Original Article

Investigation on the association between breast cancer and consumption patterns of combined oral contraceptive pills in the women of Isfahan in 2011

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Abstract

Background: Oral contraceptive pills are among the most popular contraceptive methods, but the fear of cancer and cardiovascular disease overshadows its continuous use among women. This study aimed to define the association between consumption patterns of combined oral contraceptives among women with breast cancer.

Materials and Methods: This is an analytical case–control study conducted on 175 women with breast cancer, referring to Seyed al Shohada Medical Center and private clinics in Isfahan to be treated and followed up in 2011, as well as 350 healthy women who were identical with the subjects in the study group regarding age and residential location. The data were collected using a researcher-made questionnaire. Content validity and Cronbach's alpha were employed to confirm validity and scientific reliability of the questionnaire, respectively. The data were analyzed by descriptive and analytical statistical methods through SPSS.

Results: The findings showed that there was a significant association between history of contraceptive pills' consumption and incidence of breast cancer ($P < 0.001$). It was shown that the risk of developing breast cancer is increased by 2.27-fold among those with pills' consumption compared to those with no history of that. It was also shown that pills' consumption for 36-72 months increased the risk of breast cancer by 2.18-fold, the age of the first use being less than 20 years increased the risk by 3.28-fold, and time since the last use of less than 25 years increased the risk by 2.63-fold. There was no significant association between duration of use, age of the first and last use, and time since the first and last use in the study and control groups.

Conclusion: The results showed that history of pills' consumption is associated with incidence of breast cancer regardless of the consumption pattern. Use of oral contraceptives pills at any age and for any duration can increase the risk of breast cancer.

Key words: Age at first use, breast cancer, combined oral contraceptives, duration of use

Introduction

Family planning services are known as the most effective way to reduce unwanted pregnancy, and for population control in Asian and Latin American countries.[1] Hormonal methods are highly successful among the contraceptive methods, and are counted as the most effective reversible way.[2] Women's fear and anxiety about developing cancer and cardiovascular diseases are the prohibiting factors for the constant intake of contraceptives.[3] In Ehsanpour's study[4] that compared users' attitude about common contraceptive methods, it was concluded that although a high percentage of the subjects believed contraceptives to be the most effective method, 60.8% of the women had a negative attitude toward intake of contraceptives due to their hormonal combination and side effects.

In relation to the consumption of combined contraceptives by millions of women and their concern about the effects of the hormonal combination on their health and incidence of cancer, several studies have been conducted to investigate the safety of these medications. Some studies report that intake of combined contraceptive has no significant effect on the risk of breast cancer,[5-8] while some other studies emphasize on this issue.[9-13] The existing controversy can be because of mixing up all types of the studied invasive cancers, ignoring the intake methods, and/or the type of study as well as selection of different case groups. Therefore, the researcher tried to investigate the association between consumption patterns of combined oral contraceptives (duration of use, the first and the last age of use, the time since the first and the last use) and incidence of breast cancer in the population of Isfahan.

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Materials and Methods

This is an analytical case–control, one-stage, two-group multivariable study. The subjects were 525 women (175 with breast cancer and 350 healthy women). The research was conducted in Seyed al Shohada Medical Center (which covers the whole province of Isfahan with its special and sub-special services, with a vast coverage of breast cancer) as well as private breast cancer clinics in Isfahan. At first, the researcher collected some personal information and phone numbers of the women with breast cancer through backward searching of the latest electronic and paper files that existed in breast cancer clinics. Next, regular random sampling was employed in these centers through dividing the number of breast cancer women's files by the number of subjects needed. The obtained number showed the intervals between the subjects. Then, it was tossed between number one and the obtained number to determine the first subject to start from based on the file's number. Finally, the subjects were selected by the calculated intervals. Inclusion criteria for the study group were having a medical file of breast cancer diagnosis and treatment in the mentioned centers, ability to answer the questions, personal interest to attend the study, having Iranian nationality, and residing in Isfahan. After the selection of subjects in the study group and with regard to subjects' residential location and patients' range of age (−2, +2), 350 women (two of the related neighbors for each patient, if they met the inclusion criteria) were interviewed. Inclusion criteria for the control group were: Residing in the neighborhood of the patients, being in age range identical to that of the patients (−2, +2), and normal report of breast exam conducted by a clinic specialist or a midwife in the recent past year. Data collection tool was a researcher-made questionnaire which included four sections for the study group and three sections for the control group. The data were collected until diagnosis of breast cancer in the case group and until filling the questionnaire in the control group.

