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Effectiveness of Chemopreventive and Life Style as Breast Cancer Prevention: a Literature Review

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Abstract

Background: Breast cancer is the most common cancer in women worldwide, including Indonesia. Breast cancer patients have an inherited genetic predisposition, including mutations in genes such as BRCA1 and BRCA2. Breast cancer prevention can be done through various ways, such as healthy lifestyle changes, early screening, and chemopreventive. Purpose : This study aims to assess various breast cancer prevention strategies, both through chemopreventive and lifestyle modification to determine the effectiveness of each treatment. Methods: This study used the PRISMA-ScR method (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews). Article searches were in the form of English articles relevant to the research theme with data for the last 5 years (2020-2024) and types of articles Randomized controlled trial, case control, and prospective cohort studies through PubMed, Science direct, and SpringerLink. Results: This study shows that chemopreventive, particularly low-dose tamoxifen, and lifestyle modification are promising approaches in preventing breast cancer. Low-dose tamoxifen was shown to be effective in lowering breast cancer risk with milder side effects and improved patient compliance. In addition, lifestyle modifications such as healthy diet and physical activity also play an important role in breast cancer prevention. Conclusion: The combination of chemopreventive and lifestyle modification can be a comprehensive strategy to reduce the risk of breast cancer.

Introduction Section

Breast cancer is a group of diseases characterized by the unregulated proliferation of cells within breast tissue, frequently manifesting as a palpable mass. Breast cancer is the most prevalent cancer among women globally. Based on GLOBOCAN from the International Agency for Research on Cancer (IARC) 2022, breast cancer is the most commonly diagnosed cancer after lung cancer. It accounts for 11.6% of all cancers globally. The incidence of this cancer is expected to continue to increase, with 2.3 million new cases per year in 2022. Breast cancer is also the fourth leading cause of death in 112 countries with 665,684 deaths (Bray et al., 2024). In Indonesia, cancer is the third leading cause of death after stroke and heart disease. The Global Cancer Observation Center (GLOBOCAN) recorded 408,661 new cases and 242,988 deaths caused by cancer in 2022 (Kementerian Kesehatan Republik Indonesia, 2022).

Breast cancer is a common disease affecting one in eight women during their lifetime. Its incidence rate is significant, reaching 12.9% (Jatoi, 2018). Perimenopausal and menopausal women are particularly susceptible, contributing to the overall increase in breast cancer cases. Risk factors for breast cancer can be categorized into two groups: unchangeable and changeable. Unchangeable factors include gender, age, family history, genetics, personal history, radiation exposure, race/ethnicity, breast density, and menstrual history. A small percentage (5-10%) of breast cancer cases are linked to inherited genetic mutations like BRCA1 and BRCA2. Changeable factors encompass obesity/overweight after menopause, breastfeeding, hormone, reproductive history, replacement therapy, alcohol consumption, hormonal contraceptives, physical inactivity, smoking, and DES exposure. Due to its widespread impact on health, society, and the economy, breast cancer remains a global health concern (Kolak et al., 2017)

Based on this, to reduce the incidence of breast cancer, prevention includes primary, secondary, and tertiary prevention. Primary prevention aims to reduce the risk of breast cancer development. This prevention can be done by limiting risk exposure by providing chemopreventive therapy and changing unhealthy behavior through lifestyle modification. Secondary prevention aims to detect and treat the disease early. This preventive measure involves biennial screening mammography for women aged 50 to 69, complemented by recommended practices like self-breast examination

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(SBE), clinical breast examination (CBE), and breast ultrasonography (USG) (Kolak et al., 2017). Tertiary prevention aims to reduce the impact of an existing disease or injury such as the risk of tumor recurrence after successful surgical intervention and/or chemotherapy (DeCensi et al., 2021 and Rather et al., 2022)

Chemopreventive is one of the preventive measures with the modality of chemical substances or natural compounds to prevent, suppress, and delay the initiation of carcinogenesis (Olayiwola & Gollahon, 2024). Estrogen, as a major modulator of mammary tissue growth and development, contributes to about 40% of breast cancer cases in women. The role of estrogen includes regulation of normal cell proliferation, cellular differentiation, as well as molecular mechanisms underlying breast oncogenesis. Examples of drugs approved by the FDA for chemoprevention of precancerous lesions are tamoxifen and raloxifene (Puspita, 2016; Starek-Świechowicz et al., 2021).

