Advanced breast cancer systemic therapy

THE POSSIBLE RESOLUTION OF TAMOXIFEN-INDUCED HOT FLASH BY COMBINATION WITH RISPERIDONE IN BREAST CANCER PATIENTS WITHOUT INTERFERING WITH THE EFFICACY OF TAMOXIFEN

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Hot flashes are a major problem for breast cancer patients. It has been reported that approximately 65% of women after treatment for breast cancer experiencing hot flashes, and the incidence is even higher among tamoxifen users. Hot flashes can not only greatly decrease quality of life, but they may lead to discontinuation of cancer therapies. Selective serotonin reuptake inhibitor (SSRIs) antidepressants are one of the most commonly prescribed options for hot flashes in breast cancer patients. Unfortunately, many SSRIs such as fluoxetine, are known to inhibit cytochrome P450 2D6 (CYP2D6) which is an essential isoenzyme for tamoxifen metabolism. The inhibition of CYP2D6 decreases tamoxifen metabolism, resulting in increased rates of breast cancer recurrence and mortality. Fortunately, risperidone, an anti-psychotic drug, has been proofed for treating hot flashes in hysterectomy, menopause, and perimenopause women, and it does not inhibit CYP2D6 activity. In this paper, we found that in combination with risperidone, tamoxifen-induced growth inhibition of T47D human breast cancer cells was not interfered with by risperidone while fluoxetine antagonized this effect. Cell cycle analysis and protein expression of cell cycle regulators cyclinD1, p21, and c-Myc were also examined, and none of these effects were influenced by coadministration of risperidone. Nevertheless, fluoxetine abrogated tamoxifen-induced G0/G1 arrest and down-regulation of cell cycle regulators. This is the first paper suggesting the possibility of combination treatment of tamoxifen and risperidone for hot flashes in breast cancer patients without interfering with the efficacy of tamoxifen.

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