Original Article

Effects of Various contraceptive methods on Clinical and Metabolic Parameters

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Abstract

Background: Widespread usage of contraceptive pills and Medroxyprogesterone acetate (Depo-Provera) as an injectable contraceptive can affect various biochemical and physiological factors, such as lipid profiles, fasting blood sugar (FBS) and systolic and diastolic blood pressure. The purpose of this study was to determine the relationship between the use of oral contraceptives, medroxyprogesterone acetate and natural birth control methods with biochemical and physiological markers. **Materials and Methods:** In this study, the serum samples of all subjects (200 women taking depo-Provera, 200 taking contraceptive pills and 200 women who had natural birth control) were collected. Then fast blood sugar, lipid profiles, systolic and diastolic blood pressure, and BMI were measured and recorded. **Results**: There was no significant difference between the mean and standard deviation of FBS and HDL between the three examined groups, but there were significant differences in lipid profiles biomarkers, blood pressure and BMI among three groups. Indeed, mean TG, LDL, cholesterol, BMI and systolic and diastolic blood pressure showed significant higher levels in contraceptive pills users compared to other groups. Also, in the users of depot-medroxyprogesterone acetate, the mean of TG, LDL, cholesterol, BMI and systolic blood pressure was significantly higher than the natural birth control users. There was a significant difference between the three groups in terms of the duration of the contraceptive method usage, which indicated that the depot-medroxyprogesterone acetate was utilized for a long period of time in compared to other methods. In addition, contraceptive pills users were more likely to suffer from headache and nausea, and depot-medroxyprogesterone acetate users experienced changes in their menstrual cycle, such as spotting. **Conclusion:** It seems that oral contraceptive has no significant relationship with serum HDL level, and cholesterol is more affected by contraceptive drugs.

Keywords*:* Medroxyprogesterone acetate (Depo-Provera), Oral contraceptive pills, Menstrual Cycle, Biochemical Factors, Physiological Factors.

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Introduction

Over-population is one of the most serious problems around the world, so various contraceptive methods are used to control unintended pregnancies [1]. Among these procedures, Oral contraceptive pills have been widely used as an effective method[2]. Recently, approximately 25% of women aged 15-44 uses the LD, Low Dose, as contraception. Generally, there are three types of oral contraceptives: 1) Estrogen-progesterone combination; 2) Progesterone 3) take contraceptive pill without a break[3].

Currently, various studies have been shown that the side effects of oral contraceptives are not severe and will disappear by changing to another type. The most common side effects of oral contraceptives listed as headache, nausea, pain, breast tenderness, painful proximity, spotting (changes in the menstrual period), hair loss, abdominal cramps and excessive vaginal discharge or decreased libido[4-7]. Other surveys have shown that taking contraceptive pills will have a significant effects on the metabolism of lipids, carbohydrates, as well as the blood pressure[8, 9]. In this regards, a report indicated that the levels of triglyceride, cholesterol, HDL, and LDL-C had significant increased levels in contraceptives pill users[10], while in another study, the level of LDL-c did not show the significant statistical differences among contraceptive pills users versus those who did not take these medication[11].

Medroxyprogesterone acetate, as a contraceptive drug, is a weak androgenic progesterone (injected intramuscularly every three months) which inhibits the gonadotropin activity[12]. However, women taking this contraceptive drug may have some side effects such as dysregulation in menstrual cycle, weight changes, headache, anxiety, abdominal pain, dizziness and weakness or fatigue[13]. Although a large number of researches have been conducted to evaluate the medroxyprogesterone acetate relationships with lipid profile, but, the results are not consistent in various studies[14, 15].

A study showed that in the medroxyprogesterone acetate users, cholesterol, LDL-C, VLDL, triglyceride and fasting blood glucose (FBS) levels were significantly increased in compared to untreated group, while HDL levels decreased[16]. In addition, blood sugar and insulin levels have been increased in medroxyprogesterone acetate users versus oral contraceptive pills users[17].

Other contraceptive methods include the use of natural birth control methods such as the condoms usage. It has been reported that the use of intrauterine devices reduces the frequency of sexual intercourse and sexual satisfaction due to increased irregular bleeding[18, 19]. There are few reports about the effects of using natural birth control methods on serum levels of biochemical markers, such as cholesterol, triglycerides and blood sugar. In addition, there are few studies which investigate the impacts of these contraceptive methods on clinical factors such as changing the menstrual cycle and hair loss. Therefore, studying the relationship between this contraceptive procedures and physiological and biochemical markers can be useful. Although several studies have been performed to investigate the possible relationships between taking oral contraceptives and using medroxyprogesterone acetate with lipid profiles, blood sugar, blood pressure, BMI as well as side effects such as headache, nausea, pain and chest sensation, painful sexual intercourse, spotting (changes in the menstruation cycle) and hair loss, but there are numerous inconsistencies in the results of these surveys. Hence, in this study, we examined the precise relationships between these variables.

