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Confusion over symptoms may be affecting whether women take tamoxifen for breast cancer

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Women who are at high risk of developing breast cancer may be failing to take the preventive anti-cancer drug tamoxifen because they are confusing naturally-occurring symptoms with side effects from the medicine, according to a study of nearly 4,000 women led by Queen Mary University of London (QMUL).

The researchers say that their findings have important implications about how to communicate with women, because getting it right could improve adherence to medication, thereby helping women to reduce their risk of developing breast cancer.

Tamoxifen, which is used to treat women with breast cancer driven by the oestrogen hormone, has been shown to reduce the incidence of breast cancer by at least 30 per cent if it is given before disease develops in women who are at high risk of developing it due to factors such as a family history of breast cancer.

The International Breast Intervention Study (IBIS-1)*, which has been running since 1992, has shown that the preventive effects of tamoxifen last at least 20 years. However, only one in six high-risk women opt to take the drug when it is offered and not all of them manage to take it consistently for at least five years.

In the study published in the *Journal of Clinical Oncology* researchers at

QMUL, University of Leeds, University of Manchester in the UK and Calvary Mater Newcastle Hospital in Australia analysed data on 3,823 UK women taking part in IBIS-1 who had been randomised to receive placebo or tamoxifen for five years.

Overall, 69.7 per cent of women managed to adhere to their treatment for at least 4.5 years (74 per cent taking placebo and 65.2 per cent taking tamoxifen). Symptoms that were reported included nausea or vomiting, headaches, hot flushes and gynaecological symptoms, such as irregular bleeding, vaginal dryness and vaginal discharge. Drop-out rates were highest in the first 12-18 months of follow-up (7.4 per cent on placebo versus 12.2 per cent on tamoxifen).

At six months among women who reported symptoms of nausea or vomiting, just over 40 per cent failed to adhere to their treatment, regardless of whether they were receiving placebo or tamoxifen.

Co-author of the paper Dr Ivana Sestak from QMUL said: "We found that the association between nausea, vomiting, headaches, hot flushes and gynaecological symptoms and non-adherence to treatment was largely similar between women taking placebo or tamoxifen: the greater the severity the less likely the women were to adhere to their treatment, with the exception of headaches, which were associated with increased non-adherence of 38 per cent only in the placebo group. Therefore, this suggests that women may be attributing normally-occurring, age-related symptoms, such as those experienced around the time of menopause, to their medication instead."

Co-author Dr Samuel Smith, Cancer Research UK Fellow and University Academic Fellow at the University of Leeds, said: "The fact that there was a relationship between reporting symptoms and non-adherence among women in the placebo group shows that behaviour is being affected by the symptoms, but these symptoms clearly could not

have been caused by the drug because it was a placebo."

Better communication with women is important, say the researchers. "Communicating accurate information on side effects to patients, and highlighting that some naturally-occurring symptoms may occur during the course of therapy, could be a useful approach in encouraging adherence. This is particularly important for women who are expected to experience the menopause while taking preventive therapy," said Dr Sestak. "These discussions may encourage more realistic expectations of the likelihood of experiencing side effects."

Dr Smith said: "Intervention strategies that help to communicate effectively the harms and benefits of preventive therapy to patients need to be developed. At present interventions that help to improve adherence to medications are few and far between. So we are considering ways to intervene with these patients to ensure the safe and appropriate use of preventive therapy. We are also planning a secondary analysis of the IBIS-II trial, which looked at another anti-cancer drug, anastrazole, versus placebo, to see if the same effects are observed in a separate group of women."

More information: Smith SG, Sestak I, Howell A, et al: Participant-Reported Symptoms and Their Effect on Long-Term Adherence in the International Breast Cancer Intervention Study I (IBIS I). *J Clin Oncol* DOI: 10.1200/JCO.2016.71.7439

* Women aged between 35 and 70 were recruited to the IBIS-1 study between 1992 and 2001 from various centres in the UK, Australia, New Zealand and other European countries. They were healthy at the time of enrolment, but considered to have at least a two-fold risk of developing breast cancer based on their family history. The categorisation of the women's risk was based on a woman's age, and how many first or second degree relatives with the disease they had and their age at which the

disease developed. Women with benign conditions that can be precursors for breast cancer, such as ductal carcinoma in situ (DCIS), were also eligible to join the study.

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