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Dentistry

Activity for 2020

Activity No: B10 (20) 2024

Topic

Medicine and periodontal health

Article

The association between the use of new oral contraceptive pills and periodontal health: a matched case-control study

Speciality

MP / Obstetrics / Gynaecology / DP / OH / DA

Approved for **TWO (2)** Clinical Continuing Education Units (CEU's)

The Association between the Use of New Oral Contraceptive Pills and Periodontal Health: A Matched Case–Control Study

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Abstract

Aim: The aim of this study was to evaluate the effects of oral contraceptive pills (OCPs) on the periodontal status of the women using them. **Materials and Methods:** During the period from January 2016 to June 2017, 139 oral contraceptive users (Group A) and 142 nonusers (Group B) were examined by a blinded examiner using a mouth mirror and a 15-mm conventional periodontal probe (Hu-Friedy). The dental examination included the simplified oral hygiene index (OHI-S), gingival index, sulcus bleeding index (SBI), and clinical attachment loss (CAL). A full-mouth examination excluding the third molars was performed at four sites per tooth (mesiobuccal, distobuccal, mesiolingual, and distolingual). The results of these examinations were compared between the two groups to identify significant differences. **Results:** Both groups were comparable with regard to their demographic data. Group A had a significantly higher mean OHI-S score than Group B (0.43 vs. 0.29, respectively). The gingival index score was also higher in OCP users than in nonusers (0.78 vs. 0.37, respectively). The SBI score was 0.72 in Group A and 0.41 in Group B, demonstrating a significant difference between OCP users and nonusers. The CAL score was 1.62 in Group A versus 1.11 in Group B, and this difference was statistically significant. **Conclusions:** The use of combined oral contraceptives can influence the periodontal condition of patients, resulting in increased gingival disease. This adverse effect can be enhanced by the use of newer generations of OCPs, especially in high-risk populations.

Keywords: Gingivitis, oral contraceptive pills, periodontal diseases

INTRODUCTION

Oral contraceptives have been used as a means of contraception for a long time, and millions of women have used them over the last 60 years. The use of oral contraceptives is associated with small, but serious increased risks of thromboembolic and cardiovascular complications^[1] and minor side effects, including gingival and/or periodontal disease.^[2]

The effects of sex steroids on the gingiva and periodontal status have been described by many studies that have demonstrated that endogenous sex steroid hormones play significant roles in modulating periodontal tissue responses and may alter the periodontal tissue responses to microbial plaque, thereby directly contributing to periodontal disease.^[3] Sex steroids can influence the periodontium during different life stages including puberty, menstruation, pregnancy, menopause, and postmenopause.^[3] The effect of oral contraceptives on gingival diseases has been described by many authors over the years,^[4-6] although the compositions and dosages of sex steroids in modern oral contraceptive pills (OCPs) have shifted toward

higher progestogenic doses and lower estrogenic doses.^[7] Therefore, we conducted this cross-sectional, comparative study to examine the effects of new generation of oral contraceptives on the gingival status of the women using them.

MATERIALS AND METHODS

During the period from January 2016 to June 2017, we recruited 139 women aged between 18 and 39 years who were using combined oral contraceptive (COC) pills from among the women attending a gynecology clinic at the Islamic Hospital. For the control group, we recruited 142 women who were not current users of OCPs and had not used them during the previous year. Ethical approval was granted from the Ethical

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Access this article online

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Website:
www.jioh.org

DOI:
10.4103/jioh.jioh_17_18

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How to cite this article: Smadi L, Zakaryia A. The association between the use of new oral contraceptive pills and periodontal health: A matched case–control study. *J Int Oral Health* 2018;10:127-31.

Committee of the Islamic Hospital Ethical Board (Ethical approval number IHEB 17–138), and informed consent forms were signed by all women who enrolled in the study; all informed consent was in Arabic although a translated copy to English was available for patients on requests. The inclusion criteria for the participating women were at least 1 year of continued use of combined pills and at least 24 teeth (except for third molars).

The exclusion criteria were as follows: pregnancy or delivery within 12 months before data collection; drug or alcohol abuse; history of radiotherapy or chemotherapy in the past 5 years; early or premature menopause; breastfeeding; the presence of any systemic condition that could influence the host response to plaque accumulation (e.g., diabetes mellitus); periodontal treatment, including professional prophylaxis, within the 6-month period before data collection; and the use of drugs that could induce gingival enlargement (e.g., calcium channel blockers, cyclosporine, or anticonvulsants).

