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The Correlation of the Use of Oral Contraceptive Pills and the Risk of Ischemic Heart Disease in Perimenopausal Women

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Abstract

Oral Contraceptive Pills (OCP) are known to have cardiovascular adverse effects. However, Ischemic Heart Disease (IHD) is relatively uncommon among pre-menopausal women. The aim of this study is to find out if the use of OCP is associated with increased risk of IHD in perimenopausal women.

A cross-sectional study was conducted throughout the year 2016. The study population consists of two groups; 120 non-diabetic women in the perimenopausal age between 40 and 55 years old who met the diagnostic criteria of IHD, and 120 healthy age-matched women who did not have any history of cardiovascular disease. Each woman was assessed individually using a case sheet that include complete medical & medication history, use of OCP & its duration, in addition to risk factors of IHD.

The use of OCP was found to be significantly higher among women with IHD; 96 out of 120 (67.5%), as compared with those without IHD; 33 out of 120 (27.5%) [Odds ratio (OR): 3.57, 95 % Confidence Interval (CI): 2.08 to 6.12, *P*-value 0.0001]. Also, the duration of its use was significantly longer among IHD group [*p*-value <0.0001]. Moreover, the use of OCP was associated with the occurrence of IHD among women who had risk factors of IHD: Obesity [OR: 2.45, 95 % CI: 1.25 to 4.81, *P*: 0.009], dyslipidemia [OR: 3.48, 95 % CI: 1.59 to 7.60, *P*: 0.002], hypertension [OR: 2.62, 95 % CI: 0.94 to 7.33, *P*: 0.066], smoking [OR: 6.12, 95 % CI: 1.02 to 36.89, *P*: 0.048], and family history of IHD [OR: 2.85, 95 % CI: 1.04 to 7.82, *P*: 0.042].

The use of OCP may increase the risk of IHD in perimenopausal women especially in those who already have cardiovascular risk factors.

Keywords: Oral Contraceptive Pills, Ischemic Heart Disease, Risk factors, Perimenopausal Women.

INTRODUCTION

Oral hormonal contraception is a method used to prevent unwanted pregnancy by acting on endocrine system [1]. They simulate a state of pregnancy by elevating hormonal blood level that suppresses ovulation and implantation [2]. The common hormonal contraceptive pill composed of both estrogen and progesterone. These hormones have many adverse effects on the cardiovascular system as estrogen causes decrease venous blood flow, endothelial proliferation in veins and arteries, increased coagulability of blood resulting from change in platelet functions and fibrinolytic system, and decrease plasma level of antithrombin III [3]. While progesterone especially with androgenic activity may cause decrease glucose tolerance, decrease levels of HDL, increase levels of LDL, and platelet aggregation, in addition to coronary arterial spasm [4].

Ischemic heart disease (IHD) is a status in which the blood perfusion to the heart is hindered by atheroma, thrombosis or spasm of coronary arteries. This may reduce the oxygenated blood supply to myocardium sufficiently lead to oxygen demand and myocardial ischemia which, if severe or prolonged, may cause the death of cardiac muscle cells. The consequent ischemic myocardium releases adenosine which act on the adenosine (A1) receptors located on the cardiac nerve endings to mediate chest pain [5]. There are many predisposing risk factors for induction of IHD including a family history of IHD [6], prolong stress and other psychiatric disorder [7], smoking [8,9], obesity [9,10], dyslipidemia [9,10], hypertension [9-11], diabetes [10,12], and infections with certain microorganisms [13]. It is usually rare to occur in women during the premenopausal age unless there are some predisposing risk factors especially diabetes that may lead to coronary artery disease [9,10].

The average age of menopause is 48-52 years, but for some women it may occur as early as 40 or as late as 55 years [14]. The perimenopause, or the menopausal transition, is the time leading up to a woman's last period during which menstrual periods can stop and then start again until it ends up [14].