Methods

A prospective study (descriptive-analytical type) were conducted with 600 subjects as the population study comprising the 200 women using medroxyprogesterone acetate, 200 taking oral contraceptives, and 200 who had Natural birth control. All of the research units were located in the areas covered by the Neka Health Center. The non-pregnant subject's age was range between 20 and 41 years. Also, in the past few months, all women didn't use any other contraception except for medroxyprogesterone acetate, combined contraceptive pills and natural birth control. Likewise, subjects had regular menstrual cycle and did

not complain about the studied complications, such as headache, back pain and etc .

The blood samples were drawn and serum separated. Then the serum levels of FBS, cholesterol, triglyceride and HDL-c using Pars Azmun kits (Iran) were measured. Iran. Also the LDL-c were calculated by the Friedewald equation. Systolic and diastolic blood pressure and BMI of the all subjects were also assessed and recorded. All participants were asked to complete a questionnaire including these age, number of children, type of contraception, history of using contraceptive method, headache, nausea, pain and chest sensitivity, painful sexual intercourse, marital satisfaction, spotting (dysregulation in menstrual cycle), hair loss, demographic status, the history of any disease in studied women and their family (diabetes, blood pressure, any chronic disease, history of abortion or high risk delivery). Then data accurately recorded. statistical analysis was performed using SPSS 18 software. The SMIRNOV-KOLMOGOROV test was used to assess the normal distribution of data. Then the data were analyzed by INDEPENDENT SAMPLE TEST, FISHER EXACT TEST, ONEWAY ANOVA, POST HOC TUKEY, and Chi-Square tests. $P \leq 0.05$ was considered as a significant level.

Results

The mean age in the depot-medroxyprogesterone acetate users group was 31.78 ± 5.5, in the users of contraceptive pills was 32.67 ± 4.8 and in the Natural birth control users group was 31.91 ± 5.35. As presented in Table 1, there were no significant differences in the mean age between three groups (Table 1). Depot-medroxyprogesterone acetate users (three months) had a higher number of children in compared to other groups. (P = 0.000) (Table 1).

There was a significant difference between the three groups in total duration of contraceptive use which indicated that depot-medroxyprogesterone acetate had longer use of this method (Table 1).

In evaluating the side effects, the results revealed that, contraceptive pills users were more likely to suffer from headache and nausea, and depot-medroxyprogesterone acetate users experienced dysregulation in menstrual cycle, such as spotting. There is no statistically significant difference in other complications between the groups (Table 2).

As presented in Table1, the statistical significant differences in biochemical and clinical parameters including lipid profiles, systolic & diastolic blood pressure and BMI between three groups were presented. But there are any significant differences in FBS and HDL-c levels among studied groups (Table 1). Table 3 shows the in-paired comparison of lipid profile, FBS, blood pressure and BMI between groups. As shown in Table 3, the mean levels of TG, LDL, cholesterol, BMI, systolic & diastolic blood pressure show a significant increase in contraceptive pill users compared to the other two groups. Also, the Mean levels of TG, LDL, cholesterol, BMI and systolic blood pressure were significantly higher in the depot-medroxyprogesterone acetate users in compared to natural birth control users. Although there were statistically significant differences in levels of cholesterol, triglyceride, LDL and blood pressure, but the values were within the normal range.

Table1. The mean and standard deviation of lipid profiles, FBS, blood pressure and BMI in three groups including; depot-medroxyprogesterone acetate, contraceptive pills and natural birth control users.

	Natural birth control users (Mean±SD)	LD pills users (Mean±SD)	Ampulla users (depot-medroxyprogesterone acetate) (Mean±SD)	P value
Age, years	31.91±5.35	32.67±4.8	31.78±5.5	0.19
Number of Children	1.74±0.68	1.98±0.61	2.2±0.8	0.0001
FBS, mg/dL	88.17±12.3	88.68±10.5	88.3±11.9	0.9
TG, mg/dL	121.2±57.1	144.4±46.7	133.1±48.75	0.0001
CHOL, mg/dL	153.9±37.3	187.2±21.9	169.3±35	0.0001
LDL-C, mg/dL	81.29±39	111.6±24.17	96.1±36.5	0.0001
HDL-C, mg/dL	48.4±12.9	46.75±11.15	46.56±11.4	0.2
DBP, mmHg	66.67±8.9	68.47±7.7	66.52±7.23	0.02
SBP, mmHg	107.38±12.19	110±12.9	104.8±8.25	0.0001
BMI, kg/m2	25.19±3.3	28.15±3.7	27.04±3.7	0.0001
Usage history, years	3.98±2.83	3.65±2.31	2.68±2.12	0.0001

Table 2. Side effects distribution in the depot-medroxyprogesterone acetate and contraceptive pills users.