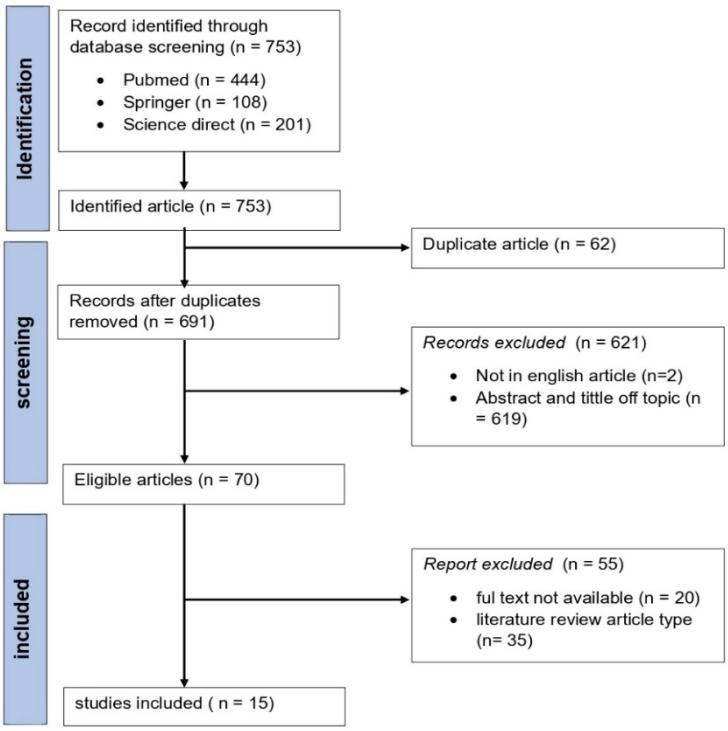
Therefore, this study was conducted to identify breast cancer prevention through primary approaches through lifestyle changes and tertiary with chemoprevention in an effort to support effective prevention strategies and reduce the incidence and mortality of breast cancer.

Method

The method used in the literature review is PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews). The article search was carried out in a four-stage selection process including identification, screening, eligible, and included. In the first stage, article identification was carried out by searching online databases with data for the last 5 years (2020-2024) with the types of articles Randomized controlled trials, case control, and prospective cohort studies through Pubmed, Science direct, and Springerlink. Then boolean operators were used to get articles with the keywords “breast cancer” AND “breast cancer prevention” AND “chemoprevention” AND “lifestyle modification” in the SpringerLink database. Science Direct and Pubmed databases used keywords (breast cancer) AND (breast cancer prevention) AND (chemoprevention) AND (lifestyle modification). In the second stage, screening was carried out by removing journals that were not in English and were out of topic/incompatible between the content of the article and PICO. In the third stage, further screening will be carried out (eligible) including articles with unavailable full text and literature review will be excluded.

Articles were selected based on PICO compliance: Population (patients at high risk of breast cancer such as perimenopausal women, postmenopausal, and patients who have undergone conservative cancer surgery), Intervention (chemopreventive or lifestyle modification), Comparison (compared to patients who were not given the intervention), Outcome (effectiveness of preventive therapy in patients at high risk of breast cancer). Then there is a fourth stage of excluded records.

Based on the final search results, 15 articles were included in the literature review. Furthermore, articles will be reviewed related to journal identity, journal objectives and methods, interventions provided, and journal conclusions.



Picture 1. Article Search Diagram

Result and Discussion

Result

The results of data searches regarding chemopreventive and lifestyle modification in breast cancer prevention for 5 years in one database, namely Springerlink as many as 108 articles, Science Direct as many as 201 articles, and Pubmed as many as 444 articles. After PRISMA-ScR and adjusted to the restriction criteria all articles were declared eligible as many as 15. The article search identified 15 studies from several countries. All study subjects were women with a range of productive ages to menopause at various study times. There are 15 research articles that have been reviewed in Table 1. The objectives, methods, interventions, and results of the studies can be compared in table 1.

