Afr J Reprod Health 2025; 29 [5s]: 97-104).*

Mots-clés: Récepteur 2 du facteur de croissance épidermique humain, cancer du sein, docétaxel, trastuzumab, chimiothérapie, qualité de vie

Introduction

Breast cancer (BC) is to a frequent disease in female, and is a malignant tumor located on the epithelial tissue of the breast gland.[1] Since the breast is not a crucial organ to keep the life activities of the human body, in situ BC is generally not fatal.[2] Nevertheless, due to the fact that BC cells lose the features of normal cells, the loose connection between cells and the probability of exfoliation is high. Free cancer cells can spread to various tissues and organs of the body, metastasizing, and even threatening the life and health of patients.[3] Early BC is not easy to detect due to the lack of typical symptoms and signs.[4] It is generally incidentally found during physical examination or during BC screening. With further development of the disease, patients may have breast masses, nipple discharge, nipple and areola abnormalities, skin changes, axillary lymph node swelling, and other symptoms.[5] Early detection and

early diagnosis of BC are important for improvement of the clinical efficacy. Therefore, once BC is diagnosed, symptomatic treatment is needed as soon as possible.[6]

Human epidermal growth factor receptor 2 (HER2) is recognized as a proto-oncogene that promotes cancer progression.[7] Studies have found that the degree of HER2 gene amplification is closely linked to the malignant degree of tumors.[8] HER2-positive cancer cells proliferate more rapidly and are less differentiated than normal cancer cells.[9] Currently, anti-HER2 drugs such as trastuzumab, lapatinib and pertuzumab are available for treating HER2-positive BC.[10] As the most widely used first-line anti-chemotherapy drugs, they can significantly improve the prognosis of HER2-positive BC patients.[11] Trastuzumab is an anti-HER2 monoclonal antibody, which can effectively stimulate human immune cells, inhibit the growth of tumor cells, as well as improve the immunity and anti-tumor effect of HER2-positive BC patients.[12]

In addition, paclitaxel is a new type of anti-microtubule drug, which is extensively used in treating BC.[13] Recently, with the improvement and exploration of taxanes preparation process, docetaxel has been developed, which has the same mechanism of action as paclitaxel, higher microtubule binding affinity, wider antitumor spectrum and higher anticancer activity.[14] Of note, it has been also reported that the combination of pertuzumab, trastuzumab together with docetaxel increase the survival of HER2-positive metastatic BC patients.[15] Nevertheless, there has been few research data on the combined application of docetaxel together with trastuzumab in HER2-positive BC.

Therefore, the objective of this study is to investigate the effectiveness of trastuzumab combined with docetaxel in treating HER2-positive BC patients.

Methods

Materials

Fifty-two HER2-positive BC patients who accepted chemotherapy at the Hangzhou Linping District Maternal & Child Health Care Hospital from January 2018 to January 2023 were chosen as the study participants. They were randomly separating into a control group (CG, n=26) and a research group (RG, n=26). As shown in Table 1, no difference was seen in general information between both groups, implying comparability.

The inclusion criteria were: (1) BC was diagnosed by pathology and immunohistochemistry; (2) patients with Her-2 positivity; (3) Eastern Cooperative Oncology Group (ECOG) score ranging 0-1; and (4) Age over 18 years old.

The exclusion criteria were: (1) presence of abnormal liver and kidney function; (2) human immunodeficiency virus (HIV) antibody positivity; (3) patients with distant metastasis; (4) patients who had accepted chemotherapy or were allergic to chemotherapy drugs; (5) patients complicated with endocrine diseases such as hyperthyroidism and diabetes mellitus, which may affect the study results; (6) pregnant women; and (7) patients with previous history of malignant tumors. All patients signed an informed consent form.

Methods

Both groups were given dexamethasone (Shanghai Xiandai Hasen (Shangqiu) Pharmaceutical Co. Ltd and omeprazole (AstraZeneca, UK) before chemotherapy to prevent the side effects of chemotherapy. Thirty minutes before chemotherapy daily, 5 mg of dexamethasone was dissolved in 100 mL of 0.9% sodium chloride injection for intravenous infusion, and 40 mg of omeprazole was dissolved in 100 mL of 0.9% normal saline for intravenous infusion.