The aim of the present study is to assess the effect of using oral contraceptive pills on the incidence of IHD in non-diabetic perimenopausal women.

MATERIALS AND METHODS

This study was designed as a case-control study, conducted throughout the year 2016. The population sample enrolled were non-diabetic women in the perimenopausal period aged between 40 and 55 years; consists of two groups of women: Group 1 includes 120 women who met the diagnostic criteria of ischemic heart disease [15], and Group 2 includes 120 healthy women who did not have any cardiovascular disease. They were seen and evaluated in the Outpatient Clinic and Women Health Clinic. All patients' consents were taken and this study was approved by the local ethical committee. Exclusion criteria were diabetes and renal or liver impairments.

Ischemic heart disease was diagnosed by specialist cardiology physician according to the European Society of Cardiology (ESC) Guidelines for the diagnosis and management of stable coronary artery disease [15].

Each woman was assessed individually using a case sheet that include age, weight and height to calculate the Body Mass Index (BMI), full medical history, past medical history (mainly hypertension), family history, smoking history, medication history especially antihypertensive & the use of combined oral contraceptive pill (OCP) and duration of use. Also, complete physical examination and full investigations were done which include Electrocardiography (ECG) at rest (for all) and during exercise test (for group1), in addition to biochemical tests as renal & liver function tests, blood glucose, hemoglobin A1c, cardiac markers & lipid profile. Blood Pressure measurement was done by mercurial sphygmomanometer recording. The presence of hypertension and response to antihypertensive treatment were categorized as: "No Hypertension" means patient has normal blood pressure, "Controlled" means patient has hypertension that is controlled on treatment, and "Uncontrolled" means patient has hypertension that is not controlled on antihypertensive treatment. The classification of BMI include; Normal 18-<25, Overweight 25-<30, and Obese ≥30. The definition of dyslipidemia according to 2016 ESC Guidelines [16] was defined as elevated total or low-density lipoprotein (LDL) cholesterol levels, or low levels of high-density lipoprotein (HDL) cholesterol.

Statistical analyses:

Statistical analyses were achieved using SPSS 19.0 for windows Inc. The data were showed as means ± SEM or as numbers & percentages and statistically analyzed by using independent-samples T test, or Chi-square and odds ratio.

P-values of < 0.05 were considered statistically significant.

Results And Discussion

The characteristics of women in two groups; those with IHD and those without IHD are shown in table 1 and figure 1. The age of both groups was matched with no statistically significant difference. The Body Mass Index (BMI), in addition to other risk factors of IHD, was significantly higher in women with IHD group. The percentage of OCP use was higher among women with IHD (67.5%) as compared with those without IHD (27.5%). Also, the duration of OCP use was longer in women with IHD group. There were statistically significant differences as shown in table 1. The effect of OCP use in women with risk factors of IHD: obesity, dyslipidemia, hypertension (HT), smoking history, and family history of IHD are shown in tables 2, 3, 4, 5 & 6 respectively.

Table 1: Characteristics of the two groups of women Expressed by Mean±SEM or by Numbers & (Percentages)

Women Characteristics	Women with IHD (N=120)	Women without IHD (N=120)	*P* value
Age (years)	45.98 ±0.45	44.82 ±0.59	0.12†
BMI (kg/m^2)	29.88 ±0.6	25.28 ±0.22	< 0.0001*
Overweight & Obese	94 (78.3%)	57 (47.5%)	< 0.0001*
Dyslipidemia	114 (95%)	42 (35%)	< 0.0001*
Hx of Hypertension	86 (71.6%)	19 (15.3%)	< 0.0001*
Controlled	36 (30.0%)	19 (15.3%)	< 0.0001*
Uncontrolled	50 (41.7%)	0 (0.0%)	< 0.0001*
Hx of Smoking	22 (18.3%)	9 (7.5%)	0.0123*
Family Hx of IHD	80 (66.7%)	21 (17.5%)	< 0.0001*
Use of OCP	69 (67.5%)	33(27.5%)	<0.0001*^
Duration of OCP (yr)	3.08±0.34	1.66±0.15	<0.0001*

†: No significant difference between the 2 groups of women.

