INPLASY PROTOCOL

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Corresponding author:
Boni Ding

dingboni@aliyun.com

Author Affiliation:
Central South University

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Influence of different order of taxanes and anthracyclines on the neoadjuvant chemotherapy for breast cancer: a Systematic review and meta-analysis

Qiu, J[1]; Ding, B[2]; Qian, L[3]; Wu, W[4]; Wen, Y[5].

Review question / Objective: **To evaluate the effect of the influence of the medication administration sequence of taxanes and anthracyclines on the therapeutic effect during neoadjuvant chemotherapy for breast cancer.**
Condition being studied: **At present, the main treatments for breast cancer include surgery, chemotherapy, radiotherapy and bio-targeted therapy, chemotherapy is the most commonly used method and one of the most effective methods.The chemotherapy scheme containing anthracyclines and taxanes has reduced the 10-year mortality rate of breast cancer by about one third.In order to improve the therapeutic effect of tumor, a combination chemotherapy of two or more drugs is often used in clinic.However, the combination of drugs may affect the therapeutic effect and toxicity of chemotherapy due to the interaction between drugs or the cycle specificity of anticancer drugs.In clinic,there is also a phenomenon of neglecting the medication order of drug.Therefore, the correct medication order is an important part of promoting the rational use of tumors.**

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INTRODUCTION

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METHODS

Participant or population: Breast cancer patients receiving neoadjuvant therapy.

Intervention: Different order of taxanes and anthracyclines on the neoadjuvant chemotherapy for breast cancer.

Comparator: Control group.

Study designs to be included: Randomized controlled trials(RCTs).

Eligibility criteria: Including all neoadjuvant chemotherapy literatures comparing the Influence of different order of taxanes and anthracyclines on the neoadjuvant chemotherapy for breast cancer.

Information sources: According to the inclusion and exclusion criteria, two researchers independently and strictly searched and screened the included literature. The databases (PubMed, Cochrane Library, Embase, CNKI, WanFang) were searched for the related studies that met the requirements.

Main outcome(s): The 5-year Overall survival(OS),5-year Disease-free survival(DFS),pathological complete response (PCR), Breast-conserving rate,objective response rate(ORR)、disease control rate(DCR),treatment adherence and toxic side effects rate were analyzed as main outcomes.

Quality assessment / Risk of bias analysis: According to the "bias risk assessment tool" recommended by Cochrane Handbook for systematic reviews of interventions version 5.1.0 to evaluate the quality of the included randomized controlled studies.The evaluation indexes include:random sequence generation, allocation concealment, blinding of participants and personnel,blinding of outcome assessment, incomplete outcome data, selective reporting, other bias.Cases of disagreement would be resolved by discussion and third parties would render assistance when necessary.

Strategy of data synthesis: Use Revman 5.3 software to analyze the extracted data. Compare OS, DFS, PCR, breast-conservation rate, ORR, DCR, treatment adherence, and toxic side effects rate in different order of taxanes and anthracyclines. This meta-analysis is an analytical study, using RR and 95% CI as the effect analysis statistics.The Q statistic test and I2 statistic test in Cochrane were used to analyze the heterogeneity of the included studies. Firstly, $\chi 2$ test was used to analyze the heterogeneity between the results of each study and the test level was set as $\alpha=0.100$. At the same time, the size of heterogeneity was determined by combining I2.If $P>0.100$ and $I2\leq 50\%$, it indicates that the homogeneity between the research results is better and the fixed effect model is used; if $P\leq 0.100$ and/or $I2>50\%$, it indicates that the heterogeneity between the results is statistically significant, then use a random effect model and analyze its heterogeneous sources at the same time.

Subgroup analysis: The characteristics of subgroup analysis were implemented to explain the sources of heterogeneity to the greatest extent possible.

Sensibility analysis: Sensitivity analyses were performed by omitting one study at a time to assess their influence (leave-one-out analysis) and to seek the sources of

heterogeneity,when the source of heterogeneity cannot be resolved or determined.

Country(ies) involved: China.

Keywords: Breast cancer; neoadjuvant chemotherapy; taxanes; anthracyclines; medication administration sequence; meta-analysis.

Contributions of each author:
Author 1 - First author of this study, study selection, data extraction, data analysis, draft the manuscript.
Author 2 - Corresponding author of this study, project, study selection, data extraction, data analysis and writing.
Author 3 - Study selection, data extraction, writing.
Author 4 - Data extraction, data analysis and writing.
Author 5 - Data extraction and writing.