Tabel 1. Article Review Result

	Title (Researcher, year/citation)	Detail		
		Aim, Methods	Intervention	Result
1.	Initiation and tolerance of chemoprevention among women with high-risk breast lesions: the potential of low-dose tamoxifen. (Bychkovsky et al., 2022)	To evaluate the adoption and tolerability of low-dose tamoxifen for breast cancer prevention in women with high-risk breast lesions, particularly after the introduction of low-dose tamoxifen as a preventive option in breast cancer clinics. Prospective cohort study	Low dose tamoxifen (5 mg)	The study found that of 660 women with high-risk lesions, 22.7% initiated chemoprevention, and low-dose tamoxifen became the most popular choice after its introduction in 2019. Results showed that discontinuation rates after one year were lower with low-dose tamoxifen (6.7%) compared with tamoxifen 20 mg, raloxifene, or aromatase inhibitors. Additionally, women of certain ages and a family history of breast cancer have a higher

				likelihood of initiating chemoprevention. Chemoprevention was not significantly different before 2019 vs. post 2019 (21.2% vs. 26.3%, p=0.16); however, post-2019, low-dose tamoxifen was the most popular choice (41.5%, 34/82).
2.	Tamoxifen and the risk of breast cancer in women with a BRCA1 or BRCA2 mutation. (Kotsopoulos et al., 2023)	To evaluate the effectiveness of tamoxifen as a chemopreventive agent in reducing the risk of primary breast cancer in women carrying BRCA1 or BRCA2 gene mutations. Prospective cohort study	Tamoxifen or raloxifene	Using tamoxifen or raloxifene can reduce the risk of breast cancer in carriers of BRCA1 and BRCA2 mutations by around 40%. Although the risk reduction was significant, this study suggests the need for further studies to confirm the benefit of this chemoprevention among a larger high-risk population. Tamoxifen/raloxifene users (10.9% of users) and 71 cases were diagnosed among non-users (14.3% of non-users; HR=0.64; 95% CI 0.40–1.03; P = 0, 07). Conclusions Chemoprevention may be an effective risk reduction option for BRCA mutation carriers, but further studies with longer follow-up are needed.
3.	Radiotherapy versus low-dose tamoxifen following breast-conserving surgery for low-risk and estrogen receptor-positive breast ductal carcinoma in situ: an international open-label randomized non-inferiority trial (TBCC-ARO DCIS Trial). (Kuo et al., 2023).	To evaluate whether low-dose tamoxifen (5 mg/day for 5 years) is less effective than radiotherapy (RT) in reducing tumor recurrence in patients with low-risk ductal carcinoma in situ (DCIS) and estrogen receptor (ER) positive status who have undergone breast-conserving surgery (BCS). Randomized controlled trial (RCT)	Low dose Tamoxifen(5 mg)	Low-dose tamoxifen was no less effective than RT in preventing tumor recurrence in the same breast or other parts of the body in patients with low-risk DCIS. If proven, low-dose tamoxifen could be an alternative for patients who do not wish to undergo RT. This study compared the effectiveness of radiotherapy (RT) and low-dose tamoxifen (5 mg/day) to prevent cancer recurrence in low-risk ductal carcinoma in situ (DCIS) patients after breast-conserving surgery. Using an open, randomized non-inferiority trial design, this study aimed to demonstrate that low-dose tamoxifen is no less effective than RT in preventing recurrence. The primary objective of the study was to measure the recurrence rate over a seven-year period, with a confidence level of 5%, power of 90%, and a non-inferiority margin of 5%. The recurrence rate in the RT group is expected to be 6%, while in the tamoxifen group it is expected to be below 10.5%. The results of statistical tests showed that there was no significant difference in the recurrence rate between RT and tamoxifen, so the small excess recurrence rate on tamoxifen was not clinically or statistically significant. This study could be an alternative treatment with lower side effects than RT, for patients who want to avoid radiotherapy.