Headache			No	Yes	Total
Group	L.D.	Count % with group	99(49.5%)	101(50.5%)	200(100%)
	DEPO.	Count % with group	175(87.5%)	25(12.5%)	200(100%)
P-Value		0.0001	---		
Nausea			No	Yes	Total
Group	L.D.	Count % with group	123(61.5%)	77(38.5%)	200(100%)
	DEPO.	Count % with group	150(75%)	50(25%)	200(100%)
P-Value		0.005	---		
Pain and chest sensation			No	Yes	Total
Group	L.D.	Count % with group	177(88.5%)	23(11.5%)	200(100%)
	DEPO.	Count % with group	174(87%)	26(13%)	200(100%)
P-Value		0.76	---		
Painful sexual intercourse			No	Yes	Total
Group	L.D.	Count % with group	133(66.5%)	67(33.5%)	200(100%)
	DEPO.	Count % with group	140(70%)	60(30%)	200(100%)
P-Value		0.51	---		
Marital Satisfaction			No	Yes	Total
Group	L.D.	Count % with group	67(33.7%)	132(66.3%)	200(100%)
	DEPO.	Count % with group	61(30.5%)	139(69.5%)	200(100%)
P-Value		0.52	---		
Spotting (changes in the menstrual period)			No	Yes	Total
Group	L.D.	Count % with group	181(90.5%)	19(9.5%)	200(100%)
	DEPO.	Count % with group	151(75.5%)	49(24.5%)	200(100%)
P-Value		0.0001	---		
Hair loss			No	Yes	Total
Group	L.D.	Count % with group	136(68%)	64(32%)	200(100%)
	DEPO.	Count % with group	147(73.5%)	53(26.5%)	200(100%)
P-Value		0.27	---		

Table 3. In paired comparison of variables in three examined groups: depot-medroxyprogesterone acetate, contraceptive pills and natural birth control users.

Dependent Variable	Group	Group	Mean Difference	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
Age, years	Natural	L.D.	-0.75	0.52	0.15	-1.78	0.27
	Natural	DEPO.	0.13	0.52	0.79	-0.89	1.16
	L.D.	DEPO.	0.89	0.52	0.09	-0.14	1.92
Number of Children	Natural	L.D.	-0.23	0.07	0.001	-0.37	-0.09
	Natural	DEPO.	-0.48	0.07	0.000	-0.62	-0.34
	L.D.	DEPO.	-0.24	0.07	0.001	-0.38	-0.1
FBS, mg/dL	Natural	L.D.	-0.5	1.16	0.66	-2.78	1.77
	Natural	DEPO.	-0.12	1.16	0.91	-2.4	2.15
	L.D.	DEPO.	0.38	1.16	0.74	-1.9	2.66
TG, mg/dL	Natural	L.D.	-23.18	5.11	0.000	-33.21	-13.14
	Natural	DEPO.	-11.88	5.11	0.02	-21.91	-1.84
	L.D.	DEPO.	11.3	5.11	0.027	1.26	21.33
CHOL, mg/dL	Natural	L.D.	-33.26	3.21	0.000	-39.5	-26.94
	Natural	DEPO.	-15.39	3.21	0.000	-21.7	-9.07
	L.D.	DEPO.	17.87	3.21	0.000	11.55	24.18
LDL-C, mg/dL	Natural	L.D.	-30.29	3.38	0.000	-36.95	-23.64
	Natural	DEPO.	-14.87	3.38	0.000	-21.53	-8.22
	L.D.	DEPO.	15.42	3.38	0.000	8.76	22.07
HDL-C, mg/dL	Natural	L.D.	1.67	1.18	0.15	-0.65	4
	Natural	DEPO.	1.86	1.18	0.11	-0.46	4.19
	L.D.	DEPO.	0.19	1.18	0.87	-2.14	2.52
DBP, mmHg	Natural	L.D.	-1.8	0.79	0.025	-3.36	-0.23
	Natural	DEPO.	0.15	0.79	0.85	-1.41	1.71
	L.D.	DEPO.	1.95	0.79	0.01	0.38	3.51
SBP, mmHg	Natural	L.D.	-2.63	1.13	0.021	-4.85	-0.4
	Natural	DEPO.	2.5	1.13	0.028	0.27	4.72
	L.D.	DEPO.	5.13	1.13	0.000	2.9	7.35
BMI, kg/m2	Natural	L.D.	-2.96	0.36	0.000	-3.66	-2.25
	Natural	DEPO.	-1.84	0.36	0.000	-2.55	-1.14
	L.D.	DEPO.	1.11	0.36	0.002	0.4	1.82
Usage history, years	Natural	L.D.	0.32	0.24	0.18	-0.15	0.8
	Natural	DEPO.	1.29	0.24	0.000	0.81	1.77
	L.D.	DEPO.	0.97	0.24	0.000	0.49	1.45

