A Retrospective Analysis of Tamoxifen and Raloxifene

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Abstract: This article focuses on the two drugs used in the treatment of cancer, tamoxifen and raloxifene. The drugs discussed in this article are the only two drugs approved by the FDA in the United States to minimize the risk of breast cancer. The research was conducted by quantitatively analyzing the existing literature and investigation on the topic was objective and unbiased. The objective is to find the most effective drug for mitigating the risk posed by breast cancer. This article also discusses the adverse outcomes associated with prolonged or brief use of these medications. We evaluate the risk versus benefits and safety that each agent represents. We then conclude with the medical best practice recommendations regarding these drugs in the mitigation of this risk. The best practices proposals established a basis for the analysis conducted and our professional opinion on the weight of each effect.

Keywords: tamoxifen, raloxifene, adverse reactions, clinical trials, drug, cancer patients, long-term health

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Tamoxifen and Raloxifene are drugs that mitigate the risk of developing breast cancer, although they cause significant side effects to warrant caution. These drugs are more advantageous to women facing the possibility of developing breast cancer. However, these drugs have many adverse effects. We conducted this quantitative study to investigate and analyze Tamoxifen and Raloxifene use in the prevention and treatment of this type of cancer. We also examine the adverse reactions profiles in clinical trials to determine the most effective drug for improving a cancer patient's long-term health. The quantitative analysis conducted with scholarly articles and reports are from reputable researchers and scientists studying the effects of these drugs.

2. Materials and Methods

We did a quantitative analysis of the existing literature and research articles on the effectiveness and side effects of Tamoxifen and Raloxifene. This research relied on articles written by several authors who conducted studies and trials on the two drugs and their efficacy in the mitigation of this type of cancer. One of the reviews studied was "*Systematic review: comparative effectiveness of medications to reduce the risk for primary breast cancer,"* written by Nelson et al. [1]. In this article, the authors review the benefits, risks and safety of three breast cancer drugs, including Tamoxifen and Raloxifene, in the mitigation of the hazard posed by breast cancer. The review focuses on women in general and in specific subgroups [1].

We also analyzed the article titled *"Comparative Tolerability of First-Generation Selective Estrogen Receptor Modulators in Breast Cancer Treatment and Prevention,"* written by Michèle G. Curtis [2]. This article discusses the benefits and risks of selective estrogen receptor modulators (SERMs), including tamoxifen for the prevention and treatment of cancer [2]. Our research focused on the

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quantitative indicators for the efficacy of Tamoxifen and its side-effects. These indicators included the number of patients treated using Tamoxifen, the number of patients who reported side effects, and other quantitative factors. Table 1 contains the results that will be used in presenting the findings of these quantitative analyses.

We also analyzed a report from the Agency for Healthcare Research & Quality titled "*Medications Effective in Reducing Risk of Breast Cancer but Increase Risk of Adverse Effects*" to understand the side-effects of Raloxifene, Tamoxifen, and Tibolone when used for breast cancer treatment [3]. These side-effects are critical in consideration of the efficacy of these drugs and for the conclusion of this research.

We also analyzed the financial gains and losses of utilizing these two drugs in preventing and mitigating this risk. This analysis was based on the article titled *"Economic evaluation of chemoprevention of breast cancer with Tamoxifen and Raloxifene among high-risk women in Japan"* by Kondo M, Hoshi S-L, and Toi M [4]. This article describes the financial losses and benefits of using these drugs in treating and preventing this type of cancer. The inferences made by these researchers were critical in the evaluation of our hypotheses.

The final material used in this research was the report by Berger JC, and Clericuzio CL [5] titled *"Pierre Robin sequence associated with first-trimester fetal tamoxifen exposure*." This report discusses the findings from the case where Tamoxifen was found to cause adverse effects on a neonatal infant. This article was critical in the determination of the harmfulness of the drugs.

