

ORIGINAL ARTICLE

HORMONAL CONTRACEPTIVES AND HORMONE REPLACEMENT THERAPY AS A POSSIBLE RISK FACTOR FOR BREAST CANCER

Lenka Predná¹, Marta Habánová¹, Eva Sláviková², Joanna Wyka^{3*}

¹Department of Human Nutrition, Slovak Agricultural University in Nitra, Slovak Republic

²Ultrasound Outpatient Clinic, Chrenová Nitra, Slovak Republic

³Department of Human Nutrition, Wrocław University of Environmental and Life Sciences, Wrocław, Poland

ABSTRACT

Background. Breast cancer is a disease with an increasing incidence, and it originates from several factors. Risk factors of this disease represent a diverse group of parameters, which also include hormonal influences.

Objective. The aim of the present study was to determine if there is a relationship between hormonal contraceptives and hormone replacement therapy in patients with diagnosed most common types of breast cancer taking into account the age at which the disease was diagnosed in selected sonographic clinic in the district of Nitra, Slovak Republic.

Material and Methods. As a part of an ongoing retrospective study from 2005, a cohort of 300 randomly selected patients aged 25-87 years with diagnosed breast cancer have been monitored in 2012. The age at which breast cancer was diagnosed, and relationship to hormone therapy were analysed based on medical documentation.

Results. Among 300 randomly selected patients with a confirmed diagnosis of breast cancer the group at the age of 40-59 was the most numerous (mean age was 53.06±11.25 years). The mean age of 45 patients who were given hormonal contraceptives (HC) was 46.44±7.34 years, whereas the mean age of 82 patients who were subjected to hormone replacement therapy (HRT) was 53.63±6.67 years. In women who took hormonal treatment, breast cancer was diagnosed at the mean age of 50.60±7.56 years, while women who never took HRT or HC, were diagnosed around the age of 53.92±12.35 years. The most common types of cancer were the infiltrating *ductal carcinoma* and *lobular carcinoma*. From all patients, the relapse occurred among 14 of them, about 4.86 years later. Only 2 patients had breast cancer on both diagnosed breast. After a surgery, the cancer was observed in 7 patients. The positive family history was confirmed with 34 patients.

Conclusions. Nowadays, the breast cancer treatment, especially at early stages, is successful, however, the malignant breast neoplasm remains the most common oncological disease causing the death amongst women. In the assessment of the impact of HC and HRT on breast cancer, it is not possible to provide a clear conclusion, because their influence on the tumour is difficult to verify.

Key words: *breast neoplasms, hormonal contraceptives, hormone replacement therapy, risk factors*

STRESZCZENIE

Wprowadzenie. Rak piersi jest chorobą, której występowanie uzależnione jest od wielu czynników. Czynniki te są zróżnicowane, a wśród nich wyróżnia się czynniki hormonalne.

Cel. Na podstawie danych medycznych podjęto próbę oceny występowania zależności różnych typów raka piersi u kobiet a stosowaniem antykoncepcji hormonalnej oraz hormonalnej terapii zastępczej.

Material i metody. Praca stanowi część trwającego od 2005 roku badania stanu zdrowia pacjentek w wieku 25-87 lat. Badaniami objęto kohortę 300 kobiet, u których w 2012 roku zdiagnozowano raka piersi. W badaniach przeprowadzonych na podstawie analizy dokumentacji medycznej oceniano zależność między wiekiem kobiety, w którym zdiagnozowano raka piersi a terapią hormonalną.

Wyniki. W grupie 300 kobiet ze zdiagnozowanym rakiem piersi, najliczniejszy udział stanowiły kobiety w wieku 40-59 lat (średnia 53.06±11.25 lat). Wśród pacjentek wyróżniono 45 kobiet stosujące HC (HC – antykoncepcję hormonalną) ze średnim wiekiem 46.44±7.34 lat oraz 82 kobiety stosujące HRT (HRT – hormonalną terapię zastępczą) ze średnim wiekiem w tej grupie 53.63±6.67 lat. Wśród kobiet, które przyjmowały preparaty hormonalne średni wiek wykrycia raka piersi wynosił 50.60±7.56 lat, w porównaniu do kobiet nie stosujących żadnej terapii hormonalnej 53.92±12.35 lat. Wśród badanych kobiet najczęściej stwierdzany był naciekający nowotwór wewnątrzprzewodowy (*ductal carcinoma*) oraz wewnątrzrzazikowy (*lobular carcinoma*). U 2 pacjentek stwierdzono dwa rodzaje nowotworu. Wśród 14 pacjentek wykryto nawrót choroby,

*Corresponding author: Joanna Wyka, Department of Human Nutrition, Wrocław University of Environmental and Life Sciences, Chelmońskiego 37/41, 51-630 Wrocław, Poland, phone: +48 71 3207757, e-mail: joanna.wyka@up.wroc.pl

średni czas od powtórnego zdiagnozowania nowotworu wynosił 4.86 lat. Po operacji chirurgicznej nowotwór wykazano u 7 kobiet. W grupie 34 pacjentek stwierdzono występowanie nowotworu piersi w rodzinie.