Content validity and test retest correlation index were employed to confirm validity and scientific reliability of the questionnaire, respectively.

The quantitative and qualitative data collected in the present study were analyzed by descriptive statistics (frequency distribution table, mean, and SD) and inferential statistical tests (χ^2 and independent *t*-test), as well as univariable regression analysis was employed to measure odds ratio using SPSS version 14.

Results

One hundred and seventy-five women with breast cancer (study group) and 350 healthy women (control group) participated in the present study. The highest frequencies of age, marital status, and marriage age were

Table 1: The distribution of frequency of demographic characteristics in cases and controls

Subject	Classification	Case		Control		χ^2	*P* value
		Number	Percent	Number	Percent		
Age (years)	≤40	34	19.4	79	22.6	0.85	0.83
	41-50	68	38.9	125	35.7		
	51-60	44	25.1	89	25.4		
	60>	29	16.6	57	16.3		
	Total	175	100.0	350	100.0		
Marital status	Single	5	2.9	13	3/7	7.11	0.06
	Married	153	87.4	277	79.1		
	Widowed	14	8.0	56	16.0		
	Divorced	3	1.7	4	1/2		
	Total	175	100.0	350	100.0		
Age at marriage (years)	≤15	40	23.5	75	22.3	5.94	0.11
	16-20	80	47.1	146	43.3		
	21-25	32	18.8	93	27.6		
	>26	18	10.6	23	6.8		
	Total	170[1]	100.0	337[2]	100.0		
Number of children	≤3	111	65.3	235	69.7	1.02	0.31
	>3	59	34.7	102	30.3		
	Total	170	100.0	337	100.0		

[1]Five persons of cases are single, [2]Thirteen persons of control are single

for the breast cancer women in the study and control groups; therefore, most of the women with breast cancer were aged 41-50 years (38.9%) and had got married at 16-20 years of age (47.1%). Most of the subjects had three or less than three children (65.3% in study and 69.7% in control) [Table 1]. Pills' consumption was significantly higher in the study group (43.4%) compared to control (25.4%) ($P < 0.001$). The risk of breast cancer was 2.27-fold more among those taking pills compared to non-consumers [Table 2]. Women with breast cancer had the highest mean duration of use, the highest mean age of the first use, the highest mean age of the last use, and the highest mean time passed since the first and last use, although the mean differences were not significant based on independent *t*-test results ($P > 0.05$) [Table 3]. Most of the subjects had consumed the first pill at the age of 21-25 years (34.3% in study and 38.2% in control group). Frequency of taking pills over 31 years of age, consumption quit over the age of 36 years, and taking pills for over 21 months were higher in women with breast cancer compared to healthy ones. The risk of breast cancer was increased by 2.18-fold for those taking the pills for 36-72 months, by 3.28-fold for age of the first use being less than 20 years, and by 2.63-fold for the age of the last use being less than 25 years, but these increases were not significant ($P > 0.05$). With regard to the time since the first and the last pills' use and incidence of breast cancer, no significant association was found [Table 2].

