

Association Between Depot-Medroxyprogesterone Acetate Injection and Periodontal Health in Reproductive Age Women: A Case Control Study in Iran

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Received 2016 February 05; Revised 2016 March 07; Accepted 2016 April 08.

Abstract

Background: It seems that depot-medroxyprogesterone acetate (DMPA) use can have an effect on a woman's oral health, and cause periodontal changes in adult women. However, there is little research in this regard and consensus has not been reached in the literature.

Objectives: This study aimed to investigate the association between DMPA injection and periodontal health in reproductive age women.

Materials and Methods: This descriptive analytical study was conducted on 194 women aged 20 - 40 years in Ahvaz health care centers, southwest of Iran, during 2015. Ninety-seven women taking DMPA were assigned to the case group and 97 women who did not use DMPA were assigned to the control group. Periodontal parameters such as bleeding on probing, probing pocket depth and clinical attachment loss were measured. Data were analyzed by SPSS software version 19 using descriptive and analytic (Chi-square, Mann-Whitney and student's t-test) statistical methods.

Results: There was a statistically significant difference regarding bleeding on probing, probing pocket depth and clinical attachment loss between the case and control groups. Totally, 56.7% of the women in the case group had periodontitis compared to 16.5% in the control group ($P < 0.0001$).

Conclusions: Based on our findings, the use of DMPA can affect the periodontal health status of women. Therefore, women who use this method must have a strict oral hygiene care program.

Keywords: Depot Medroxyprogesterone Acetate, Progesterone, Periodontal Disease, Women, Iran

1. Background

Hormonal contraceptives are the most effective method of birth spacing (1). One of the most common injectable hormonal contraceptive is depot medroxyprogesterone acetate (DMPA), known as Depo-Provera (2). Depot medroxyprogesterone acetate is a highly efficacious long lasting progestin-only injectable hormonal contraceptive, which is administered by intramuscular injection every 3 months (3). The contraceptive action of DMPA results from its suppression of gonadotropin secretion which in turn inhibits ovarian estradiol production and prevents ovarian follicular maturation and ovulation (4). The use of DMPA is a highly effective method, and it is favored because of its simplicity and noninterference with sexual intercourse (5). Today, DMPA is a contraceptive widely used by 90 million women in 130 countries due to its high efficiency and ease of use (6). A National study re-

ports that between 3% - 12% of women in the United States between the ages of 15 - 44 years use DMPA (7). Despite the advantages of DMPA, it causes some changes in menstrual bleeding patterns (amenorrhea, spotting and prolonged bleedings) (8, 9) as well as libido and sexual pain (10), and might also cause low bone mass and osteoporosis in long term (11).

Today, some studies reported that DMPA may impact on woman's oral health, although a consensus has not been reached in the literature. It seems that progestin only contraceptive use has been associated with periodontal changes in adult women (12-15). Tilakaratne et al. reported that DMPA use may be associated with an increase in adverse periodontal changes including gingival bleeding and periodontitis (15). In a clinical study by Seck-Diallo et al. women using DMPA demonstrated more gingival inflammation, periodontal pocketing and clinical attach-

ment loss than nonusers (12). It has been suggested that progestins may have an inflammatory component and/or increase in prostaglandin synthesis. Thus, extended progestin use may be associated with higher risk of periodontal diseases (13).

2. Objectives

Depot medroxyprogesterone acetate is one of the most widely contraceptive methods for birth control. Recent studies have reported that DMPA may impact on oral health; however, there is little research in this regard. Therefore, the present study was performed to evaluate the relationship between DMPA use and periodontal health in reproductive age women.

3. Materials and Methods

This descriptive analytical research was performed on 194 women aged 20 - 40 years, who were using DMPA (two times and for 6 months regularly) and were affiliated to Ahvaz Health Care Centers, southwest of Iran, during 2015. Exclusion criteria were current pregnancy or delivery within 12 months prior to data collection, smoking or former smokers, drugs or alcohol abuse, presence of any systemic condition that could influence the healing and viability of periodontal tissues (e.g., diabetes mellitus, leukemia, neutrophil defects), presence of gingival ulceration, sever gingivitis, gingival overgrowth and periodontal abscesses, use of wide-spectrum antibiotics and nonsteroidal or steroidal anti-inflammatory drugs for the previous 6 months, use of medications or hormones during last 6 months that could predisposed women to gingival overgrowth (such as immunosuppressive agents and calcium channel blockers), periodontal treatment including professional prophylaxis within the 6 months period prior to data collection, and hormone replacement therapy.

To estimate the sample size, a pilot study was conducted on 30 women (not included for the main sample). Based on the results and using the sample size formula with a confidence level of 97%, power: 90%, $P_1 = 0.267$ and $P_2 = 0.1$, the number of needed samples was calculated as 194. Women were allocated to case and control groups equally. Ninety-seven women who did not use DMPA were assigned to the control group, and 97 women taking DMPA were assigned to the case group. For each woman included in the case group, a woman at the same or similar age who did not report the use of DMPA and did not have any of the exclusion criteria was selected to compose the control group, in such a way that the case and control groups were composed by 97 age-matched women.