Wnioski. W obecnych czasach leczenie nowotworu piersi, szczególnie we wczesnych stadiach choroby przynosi satysfakcjonujące rezultaty. Jednak złośliwe postaci nowotworu nadal są przyczyną wysokiej śmiertelności wśród kobiet. W niniejszym badaniu nie udało się wskazać istotnej zależności pomiędzy występowaniem nowotworu piersi a stosowaniem HC i HRT wśród badanych kobiet.

Słowa kluczowe: nowotwór piersi, antykoncepcja hormonalna, hormonalna terapia zastępcza, czynniki ryzyka

INTRODUCTION

Breast cancer is the most common invasive cancer in women and its etiology is not fully defined [8]. The current incidence of this disease has increased since 1980 in all European countries [3], and breast cancer mainly concerned oncological women diseases in 2012 (49-148/100 000). High incidence was recorded in Western European countries, notably in Belgium (147/100 000), France (137/100 000), the Netherlands (131/100 000) and in Northern Europe, especially in the UK (129/100 000) and the Nordic countries such as Denmark (143/100 000), Iceland (131/100 000) and Finland (121/100 000). The incidence in Eastern European countries, such as Ukraine (54/100 000) and Moldova (53/100 000) was much lower [14]. Also breast cancer is the most common malignant tumour among women in Slovakia. Estimated age-standardised incidence rates (European standard) per 100 000 was 69.7 (in Poland 74.1) and mortality was 21.2 (in Poland 20.9) [13]. However, the decreasing trend in mortality is observed in recent years. The largest decline was recorded in the Northern European countries, but declines were also observed in Central and Eastern Europe, which mainly caused by the advances in therapy [2], particularly the introduction of organised mammography screening programmes [27].

The high rates of breast cancer in developed countries are the consequence of a higher prevalence of the known risk factors for the disease [19]. The most important risk factors include age, family history and reproductive factors. Also the risk of breast cancer is associated with lifestyle and hormonal factors [28]. Possible relationship between hormonal contraceptives and breast cancer was the subject of several epidemiological studies [9,23].

The aim of the present study was to determine if there is a relationship between hormonal contraceptives and

hormone replacement therapy in patients with a positive diagnosis of breast cancer, age at which the disease was diagnosed taking into account the most common types of breast cancers in selected sonographic clinic in the district of Nitra, Slovak Republic.

MATERIALS AND METHODS

The research was performed in outpatient sonographic Clinics Chrenova in Nitra, in 2012. The study included 300 randomly selected female patients, aged 29-79 who had histologically confirmed breast cancer. The age at which breast cancer was diagnosed, and relationship to hormone therapy with maintaining the anonymity of patients were analysed based on medical documentation. Studied group was divided into three subgroups: (1) patients taking hormonal contraceptives (HC), (2) patients subjected to hormone replacement therapy (HRT) and (3) patients who never took such treatment served as a reference group for this study. Duration (in months) of taking the hormonal contraceptives or hormone replacement therapy was analysed. The most common types of breast cancers in this group were regarded in this study.

RESULTS

Based on medical history of a monitored cohort, there was found that 173 women had never received hormonal contraceptives (HC) or hormone replacement therapy (HRT), whereas 127 declared this treatment (Table 1). The mean age of breast cancer in monitored group was 53.06 ± 11.25 years. The youngest woman diagnosed with breast cancer was 25 years old and the oldest one was 87 years. The mean age of diagnosed breast cancer in women who took HC was 46.44 ± 7.34

Table 1. Evaluation of monitored indicators

Monitored indicators	Number of patients	Mean age	s_x	Confidence interval
Patients with HC	45	46.44	7.34	39.10±54.00
Patients with HRT	82	53.63	6.67	46.96±60.30
Patients with HC and HRT	127	50.03	7.56	43.04±58.16
Patients without HC and HRT	173	53.92	12.35	41.57±66.27
Together	300	53.06	11.25	41.81±64.31