4.	Use of anastrozole for breast cancer prevention (IBIS-II): long-term results of a randomized controlled trial (Cuzick et al., 2020).	To assess the effectiveness of administering anastrozole in the post-treatment period as a preventive measure for ca mammae Randomized controlled trial (RCT)	Anastrozole 1 mg/day and placebo	Long-term use of anastrozole can be used for preventive treatment of ca mammae in high-risk postmenopausal women ($p < 0.0001$). No new major adverse events occurred with long-term use of anastrozole.
5.	Low-Dose Tamoxifen for Mammographic Density Reduction: A Randomized Controlled Trial (Eriksson et al., 2021)	To examine the reduction in mammographic image density levels in the low-dose tamoxifen intervention and its association with fewer symptoms. Randomized controlled trial (RCT)	Tamoxifen 1 mg 2,5 mg; 5 mg; 10 mg; 20 mg; dan placebo	In the 20 mg tamoxifen control group, a decrease in density results was found to be 9.6%, a decrease in density was also obtained in the tamoxifen 2.5 mg and 5 mg control groups but no decrease in density was found in the placebo group and the tamoxifen 1 mg control group. Tamoxifen decreased 18.5% of mammographic image density in pre-menopausal women who received tamoxifen 20 mg. Vasomotor symptoms in respondents who received tamoxifen 20 mg experienced more severe vasomotor symptoms compared to respondents who received tamoxifen 1 mg; 2.5 mg; 5 mg.
6.	The Effect of Diet on Breast Cancer Recurrence: The DIANA-5 Randomized Trial. (Wernli et al., 2021)	To assess the effectiveness of macro-mediterranean diet in reducing ca mammary recurrence Randomized controlled trial	Recommended drugs for preventive ca mammae medication accompanied by The DIANA-5 Diet intervention	over the 5 years of the study, both intervention and control groups experienced mammary ca recurrence (HR: 0.99). Participants with high dietary adherence had an HR: 0.59 for mammary ca recurrence. This study also emphasizes that new research needs to focus on adherence in dietary intervention studies so that it can get clearer results.
7.	Association of Menopausal Hormone Therapy With Breast Cancer Incidence and Mortality During Long-term Follow-up of the Women's Health Initiative Randomized Clinical Trials (Chlebowski et al., 2020)	To determine the long-term effects of menopausal hormone therapy (MHT) on breast cancer incidence and mortality among postmenopausal women, and to compare the effectiveness of the two hormones, namely CEE and MPA. Randomized placebo-controlled trial (RCT)	CEE was given to women who had undergone hysterectomy and CEE plus MPA was given to women with an intact uterus.	CEE reduced breast cancer incidence and mortality, while CEE plus MPA increased breast cancer incidence without significantly affecting mortality. CEE compared with placebo with a history of hysterectomy was associated with a statistically significantly lower incidence of breast cancer ($P = .005$) and was associated with a statistically significantly lower breast cancer mortality ($HR = .60$ and $P = .04$). In contrast, CEE plus MPA compared with placebo with a uterus was associated