The method used in this research was straightforward and valuable. We decided to examine all numerical data presented in these articles and studies and all quantifiable data to determine if the positive outweighed the negative or vice-versa. These figures and quantities included the number of successful treatments, the number of reported side-effects, the number of withdrawals from therapy, and all other quantifiable data presented in the articles. We then considered the advantages and disadvantages of each quantity by looking at the number of positive versus adverse outcomes. Positive outcomes were considered as outcomes that led to the conclusion that these drugs were recommendable for the treatment of breast cancer. Adverse outcomes were considered as outcomes that led to the belief that these drugs caused more harm than good to the patients. The weight assigned to each factor was based on our professional knowledge and expertise, and the final results and recommendations reflected part of our expert opinion as researchers and medical practitioners.

3. Results

The analysis of the article by Nelson et al. on the efficacy of the two drugs [1] revealed that these drugs were critical in mitigating the threat posed by breast cancer. This benefit was exceptionally fortuitous for women facing a more significant danger of developing this kind of disease. However, the researchers noted that each drug possessed side-effects. The researchers pointed out that all three drugs reduced this threat in women in their middle ages and above by 30% to 68% [1]. The women considered in this bracket had no pre-existing breast cancer. The effects of Raloxifene and Tamoxifen were noted to be similar in the head-to-head trials conducted between the drugs [1]. These trials also demonstrated additional benefits for women, such as the risk reduction for fractures. In the United States, Raloxifene is preferred for post-menopausal women and Tamoxifen for pre and post-menopausal women.
The research by Nelson et al. also demonstrated several adverse and potentially life-threatening side-effects [1]. The drugs increased the potential for developing thromboembolic events, more so in Tamoxifen than in Raloxifene [1]. The investigators indicated that this risk could be mitigated if the drug was to be administered only to women who have had hysterectomies [1]. Physicians noted the need for close monitoring of the uterine effects of Tamoxifen in some pre-menopausal women [1]. Tamoxifen and Raloxifene also cause life-altering side-effects, such as musculoskeletal symptoms, vaginal symptoms,

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and hot flashes. Their effects on endometrial cancer and endometrial hyperplasia are also of concern to researchers [1].

The article by Curtis on the tolerance of SERMS [2] indicated that Tamoxifen had been utilized in the last several decades to treat breast cancer. A research posted in 1998 demonstrated that Tamoxifen used for more than five years lowers the potential of developing cancer in women with ER-positive tumors [2]. Tamoxifen reduces the threat of developing breast cancer by 50% and developing ER-positive cancer by 69% [2]. Raloxifene is also noted to mitigate the risk of this type of cancer compared to placebo experiments [2]. At the time of the research, Raloxifene was undergoing clinical trials to determine its effects and applications in treating breast cancer. The impact of Tamoxifen and Raloxifene on other conditions such as endometrial and hepatic tumors was also profoundly analyzed in this article. Although these discussions were beyond the scope of this research, they contributed significantly to the recommendations and inferences presented in this article.

The article by the Agency for Healthcare Research & Quality [3] outlines some of the recorded side-effects of Tamoxifen and Raloxifene. These side-effects include vasomotor symptoms such as night sweats and hot flashes. In addition, they can cause vaginal pruritus as well as vaginal dryness and vaginal discharge. Tamoxifen increases the potential for developing cataracts, hysterectomies, and endometrial cancer. These side-effects form the case against the advocacy for the utilization of these drugs. The threat of blood clots and leg cramps is higher when using Raloxifene.

Kondo and Hoshi [4] discuss the financial benefits and dangers that accompany the utilization of the two drugs by women. Based on their research conducted in Japan, the researchers noted that the use of the two drugs was cost-effective for women predisposed to breast cancer. The study indicated that the use of the two drugs to prevent cancer at a younger age provided more benefit in terms of life-years gained at a recurring or increasing cost of about 30,000 dollars or lower [2]. The research also indicated a more significant interest in the switch to Raloxifene by women with Atypical Hyperplasia (A.H.) and Lobular Carcinoma in Situ (LCIS) [2]. We used this study to give more weight to the benefits of using these drugs to treat and prevent breast cancer before making our inferences.