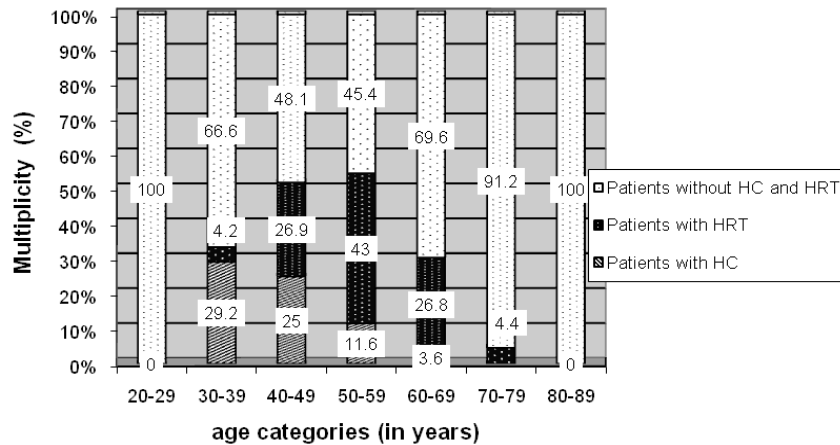


Figure 1. Monitored groups of patients

years, and 53.63 ± 6.67 years in women who received HRT.

The youngest patient with breast cancer who received HC for 42 months, was 36 years old woman. Whereas, the oldest patient with positive relation to HRT, was 69 years old woman, who was subjected to the replacement therapy for 60 months.

Figure 1 shows the number of patients from different age groups subjected to HC or HRT. It follows that women aged 30-39 (29.2%) and 40-49 (26.9%) comprised the largest group of patients receiving HC. The highest percentage of patients receiving HRT were at the age 50-59 (43%), and almost equally represented were patients subjected to HRT aged 40-49 (26.9%) and 60-69 (26.8%). The alleviating menopausal symptoms were the main reasons why women received HRT.

The youngest woman, aged 38, diagnosed with breast cancer, received HRT for 24 months (2 years). The oldest one, diagnosed at the age of 78 year, has been taking HRT for 36 months (3 years). Patients who were not subjected to HRT or HC therapy were on average aged 53.92 ± 12.35 years. However, the youngest patient, who did not receive HRT and HC, was diagnosed with breast cancer at 25 years. Moreover, the oldest ones, who were not subjected to hormonal therapy, were diagnosed with breast cancer at the age of 87. The mean age of patients with breast cancer, who received HRT or HC, was 50.60 ± 7.56 years. These results confirm the fact, that age when the breast cancer has been diagnosed

for the first time, decreased. This problem concerns all women at risk age, not only women subjected to HRT or HC therapy. However, the positive aspect is that the women who received HRT and HC are under constant supervision of gynaecologist. With breast cancer, early diagnosis and treatment are successful. On average, 45 women were subjected to HC therapy for 44.6 months (3.7 years), whereas 3 months were the minimum duration of treatment and the maximum was 192 months (16 years). 82 women were subjected to HRT with an average period of 45.66 months (3.8 years) and the minimum duration of treatment was one month and a maximum was 168 months (14 years).

Table 2 shows the type of breast cancer detected in the examined group of women. It indicates that tumours with infiltrating ductal and lobular carcinoma were the most frequently diagnosed. All observed facts depended on the accuracy and completeness of keeping the medical records in the sonography surgery clinic. However, some patients, after being diagnosed, chose another clinics, for that reason the data were not complete. From all patients, only 14 cases of relapse were diagnosed. Relapses appeared after 4.86 year. 2 patients had breast cancer on both diagnosed breasts. 7 patients came down with cancer after the accident. 34 patients confirmed positive family history.

This issue is very complex and needs to be solve in future long-term epidemiological studies.

Table 2. Types of breast cancer in monitored group

Age intervals (in years)	20-29	30-39	40-49	50-59	60-69	70-79	80-89
Ductal carcinoma <i>in situ</i>			4	2	4		
Lobular carcinoma <i>in situ</i>			1				
Infiltrating ductal carcinoma		9	44	48	18	8	
Infiltrating lobular carcinoma			9	4	9	2	
Infiltrating tubular carcinoma			1	2	2		1
Infiltrating medullary carcinoma	1	3	3	1			
Infiltrating mucinous carcinoma					1		
Infiltrating papillary carcinoma		1			1		

