Molecular and Histological Study of the Single and Combined Effects of Trastuzumab and Docetaxel on Fetal Rat Liver

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ABSTRACT

Background: Trastuzumab (TZM) and docetaxel (DTX) are commonly employed in the treatment of breast cancer. This study aimed to investigate the histopathological and molecular effects of TZM and DTX alone and in combination on fetal rat liver.

Materials and Methods: Forty pregnant albino rats were divided into four equal groups. Group 1 was used as the control group and injected with normal saline only. Group 2 (TZM alone) was injected subcutaneously with TZM at a dose of 10 mg/kg body weight. Group 3 (DTX alone) was injected intraperitoneally with DTX at a dose of 15 mg/kg body weight. Group 4 (TZM and DTX combination) was injected with a combination of TZM (10 mg/kg) and DTX (15 mg/kg). All groups were injected on the 6th day of gestation. The pregnant rats from the control and treated groups were sacrificed on day 19 of gestation.

Results: As demonstrated in our study, the histological examination of fetal liver sections of the TZM alone (Group 2) and DTX alone (Group 3) revealed several histopathological alterations, while the TZM and DTX combination (Group 4) showed severe histopathological lesions of hepatic cords and their vasculatures. On the molecular level, the results of this study revealed many mutation types in exon 1 of the BCL2 gene, such as deletion, transition, and transversion after exposure to DTX alone and a combination of TZM and DTX, but the mutation level was higher in the combination treatment, while in exon 24 of the ErbB2/HER2 gene no mutation had occurred.

Conclusion: These findings confirmed the occurrence of a synergistic effect between TZM and DTX, which caused more severe damage to the liver of albino rat fetuses than the effect of either therapy alone and increased DNA mutation levels.

Keywords: Trastuzumab, docetaxel, fetal liver

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