*: Significant difference between the 2 groups of women.

^ Odds ratio: 3.57 95 % CI: 2.08 to 6.12

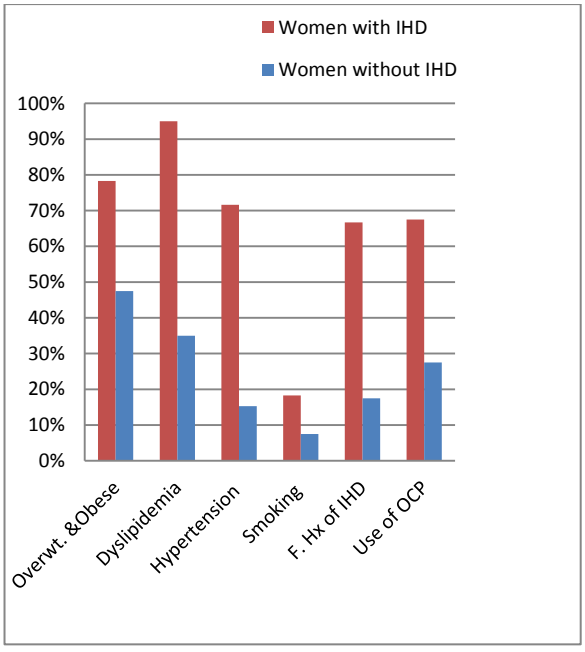

Figure 1: The characteristics of the two groups: (a) women with IHD in red color (aliened to the left) and (b) women without IHD in blue color (aliened to the right).

Table 2: The effect of OCP use in women with Obesity

Groups of overweight & obese women	Use of OCP		Total
	Yes	No	
Women with IHD	57 (60.6%)	37 (39.4%)	94 (100%)
Women without IHD	22 (38.5%)	35 (61.5%)	57 (100%)
Total	79 (52.3%)	72 (47.7%)	151 (100%)

Odds ratio: 2.45 95 % CI: 1.25 to 4.81 *P*-value: 0.009

Table 3: The effect of OCP use in women with Dyslipidemia

Groups of women with Dyslipidemia	Use of OCP		Total
	Yes	No	
Women with IHD	63 (55.3%)	51 (44.7%)	114 (100%)
Women without IHD	11 (26.1%)	31 (73.8%)	42 (100%)
Total	74 (47.4%)	82 (52.6%)	156 (100%)

Odds ratio: 3.48 95 % CI: 1.59 to 7.60 *P*-value: 0.002

Table 4: The effect of OCP use in women with Hypertension

Groups of HT women	Use of OCP		Total
	Yes	No	
Women with IHD	52 (60.5%)	34 (39.5%)	86 (100%)
Women without IHD	7 (36.8%)	12 (63.2%)	19 (100%)
Total	56 (53.3%)	49 (46.7%)	105 (100%)

Odds ratio: 2.62 95 % CI: 0.94 to 7.33 *P*-value: 0.066

Table 5: The effect of OCP use in women with Smoking Hx

Groups of Smoker women	Use of OCP		Total
	Yes	No	
Women with IHD	14 (63.6%)	8(36.4%)	22 (100%)
Women without IHD	2 (22.2%)	7 (77.8%)	9 (100%)
Total	19 (61.3%)	12 (38.7%)	31 (100%)

Odds ratio: 6.12 95 % CI: 1.02 to 36.89 *P*-value: 0.048

Table 6: The effect of OCP use in women with Family Hx of IHD

Groups of women with Family Hx of IHD	Use of OCP		Total
	Yes	No	
Women with IHD	47 (58.8%)	33 (41.2%)	80 (100%)
Women without IHD	7 (33.3%)	14 (66.7%)	21 (100%)
Total	54 (53.5%)	47 (46.5%)	101 (100%)