Discussion

The obtained results of the present study showed that there was a significant association between history of pills' consumption and incidence of breast cancer. Higher risk of breast cancer as a result of contraceptive pills had also

Table 2: Frequency distribution of history in OCP consumption and OCP pattern of use in case and control subjects [with OR (95% CI)]

Subject	Classification	Case		Control		OR (95% CI)	*P* value
		Number	Percent	Number	Percent		
History of OCP consumption	Yes	76	43.4	89	25.4	2.27 (1.53-3/33)	>0.001
	No use	99	56.6	261	74.6	Referent	
	Total	175	100.0	350	100.0		
Duration of use (months)	≤36	24	31.6	26	29.2	1.53 (0.75-3.20)	0.38
	37-72	16	21.1	28	31.5	2.18 (0.89-5/37)	
	73-120	16	21.1	19	21.3	1.4 (0.58-3.78)	
	≥121	20	26.2	16	18.0	Referent	
	Total	76	100.0	89	100.0		
Age at first use (years)	≤20	14	18.4	23	25.8	3.28 (0.90-9.13)	0.18
	21-25	26	34.3	34	38.2	2/61 (0.92-7/40)	
	26-30	22	28/9	25	28/1	2/27 (0/77-6/64)	
	≥31	14	18.4	7	7/9	Referent	
	Total	76	100.0	89	100.0		
Age at last use (years)	≤25	11	14.5	22	24.7	2.63 (0.86-8.01)	0/22
	26-30	19	25.0	25	28.2	1.62 (0.62-4.21)	
	31-35	21	27.6	23	25.8	1.28 (0.51-3.19)	
	≥36	25	32.9	19	21.3	Referent	
	Total	76	100.0	89	100.0		
Time since first use (years)	≤12	9	11.8	16	18.0	2.32 (0.33-16.36)	0.33
	13-24	40	52.6	38	42/7	0.92 (0.19-4/33)	
	25-36	19	25.1	29	32.6	1.26 (0.28-5.58)	
	≥37	8	10.5	6	6.7	Referent	
	Total	76	100.	89	100.0		
Time since last use (years)	≤8	21	27.6	22	24.7	0.65 (0.23-30.11)	0/22
	9-16	27	35/5	26	29/2	3/10 (0/34-27/71)	
	17-32	23	30.3	39	43.8	4.31 (0.55-33.39)	
	≥33	5	6.6	2	2.3	Referent	
	Total	76	100.0	89	100.0		

Table 3: The comparison between the mean of the pattern of use of OCP in cases and controls

Group subject	Case	Control	*P* value
Duration of use (months)	92.19 (±52.42)	79.30 (±55.91)	0.40
Age at first use (years)	25.52 (±6.18)	24.03 (±5.03)	0.08
Age at last use (years)	33.10 (±7.19)	30.60 (±7.22)	0.08
Time since first use (years)	22.26 (±9.24)	20.55 (±9.30)	0.84
Time since last use (years)	15.75 (±9.36)	14.77 (±9.96)	0.51

been reported by Ozmen,[14] Nojoumi,[15] Kahlenborn,[16] Yavari,[17] and Tehranian.[13] On the contrary, the findings of Hajian Tilaki[18] and Hunter[19] showed no significant association between oral contraceptives' consumption and risk of breast cancer. Narvaize *et al*.[19] showed that a noticeable change in periodical epithelial breast tissue changeability occurs after a 21-day use of combined oral contraceptives.

It should be also indicated that epithelial breast tissue can show various hormonal reactions due to expression of numerous indexes of differentiation and development.[20,21]

The findings of the present study showed no significant association between duration of use and incidence of breast cancer, which concords with the findings of the other studies.[8,22-24] Lack of a significant association between the age of the first use and incidence of breast cancer, found in the present study, was consistent with the results of Nichols' study.[25] March Banks[8] also emphasized on lack of any association between the age of the first use and the time since the last use, which is consistent with the results of the present study. However, with regard to the limited studies conducted on length of use, age of the first and last use, the time passed since the first and last use, further studies in various societies are needed to conclude the association between contraceptive pills' consumption patterns and breast cancer.

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