Bangladesh J Obstet Gynaecol, 2019; Vol. 34(2): 106-111

# Effects of Long-Term Use of Depomedroxy Progesterone Acetate on Serum Lipids

SHAHRIN FERDOUS[1], MUMTAHENA AMIR[2], SALEHA BEGUM CHOWDHURY[3], BEGUM NASRIN[4], FARZANA HAMID[5], SHABNAM BANU[6]

**Abstract**

***Introduction:*** *Long Acting Reversible Contraceptive (LARC) is one of the most popular method of family planning. The Aim of the study was to explore the effects of long-term use of Depomedroxyprogesterone acetate (DMPA) which is the most commonly used LARC, on serum lipid profile.*

***Methods:*** *This cross-sectional analytical study was carried out in the Department of Obstetrics and Gynaecology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period December 2015 to September 2016. A total 70 married women at the age range of 20-35 years attending, the family planning clinic of BSMMU were included in this study. Out of them 35 subjects who had been using DMPA for ≥ two years uninterruptedly were considered as cases and another 35 subjects who did not use any hormonal contraceptives were labeled as control. In both the groups, age and BMI were matched. All the study subjects in both groups were apparently healthy. Fasting blood samples were collected from each subject for the estimation of Total Cholesterol (TC), Triglyceride (TG), High-density Lipoprotein Cholesterol (HDLC) and Low-density Lipoprotein Cholesterol (LDLC). The data were collected in a pre-designed data sheet and analyzed with student T-test for the statistical significance.*

***Results:*** *Serum TC and LDLC level in group-I (cases) were significantly higher compared to group-II (control) and the difference was statistically significant ($p<0.05$). Serum High-density Lipoprotein Cholesterol (HDLC) level in group-I was lower than group-II which was also statistically significant ($p=0.001$). Serum Triglyceride level in group-I was higher than group-II, however the difference was not statistically significant ($p=0.177$).*

***Conclusion:*** *DMPA use for ≥ two years increases serum TC and LDLC and decrease serum HDLC, which may increase the risk of atherosclerosis.*

***Key words:*** *Long Acting Reversible Contraceptive (LARC), Depomedroxyprogesterone acetate (DMPA), Lipid profile.*

**Introduction:**

Depomedroxyprogesterone acetate (DMPA) is an injectable progestin only contraceptive method that provides highly effective, convenient, reversible contraception with a very low failure rate [1].

DMPA is available in two formulations;150mg/1ml for intramuscular injection and 104mg/0.65ml for subcutaneous injection. The 150mg/1ml formulation is mostly used by women of low socio-economic status of Bangladesh because the method is

1. Dr. Shahrin Ferdous, Medical Officer, UHC, Singair, Manikganj.
2. Dr. Mumtahena Amir, Resident Surgeon, Dept. of Obstetrics and Gynaecology, Mugda Medical College Hospital
3. Prof. Saleha Begum Chowdhury, Professor, Dept. of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University
4. Prof. Begum Nasrin, Professor, Dept. of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University
5. Dr. Farzana Hamid, Medical Officer, Dept. of Obstetrics and Gynaecology, Mugda Medical College Hospital
6. Dr. Shabnam Banu, Junior Consultant, UHC, Singair, Manikganj.

**Address of Correspondence:** Dr. Shahrin Ferdous, Medical Officer, UHC, Singair, Manikganj, Mobile: 01716153050, Email: rushia2012@gmail.com

incorporated in the family planning program of Government of Bangladesh at free of cost. Because of low solubility of the microcrystals at the injection site pharmacologically active drug levels persists for three months. Following 150 mg IM dose of DMPA, it takes approximately three weeks to reach peak plasma concentration of one to seven ng/ml. The level then decrease exponentially until they become undetectable (<.1 ng/ml) between 120 to 200 days following a single injection.

DMPA is derived from the natural progesterone hormone [2]. The contraceptive appears to be a potent inhibitor of gonadotrophins [3] and there by negative, effect on estrogen and progesterone production. It is highly effective contraceptive method yet its use is not without its side effects among the users. The adverse effect of DMPA on lipid metabolism is related to its weak androgenic effect, which can counteract the effects of estrogen. It is associated with significant increase in fasting blood glucose, pyruvate and insulin level [4]. Elevated serum insulin level stimulates increased synthesis of triacylglycerol by liver. Synthetic progestin was found to decrease high-density lipoprotein (HDL) and increase low-density lipoprotein (LDL) by decreasing apoprotein-A and apoprotein-B concentration respectively. Suppression of estrogen by DMPA may also modify lipid profiles and endothelial function.[5]

Although, a few studies has been conducted on the relationship between DMPA and lipid profile, results are not consistent among studies,[3,6, 7, 8], therefore the present study was designed to evaluate the effect of long-term use of DMPA on lipid profile among Bangladeshi women.