				with a statistically significantly higher incidence of breast cancer (HR, 1.28 and P < .001) and no significant difference in breast cancer mortality (HR = .11 and P = .11).
8.	Topical Endoxifen for Mammographic Density Reduction—A Randomized Controlled Trial (Bäcklund, Eriksson, Gabrielson, et al., 2022)	To evaluate the effectiveness of topical endoxifen, a metabolite of tamoxifen, in reducing mammography as a potential method for breast cancer prevention and to assess the impact of different doses of topical endoxifen on mammography in women in order to determine its feasibility and effectiveness as a preventive treatment for breast cancer. Randomized placebo-controlled trial (RCT)	Use of topical endoxifen, specifically Z-endoxifen, in various doses (0 mg, 10 mg, and 20 mg) and performing mammograms and completing questionnaires regarding symptoms associated with tamoxifen exposure at various intervals during the study.	Topical endoxifen has shown potential to reduce mammography-related breast cancer incidence, but there is a concern about skin toxicity. The absolute reduction in mammography history during follow-up compared with baseline was 0.3% (P = 0.12), 0.9% (P = 0.04), and 1.9% (P = 0.03) per month in the placebo, 10mg, and 20mg groups, respectively.
9.	Identifying actionable druggable targets for breast cancer: Mendelian randomization and population-based analyses (Zhang et al., 2023)	To examine the association between various drugs and breast cancer risk, with a particular focus on the repurposing of existing non-oncology drugs for the prevention and treatment of breast cancer. Case control	Raloxifen, estradiol, Tolterodine dan Nitrofurantoin	Raloxifene use was associated with a reduced risk of breast cancer, consistent with the STAR trial and providing further evidence that the MR study. In contrast, use of estradiol, tolterodine, and nitrofurantoin may increase the risk of breast cancer. Raloxifene use was associated with a 35% reduced risk of breast cancer (P = 0.0004). In contrast, use of estradiol, tolterodine, and nitrofurantoin was associated with an increased risk of breast cancer, with adjusted ORs of 1.10 (P < 0.0001), 1.16 (P < 0.0001), and 1.09 (P < 0.0001). The effect of raloxifene was marginally significant due to insufficient sample size (P = 0.064) and there was no significant association between tolterodine and breast cancer risk (P = 0.711).
10.	Effects of Raloxifene Combined with Low-dose Conjugated Estrogen on the Endometrium in Menopausal Women at High Risk for Breast Cancer (Carneiro et al., 2021).	The aim of this study was to compare the effects of low-dose conjugated estrogens (CE), raloxifene, and their combination on vasomotor symptoms and endometrial thickening in postmenopausal women at risk of breast cancer.	Low-dose conjugated estrogens/CE (0.3 mg), raloxifene (60 mg), or combined therapy for 1 year.	Vasomotor symptoms decreased significantly in the CE group and combination group than the raloxifene group (p=0.002) after 6 months and (p=0.003) after 12 months. Whereas in the CE group, endometrial thickening increased progressively than the other groups (p=0.040 and p=0.049) . The combination of raloxifene and CE is a good option for managing vasomotor symptoms and preventing endometrial

		RCT (Randomized Controlled Trial)		thickening in postmenopausal women with moderate-high risk of breast cancer.
11.	A Randomized Phase IIb Study of Low-dose Tamoxifen in Chestirradiated Cancer Survivors at risk for Breast Cancer (Bhatia et al., 2021).	This study evaluated low-dose tamoxifen treatment (5 mg/day) in cancer survivors who previously underwent chest radiation and were at high risk of developing breast cancer. Breast cancer evaluation was assessed using mammographic density, insulin-like growth factor-1 (IGF-1) levels and insulin-like growth factor binding protein-3 (IGFBP-3) levels, which are biomarkers of breast cancer risk. RCT (Randomized Controlled Trial)	Low-dose tamoxifen (5mg/day)	Low-dose tamoxifen effectively reduced mammographic density than the placebo group (p=0.02) after 1 year and (p=0.03) after 2 years. IGF-1 levels decreased significantly in the tamoxifen group, with significance at 1 year (p<0.0001) and 2 years (p=0.008). IGFBP-3 levels increased significantly in the tamoxifen group after 2 years (p=0.02). There was no significant difference in side effects between the tamoxifen and placebo groups (p=0.5225) in grade 3-4 and (p=1.0) in grade 1-2.
12.	Time to Mammographic Density Decrease After Exposure to Tamoxifen (Bäcklund, Eriksson, Hammarström, et al., 2022)	The aim of this study was to identify medication adherence, adverse events, and mammographic density by using tamoxifen 10mg/day and 20 mg/day for 9 months. RCT (Randomized Controlled Trial)	Tamoxifen 10 mg and 20 mg	Using tamoxifen for 9 months significantly decrease mammographic density -1.8% (95% CI: -3.3% to -0.2%) after 3 months, -2.2% (95% CI: -4.2% to -0.3%) after 6 months, and -2.9% (95% CI: -5.0% to -0.9%) after 9 months. Using tamoxifen between 10 mg and 20 mg for 9 months showed no significant difference in side effects and density reduction. At the 10 mg dose, the mean decrease in mammographic density was -3.3% (95% CI: -6.1 to -0.5) and the change in symptom score was 1.8 (95% CI: -0.8 to 4.5). Whereas at the 20 mg dose, the mean decrease in mammographic density was -2.5% (95% CI: -5.7 to 0.8) and the change in symptom score was 3.7 (95% CI: 0.5 to 6.8).
13.	Assessing nutrition-related knowledge,attitudes, and practices towards breast cancer prevention among female students at the Federal University of Oye-Ekiti, Nigeria (Kolawole et al., 2024)	The aim of this research is to evaluate knowledge, nutrition, and practice of lifestyle changes in preventing breast cancer cross sectional	Participants fill out questionnaires related to the food frequency questionnaire (FFQ) to assess	It was found that only 30% of respondents consumed healthy foods such as vegetables and fruit, which increased the risk of breast cancer. 68% of respondents consume fish which is a protective factor against breast cancer. Inadequate knowledge and a sedentary lifestyle are associated with an increased risk of breast cancer.

