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EFFECT OF AROMATASE INHIBITORS ON BONE TURNOVER MARKERS IN VINYL CYCLOHEXENE DIEPOXIDE TREATED OVOTOXIC FEMALE MICE

Background and Aim: The third generation aromatase inhibitors are currently the drugs of choice for treatment of early and advanced breast cancer in postmenopausal women (1). One of the significant limiting factor during therapy is their negative impact on bone health (2). In the present study, we compared the effects of a non-steroidal (letrozole) and a steroidal aromatase inhibitor (exemestane) on markers of bone turnover in vinlycyclohexene di epoxide (VCD)-induced ovotoxic female mice.

Method: Ovotoxicity was developed by VCD (vinlycyclohexene di epoxide) administration for 15 days followed by a drug-free period of 30 days which mimicked a postmenopausal state and it was confirmed by significant reduction of primary ovarian follicles and reduced serum estradiol levels.

Result and Discussion: Ovotoxicity was accompanied by reduced alkaline phosphatase (ALP) and hydroxyproline (HxP) and enhanced tartrate-resistant acid phosphatase activity in femoral epiphysis and lumbar vertebrae of mice. Letrozole (1mg/kg) treatment for one month enhanced bone turnover in ovotoxic mice. Exemestane (3.25 mg/kg) administration was devoid of such effects in both normal and ovotoxic mice. It, however, reduced ALP in femoral epiphysis of ovotoxic mice. In addition, letrozole depleted estradiol levels in ovotoxic mice and enhanced receptor activator of nuclear factor kappa-B ligand (RANKL) activity while exemestane neither affected estradiol nor RANKL in both normal and ovotoxic mice. Further, ovotoxic and letrozole treated animals exhibited higher sclerostin and DKK-1 in femoral epiphysis and lumbar bones. Exemestane enhanced sclerostin and DKK-1 in femoral epiphysis only but not in lumbar bones. Results are expressed as mean± SEM and were compared using one way analysis of variance with Tukey's post hoc test.

Conclusion: The study indicates that the two aromatase inhibitors possesses differential profile in terms of their effects on bone and that exemestane could be a better option for the treatment of breast cancer in postmenopausal women at least in terms of its effects on bone.

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