**Materials and Methods:**

This was a cross sectional analytical study carried out in the department of obstetrics & gynaecology, BSMMU. Study subjects were collected from the Family Planning Clinic of BSMMU from December, 2015 to September, 2016. Thirty five married women of 20-35 years of age, who were receiving DMPA injection for ≥ two years uninterruptedly were the study cases. Another thirty five (35), age and BMI matched married women who did not use any hormonal contraceptives were enrolled as control in this study. Women having BMI ≥25 kg/m$^2$, or suffering from chronic diseases like diabetes mellitus, hypertension, thyroid disorder, chronic liver disease, kidney disease which may affect lipid metabolism or taking any medications like lipid lowering agent, steroid, anti-hypertensive, chemotherapeutic agent, thiazide diuretics, smoking or alcoholic were excluded from the study. The subjects were divided into two groups, subjects who were receiving DMPA injection for ≥ two years uninterruptedly were labeled as group I and subjects who did not use any hormonal contraceptives were labeled as group II. Purposive sampling was done according to the availability of the subjects.

A total 70 samples were collected. Among them 35 were in group I and 35 were in group II. A pre-designed structured data collection sheet was made. At first the purpose and procedure of the study was discussed with the subjects. Study subjects were selected by taking details history and clinical examination. Written consent was taken from those who agreed to participate in the study. Subjects were requested for overnight fasting (10-12 hours) and to report at around 9 am at BSMMU for laboratory test. Five milliliter fasting blood samples was collected into a plain test tube from each subject with disposable syringe by antecubital venipuncture. To avoid diurnal variation, samples were collected always between 8-9 am. Measurement of serum TC and TG concentration were done by enzymatic colorimetric method, serum HDL was measured by the precipitation method, and serum LDL was calculated by using Friedwald's Equation.

The tests were done at the Biochemistry Department of BSMMU. The subjects personal, clinical and laboratory data were collected in the predesigned Data collection sheet. All the data were compiled and analyzed by using student's t-test for comparative study.

**Results:**

Results of this cross sectional analytic study were expressed in percentage. For comparison of lipid profile and other factors between two groups, P-value was calculated. P-value < 0.05 was considered as significant difference.

Table I shows the percentage of women in different age groups, the mean ±SD age of group-I and group-II which were 26.71±3.59 and 26.11±3.95 respectively. The age range was 20-35 in both groups. The difference was not statistically significant between two groups (P>0.508).

**Table-I**

*Distribution of study subjects by age (n=70)*

| Age (in years) | Groups under study | | p value* |
|---|---|---|---|
| | Group-I (35) | Group-II (35) | |
| 20-25 | 17 (48.6%) | 15 (42.8%) | 0.508$^{ns}$ |
| 26-30 | 13 (37.1%) | 17 (48.6%) | |
| 31-35 | 5 (14.3%) | 3 (8.6%) | |
| Total | 35 (100.0) | 35 (100.0) | |
| Mean ± SD(Range) | 26.71 ± 3.59(20-34) | 26.11 ± 3.95(20-35) | |

**t* test was done to measure the level of significance.
Figure within parentheses indicates in percentage.
ns = Not significant
Group-I = (Cases)
Group-II = (Control)

Table- II shows that in both groups the maximum study subjects were house wife 17 (48.6%) and 16(45.7%) respectively. In group-I maximum had primary education 17 (48.6%) compared to group-II in which maximum education level was HSC 13 (37.1%).

There was difference in graduation level education in two groups also, among group-I 1(2.9%) and group II 5(14.3%) were graduate.

Table III shows the comparison of BMI among two groups. Mean (±SD) BMI of group-I and group-II were 22.48± 1.46 and 22.27± 1.48 respectively, which showed statistically no significant difference (p value 0.556).

Table IV shows the percentage of women using DMPA for 2 years and percentage of women using DMPA for more than two years.

Out of 35 DMPA users 20(57.1%) used for more than 2 years and 15(42.9%) for 2 years.

Table V shows the comparative analysis of serum lipid profile between two groups.

