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**Original Research Article**

# Efficacy of epirubicin plus docetaxel or paclitaxel in the treatment of breast cancer

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## Abstract

***Purpose:*** *To determine the clinical efficacy of epirubicin plus docetaxel or paclitaxel in the management of breast cancer.*
***Methods:*** *This study was a randomized controlled trial that recruited 78 patients with breast cancer treated in The First People's Hospital of Anqing between December 2018 and March 2021. The participants were randomized to receive either epirubicin plus docetaxel (control group) or epirubicin plus paclitaxel (study group), with 39 cases in each group. Clinical outcomes, adverse events, quality of life, and prognosis of the two groups were compared.*
***Results:*** *Epirubicin plus paclitaxel produced greater efficacy than epirubicin plus docetaxel ($p < 0.05$). The combination also exhibited a higher safety profile versus epirubicin with docetaxel, as evidenced by lower incidences of nausea and vomiting, intestinal discomfort, muscle pain, and dyspnea reactions ($p < 0.05$). Epirubicin with paclitaxel resulted in greater improvement in quality of life in patients than epirubicin plus docetaxel ($p < 0.05$) as well as provided more benefits in terms of survival and recurrence control than epirubicin plus docetaxel ($p < 0.05$).*
***Conclusion:*** *Epirubicin/paclitaxel combination alleviates clinical symptoms, reduces adverse events, enhances patient prognosis, lowers the risk of postoperative recurrence, and provides superior quality of life when compared to epirubicin/docetaxel combination in breast cancer patients. Nonetheless, large-scale and better-randomized clinical trials are required to validate the findings of this study.*

***Keywords:*** *Epirubicin, Docetaxel, Paclitaxel, Breast cancer, Adverse effects*



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## INTRODUCTION

Breast cancer is a common gynecologic malignancy arising from the uncontrolled proliferation of breast epithelial cells [1]. Clinical data reveal the presence of advanced clinical features in patients first diagnosed with breast cancer, 30 – 40 % of whom experience rapid disease progression to locally advanced cancer mostly with metastasis. Moreover, breast cancer patients are prone to easy recurrence, a somber prognosis, and high mortality [2]. The prevalence of breast cancer has shown a rising trend among women across all age groups, posing a substantial health risk for women [3]. Research has found that female individuals with risk factors have a higher incidence rate of breast cancer,

while male patients only account for a very small percentage [4].

The absence of specific early symptoms of breast cancer frequently causes delayed diagnosis and unhampered disease progression, which complicate the clinical treatment [5]. Chemotherapy was highly encouraged for patients with advanced breast cancer to preoperatively reduce tumor size and facilitate radical tumor resection. Clinical research has shown that neoadjuvant chemotherapy reduces the primary tumor lesions, shortens the clinical stage of tumors, increases the feasibility of surgery, and prolongs the survival of patients [6]. Hence, there exists an urgent need to look for a safer and more effective multi-drug regimen to provide better therapeutic benefits. Epirubicin is a common anthracycline anticancer drug that interferes with DNA and RNA synthesis [7]. Docetaxel inhibits microtubule depolymerization and enhances microtubule polymerization. Paclitaxel is a common anti-tubulin drug that can arrest breast cancer cells in the G2/M phase and induce cancer cell death, thereby providing a good antitumor activity [8]. A combination of therapeutic interventions offers maximum therapeutic benefits while minimizing or eliminating disease recurrence, drug resistance, and toxic side effects, and ensuring a good quality of life. The present study was performed to compare the clinical efficacy of epirubicin plus docetaxel or paclitaxel in the clinical management of breast cancer.

## METHODS

### Study design

This study was a randomized controlled trial recruiting 80 patients with breast cancer treated in The First People's Hospital of Anqing between December 2018 and March 2021 for analysis. The 78 participants were randomized to receive either epirubicin plus docetaxel (control group) or epirubicin plus paclitaxel (study group), with 39 cases in each group.

### Ethical matters

The study was approved by the ethics committee of The First People's Hospital of Anqing (approval no. AQ02301) and was conducted in strict compliance with the Declaration of Helsinki [9]. All patients signed the consent form.