Patients in the CG were given docetaxel injection, 75 mg/m^2, intravenous drip, which was completed within 1 hour. The drug was used again at an interval of 21 days, and the treatment repeated over 4 times.

In addition to treatment given to the CG, patients in the RG were given trastuzumab, intravenous infusion, trastuzumab was dissolved by mixing with 250 mL of normal saline, the first dose of 4 mg/kg, which was completed within 90 minutes, and then 2 mg/kg for maintenance, once a week.

Table 1: General data in both groups

Items		Control group (n=26)	Research group (n=26)	P
Age (years)		40.3±3.6	40.5±4.1	>0.05
Marital status	Unmarried/married	1/25	2/24	>0.05
Location of the lesion	Left side	11	12	>0.05
	Right side	12	13	
	Two-side	3	1	
Stage	Stage II	15	16	>0.05
	Stage III	11	10	

Observed indices

(1) Clinical efficacy evaluation criteria: Following the tumor evaluation criteria, the clinical efficacy was assessed and separated into complete remission (CR), partial remission (PR), stable disease (SD), as well as progressive disease (PD). CR: the visible lesions had completely disappeared. PR: lesion reduction and >30% reduction in the sum of the radii. SD: the total of the radii of the lesions was decreased by <30%, or the total of the radii was elevated by <20%. PD: the total of the radius of the lesions was elevated by more than 20% or new lesions arose. Objective response rate = (CR + PR)/26 ×100%. Disease control rate = (CR + PR + SD)/26 ×100%.
(2) The venous blood (4 mL) of the patients was obtained and centrifuged, and serum carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125) along with carbohydrate antigen 153 (CA153) levels were examined utilizing enzyme linked immunosorbent assay (ELISA).
(3) Levels of inflammatory markers including interleukin-6 (IL-6), interleukin-8 (IL-8) and tumor necrosis factor-α (TNF-α) were detected utilizing ELISA.
(4) Adverse reactions included bone marrow suppression, gastrointestinal reactions, liver function damage, and cardiotoxicity in both groups were counted.
(5) Utilizing the 36-item Short Form Health Survey (SF-36), patients' quality of life was assessed.[16] Scores were proportional to quality of life.
(6) Long-term efficacy of patients included 5-year overall survival (OS) as well as 5-year disease-free survival (DFS) was recorded.

Statistical analysis

Using SPSS 21.0 statistical software, data analysis was performed. Count data exhibited as % were analyzed using χ^2 test. Measurement data exhibited as mean ± standard deviation were analyzed by means of t test. $P<0.05$ represented the difference was significant.

Ethical clearance

This study was consistent with the ethical standards of the 1964 Declaration of Helsinki and its later amendments, and was approved by the Ethics Committee of Hangzhou Linping District Maternal & Child Health Care Hospital.

Results

Clinical efficacy in both groups

The objective response rate as well as disease control rate in the RG were 84.6% and 96.2%, respectively, which were higher relative to the CG ($P<0.05$, Table 2).

Levels of CEA, CA125 and CA153 in both groups

As shown in Figure 1, the levels of CEA, CA125, and CA153 were not significantly different between both groups prior to treatment ($P>0.05$). The levels of the above tumor markers in both groups declined after treatment ($P<0.05$). However, relative to the CG, the RG had lower levels of the above tumor markers ($P<0.05$).

Table 2: Clinical efficacy in both groups (n, %)

Groups	CR	PR	SD	PD	Objective response rate	Disease control rate
Control group (n=26)	6	8	5	7	53.8%	73.1%
Research group (n=26)	10	12	3	1	84.6%	96.2%
χ^2					5.8	5.3
P					<0.05	<0.05

