EFFECTS OF PHARMACEUTICALS USED FOR BREAST CANCER TREATMENT ON REPRODUCTION AND AROMATASE ACTIVITY IN A MARINE FISH

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Laboratory experiments were conducted with the marine fish cunner (*Tautogolabrus adspersus*) to evaluate whether four pharmaceuticals used in breast cancer treatment have an impact on reproduction or aromatase activity. Tamoxifen binds to estrogen receptors, while anastrozole, letrozole and exemestane are all aromatase inhibitors. Aromatase, a key enzyme in estrogen biosynthesis, is critical to normal reproduction in fish, just as in mammals. Spawning cunner were treated with tamoxifen (0, 0.5 or 5 mg/kg) or one of the three aromatase inhibitors (0, 75 or 750 µg/kg) administered by oral gavage on days 0, 4, 8, 12 and 16 of each experiment. Egg production, viability and fertility were determined daily. On day 17, gonadosomatic index (GSI) was determined, and brain and ovary tissues were flash-frozen for later analysis of aromatase activity. In tamoxifen-treated fish, egg production was significantly reduced, but downward trends in egg fertility and viability were not significant. Ovarian aromatase activity was significantly increased in fish treated with 5 mg/kg tamoxifen. Of the aromatase inhibitors, anastrozole and letrozole significantly decreased egg production in fish treated with the high concentration (750 µg/kg), while exemestane had no effect. There was no effect on egg fertility or viability in fish treated with any aromatase inhibitor. Female GSI was significantly reduced in the anastrozole treatments, significantly increased in 75 µg/kg letrozole treatment, and unaffected by exemestane treatment. Effects on aromatase activity were variable depending on treatment and tissue (brain or ovary). For example, in fish treated with anastrozole, aromatase activity was significantly decreased in brains, while activity was increased in ovaries. Results indicate tamoxifen and aromatase inhibitors can impact fish reproduction. The effect of these pharmaceuticals on aromatase activity appears to be chemical- and tissue-specific.