A detailed questionnaire was completed by all patients included in the study that collected their full medical history and COC intake before the clinical examination. The test group volunteers were questioned about the name, dose, and total length of uninterrupted use of COCs, which were recorded in the patient’s record.

The periodontal status of the patients was evaluated by a single-blinded examiner using a mouth mirror and a 15-mm conventional periodontal probe (Hu-Friedy). The dental examination included simplified oral hygiene index (OHI-S),^[8] gingival index (GI),^[9] sulcus bleeding index (SBI),^[10] and clinical attachment loss (CAL).^[11] A full-mouth examination

excluding the third molars was performed at four sites per tooth (mesiobuccal, distobuccal, mesiolingual, and distolingual).

Statistical analysis

The Kruskal–Wallis or Fisher’s exact test was used to compare the median or mean values for the patient characteristics and the outcomes related to the *in vitro* fertilization (IVF) treatment. Student’s *t*-test with Bonferroni correction or one-way ANOVA was used to compare two or more mean values of the indices before and after IVF. Statistical analyses were conducted using SPSS version 18 software (PASW®, IBM, Chicago, USA). The level of statistical significance of all comparisons was set at 5% ($P \leq 0.05$).

RESULTS

A total of 376 women were interviewed for enrollment, including 273 OCP users and 203 nonusers. Of the women interviewed, 141 of the OCP users fulfilled the inclusion criteria, but two of them opted to withdraw from the study after their initial acceptance, resulting in data from a total of 139 OCP users.

In the control group, 147 women fulfilled the inclusion criteria, but five of them opted to withdraw from the analysis, resulting in 142 women enrolled in the control group (Group B). Flowchart 1 demonstrates the inclusion process [Figure 1].

Both groups were comparable, with no significant differences in age, weight, previous pregnancies, previous use of OCP 1 year or more before their enrollment in the study, or medical diseases necessitating medical treatment apart from the diseases mentioned in the exclusion criteria [Table 1].

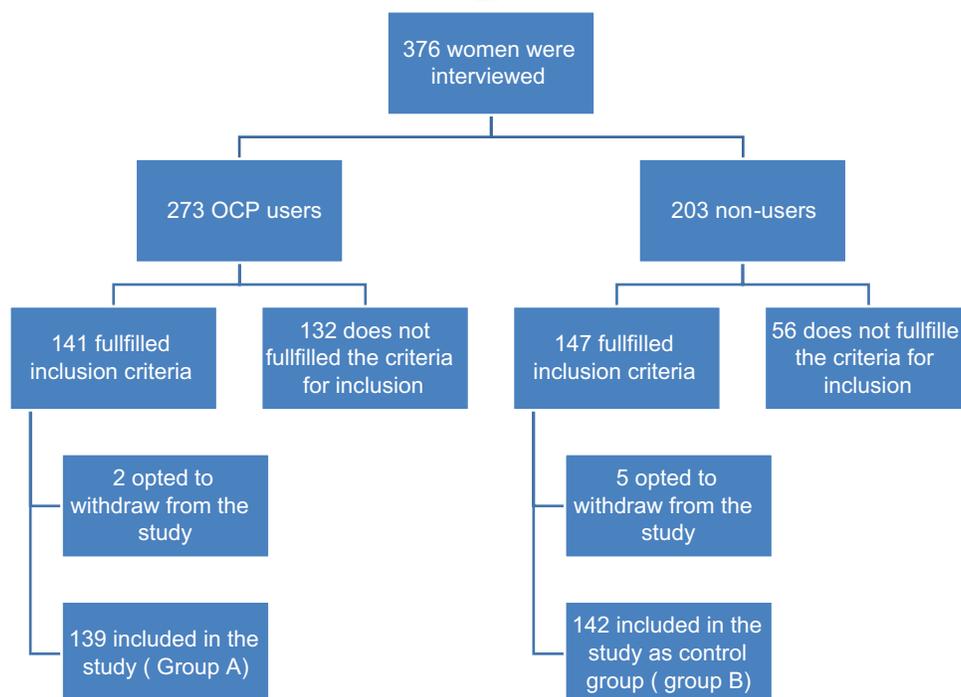


Figure 1: Flowchart for inclusion process

Table 2 lists the type and composition of OCPs used by the women in Group A, showing that 38.9% of OCP users use the newer generation of OCP with higher progesterone affinity while 41.7% use two different products in which the progesterone has a spironolactone analog effect.

The average duration of use of OCP by Group A was 2.3 ± 0.4 years. The Pearson's correlation coefficient was used to test the effect of duration of use of OCP on periodontal indexes. Table 3 demonstrates the results of this analysis. For the control group, the same test was used to demonstrate the effect of age of women on the periodontal indexes; the results are shown in Table 4.