#### *Inclusion criteria*

Female patients who were pathologically diagnosed with breast cancer and had not received chemotherapy six months before enrollment, with good tolerance to chemotherapy and good compliance to therapy were included.

#### *Exclusion criteria*

Patients with allergies to the studied drugs, abnormal liver, and kidney function, autoimmune system diseases, or a history of psychiatric diseases were excluded.

### Treatments

All patients were routinely examined upon admission and given prophylactic medication. Patients in the control group received epirubicin (Guodianzhi H20000496, Pfizer Pharmaceutical Co., Ltd.) at a dose of 60 mg/m$^2$ through intravenous drip within 30 min and docetaxel (Guodianzhi H20093738, Beijing Union Pharmaceutical Co., Ltd.), at a dose of 75 mg/m$^2$, dissolved in 250 mL of normal saline (Guodianzhi H61022096, Xi'an Anjian Pharmaceutical Co., Ltd.) through intravenous drip, and the administration duration was kept within 30-60 min. The treatment was performed once daily for 3 weeks.

Patients in the study group received epirubicin (consistent with the control group) plus paclitaxel liposomes (Guo medicine quanzhi H10980068, Beijing Xiehe Pharmaceutical factory) at a dose of 175 mg/m$^2$ dissolved in 500 mL of 5 % glucose solution (GuoPharm QuanZi H61022096, Xi'an AnJian Pharmaceutical Co., Ltd.) through intravenous drip, and the administration duration was kept within 200 min. The patients were closely monitored in terms of heart rate, respiration, and blood pressure. The treatment was performed once daily for 3 weeks.

### Determination of parameters/indices

The treatment efficacy was evaluated according to the Evaluation Criteria for Treatment Efficacy of Solid Tumors and was classified as complete (C) remission (disappearance of all visible lesions for more than 4 weeks), partial (P) remission (tumor shrinkage of more than 50 % for more than 4 weeks without new lesions), mild (M) remission (tumor shrinkage between 25 and 50 % without new lesions), stable disease (tumor shrinkage or enlargement of 25 % or less without new lesions), and progressive disease (tumor enlargement of over 25 %). Tumor remission rate (Tr) was calculated using Eq 1.

$$Tr = \{(C+P+M)/T\}100 \quad \ldots\ldots. (1)$$

where T = total number of cases

Adverse events, including anemia, diarrhea, alopecia, rash, phlebitis, nausea and vomiting, intestinal discomfort, muscle pain, dyspnea, leukopenia, thrombocytopenia, and elevated glutamate transaminase, were recorded.

The quality of life of all patients was evaluated by the Quality-of-Life Measurement Scale short form. High scores indicate better quality of life. The patients were followed up for one year to document their survival and recurrence data.

### Statistical analysis

The data of this study were analyzed using SPSS 22.0, and GraphPad Prism 8 was used to plot graphics. Measurement data are expressed as mean ± standard deviation (SD) and tested using *t*-test. Count data was expressed as the n (%) and tested using chi-square ($\chi^2$) test. Statistically significant differences were indicated at $P < 0.05$.

## RESULTS

### Baseline patient profiles

In the control group, there were 39 patients comprising 31 married patients and 8 unmarried patients, aged 30 – 65 years, with a body weight of 58.21 ± 8.31 kg, BMI of 23.58 ± 2.55 kg/m$^2$, disease duration of 1 - 12 years, TNM stage II in 31 cases, stage III in 8 cases, tumor diameter of 2.3 - 7.8 cm, 29 cases of invasive ductal carcinoma, 8 cases of invasive lobular carcinoma, and 2 cases of medullary carcinoma. In the study group, there were 29 patients, 10 married cases and 8 unmarried cases, aged 30 - 65 years, with a body weight of 58.47 ± 8.01 kg, BMI of 23.41 ± 2.32 kg/m$^2$, disease duration of 1 - 12 years, TNM stage II in 32 cases, stage III in 7 cases, tumor diameter of 2.3 - 8.0 cm, 28 cases of invasive ductal carcinoma, 10 cases of invasive lobular carcinoma, and 1 case of medullary carcinoma. The two groups were well-balanced in terms of baseline patient profiles ($p > 0.05$) (Table 1).