14.	Adherence to Cancer Prevention Lifestyle Recommendations Before, During, and 2 Years After Treatment for High-risk Breast Cancer (Cannioto et al., 2023).	The aim of this study is to determine lifestyle modifications that influence cancer prevention (such as diet and physical activity) before, during, and 1-2 years after breast cancer treatment in high-risk patients. Kohort Prospektif	Patients assessed lifestyle changes with the delcap questionnaire (The Diet, exercise, Lifestyles, and Cancer Prognosis (DELCaP)).	Research comparing lifestyle changes found a 58% reduction in mortality and a 37% reduction in breast cancer recurrence. significant figure. Changing activities, avoiding sugary drinks, and consuming vegetables and fruit were found to be significant in reducing mortality rates. A low lifestyle index in sufferers with a p value <0.05 is considered significant for an increased risk of breast cancer recurrence.
15.	Effect Modifiers of Low-Dose Tamoxifen in a Randomized Trial in Breast Noninvasive Disease. (De Censi et al., 2023).	The aim of this study was to compare the effects of low-dose tamoxifen (5 mg/day) versus placebo for 3 years in women with non-invasive breast disease who had been operated on. RCT (Randomized Controlled Trial)	Tamoxifen 5mg/ day compared with placebo	Low-dose tamoxifen was more effective in post-menopausal women (HR = 0.30) compared with pre-menopausal women (HR = 0.73), although this difference was not statistically significant. Women with low estradiol levels (<15.8 pg/mL) showed a better response to low-dose tamoxifen (HR = 0.23) compared with those with high estradiol

Discussion

This review synthesizes research exploring chemopreventive and lifestyle modification strategies to mitigate breast cancer risk in high-risk populations. Notably, Indonesia has witnessed a significant surge in breast cancer incidence, with a 16.6% increase to 369,914 cases and a mortality rate exceeding 22,000 individuals (Kementerian Kesehatan Republik Indonesia, 2022). Women carrying BRCA1 or BRCA2 gene mutations are at exceptionally high lifetime risk of developing breast cancer. Currently, treatment options to reduce this risk can include magnetic resonance imaging (MRI), mammography, bilateral mastectomy, and the use of preventive medications such as tamoxifen, raloxifene, anastrozole, conjugated estrogens, etc. While the primary treatment of breast cancer is surgery with or without chemotherapy, radiotherapy, and continued hormone therapy, these treatment options are not suitable for all patients. (Kotsopoulos et al., 2023)

Tamoxifen is a selective estrogen receptor modulator (SERM) that functions to inhibit estrogenic activity in breast tissue. Additionally, tamoxifen binds to estrogen receptors in the uterus and bones, thereby acting as an activator or cell growth stimulant agent in endometrial tissue, exhibiting effects comparable to those of natural estrogen. Tamoxifen is employed not only as a therapeutic agent for breast cancer in patients who have undergone surgery or chemotherapy, but also as a prophylactic measure for women at high risk of developing the disease. A cohort study conducted by Kotsopoulos et al. (2023) revealed significant differences in the incidence of breast cancer between users and non-users of tamoxifen/raloxifen. A total of 22 cases of breast cancer were observed among tamoxifen/raloxifen users, whereas 71 cases were identified among non-users (Kotsopoulos et al., 2023). However, the use of this drug is often accompanied by a range of adverse effects, including hot flashes (1264 or 40.9%) and nausea, vomiting (384 or 12.4%), fatigue (544 or 17.6%), joint pain (911 or 29.4%). There were also incidences of stroke (88 patients, 2.8%), thromboembolism (214 patients, 6.9%), and endometrial cancer (17 patients, 0.8%). (Effendi et al., 2023; Fadhil et al., 2019; Gu et al., 2012).