OCP users had a significantly higher mean OHI-S score than nonusers (0.43 vs. 0.29, respectively). The GI score was also higher in OCP users compared to nonusers, with a GI index of 0.78 in Group A compared to 0.37 in Group B. The SBI score was 0.72 in Group A compared to 0.41 in Group B, showing a significant difference between OCP users and nonusers. CAL was 1.62 in Group A versus 1.11 in Group B, and this difference was statistically significant. Table 5 demonstrates these findings.

DISCUSSION

Our results were in accordance with the findings from previous similar studies, in which Kalkwarf, as early as 1978, reported an increased gingival inflammatory index score in OCP users.^[12] Tilakaratne *et al.* found an increased risk of gingival disease, as expressed by an increase in the mean GI score, in

OCP users compared to nonusers in Sri Lankan women.^[13] In 2010, two studies showed similar results of increased GI scores in OCP users compared to nonusers.^[14,15] The study by Haerian-Ardakani *et al.* showed an increase in the mean GI score, pocket depth, and attachment loss in oral contraceptive users compared to nonoral contraceptive users.

Domingues *et al.*, in a 2011 report, demonstrated both increased probing depth and increased SBI scores in OCP users compared to nonusers.^[16]

On the other hand, there were a few studies failed to demonstrate an increased risk of gingival disease in OCP users. Arumugam *et al.* reported nonsignificant differences in the mean GI scores, mean probing depths, and mean clinical attachment levels between contraceptive users and nonusers.^[17]

Knight^[18] reported a nonsignificant difference in the mean GI scores between contraceptive users and nonusers, but they showed a greater loss of attachment in women who had used OCPs for more than 1.5 years compared to those who had taken oral contraceptives for a shorter period.

Our study confirmed the effect of the duration of OCP use on the gingival diseases parameters, showed by other studies which demonstrate an increase in disease with a longer duration of OCP use.^[14-18]

Our study included more patients in both groups than all other previous studies, which enhance the significance of our study.

In our study, the effect of OCP use on gingival disease was significant after only 1 year of use, which can be explained by the fact that the Jordanian population might be at higher risk for the development of periodontal diseases.^[19] This enhanced predisposition for periodontal disease should explain the similarity between our results and the results from underdeveloped countries such as Sri Lanka and Iraq.^[13,20]

Both estrogen and progesterone have receptors on the gingiva.^[21,22] Estrogen receptors are also found on periosteal fibroblasts, scattered fibroblasts of the lamina propria, and periodontal ligament fibroblasts and osteoblasts, resulting in complex effects that enhance the probability of gingival and periodontal changes in women exposed to either endogenous sex steroids such as during puberty and pregnancy or exogenous sex steroids such as those resulting from the use of OCP. This effect has been demonstrated clinically, and

Table 1: Demographic data

	Group A	Group B	P
Number of patients	139	142	
Age (years)*	26.7±7.5	24.5±6.9	0.1231
Previous pregnancy**	76/139	79/142	0.6855
Weight (kg)*	64.3±9.12	67±8.9	0.1164
History of previous use of OCP >1 year before the study**	21	19	0.3632
History of medical illness necessitating the use of medications (other than DM)**	15	9	0.0126

*Data presented as the mean±SD for age and weight, and the statistical analysis was performed with unpaired *t*-tests for age and weight. **Numbers were used for parity, medical history, and allergies, and Fisher's exact test was used for the statistical analysis. SD: Standard deviation, OCP: Oral contraceptive, DM: Diabetes mellitus

Table 2: Type and composition of oral contraceptive used by women

Trade name	Oestrogen component	Progesterone component	Properties of progesterone	Number of users (%)
Yaz™	20 µg ethinylestradiol	3 mg drospirenone	Spironolactone analogue	21 (15.1)
Marvelon™	30 µg ethinylestradiol	150 µg desogestrel	Higher affinity for progesterone receptors	54 (38.9)
Yasmin™	30 µg ethinylestradiol	3 mg drospirenone	Spironolactone analogue	37 (26.6)
Microgynon 30™	30 µg ethinylestradiol	100 mg levonorgestrel	Progestogenic	12 (8.6)
Dian™	35 µg ethinylestradiol	2 mg cyproterone acetate	Anti-androgenic	10 (7.2)
Others	—	—		5 (3.6)

Table 3: Correlation between age, total duration of oral contraceptive therapy, and clinical periodontal parameters in test group