### Clinical outcomes

In the control group, there were 5 cases of complete remission, 11 cases of partial remission, 13 cases of mild remission, 6 cases of stable disease, and 4 cases of progressive disease, with an overall remission rate of 74.36 %. In the study group, there were 11 cases of complete remission, 14 cases of partial remission, 12 cases of mild remission, 1 case of stable disease, and 1 case of progressive disease, with an overall remission rate of 94.87 %. Epirubicin plus paclitaxel was associated with markedly potent treatment efficacy versus epirubicin plus docetaxel ($p < 0.05$) (Figure 1).

### Incidence of adverse events

Epirubicin plus paclitaxel exhibited a higher safety profile than epirubicin plus docetaxel ($p < 0.05$; Table 2).

**Table 1:** Patient characteristics (n = 39)

| Parameter | | Control group | Study group | $t/x^2$ | *P*-value |
|---|---|---|---|---|---|
| Marriage | Married | 31 | 29 | 0.289 | 0.591 |
| | Unmarried | 8 | 10 | - | - |
| Age (year) | - | 30-65 | 30-65 | - | - |
| | Mean | 40.44±8.17 | 40.87±8.26 | 0.231 | 0.818 |
| Weight (kg) | | 58.21±8.31 | 58.47±8.01 | 0.141 | 0.888 |
| BMI (kg/m$^2$) | | 23.58±2.55 | 23.41±2.32 | 0.308 | 0.759 |
| Disease course (year) | - | 1-12 | 1-12 | - | - |
| | Mean | 5.08±0.32 | 5.11±0.28 | 0.441 | 0.660 |
| TNM stage | Ⅱ | 31 | 32 | 0.083 | 0.774 |
| | Ⅲ | 8 | 7 | - | - |
| Tumor diameter (cm) | - | 2.3-7.8 | 2.3-8.0 | - | - |
| | Mean | 5.17±2.01 | 5.23±2.04 | 0.131 | 0.896 |
| Pathology | Invasive ductal carcinoma | 29 | 28 | 0.065 | 0.799 |
| | Infiltrating lobular carcinoma | 8 | 10 | - | - |
| | Medullary carcinoma | 2 | 1 | - | - |