The report by Berger JC and Clericuzio CL [5] discusses a case of Pierre Robin sequence diagnosed in a neonate after the mother was exposed to Tamoxifen. The neonate still demonstrated the effects of the drug even after it was discontinued after six weeks of exposure [5]. At week 30, the neonate showed signs of clubfoot and a questionable palette in an ultrasound [5]. The baby was born at week 32 and 3 days with APGAR scores of 6 (1 min) and 8 (5 min) [5]. The baby was born with poor health and developed airway obstruction after he was born [5]. The effect of Tamoxifen on neonates was also a contributing factor in the recommendations presented in this report.

The compounded data was analyzed based on the usefulness of the drugs in preventing or mitigating the threat. We noted that the drugs were positively proven to minimize the danger of developing this type of cancer by 50% or more. Researchers also pointed out that the drugs increased the life-years gained by women facing the risk of developing breast cancer, and building on the recommendations by Kondo and Hoshi, we noted that the financial benefits of these two drugs were worthwhile. Tamoxifen and Raloxifene also had other positive befits such as the reduction of risk for different types of cancer such as Hepatic Tumors. Researchers from each study and research group all noted the positive outcomes of using these drugs to treat and prevent breast cancer, especially in women predisposed to this type of cancer. The FDA also approves both drugs. Tamoxifen has been in use for several decades with acceptable outcomes so far. Raloxifene has been noted to improve on the benefits provided by Tamoxifen while reducing some of the adverse effects. However, both drugs cause significant harmful side-effects that make them unfavorable for women not facing the threat of developing breast cancer.

4. Discussion

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Both Tamoxifen and Raloxifene are two drugs that are specific estrogen receptor modulators (SERMs) [2]. They square with estrogen (which is a female hormone) in particular organs of the body and yet behave similarly to estrogen in other parts. Estrogen increases the rate of formation of cancer growth cells in the breast. Raloxifene and Tamoxifen act against the estrogen in breast cells, making them very valuable in bringing down the threat of developing this type of cancer. Tamoxifen treatment utilizes, for the most part, mitigation of the threat posed by the hormone receptor-positive breast disease (breast cancer growth with cells that have estrogen and additionally progesterone receptors on them). Raloxifene administration is generally to counteract and treat osteoporosis (exceptionally frail bones) in women who are undergoing the post-menopause period in their life [1]. Tamoxifen applications are significant whether the woman has experienced menopause or not. However, Raloxifene for post-menopausal women is affirmed [1].

The overall decrease in the threat of breast cancer attributed to these medications is more than 50% (over a half), based on the research conducted. Compared to the risk carried by breast cancer, a 50% reduction of risk is a massive benefit for the women facing a higher risk of developing breast cancer. Therefore, the recommendation of tamoxifen is for these women, women predisposed to breast cancer, but have yet to undergo menopause since it reduces their risk tremendously despite the adverse side effects. However, these adverse effects can be lower if the woman has had a hysterectomy.
Both Tamoxifen and Raloxifene can also help avert osteoporosis, a severe, debilitating of the bones that occur in women after menopause. These drugs provide additional benefits for women apart from the mitigation of the threat of breast cancer. Researchers have noted that the two breast cancer mitigation drugs also lessen the risk for fractures [6]. Currently, the two breast cancer prevention drugs are in wide use by physicians in the U.S. to mitigate the threat posed by breast cancer despite the adverse effect of its use [1]. Physicians have the responsibility of ensuring that women facing a more significant risk of developing cancer understand their predicament and options. This knowledge can help these women balance this risk with the side effects of the Tamoxifen and Raloxifene [1].
Consumption of these medications is for an extended period in order to reduce the danger of breast cancer cell growth. Based on previous studies and observations, prescribing of these drugs extend for long periods, stretching beyond five years [2]. The most well known reactions of these medications are the side effects of menopause. These incorporate hot flashes and night sweats. Tamoxifen can likewise lead to vaginal dryness and vaginal release of fluids. Women who have not undergone menopause and taking Tamoxifen can encounter fluctuations in their menstrual cycles [7]. Menstrual periods can end up sporadic or even come to a halt altogether. Both Tamoxifen and Raloxifene increment the danger of creating blood clusters in leg veins of women, known as deep venous thrombosis, or the lungs, pulmonary embolism. This coagulation can now and then cause significant issues, and even be as grave as death.