This study was approved by the ethics committee of Ahvaz University of Medical Sciences, Ahvaz, Iran. After obtaining an introduction letter from this committee and representing it to health care center managers and after obtaining an informed consent from all the participants and providing verbal explanation about the research and assurance of confidentiality and anonymity, the researcher recorded their sociodemographic information (age, education level, ethnicity, occupation, gestational time, number of children) and DMPA use data (duration of use, age of initiation and injection time). Data were gathered by interview and periodontal examination. Depot medroxyprogesterone acetate use was ascertained based on respondents' report and their medical record that was on recruitment centers. Periodontal parameters including pocket probing depth, clinical attachment loss and bleeding on probing was assessed by a previously calibrated ($K = 0.92$ for probing depth and $K = 0.89$ for clinical attachment loss) and single-blinded examiner. All women were examined using good illumination and standardized conditions. Full-mouth examination was performed at six sites per teeth for all indices. Pocket probing depth measured with a 15 mm periodontal probe (Williams, Chicago, IL, USA), determined by the distance from gingival margin to the bottom of the gingival sulcus or pocket. Clinical attachment loss defined as the distance from cemento-enamel junction to the bottom of the sulcus or pocket and categorized into weak (1 - 2 mm), moderate (3 - 4 mm) and severe (≥ 5 mm). Bleeding on probing considered as the occurrence of bleeding on gentle probing was observed immediately or within 30 seconds after removal of the probe from the sulcus and recorded as present or absent. Periodontitis was defined as at least two sites with 4 mm of clinical attachment loss and a probing pocket depth ≥ 4 mm following previously published reports (13, 16).

Data were analyzed by SPSS software version 19 (SPSS Inc., Chicago, Illinois, USA) using descriptive statistical tests (mean, standard deviation, numbers and percent), Chi-square and Mann-Whitney test for comparing qualitative data between the two groups and t-test for comparing quantitative data between the two groups. P value < 0.05 was considered as a significant level.

3.1. Ethical Considerations

This study was conducted after obtaining confirmation of Ahvaz Jundishapur ethics committee (ajums.res.13920253), and informed consent from all subjects participating in the study.

4. Results

The mean ages of the women in the case and control groups were 31.55 ± 5.57 and 32.08 ± 5.54 years, respectively and t-test showed no significant difference between the two groups ($P = 0.498$). Findings indicated that the mean duration of DMPA use and the mean age of initiation use were 48.39 ± 0.712 months and 32.12 ± 0.615 years in the case group, respectively. Regarding to DMPA injection time in the case group, most of the women (71%) had 2 times injection and less (29%) had 3 or more times. Other sociodemographic characteristics of women are shown in Table 1. Based on the chi-square test, there was no significant difference between the two groups.

Clinical periodontal parameters of women in the case and control groups are shown at Table 2. The Student's t-test showed a statistically significant difference in the case and control groups regarding to probing pocket depth ($P < 0.001$) and clinical attachment loss ($P < 0.001$). The chi-square test showed a statistically significant difference in the case and control groups regarding bleeding on probing ($P < 0.0001$), probing pocket depth ($P < 0.0001$) and clinical attachment loss ($P < 0.0001$). Totally, 56.7% of the women in the case group had periodontitis compared to 16.5% in the control group ($P < 0.0001$).

5. Discussion

Our results showed that women who used DMPA had more pocket probing depth, clinical attachment loss, bleeding on probing and periodontitis than their matched control, and the differences was significant. Our study confirms and expands the findings of previous studies, which suggest that DMPA use may influence periodontal health. In concordance with our results, in a cross-sectional study (national health and nutrition examination surveys) among US females (15 to 44 years of age), Taichman et al. reported that past users of DMPA were more likely to have periodontitis (12.0% vs. 8.0%), and a significant differences was reported regarding to pocket probing depth and bleeding on probing among current and past DMPA users as compared to never users ($P < 0.001$) (13). Also, in a clinical study by Seck-Diallo et al. women using injectable progestin-only contraceptives demonstrated more periodontal pocket probing depth (3.01 ± 0.04 vs 1.12 ± 0.61 , $P < 0.0001$) and clinical attachment loss (3.19 ± 0.08 vs 1.94 ± 0.11 , $P < 0.0001$) than nonusers (12). In the present study, the mean pocket probing depth was much higher as compared to the two above-mentioned studies, which may be attributed to the duration of DMPA use. However, as the above studies did not disclose the duration of DMPA use of their population, it is dif-

Table 1. Socio-Demographic Characteristics of the Women in the Case and Control Groups^a