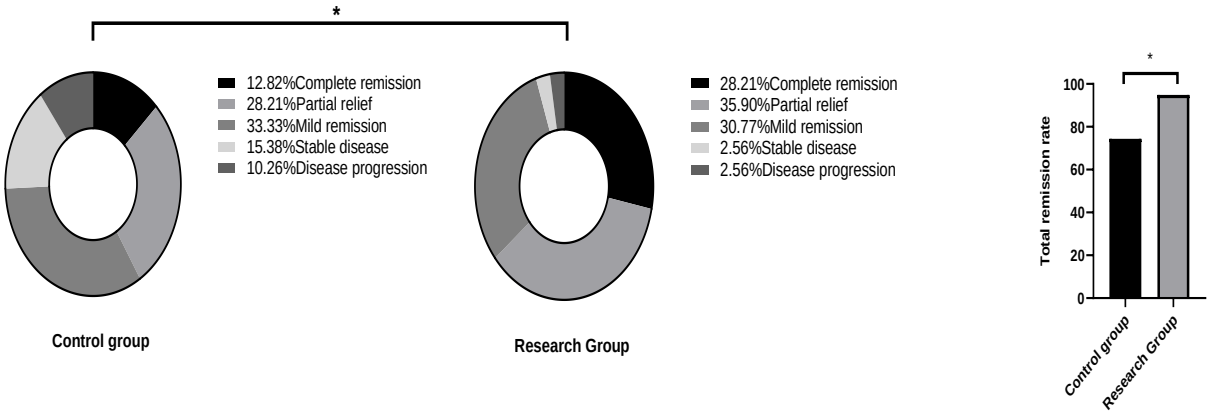


**Figure 1**: Clinical efficacy. Note: * indicates P<0.05 when compared with the control group

**Table 2:** Adverse events (n=39)

| Parameter | Control group | Study group | $x^2$ | *P*-value |
|---|---|---|---|---|
| Anemia | 7 | 3 | 1.835 | 0.176 |
| Diarrhea | 5 | 2 | 1.412 | 0.235 |
| Hair loss | 14 | 8 | 2.279 | 0.131 |
| Skin rash | 2 | 1 | 0.347 | 0.556 |
| Phlebitis | 11 | 6 | 1.880 | 0.170 |
| Nausea and vomiting | 20 | 4 | 15.407 | <0.001 |
| Intestinal discomfort | 13 | 2 | 9.987 | 0.002 |
| Muscle pain | 9 | 2 | 5.186 | 0.023 |
| Breathing difficulties | 7 | 1 | 5.014 | 0.025 |
| Leukopenia | 9 | 6 | 0.743 | 0.389 |
| Thrombocytopenia | 8 | 7 | 0.083 | 0.774 |
| Elevated glutamate transaminase | 6 | 4 | 0.459 | 0.498 |

## Quality-of-life

The quality-of-life scores of patients in the control group were 50.41 ± 5.14 before and 57.98 ± 4.94 after treatment, and those in the study group were 50.38 ± 4.98 before and 68.41 ± 4.52 after treatment. Epirubicin with paclitaxel resulted in more improvement in quality of life in patients than epirubicin plus docetaxel ($p < 0.05$, Figure 2).

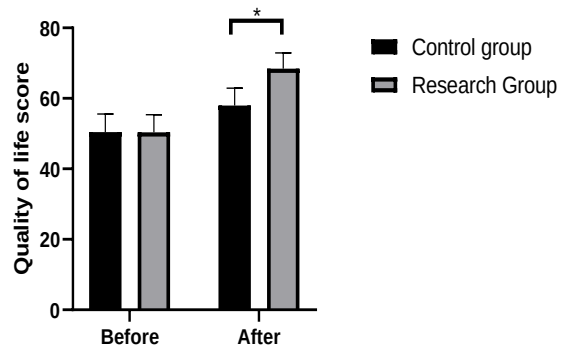


**Figure 2:** Quality of life. Note: *$P < 0.05$ when compared with the control group

## Clinical prognosis

In the control group, there were 26 survivors and 11 cases of recurrence within 1 year, and in the study group, there were 36 survivors and 3 cases of recurrence within 1 year. Epirubicin plus paclitaxel provided more benefits in survival and recurrence control than epirubicin plus docetaxel ($p < 0.05$) (Figure 3).

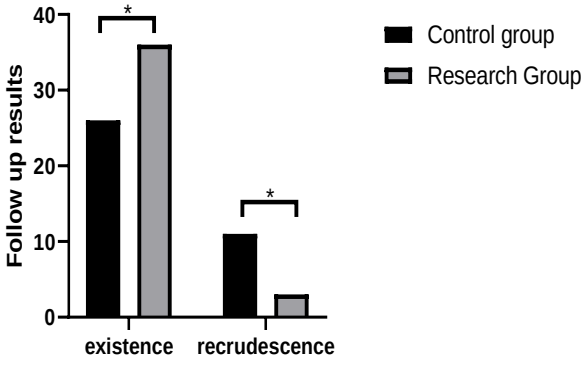


**Figure 3**: Clinical prognosis.
Note: *$P < 0.05$ when compared with the control group

## DISCUSSION

Breast cancer is associated with numerous high-risk factors, including emotional depression, premature menopause, obesity, long-term large-scale use of exogenous estrogens, poor lifestyle habits, abortions, and a family history of breast cancer. Common clinical symptoms of breast cancer include chest fracture, exudation, infiltration, breast swelling, bone pain, and chest pain [10]. Untimely interventions may result in rapid disease progression and high mortality in patients.

Neoadjuvant chemotherapy is a systemic and systemic oncology treatment prior to local breast cancer treatment; it reverses the clinical stage of cancer, inhibits tumor metastasis and resistance to cancer cell drugs, and provides drug sensitivity information and a basis for a rational chemotherapy regimen selection after surgery. A previous clinical trial suggested that neoadjuvant chemotherapy with epirubicin plus docetaxel improved the treatment outcome in breast cancer patients [11].