Tamoxifen can elevate the threat of developing cancer in the endometrium and uterine sarcoma (which are tumors of the uterus) because it behaves like estrogen in the uterus. It, likewise, connects to a greater danger of endometrial pre-malignant growths. Raloxifene does not act like estrogen in the womb and is unrelated to an expanded risk of malignant uterine growth. Although Tamoxifen increases the danger of uterine cancer growth, the general increment in hazard is low (under 1%). The threat of uterine cancer growth returns to typical risk inside a couple of long periods of halting the medication. The expanded risk appears to influence women at the age of more than 50, however [7].
After understanding the benefits and risks associated with both risk-reducing drugs, we can make our inferences and recommend that women facing the threat of developing breast cancer should use Tamoxifen and Raloxifene. We made this recommendation because the economic and general benefits brought about by the lowering of the threat of breast cancer outweigh the adverse outcomes associated with the drugs. Breast cancer is a life-threatening disease, and women predisposed to this type of cancer often develop cancerous cells in the breast at a later age [8]. We advocate for the chance of reducing the high risk of a life-threatening condition before it can become lethal. Therefore, these

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drugs are most beneficial to women with very high chances of developing this type of cancer. Research also indicated that the drugs were also useful in the treatment of this type of cancer in advanced stages. Therefore, best practices recommend tamoxifen and raloxifene for women.

Table 1. Table indicating the weighted factors in the Quantitative Analysis

Factor	**Weight**	**Outcome**
The reduction of the threat of developing breast cancer	750	Positive
Treatment of breast cancer	750	Positive
Other benefits such as the reduction of risk for fractures	300	Positive
Increased risk for other adverse conditions such as endometrial cancer	-300	Negative
Increased danger for neonates accidentally exposed to the drugs	-300	Negative
The financial cost for the risk-reduction	-100	Negative
Increased risk for hysterectomy	-200	Negative
Total Benefit	**900**	**Positive**

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Adverse effects	Tamoxifen
Carcinogenic effects	
Liver	Tumourogenic in rats
	Nontumourogenic in humans
Endometrium	Uterotrophic
MCF-7 human breast cancer cells	Resistance and stimulation of growth occurs with prolonged treatment
Other effects	
Vasomotor	Hot flushes reported in ≈50% of patients
Thromboembolism	3-fold increased risk of events
Ocular	Low incidence of ocular toxicity. Increased risk for cataracts
Hepatic	Abnormal enzyme values. Fatty liver in 30% of patients
Uterine	Endometrial hyperplasia, cysts, and fibroids

Figure 1. Tolerance to Tamoxifen [2].

4. Conclusions

The research presented sought to investigate the advocacy e of Raloxifene and Tamoxifen in the reduction of the threat posed by cancer of the breast. We conducted a quantitative analysis of academic studies and medical investigations on the utilization of these drugs in the mitigation of the threat posed by cancer. The research utilized various academic literature on the subject matter, and the results tabulated to aid in the decision-making process. These two breast cancer mitigation drugs are beneficial in the reduction of this risk, although they come with various adverse side effects. The benefit for the women naturally predisposed to this kind of cancer is, therefore, higher than women with low risk. We, therefore, recommend that women facing a higher risk of developing this type of cancer and women with preexisting breast cancer should use Tamoxifen and Raloxifene because these drugs are actively effective against breast cancer. Although the side effects of these drugs can be severe, there have been very few cases of critically life-threatening side effects.

Potential Conflicts of Interest

The authors declare no conflict of interest.

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