Do antidepressants interact with tamoxifen?

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Background:

Breast cancer (BC) is the **most common** cancer in women worldwide with 2 million new cases in 2018. **Tamoxifen** is a selective oestrogen receptor modulator used in patients with early stage oestrogen receptor positive BC, **reducing** the risk of BC **recurrence** and **death**. It is an inactive pro-drug which is metabolised by the cytochrome P450(CYP)2D6 to its main active metabolite **endoxifen**, with 100-fold more affinity for the oestrogen receptor (Figure 1).

Figure 1. Tamoxifen conversion to endoxifen by CYP2D6

BC has a known significant **negative impact** in women's **physical** and **psychological** wellbeing. Anxiety and depressive symptoms frequently appear, with up to **one-quarter** of women with BC being diagnosed with **depressive disorder**.

Newer **antidepressants** are an important therapeutic option to treat these conditions, being also prescribed for tamoxifen-related hot flashes. However pharmacokinetic drug interactions between hormone therapy and antidepressants may exist.

Aims:

The aim of this study is to systematically review the current scientific literature regarding the interactions between antidepressants and tamoxifen.

Methods:

The authors used the search engine PubMed® and selected all the articles published in English in the last ten years with the words “tamoxifen” and “antidepressants” in the title and/or abstract.

Results:

- Drugs known to be potent **CYP2D6 inhibitors** **decrease** endoxifen plasma level and compromise hormone therapy efficiency.
- Selective serotonin reuptake inhibitors (**SSRIs**) and serotonin and norepinephrine reuptake inhibitor (**SNRIs**) are commonly prescribed for treatment of depressive and anxiety disorders and they are known to **inhibit CYP2D6** to varying degrees **reducing endoxifen** plasma levels.
- **Strong CYP2D6 inhibitors** include **paroxetine**, **fluoxetine** and **bupropion** and they must be avoided
- **Paroxetine** is associated to tamoxifen **treatment failure**, leading to a **higher** risk of breast cancer **recurrence** and increased **mortality**.
- The risk is related to the **duration** of co-exposure.
- Antidepressants that are **weak CYP2D6 inhibitors** do not lower the concentration of endoxifen and include **venlafaxine**, **sertraline** and **citalopram**
- These drugs are safer and must be rather **preferred** as reasonable choices.

Conclusions:

Pharmacokinetics **interactions** must be considered whenever prescribing **antidepressant** drugs in tamoxifen-treated patients since some of these psychotropic drugs can significantly **impact** the **prognosis** of **cancer disease**.