The study conducted by Backlund and colleagues (2022) indicates that the administration of tamoxifen at doses of 10 mg or 20 mg for a period of three months can result in a reduction in mammographic density. However, no significant differences were observed between the two doses in terms of the incidence of adverse effects or the extent of density reduction. Additionally, low-dose tamoxifen (2.5 or 5 mg) has been demonstrated to exhibit preventive and adjuvant effects comparable to those of 20 mg. Recent research has explored the potential benefits of lower-dose tamoxifen to minimize adverse effects while preserving its protective properties. A study by Bhatia et al. (2021) demonstrated that low-dose tamoxifen effectively reduced mammographic density and modulated levels of IGF-1 and IGFBP-3 in high-risk breast cancer patients (Bhatia et al., 2021) . Additionally, a cohort study compared the efficacy of low-dose (5 mg) and standard-

dose (20 mg) tamoxifen as chemopreventive agents in high-risk women. The findings supported the use of low-dose tamoxifen as an effective breast cancer prevention strategy. Notably, 22.7% of the 660 eligible women opted for low-dose tamoxifen chemoprevention, indicating superior adherence compared to 20 mg tamoxifen or raloxifene (Bychkovsky et al., 2022).

Recent research (2023) has indicated that low-dose tamoxifen is an effective intervention for reducing breast cancer risk, associated with fewer side effects and improved patient adherence to long-term treatment (Kotsopoulos et al., 2023). This study compared the efficacy of low-dose tamoxifen (5 mg/day) with radiotherapy (RT) in women with estrogen receptor-positive, low-risk ductal carcinoma in situ (DCIS). The findings indicated that low-dose tamoxifen exhibited a similar efficacy to RT in reducing the recurrence of breast cancer, while also demonstrating a more favorable side effect profile (Kuo et al., 2023). Additional studies provide further support for the use of low dose tamoxifen as an economical and effective alternative for recurrence prevention in low-risk DCIS (Lazzeroni, 2023). In a study conducted by Eriksson, M. et al. (2021), the efficacy of low-dose tamoxifen (2.5 mg, 5 mg, and 10 mg) in reducing mammographic density in women aged 40-74 years was also evaluated (Eriksson et al., 2021). The findings indicated that the low dose was as efficacious as the standard dose of 20 mg in reducing mammographic density in premenopausal women, although this was not the case in postmenopausal women. The low-dose group exhibited reduced incidence of adverse effects, such as vasomotor symptoms, which may enhance long-term compliance (De Censi et al., 2023).

In addition to tamoxifen, raloxifen is also employed as an alternative for breast cancer prevention, exhibiting a reduced incidence of adverse effects. The research conducted by Zhang N., et al. (2023) aimed to identify drug targets using Mendeley randomization. The findings indicate that raloxifen is an effective chemopreventive agent for mammary carcinoma, with the potential to reduce the risk of developing the disease by 35% (Zhang et al., 2023) . Additionally, raloxifen is utilized for the prevention and treatment of postmenopausal osteoporosis. Concurrently, research conducted by Carneiro, A., et al. (2021) over the course of one year revealed that the efficacy of the combination of raloxifen with low-dose conjugated estrogens was comparable to that of conjugated estrogens administered without the combination in the reduction of postmenopausal vasomotor symptoms (p=0.457). Furthermore, it is comparable to raloxifen in the prevention of endometrial thickening in postmenopausal women (P=0.04 and P=0.49). This combination therapy is regarded as a viable approach for addressing vasomotor symptoms and preventing endometrial thickening, although the outcomes are not significantly distinct from those observed with monotherapy (Carneiro et al., 2021). Conjugated equine estrogen (CEE) represents a menopausal hormone therapy comprising estrogen. Chlebowski et al. (2020) aimed to investigate the association between combined conjugated equine estrogen (CEE) and medroxyprogesterone acetate (MPA) use and breast cancer incidence and mortality in postmenopausal women. The study revealed a decreased risk of breast cancer incidence and mortality (0.30%) among hysterectomized women using CEE. However, combined CEE and MPA use in non-hysterectomized women was linked to an increased risk of breast cancer (0.45%) without a significant impact on mortality (Chlebowski et al., 2020).