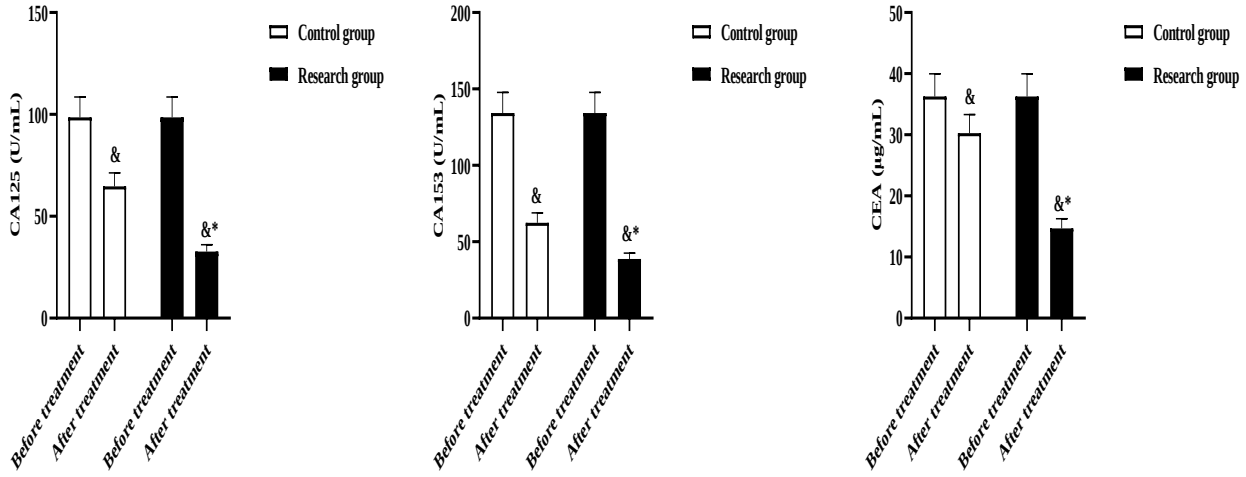

Figure 1: Levels of CEA, CA125 and CA153 in both groups. &P<0.05, compared to before treatment. *P<0.05, compared to the CG

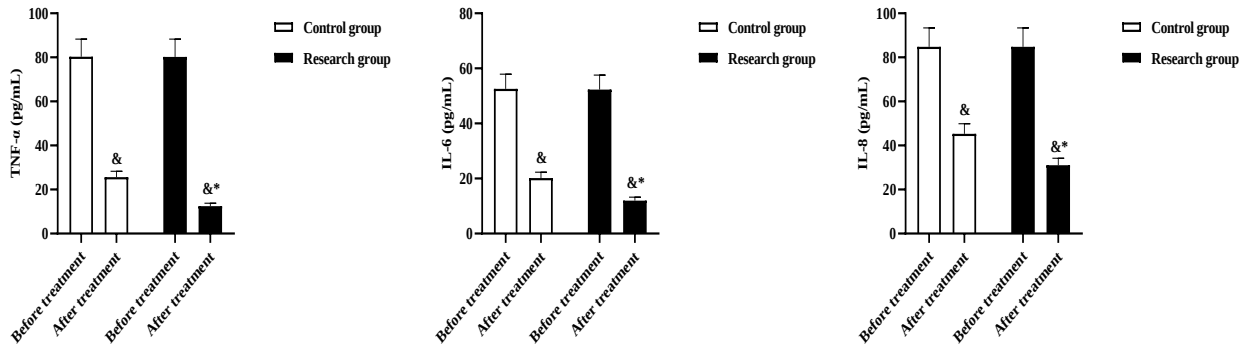

Figure 2: Levels of inflammatory cytokines in both groups. &P<0.05, compared to before treatment. *P<0.05, compared to the CG

Levels of inflammatory cytokines in both groups

As shown in Figure 2, the levels of TNF-α, IL-6, and IL-8 levels, there was no significant difference between both groups prior to treatment (P>0.05). Levels of the above inflammatory cytokines in both groups were declined after treatment (P<0.05). Importantly, relative to the CG, the RG had lower levels of the above inflammatory cytokines (P<0.05).