Epirubicin is an anthraquinone compound with promising antitumor effects and high safety. Paclitaxel is a complex secondary metabolite of Erythroxylon with a long half-life, easy uptake by human cells, and long intracellular residence time. It suppresses the differentiation and depolymerization of cancer cells, promotes tubule aggregation, and exerts anti-tumor effects [12].

In the current investigation, paclitaxel was substituted with paclitaxel liposomes. This choice was made based on the fact that paclitaxel liposomes are enclosed by cholesterol and bilayer phospholipid molecules, which greatly improve the histocompatibility and stability of the drug, impart strong cellular affinity, and exhibit no immune response after intravenous administration. Furthermore, paclitaxel liposomes exhibit a potent inhibitory effect on cancer cells with low toxicity [13].

In this study, epirubicin plus paclitaxel resulted in better efficacy and a higher safety profile than epirubicin plus docetaxel. The findings of this study indicate that paclitaxel provides greater mitigation of adverse events for breast cancer than docetaxel. Epirubicin decelerates nucleic acid formation and intercalates DNA base pairs within cells upon entering the nucleus, leading to the inhibition of mRNA formation, as well as mitosis and nucleic acid synthesis. Additionally, it inhibits tumor DNA polymerase α and DNA polymerin β, ultimately resulting in tumor cell death and exerting excellent anti-tumor effects. Furthermore, its low cardiotoxicity results in mild adverse events and side effects [14].

Paclitaxel is a novel botanical antitumor drug with strong histocompatibility, drug stability, and cellular affinity [15,16]. It rapidly binds to the B site in the vasculature and controls cell mitosis and differentiation. Cells in contact with paclitaxel accumulate massive microtubules, which disrupt tumor cell function and prevent tumor cell division during mitosis, thereby inducing cancer cell death [17,18]. Similar to paclitaxel, docetaxel exerts its anticancer effects by disrupting the microtubule network required for cytokinesis and cell mitosis. The paclitaxel liposomes used in this study showed significant improvement in drug stability, histocompatibility, and cellular affinity due to their encapsulation by phospholipid and cholesterol molecules. Hence, the chemotherapy regimen of paclitaxel liposomes plus epirubicin shows promising effectiveness in enhancing chemotherapeutic outcomes without eliciting side effects.

This research has shown that epirubicin with paclitaxel reduced the incidence of shortness of breath, rash, nausea and vomiting, and muscle pain in patients than with docetaxel. Furthermore, epirubicin with paclitaxel resulted in good improvement in quality of life, survival, and recurrence control benefits than when compared with epirubicin plus docetaxel. This may be attributed to the ability of paclitaxel to maintain high intracellular drug concentrations, which contributes to prolonging patient survival and preventing tumor recurrence, thereby improving patient quality of life. The current research results evinced the potent efficacy of paclitaxel plus epirubicin in breast cancer management with high safety and patient tolerability. Current clinical studies also suggest that breast cancer patients experience high remission rates with chemotherapy and a favorable long-term prognosis.

### Limitations of this study

During probability/random sampling, the sample may not be fully representative of the study population, and there may be "sampling bias" or "selection bias". The present study also lacks effective observation and long-term follow-ups.

## CONCLUSION

Epirubicin with paclitaxel effectively alleviates clinical symptoms, reduced adverse events, enhanced patient prognosis, lowered the risk of postoperative recurrence, and provided superior

quality of life for patients. Future studies on a larger scale, with long-term follow-up and a modified sampling technique will be required to provide more reliable data.

## DECLARATIONS


### *Acknowledgements*

None provided.

### *Funding*

None provided.


### *Ethical approval*

The study was approved by the ethics committee of The First People's Hospital of Anqing (approval no. AQ02301).

### *Availability of data and materials*

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### *Conflict of Interest*

No conflict of interest associated with this work.

### *Contribution of Authors*

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

### *Open Access*



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