Discussion

Uncontrolled pregnancy is one of the most important challenges of the century. Recently, various pharmaceutical and physical procedures are now used as contraceptive methods, which each procedures is accompanied with many challenges and complications[20, 21].

In this regards, several side effects such as headache, nausea, pain and breast tenderness, painful sexual intercourse, spotting (menstrual cycle dysregulation), and hair loss have been reported[22]. Therefore, numerous studies have been conducted to evaluate the lipid profiles, blood sugar and other relevant biochemical indices to further explore the risk of using contraceptives. On the other hand, the use of natural birth control methods such as condoms reduces sexual satisfaction and increases the risk of vaginal infections and unwanted pregnancy[23, 24].

Therefore, the replacement of natural birth control methods with drug based methods can overcome these challenges. At the same time, careful evaluations of the contraceptives effects on individual health are required. Due to need for accurate evaluation of contraceptive drugs side effects, we aimed to study

the biochemical biomarkers such as FBS, cholesterol, triglyceride, HDL, and LDL.

The results of our study emphasized that nevertheless the contraceptives effects on lipid profile (despite its significant impacts) these methods could be a good alternative to natural methods. However, in some high-risk groups (such as cardiovascular patients and people with lipid metabolism disorders), it should be prescribed and administered more precisely.

The results of this study showed that there is no significant relationship between different contraceptive methods (depot-medroxyprogesterone acetate, contraceptive pills and natural birth control users) in fast blood sugar level (Table 1). Therefore, it could be proposed that carbohydrate metabolic pathways do not affected by pregnancy medications.

Therefore, it could be suggested that the individual's situations which are predispose to metabolic carbohydrate diseases (including diabetes), is not decisive in determining the methods of contraception. In this regards, Beasley et al. (2012) did not show a significant correlation between serum FBS levels and oral contraceptive use[25].

Our study showed that (based on the contraceptive methods type), among the measured lipid profile bio markers, the greatest effects were exerted on the levels of triglycerides, cholesterol and LDL. So that, LD use increases the mean of all three mentioned lipid parameters. Likewise, Fadlalmola et al, in 2019 showed that oral contraceptive use has a significant relationship with serum cholesterol levels in the studied subjects[26]. A study by Muhsin et al (2019) in Samarra, Iraq, confirmed the association of contraceptive use with a significant increase in lipid profiles[27].

The use of depot-medroxyprogesterone acetate increases the mean of studied biomarkers. But, the amounts of increase were less than that of contraceptive pill users. With all the above, it can be concluded that taking contraceptive drugs interferes with lipid metabolism pathways. On the other hand, the average increase in lipid profile biomarkers is within the normal range. So, it is not necessary to remove the contraceptive drug from the treatment cycle (in terms of changing the risk of atherosclerotic complications). However, it is suggested that contraceptive drugs should be used with caution in disorders of Lipid Metabolism, as well as those at risk for heart disease and atherosclerotic individuals. In addition, our findings which show the significant relationship between the contraception pathway with systolic and diastolic blood pressure and BMI confirmed this important issue.

A study by Beasley et al. (2012) also found that there were significant relationships between serum LDL levels and oral contraceptives use. Though Khatun et al. research in 2019 was not in accordance with our results. In this study, which was conducted in Dhaka, Bangladesh (in the long-term follow-up), there was no significant statistical relationship between contraceptive use and lipid profile increase[28].

Conclusion

In summary, according to the results of presented survey, oral contraceptive use has no significant relationship with serum HDL level, so, it could be suggested that cholesterol (the most different lipid factor in terms of placement in LDL and HDL lipoprotein structure) more affected by contraceptive drugs. Considering the significant relationship between contraception method and most measured variables, it could be suggested that the further studies should be designed and continued to examine other important biochemical indices. In addition, long-term follow-up can reflect a more reliable situation in assessing the effects of contraceptive methods on individual health

Conflict of Interest

The authors declared no conflict of interest.

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