Odds ratio: 2.85 95 % CI: 1.04 to 7.82 *P*-value: 0.042

The use of OCP is widely spread in recent decades throughout the world due to simplicity of available regimens, low cost and more accepted by women compared to other non-hormonal contraceptive methods. OCP prevent ovulation, implantation and therefore pregnancy by its action on endocrine system. Low levels of living because of lower security and socioeconomic states encourage Iraqi women to use OCP, beside that the incidence of IHD is increasing in younger age and in women, which attract our attention to study the relationship between the use of oral contraceptive and the risk of IHD, especially the traditional OCP that is mostly used in Iraq such as *Microgynon* which is inexpensive and widely prescribed.

The results of this study showed that the use of OCP was significantly higher among women with IHD in the perimenopausal age as compared with women without IHD of the same age group (Odds ratio was 3.57, 95 % CI: 2.08 to 6.12, p-value: <0.0001). This was agreed with a study done by Roach R.E.J. et al. 2015 which revealed that the risk of myocardial infarction was increased 1.6 fold in women using OCP [17].

It is well known that obesity is strongly related to other risk factors of IHD such as hypertension, hypercholesterolemia and insulin resistance and it is a modifiable risk factor of IHD [18]. However, obesity may be associated with the use of OCP, as what was recognized by Mohammad NS, et al. 2013 that the BMI in women using OCP was found to be significantly high when compared with control of their respective age groups [19]. Besides, this study revealed that the use of OCP may lead to a significant increase in the incidence of IHD in overweight and obese women (Odds ratio: 2.45, 95 % CI: 1.25 to 4.81, P-value: 0.009). Also, it was found that the use of OCP was associated with significantly higher incidence of IHD in women with dyslipidemia (Odds ratio: 3.48, 95 % CI: 1.59 to 7.60, P-value: 0.002). Similarly, it was stated that women with controlled dyslipidemia can use low-dose OCP, with periodic monitoring of fasting lipid profiles, and women with uncontrolled dyslipidemia or with additional risk factors (e.g., coronary artery disease, diabetes, hypertension, smoking, or a positive family history) should use an alternative method of contraception [20]. Additionally, Skouby S. et al. 2005 mentioned that OCP even in low dose causes decrease HDL and increase LDL, VLDL, and triglyceride [21].

Furthermore, our study showed that the use of OCP was associated with increased incidence of IHD in women who have hypertension (Odds ratio: 2.62, 95 % CI: 0.94 to 7.33, P-value: 0.066), or history of smoking (Odds ratio: 6.12, 95 % CI: 1.02 to 36.89, P-value: 0.048), or family history of IHD (Odds ratio: 2.85, 95 % CI: 1.04 to 7.82, P-value: 0.042). It is well-known that oral contraceptives may lead to raise blood pressure and increase the risk of hypertension which in turn can result in IHD [19, 20]. On the other hand, it was proved that smoking acts synergistically with other risk factors to induce IHD [22]. So, the World Health Organization (WHO) at 2004 publicized that smoking acts as risk factor and enhance cardiovascular effect of OCP, and smokers over 35 years old should not use estrogen-containing contraceptives [23]. Also, women who had family history of cardiovascular diseases may possess an increased risk of early occurrence of IHD [24].

The duration of OCP use may also affect the occurrence of IHD, since those women with IHD had used OCP for longer period in comparison with women without IHD. Further back, Stampfer MJ. et al. 1990 revealed that women using OCP for long period are more liable for exposure to myocardial infarction than newer using women or those who do not use [25]. In the same way, Szarewski A. et al. 2005 mentioned that the use of estrogen-containing contraceptives is contraindicated for women with a history of ischemic heart disease or stroke [26].

CONCLUSION

This study has confirmed the aforementioned findings in which the use of OCP may increase the risk of IHD in perimenopausal women especially in those who already have risk factors of IHD.

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