The primary source of estrogen in menopausal women is the enzyme aromatase, which is responsible for converting androgens to estrogen in peripheral tissues, such as breast tissue. Anastrozole and exemestane function by reducing the amount of circulating estrogen, thereby more effectively reducing the proliferation and growth of estrogen-dependent cancer cells (Zuffo et al., 2023). Anastrozole is an aromatase inhibitor that impedes tumor growth by inhibiting the CYP19A1 enzyme and reducing estrogen production from androgenic precursors (Haddad et al., 2024). A recent analysis of the IBIS-II trial provides evidence supporting the use of anastrozole for breast cancer prevention in high-risk postmenopausal women. Cuzick, J., et al. (2020) investigated the long-term impact of anastrozole on breast cancer risk, including its effects on estrogen receptor-positive invasive cancer and ductal carcinoma in situ. The study also evaluated the drug's safety profile in terms of adverse effects and mortality. Findings indicate that long-term anastrozole treatment is an effective preventive strategy for breast cancer in high-risk postmenopausal women ($p < 0.0001$). The administration of anastrozole did not result in the emergence of any novel, significant adverse effects. However, the most commonly observed effects were those associated with the reduction in estrogen levels, including bone, joint, and menopausal symptoms (Cuzick et al., 2020).

In addition to medical efforts through chemoprevention, which involves the use of drugs to reduce the risk of cancer, breast cancer prevention can also be achieved through lifestyle modification. The efficacy of lifestyle modifications for primary, secondary, and tertiary prevention of breast cancer can be evaluated based on an individual's level of knowledge regarding healthy lifestyle and appropriate dietary behavior. The most recent innovation in the field of breast cancer prevention is the implementation of DIANA-5. This innovation aims to deepen our understanding of hormonal and metabolic factors influencing breast cancer development. Previous research highlights body weight, metabolic syndrome

parameters, insulin levels, and testosterone levels as prognostic factors. The study findings indicate a 41% reduction in recurrence risk among women adhering to an effective diet strategy. The DIANA-5 trial further supports these findings, demonstrating the prevention pattern's efficacy in reducing body weight and metabolic syndrome in high-risk women (Berrino et al., 2024). A review of 13 academic journals explores the interplay between habits, knowledge, and consumption patterns in high-risk women. Notably, women with a family history of breast cancer, despite possessing good knowledge (52.3%), did not exhibit statistically significant differences ($p>0.05$) compared to those without a family history. With regard to food consumption, namely fruits and vegetables, the percentage of respondents who reported consuming these items was 30 and 21%, respectively. Furthermore, the findings of this study lend support to the notion that lifestyle modifications may prove an effective strategy for the prevention of recurrence in breast cancer patients. A p-value of less than 0.05 was obtained for the variable of smoking status, which has been demonstrated to increase the risk of breast cancer recurrence. A low lifestyle index with a p-value of less than 0.04 is considered to be a meaningful factor in the increased risk of breast cancer recurrence (Cannioto et al., 2023).

Conclusion

Breast cancer represents a significant global health concern. The findings of this study indicate that chemopreventive approaches, particularly low-dose tamoxifen, and lifestyle modification represent promising avenues for the prevention of breast cancer. The administration of low-dose tamoxifen has been demonstrated to effectively reduce the risk of developing breast cancer, while simultaneously minimizing the incidence of adverse effects and enhancing patient compliance. Furthermore, the incorporation of lifestyle modifications, such as a nutritious diet and regular physical activity, has been shown to be a valuable adjunctive measure in the prevention of breast cancer. The combination of chemopreventive agents and lifestyle modifications represents a promising approach to the reduction of the global burden of breast cancer.

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