	Duration of use	OHI-S	GI	SBI	CAL
Age	$r=0.321$ $P=0.071^*$	$r=-0.721$ $P=0.016^{**}$	$r=-0.633$ $P=0.028^{**}$	$r=-0.481$ $P=0.063^*$	$r=0.523$ $P=0.075^*$
Duration of use	****	$r=-0.427$ $P=0.059^*$	$r=-0.537$ $P=0.068^*$	$r=-0.451$ $P=0.057^*$	$r=-0.65$ $P=0.078^*$
OHI-S	$r=-0.427$ $P=0.065^*$	****	$r=-0.239$ $P=0.01^{**}$	$r=0.422$ $P=0.037^{**}$	$r=-0.218$ $P=0.002^{**}$
GI	$r=-0.537$ $P=0.074^*$	$r=-0.239$ $P=0.01^{**}$	****	$r=0.717$ $P=0.001^{**}$	$r=0.461$ $P=0.031^{**}$
SBI	$r=-0.451$ $P=0.057^*$	$r=0.422$ $P=0.04^{**}$	$r=0.717$ $P=0.001^{**}$	****	$r=0.624$ $P=0.069^*$
CAL	$r=-0.65$ $P=0.078^*$	$r=-0.218$ $P=0.002^{**}$	$r=0.461$ $P=0.031^{**}$	$r=0.624$ $P=0.069^*$	****

**Significant if $P<0.05$, *Nonsignificant if $P>0.05$. r : Correlation coefficient (using Pearson's correlation test). OHI-S: Simplified oral hygiene index, CAL: Clinical attachment loss, SBI: Sulcus bleeding index, GI: Gingival index

Table 4: Correlation between age and clinical periodontal parameters in control group

	OHI-S	GI	SBI	CAL
Age	$r=-0.653$ $P=0.012^{**}$	$r=-0.573$ $P=0.043^{**}$	$r=-0.562$ $P=0.021^{**}$	$r=0.627$ $P=0.061^*$
OHI-S	****	$r=-0.310$ $P=0.02^{**}$	$r=0.467$ $P=0.039^{**}$	$r=-0.351$ $P=0.003^{**}$
GI	$r=-0.310$ $P=0.02^{**}$	****	$r=0.717$ $P=0.001^{**}$	$r=0.381$ $P=0.020^{**}$
SBI	$r=0.467$ $P=0.042^{**}$	$r=0.655$ $P=0.024^{**}$	****	$r=0.499$ $P=0.052^*$
CAL	$r=-0.351$ $P=0.003^{**}$	$r=0.381$ $P=0.022^{**}$	$r=0.499$ $P=0.052^*$	****

**Significant if $P<0.05$, *Nonsignificant if $P>0.05$. r : Correlation coefficient (using Pearson's correlation test). OHI-S: Simplified oral hygiene index, CAL: Clinical attachment level, SBI: Sulcus bleeding index, GI: Gingival index

Table 5: Periodontal status parameters among oral contraceptive users and nonusers

Periodontal status parameters	Group A		Group B		P
	n	Mean±SD	Number of teeth examined	Mean±SD	
OHI-S	1668	0.43±0.031	1704	0.29±0.015	0.002
GI	3336	0.78±0.042	3408	0.37±0.029	0.001
SBI	8896	0.72±0.029	9088	0.41±0.31	0.001
CAL	20,850	1.62±0.14	21,300	1.11±0.17	0.003

*Significant if $P<0.05$. OHI-S: Simplified oral hygiene index, CAL: Clinical attachment level, SBI: Sulcus bleeding index, GI: Gingival index, SD: Standard deviation

a positive correlation has been identified between estradiol and progesterone serum levels and GI inflammation in many clinical situations, including pregnancy, puberty, infertility treatment, and even during menstrual cycles.^[23-26]

The effect of the sex steroids in OCPs will not only manifest direct effects on the gingiva the periosteum or the fibroblasts but will also significantly increase the *Bacteroides* species in the oral cavities of OCP users,^[27] incidence of localized osteitis,^[28] and variation in the coagulation and fibrinolytic factors, leading to a greater incidence of clot lysis.^[29]

Despite the lower doses of estrogen in the newer generations of OCP (20–30 µg compared to 50 µg in older generations of ethinylestradiol), the effects of the sex steroids in OCPs are still evident. The results in our study may be unequivocal to the results of previous studies because the progesterone component in the current OCPs has a more pronounced progestogen effect than in the older generations in which the progesterone component had more androgenic effect [Table 2].