DISCUSSION

Hormonal contraceptives are among the most popular, safe and effective methods of reversible contraception [4]. Hormone replacement therapy (HRT), when is used at early stage, can minimize the dose and individual approach suitable for acute treatment of climacteric syndrome. Menopause is generally defined as the ending of menstruation [30]. While some patients go through this period with mild complaints, the others can have a series of symptoms of physiological changes such as feeling hot, vasomotor symptoms, changes in mood, sleep disorders and somatic complaints. The effects on cognitive functions can reduce the quality of life and social relationships. The aim of post-menopausal hormone therapy is to improve the quality of the patient's life and prevent the negative changes affecting the patient's life. Acute menopausal symptoms are an effect of a decrease in estrogen levels [16, 22]. However, some of the HRT preparations used for treatment are thought to worsen the woman's current psychological situation. Among the explanations proposed for the fact that psychological symptoms deteriorate with HRT are a pre-morbid personality structure reacting to different progesterone types, or the structural sensitivity of women with individual predispositions [10]. The authors concluded that the use of dienogest in continuous combined hormone replacement treatment was specifically indicated for postmenopausal women with disorders of alertness and mood [5, 24].

Hormone replacement therapy with the lowest dosage, early start and individual approach is the first-choice drug for acute climacteric syndrome. It has been safe for cardiovascular disease so as for breast cancer in acceptance of contraindications. The early start of therapy is connected with lowering of cardiovascular risk in the sharp difference from later initiation. Hormone replacement therapy should be given to the basic position of osteoporosis prevention in connection with vitamin D and calcium intake. The rational and safety hormonal substitution are based on annual discussion about risk/benefit ratio [12]. Other studies designed to analyse the influence of hormonal preparations on breast cancer do not provide direct conclusions [1]. The large randomized study of WHI (Women's Health Initiative) [29] stated that breast cancer incidence increased up to 26% among women subjected to HRT for 5.2 years. Whereas, according to the HERS study (Heart and Estrogen / progestin Replacement Study) [18], it is even higher, and reached 30%. These studies consistently referred that increased exposure to female sex HRT hormones caused an increase in the incidence of breast cancer [6]. Generally, it can be stated that women taking these preparations, only insignificantly can increase

the risk of breast cancer [17]. Time and age at which those preparations are taken is important [20]. The most available information related to older, high-dose hormonal preparations. Among users of low-dose oral contraceptives, cardiovascular diseases occur mainly in smokers and women with predisposing factors. Every effort should be made to encourage smoking cessation among potential users of oral contraceptives [7]. Our results stated that the mean age of women subjected to HC was 46.44 years. Comparing the results since 2005 [15], the age decreased by 5.36 year. Age at diagnosis of breast cancer varies considerably among different populations [11]. The exact reasons why the disease moves to younger grades are still not known. Consideration is being given to the possible effect of hormonal contraceptives, but its share of the tumour is difficult to verify. It is assumed, that the increase in incidence may be associated with an increased incidence of the disease users in their regular screening [21]. Taking HRT before diagnosis of breast cancer prognosis did not negatively affect the biological behaviour of the tumour. On the contrary, carcinomas behaved less aggressively, metastasis-free interval and survival in women subjected to HRT longer [25]. Risk assessment is a key component for determining an individual's options for breast cancer screening and prevention. A primary care clinician needs to be able to identify risk factors that place a woman at higher-than-average risk for breast cancer, and if needed, place the appropriate referral for genetic consultation and risk-reduction assessment. Mammography is universally recommended for women aged 50 to 74, with the frequency of screening (annually or biennially) to be determined by individual patient preferences and a balance of net harms and benefits. Although guidelines generally recommend offering screening for women at age 40 to 49, some place additional emphasis on a shared decision-making model between patient and providers. Preventive measures, such as physical activity, tobacco cessation, limiting alcohol use, and maintaining a recommended body mass, should be encouraged for all women to reduce breast cancer risk including chemoprevention with selective estrogenic receptor modulators is an important consideration for women at high risk from breast cancer [26].

CONCLUSIONS

Based on a retrospective analysis of 300 medical records of patients there can be concluded that the largest group was aged between 40-59. This fact confirms the trend of gradual decrease in age of diagnosing this disease in recent years. The mean age of a reference group was 53.06 ± 11.25 years. For women who were subjected to HC it was 46.44 ± 7.34 years, and incre-

ased to 53.63±6.67 years for taking HRT. Moreover, the result was that women who have taken hormonal preparations were diagnosed with breast cancer at an average age of 50.57±7.56 years, whereas women who never took HRT or HC were diagnosed at an average age 53.92±12.35 years. Based on types of diagnosed cancer, it may be concluded that the most common cancer was infiltrating ductal and lobular carcinoma observed in the age of 40-69. Out of all patients the relapse occurred in 14 patients, after about 4.86 years. Breast cancer in both breasts was diagnosed in 2 patients. Cancer after the injury occurred in 7 patients. 34 patients confirmed positive family history.

Conflict of interest

The authors declare no conflict of interest.

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