Table 3: Occurrence of adverse reactions in both groups (n, %)

Groups	Bone marrow suppression	Gastrointestinal reactions	Liver function damage	Cardiotoxicity	Total incidence rate
Control group (n=26)	4	2	2	1	9 (34.6%)
Research group (n=26)	1	0	1	0	2 (7.7%)
χ^2	5.7				
P	<0.05				

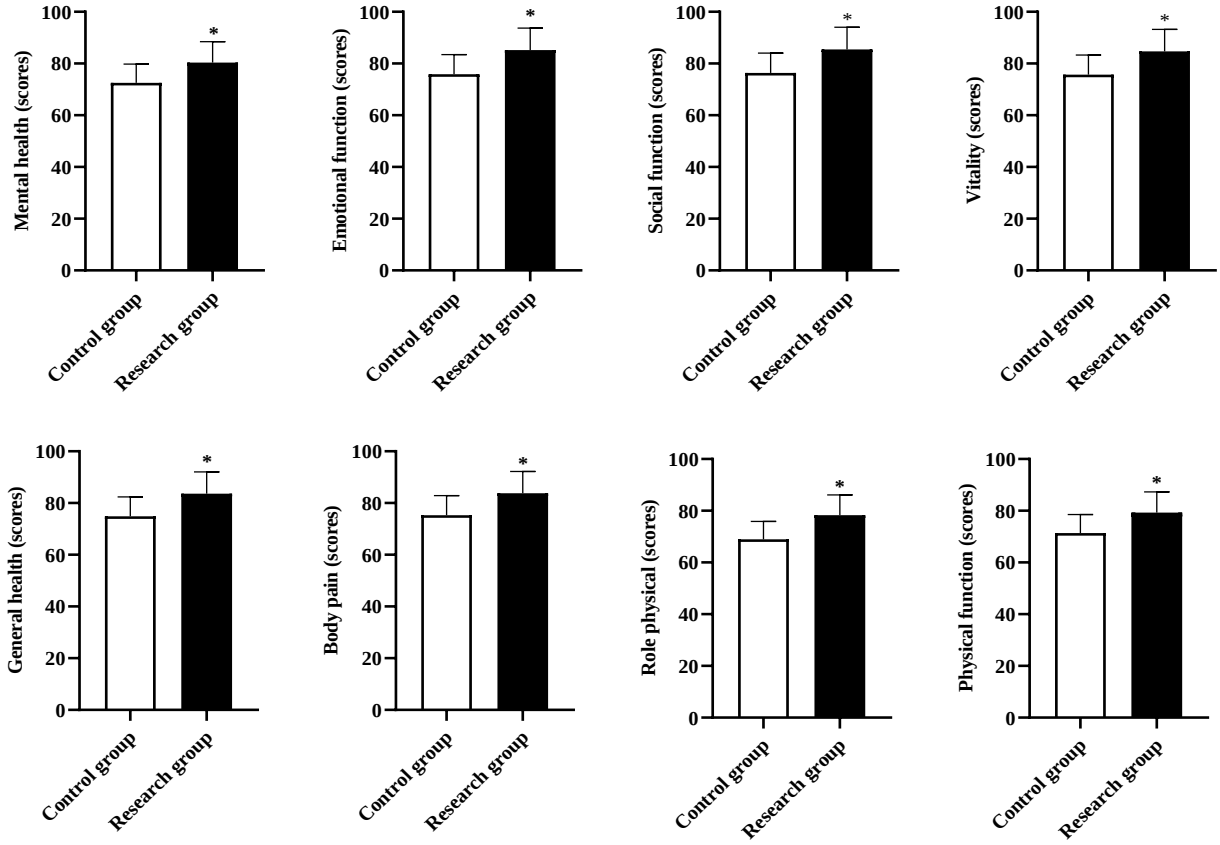

Figure 3: Quality of life scores in both groups. *P<0.05

Table 4: Long-term efficacy of patients in both groups (n, %)

Groups	5-year OS	5-year DFS
Control group (n=26)	11 (42.3%)	17 (65.4%)
Research group (n=26)	19 (73.1%)	23 (88.5%)
χ^2	5.0	3.9
P	<0.05	<0.05

Occurrence of adverse reactions in both groups

Relative to the CG, the RG had lower occurrence of adverse reactions (P<0.05, Table 3).