TC and LDL showed statistically significant difference between two groups. The TG level in Group-I was higher than Group-II, however difference was not statistically significant (p=0.177). The serum HDL level in Group-I was significantly decreased compared to Group-II (p=0.001).

**Table-II**

*Distribution of study subjects by their occupation and education (n=70)*

| Parameters | Group-I (35) | Group-II (35) |
|---|---|---|
| Occupation | | |
| Housewife | 17 (48.6%) | 16 (45.7%) |
| Service holder | 15 (42.8%) | 14 (40.0%) |
| Student | 3 (8.6%) | 5 (14.3%) |
| Educational status | | |
| Primary | 17 (48.6%) | 12 (34.3%) |
| SSC | 11 (31.4%) | 5 (14.3%) |
| HSC | 6 (17.1%) | 13 (37.1%) |
| Graduate | 1 (2.9%) | 5 (14.3%) |

SSC-Secondary School Certificate, HSC-Higher Secondary School Certificate

**Table-III**

*Comparison of study subjects according to BMI (n=70)*

| Variables | Group-I | Group-II | p value* |
|---|---|---|---|
| BMI (kg/m$^2$) | 22.48 ± 1.46 | 22.27 ± 1.48 | 0.556$^{ns}$ |

NS-Not significant

**Table-IV**

*Distribution of the duration of use of DMPA (n=35)*

| Duration of DMPA | Frequency | Percent (%) |
|---|---|---|
| 2 years | 15 | 42.9% |
| >2 years | 20 | 57.1% |
| Total | 35 | 100.0 |

**Table- V**

*Comparison of serum lipid profile between two groups (n=70)*

| Lipid profile (mg/dl) | Group-I | Group-II | p value* |
|---|---|---|---|
| TC | 232.03 ± 45.24 | 175.83 ± 24.32 | 0.001$^{s}$ |
| TG | 117.65 ± 35.89 | 110.03 ± 27.52 | 0.177$^{ns}$ |
| HDL | 39.54 ± 5.89 | 46.54 ± 6.84 | 0.001$^{s}$ |
| LDL | 168.45 ± 46.76 | 107.34 ± 21.47 | 0.001$^{s}$ |

S-Significant, ns-not significant, TC-Total Cholesterol, TG-Triglyceride, HDL-High density Lipo protein, LDL-Low density Lipo protein.

**Discussion:**

This cross sectional analytical study was conducted in the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from December, 2015 to September, 2016. The aim of this study was to explore the effect of long term use of DMPA on serum lipids. The present study findings and comparative discussion with previously published relevant studies are presented.

The mean total cholesterol was significantly higher in Group-I (DMPA users) than that of Group-II (no hormonal contraceptive users) and the difference was statistically significant (p=<0.001). This result of the present study is in agreement with those of Fekedie et al. (2016)[6]; Yadav et al. (2011)[3,] studies, where they have shown the TC level in long term DMPA users was significantly higher (P=.001) than controls.

In another study conducted by Asare et al. (2014)[8] significant elevation in serum TC level was observed among DMPA users compared to controls (P=0.018), similar to the present study. Similar observation was reported in an experimental study made on rats by Bakry and Abdullah, (2009)[2]; Bakry et al. (2010), to investigate the effect of DMPA on serum lipid profile in rats treated with DMPA.

Unlike finding of the present study, cross sectional study performed by Faddah et al. (2005)[9] and cohort study by Berenson et al. (2009)[10]; reported changes in mean serum TC level of DMPA users were not significant. Contrary to the present study, a study performed by Lizarelli et al. (2009)[11] aimed to determine whether the use of Combined Oral Contraceptives (COC) or DMPA interferes with endothelial function. They suggested a beneficial effect of DMPA, where DMPA group had lower values of TC than the control group. This finding of Lizarelli et al, was supported by a cross sectional study performed on 54 young Pakistani females of age ranging from 26-32 years aimed to compare the extent of cardiovascular atherosclerotic risk associated with the lipid metabolism in women using hormonal contraceptives including COC, DMPA,