Demographic	Case (n = 97)	Control (n = 97)	P Value ^b
Educational level			0.316
Illiterate	7 (7.2)	3 (3.1)	
Less than diploma	51 (52.6)	54 (55.7)	
Diploma	34 (35.1)	29 (29.9)	
Collegiate	5 (5.2)	11 (11.3)	
Ethnicity			0.195
Fars	40 (41.2)	42 (43.3)	
Arab	53 (54.6)	45 (46.4)	
Other	4 (4.1)	10 (10.3)	
Occupation			0.352
Housewife	93 (95.9)	90 (92.8)	
Employee	4 (4.1)	7 (7.2)	
Income			0.461
Low income (less than '5,000,000' RIs)	34 (35.1)	26 (26.8)	
Moderate (between '5,000,000 and 10,000,000' RIs)	42 (43.3)	47 (48.5)	
High income (more than 10,000,000' RIs)	21 (21.6)	24 (24.7)	
Gestational time			0.541
1	14 (14.4)	19 (19.6)	
2	43 (44.3)	41 (42.3)	
3 or more	40 (41.3)	37 (38.2)	
Number of children			0.731
0	15 (15.4)	17 (17.5)	
1	40 (41.2)	45 (22.5)	
2	28 (28.8)	27 (25)	
3 or more	14 (14.6)	8 (20)	

^aValues are expressed as No. (%).

^bObtained from the chi-square test.

ficult to make comparison. In another study, Tilakaratne et al. showed a statistically significant increase in clinical attachment loss among DMPA users as compared to nonusers ($P < 0.0001$), which is in accordance with our findings (15). However, this study is in accordance with our result, their study has low number of DMPA users and DMPA use was assessed in combination of oral contraceptives. In a prospective 6-month clinical study conducted by Kazerooni et al. women using the progestin implant contraceptive (levonorgestrel) exhibited a statistically signifi-

Table 2. Clinical Periodontal Parameters in the Case and Control Groups^a

Variables	Case (n = 97)	Control (n = 97)	P Value
Clinical attachment loss			< 0.002 ^b
Healthy	55 (56.7)	79 (81.4)	
Weak (1 - 2 mm)	24 (24.7)	12 (12.4)	
Moderate (2 - 3 mm)	13 (13.4)	4 (4.1)	
Sever (\geq 5 mm)	5 (5.2)	2 (2.1)	< 0.001 ^c
Total, mm	1.42 \pm 2.231	0.98 \pm 1.231	
Probing pocket depth			< 0.0001 ^b
Healthy (< 4 mm)	56 (57.7)	80 (82.5)	
Unhealthy (\geq 4 mm)	41 (42.3)	17 (17.5)	< 0.001 ^c
Total, mm	3.20 \pm 1.187	2.52 \pm 1.091	
Bleeding on probing			< 0.0001 ^b
Yes	72 (74.2)	37 (38.1)	
No	25 (25.8)	60 (61.9)	
Periodontitis			< 0.0001 ^b
Yes	55 (56.7)	16 (16.5)	
No	42 (43.3)	81 (83.5)	

^aValues are expressed as No. (%) or mean \pm SD.

^bObtained from the chi-square test.

^cObtained from the unpaired t-test.

cant increase in gingival pocket depths over the study period as compared to nonusers, except around the distal aspect of the premolars ($P = 0.09$) and the mesial aspect of the anterior teeth ($P = 0.07$). Also, in this study the gingival index in the case group was significantly increased for the molar and premolar teeth at 6 months ($P = 0.03$ and $P = 0.04$) compared to baseline (14).

A suggested mechanism for DMPA's effect on periodontal tissues is that progestins, in its active form, may stimulate the synthesis of prostaglandins, thereby contributing to increased vascular permeability within the chronically inflamed periodontium (17). Other possibility is that progestins may promote tissue catabolism possibly resulting in increased periodontal attachment loss (18). So that DMPA suppresses estradiol concentrations, and estrogen deprivation has been associated with teeth loss, alveolar bone loss and periodontal attachment loss, there is a possibility that DMPA could adversely affect the periodontal structure (7).

Our study involved some limitations that should be considered. First, this study is cross-sectional in design and because DMPA use and periodontal status were measured

at one point in time, it is impossible to know whether the use of DMPA causes adverse periodontal changes. Furthermore, unmeasured variables related to oral health or other non-contraceptive use in DMPA users may have influenced the results. Despite these limitations, in this study duration of DMPA use and age of initiation as well as injection time were assessed compared to previous studies. To fully understand the mechanism of DMPA effect on periodontal health, future studies are needed. Also, use of more longitudinal and RCT designs are suggested.

5.1. Conclusions

Findings of the current study showed that the use of DMPA may affect the periodontal health status of women. Therefore, it is recommended that women, who use this method, observe a strict oral hygiene care program.

Acknowledgments

We appreciate the research deputy vice-chancellor for research affairs of Ahvaz Jundishapur University of Medical Sciences for technical support as well as venerable staff of Ahvaz Health care centers and all the participants.

Footnotes

Authors' Contribution: Firozeh Bagheri devised the concept for the study, developed the study design, collected data, was involved in the conception of the study, and performed the analyses and final preparation of the manuscript. Mitra Tadayon and Poorandokht Afshari supervised data collection and analysis, contributed to the study design and final preparation of the manuscript. Mahmoud Jahangirneghad assisted in data gathering and ran the women dental examination and was involved in study coordination. Mohammad Hosein Haghhighizadeh performed the analyses.

Funding/Support: This manuscript was adopted from MSc thesis of midwifery, which supported by Ahvaz Jundishapur University of Medical Sciences.

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