Quality of life in both groups

Relative to the CG, the RG had higher SF-36 scores on all dimensions at the end of treatment (P<0.05, Figure 3).

Long-term efficacy of patients in both groups

Relative to the CG, the RG had higher 5-year OS together with 5-year DFS (P<0.05, Table 4).

Discussion

In clinical practice, BC treatment is mainly surgical, supplemented by postoperative comprehensive treatment.[17] Chemotherapy is a systemic adjuvant treatment. Scientific and reasonable chemotherapy can significantly reduce or eliminate the primary BC and consolidate the surgical effect.[18]

HER2 is one of the oncogenes, which is closely linked to the prognosis of BC patients, and is one of the main targets for the selection of targeted therapeutic drugs.[19] The condition of HER2-positive BC patients changes greatly, progresses rapidly, and has a high degree of malignancy.[20] The disease-free survival (DFS) and overall survival (OS) of HER2-positive BC patients are significantly shorter than those of HER2-negative patients.[21] Docetaxel is an anti-tubulin depolymerizing drug, belonging to the taxol class. After entering the human body, it can combine with tubulin, destroy microtubule stability, and promote the phosphorylation of B cell lymphoma-2 (Bcl-2).[22] In addition, docetaxel can block the tumor cells in G2/M phase, repress the proliferation of cancer cells.[23] Trastuzumab is a human monoclonal antibody designed according to HER2, which can effectively antagonise the HER2 gene signal transduction pathway, significantly increase the antibody-dependent cell-mediated cytotoxicity, and effectively hinder the growth of tumor blood vessels.[24]

In this study, relative to the CG, the RG had higher objective response rate as well as disease control rate. Therefore, docetaxel combined with trastuzumab could achieve good results in treating HER2-positive BC patients. The level of tumor markers has a critical role in the development of tumors.[25] Carcinoembryonic antigen (CEA) is derived from epithelial tumors and is often used in combination of other indicators.[26] CEA expression in normal cells is low, when its concentration is significantly increased, it indicates that the patient is in the advanced stage of the tumor or has systemic metastasis.[27] Carbohydrate antigen 153 (CA153) is a recognized BC-associated antigen with high specificity.[28] Carbohydrate antigen 125 (CA125) is often used as a tumor marker in the female reproductive system.[29] Herein, after treatment, relative to the CG, the RG had lower CEA, CA125 along with CA153 levels, suggesting that docetaxel plus trastuzumab chemotherapy was more effective in reducing tumor marker levels in HER2-positive BC patients, which was also consistent with former studies.[30] Considerable clinical reports has built a strong relation between inflammation and HER2-positive BC development.[31] In this study, relative to the CG, the RG had lower interleukin-6 (IL-6), interleukin-8 (IL-8) and tumor necrosis factor-α (TNF-α) levels, which implied that docetaxel plus trastuzumab chemotherapy was more effective in reducing inflammatory response in HER2-positive BC patients. Moreover, relative to the CG, the RG had lower occurrence of adverse reactions, reflecting that the safety of combination therapy was relatively high. In addition, at the end of treatment, relative to the CG, the RG had higher SF-36 scores, higher 5-year OS as well as 5-year DFS, which demonstrated that docetaxel plus trastuzumab could significantly promote quality of life as well as prolong the survival time in HER2-positive BC patients.

Strengths and limitations

Strengths include studying the effect of docetaxel combined with trastuzumab chemotherapy on survival time of HER2-positive BC patients, which possesses important reference value for clinical

treatment. Limitations include a single center study and a small-scale population.

Conclusion

Docetaxel combined with trastuzumab chemotherapy can promote the clinical efficacy, lessen the levels of tumor markers and inflammatory cytokines, lessen the adverse reactions, and promote quality of life and survival time of HER2-positive BC patients, which possesses important reference value for clinical treatment.

Competing interests

The authors report no actual or potential conflicts of interest.

Contribution of authors

Jian Qian, Yunxia Xu: conceived and designed the study, as well as collected and analysed the data. Xiaokai Ling, Fenhua Wang: prepared the manuscript. All authors mentioned in the article approved the manuscript.

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