一般的な抗うつ薬のタモキシフェンの有効性に関する影響
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ホットフラッシュの治療に一般的に用いられる抗うつ薬が乳がん再発予防目的に使用されるタモキシフェンの有効性に影響するか否かに関するスタディの結果は一致していない

Studies report mixed findings on whether antidepressants commonly used to treat hot flashes impact effectiveness of tamoxifen for preventing breast cancer recurrence

第45回American Society of Clinical Oncology学会で発表された、2D6阻害薬がタモキシフェンの乳がん再発予防効果を低下させるか否かについての二つのレトロスペクティブスタディの結果は異なっていた。ホットフラッシュ治療にタモキシフェンと同時に用いられる最も一般的な2D6阻害薬は、抗うつ薬のfluoxetineおよびパロキセチンである。一つのスタディでは、米国の薬剤給付管理会社Medcoのデータベースで、乳がん治療を受けその後再発予防目的でタモキシフェンを投与された女性を調査した。タモキシフェンのみを内服した患者の2年間の再発率は7.5%であり、一方タモキシフェンと2D6阻害薬の両者を内服した女性（両薬剤の平均重複内服期間は255日）の再発率は13.9%であった。これらの結果から抗うつ薬SSRIがタモキシフェン療法の有効性を低下させる可能性が示唆された。他のスタディではオランダの3つのデータベースを解析し、早期乳がんの手術後にタモキシフェンを投与された女性1,962人を抽出した。タモキシフェンのみを内服した女性または2D6阻害薬内服期間が60日未満であった女性（1,812人）の再発率は14.6%であった。一方タモキシフェンを2D6阻害薬と同時に内服した期間が60日以上であった患者（150人）の再発率は13.3%であった。これらの相違を解決するにはさらなるリサーチが必要である。

Full Text

Hot flashes are a common side effect of tamoxifen treatment to prevent breast cancer recurrence, and are often managed with the antidepressant drugs fluoxetine and paroxetine. Two retrospective studies report mixed results on whether 2D6 inhibitors reduce the effectiveness of tamoxifen for preventing breast cancer recurrence. Additional research is needed to resolve these differences, though women may want to consider alternative antidepressants in the meantime.

In the body, tamoxifen is broken down to several active compounds; endoxifen is one of the most biologically active of these metabolites. Previous research has shown women who have a gene mutation that prevents them from making the 2D6 enzyme, which converts tamoxifen to endoxifen, do not get the same benefit from tamoxifen as women with a normal version of the gene. Other studies have suggested that drugs that inhibit the 2D6 enzyme reduce blood levels of endoxifen in women taking tamoxifen.

2D6 inhibitors include a variety of drugs, but the two most common are fluoxetine and paroxetine. These drugs, known as selective serotonin reuptake inhibitors (SSRIs), have often been prescribed to reduce hot flashes caused by tamoxifen. Similar drugs can be used to treat both hot flashes and depression that do not inhibit 2D6.

U.S. study finds women taking 2D6 inhibitors with tamoxifen have higher rates of breast cancer recurrence
This study, conducted by the U.S. pharmacy benefit management company Medco, examined women in Medco's database who were treated for breast cancer and then initiated and were adherent to tamoxifen therapy to prevent recurrence. The study identified 945 women who took tamoxifen alone and an additional 353 who were treated with both tamoxifen and a 2D6.

The researchers found that women taking tamoxifen alone had a recurrence rate of 7.5 percent over a two-year period, compared with a 13.9 percent recurrence rate for women taking tamoxifen and a 2D6 inhibitor. The average time of overlap when both drugs were taken was 255 days.

"These findings suggest that some drugs commonly prescribed to help reduce hot flashes associated with tamoxifen therapy may be decreasing the effectiveness of their anti-cancer treatment," said Robert Epstein, M.D., Chief Medical Officer at Medco and one of the study's authors. "If women are taking tamoxifen and need an SSRI to reduce their hot flashes, there are other SSRI drug options that don't inhibit 2D6 or result in the higher recurrence rates."

Dutch study finds 2D6 inhibitors have little effect on breast cancer recurrence rate
A study from Holland analyzed data from three national databases, and identified 1,962 women who were treated with tamoxifen following surgery for early-stage breast cancer. The researchers found that about 11 percent had taken a 2D6 inhibitor at some point while they were also taking tamoxifen.

After a median follow-up time of 4.1 years (for patients who are event-free at time of analysis), the researchers found that among women who took tamoxifen alone or took a 2D6 inhibitor for less than 60 days (1,812 women), 14.6 percent experienced a recurrence. Among patients who took tamoxifen at the same time as a 2D6 inhibitor for 60 days or more (150 women), 13.3 percent experienced a breast cancer recurrence.

"Based on our findings and previous studies, we don't have strong evidence that it's unsafe to use 2D6 inhibitors during tamoxifen therapy," said Vincent O. Dezentje, M.D., a trainee in oncology at Leiden University Medical Center and the study's first author. "But because the number of patients on both tamoxifen and 2D6 inhibitors was small in our study (and because of a possible confounding or modifying effect of CYP2D6 genotype), our findings will need to be confirmed in larger trials. Until a link between 2D6 inhibitors can be definitively confirmed, doctors and patients should be cautious about using these drugs together."

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