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Systematic Review

Factors Influencing Pharmacokinetics of Tamoxifen in Breast Cancer Patients: A Systematic Review of Population Pharmacokinetic Models

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Simple Summary: Breast cancer is the most common type of cancer in women. Tamoxifen is the most preferred drug used to treat breast cancer. It has been reported that tamoxifen and its metabolites have significant variability in their pharmacokinetics. This systematic review identified five population pharmacokinetic model studies for tamoxifen. These studies were summarized, and various factors affecting tamoxifen's and its metabolites pharmacokinetics have been reported in this review. Most studies reported a two-compartment model with first-order absorption and elimination. Various factors, such as genetic variation, age, gender, BMI, co-medication, and postmenopausal status are reported to affect the disposition of tamoxifen and its metabolites. So, while addressing the pharmacokinetic variability of this drug, all these factors must be considered. These models should be externally evaluated to verify the model's generalizability and for model-informed dosing in the clinical setup.

Abstract: Background: Tamoxifen is useful in managing breast cancer and it is reported to have significant variability in its pharmacokinetics. This review aimed to summarize reported population pharmacokinetics studies of tamoxifen and to identify the factors affecting the pharmacokinetics of tamoxifen in adult breast cancer patients. Method: A systematic search was undertaken in Scopus, Web of Science, and PubMed for papers published in the English language from inception to 20 August 2022. Studies were included in the review if the population pharmacokinetic modeling was based on non-linear mixed-effects modeling with a parametric approach for tamoxifen in breast cancer patients. Results: After initial selection, 671 records were taken for screening. A total of fivestudies were selected from Scopus, Web of Science, PubMed, and by manual searching. The majority of the studies were two-compartment models with first-order absorption and elimination to describe tamoxifen and its metabolites' disposition. The CYP2D6 phenotype and CYP3A4 genotype were the main covariates that affected the metabolism of tamoxifen and its metabolites. Other factors influencing the drug's pharmacokinetics included age, co-medication, BMI, medication adherence, CYP2B6, and CYP2C19 genotype. Conclusion: The disposition of tamoxifen and its metabolites varies primarily due to the CYP2D6 phenotype and CYP3A4 genotype. However, other factors, such as anthropometric characteristics and menopausal status, should also be addressed when accounting for this variability. All these studies should be externally evaluated to assess their applicability in different populations and to use model-informed dosing in the clinical setting.

Keywords: tamoxifen; systematic review; population pharmacokinetics; breast cancer

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