Androgens may play a significant role in the maintenance of bone mass and may inhibit osteoclastic functions, inhibit prostaglandin synthesis, and reduce interleukin-6 production during inflammation. Testosterone also stimulates bone cell proliferation and differentiation and therefore has a positive effect on bone metabolism and enhances matrix syntheses by periodontal ligament fibroblasts and osteoblasts.^[30]

This study demonstrates possible effect of type of hormones used in OCP on oral health effect of the drug, raising possible future research opportunities looking at the effect of type of progesterone on the oral health, including progesterone used in other types or routes of contraception such as injectable, patches, or intrauterine. Such studies may include as well other hormone-dependent diseases which may necessitate the use of progesterone-like treatment of polycystic diseases.^[31] The studies until now looked at the effect of hormonal changes of the disease on oral health but did not investigate the effect of hormonal therapy which includes both androgen and progesterone.

CONCLUSIONS

Our results suggest that the use of COCs can influence the periodontal conditions of patients, resulting in increased gingival disease. This adverse effect can be enhanced by the use of newer generations of OCPs that lack the possible protective effect of the androgenic properties of older OCPs, especially in high-risk populations.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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QUESTIONNAIRE

B10(20)

The association between the use of new oral contraceptive pills and periodontal health: a matched case-control study

INSTRUCTIONS

- Read through the article and answer the multiple-choice questions provided below.
- Some questions may have more than one correct answer; in which case you must please mark all the correct answers.

Question 1: You are revising your patient history form in the practice and notice that the previous partner included the use of contraceptive pills. In general, you know the newer generation COCs are safer, but wonder about their impact on periodontal health. In doing some research, which of the following do you find?

- A:** The effect of sex steroids on the gingiva and periodontal status have not been well studied
- B:** Many studies have demonstrated that sex steroid hormones contribute to periodontal disease
- C:** Sex steroid hormones modulate periodontal tissue response
- D:** All of the above

Question 2: Is it TRUE that sex steroids can influence the periodontium during puberty, pregnancy and menopause but not post-menopause?

- A:** YES
- B:** NO

Question 3: What is the composition of modern oral contraceptive pills?

- A:** Higher progestogenic and oestrogenic doses
- B:** Lower progestogenic doses and higher oestrogenic doses
- C:** Higher progestogenic doses and lower oestrogenic doses
- D:** Lower progestogenic and oestrogenic doses

Question 4: Which drugs may induce gingival enlargement?

- A:** Cyclosporine
- B:** Anticonvulsants
- C:** Macrolide antibiotics
- D:** Calcium channel blockers

Question 5: At which tooth sites was a full-mouth examination performed?

- A:** Mesiobuccal, distobuccal
- B:** Occlusal, mesiobuccal
- C:** Mesiolingual, distolingual
- D:** Distolingual, facial labial

Question 6: Which of the following are progesterone properties in oral contraceptives?

- A:** Ethinyl levonorgestrel
- B:** Drospirenone
- C:** Cyproterone acetate
- D:** Levonorgestrel

Question 7: With reference to the results of other studies, which of the following are TRUE?

- A:** The study by *Haerian-Ardakani et al.* showed an increase in the mean GI score, pocket depth, and attachment loss in oral contraceptive users compared to non-oral contraceptive users
- B:** *Domingues et al.* in a 2011 report, demonstrated both increased probing depth and increased SBI scores in OCP users compared to non-users
- C:** *Tilakaratne et al.* found an increased risk of gingival disease, as expressed by an increase in the mean GI score, in OCP users compared to non-users
- D:** None of the above

Question 8: Is it TRUE or FALSE that this study confirmed that with a longer duration of oral contraceptive pill use there is an increase in gingival disease?

- A:** TRUE
- B:** FALSE

Question 9: What are the effects of sex steroid hormones in oral contraceptive pills (OCP)?

- A:** Significantly increases the *Bacteroides* species in the oral cavity of OCP users
- B:** Increases the incidence of localised osteitis
- C:** Increase in scattered fibroblasts of the lamina propria
- D:** Greater incidence of clot lysis due to variation in the coagulation and fibrinolytic factors

Question 10: Against the background of the results of this study, will you.....?

- A:** Revisit your patient history form and check if the use of OCPs is included
- B:** If not included, discuss it with the dental team
- C:** Not do any one of the above because you do not see the oral effect of OCP use in your practice
- D:** Not do anything because you don't take any form of patient history

END



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ANSWER SHEET

B10 (20)

The association between the use of new oral contraceptive pills and periodontal health: a matched case-control study

	A	B	C	D	E		A	B	C	D	E
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2						7					
3						8					
4						9					
5						10					

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