implant and non hormonal IUCD. DMPA group poses the lowest TC value compared to other hormonal methods of contraceptive next to implant (Jamil and Siddiq, 2012)[12]. This discrepancy could be due to the difference in protocol between Lizarelli et al and the present study. Berenson et al. (2009) done a cohort study on 703 participants as opposed to cross sectional study in the present relatively small sample size (70 women). The discrepancy may also be due to age difference between the study participants. In the study of Faddah et al. (2005), participants were aged between 25-30 years, in the study of Berenson et al.(2009), the age range was 16-33 years and in the study of Rabeya et al. (2014)[7], the age range was 15-40 years. But in our study, the study subjects were taken from age range of 20 to 35 years and maximum number of subjects belonged to age range of 20 to 30 years. All the subjects in all the studies were less than 40 years age. Therefore, possibility of age related elevation in serum total cholesterol is almost impossible. It is noteworthy that all the chronic and metabolic diseases were excluded before. So, it can be claimed that the increased serum cholesterol in DMPA users is solely due to hormone influence.

According to present study, serum TG level of DMPA users was found to be higher compared to non-user however, this difference was not statistically significant (p=0.177). This finding of the present study is consistent with study of Yadav et al. (2011)[3], who demonstrated the elevation of serum TG level in DMPA users compared to controls. But, the difference was not statistically significant (P=0.44). However another study suggested that serum TG level was not affected by DMPA use (Faddah et al, 2005)[9].

Mean ±SD serum HDLC level of DMPA users was lower compared to non-users which was statistically significant (p=0.001). This support results reported by other studies (Berenson et al. 2009[10]; Lizarelli et al[11] 2009; Faddah et al. 2005[9];). Whereas, another study reported that DMPA did not cause any significant changes in mean serum HDLC level (Yadav et al. 2011). Contrary to the present study, Jamil and Siddiq (2012) reported DMPA users had higher value of HDLC compared to controls. This discrepancy could be due to different dietary habit, ethnicity and poor counseling on use of DMPA.

DMPA users experienced significant increase in serum LDLC level compared to non-hormonal contraceptive users (p=0.001). Similar observations were reported by Yadav et al. (2011); Asare et al. (2014) where, significant elevation were observed in serum LDLC level in DMPA group compared to controls. The study done by Faddah et al. (2005) also revealed that the use of DMPA as contraceptive caused a significant increase (P<0.01) in LDLC. Whereas some study reported that DMPA did not cause significant change in mean serum LDLC level (Berenson et al. 2009).Contrary to the present study, DMPA group were reported with lower values of LDLC than control group (Lizarelli et al. 2009; (Jamil and Siddiq, 2012)[12].

According to our study, significant increase in serum TC and serum LDLC but significant decrease in serum HDLC were observed among DMPA users compared to non-hormonal contraceptive users. Serum Triglyceride level in DMPA users was higher than non-hormonal contraceptive users, however the difference was not statistically significant. This significant increase in TC and LDLC may have an adverse effect on cardiac function of the women. On the other hand decrease in HDLC which is cardio protective may have on adverse effect on heart of the DMPA users.

**Conclusion:**

This study showed that long term use of DMPA induces changes in lipid profile. However, further larger multi-centered study with larger sample size is needed for a general recommendation.

**References:**

1. Prata N, Weidert K, Fraser A, Gessessew A. Meeting rural demand: a case for combining community-based distribution and social marketing of injectable contraceptives in Tigray, Ethiopia. PLoS One. 2013 Jul 12;8(7): e68794.
2. Bakry S, Abdullah A. Effect of depot medroxyprogesterone (DMPA) on body weight and serum lipid profile in adult female rats. Egyptian Journal of Biochemistry and Molecular Biology. 2009 Jun 17;27(1):17-30.
3. Yadav BK, Gupta RK, Gyawali P, Shrestha R, Poudel B, Sigdel M, Jha B. Effects of long-term use of depo-medroxyprogesterone acetate on lipid metabolism in Nepalese women. The Korean journal of laboratory medicine. 2011 Apr 1;31(2):95-7.

4. Fahmy K, Khairy M, Allam G, Gobran F, Alloush M. Effect of depo-medroxyprogesterone acetate on coagulation factors and serum lipids in Egyptian women. Contraception. 1991 Oct 1;44(4):431-44.

5. Torgrimson BN, Meendering JR, Kaplan PF, Minson CT. Depot-medroxyprogesterone acetate and endothelial function before and after acute oral, vaginal, and transdermal estradiol treatment. Hypertension. 2011 Apr;57(4): 819-24.

6. Fekadie M, Seifu D, Kumpi S, Kokeb A. Effect of Depo-medroxyprogesterone acetate (DMPA) on Lipid Metabolism.

7. Rabeya S, Muttalib MA, Mia AR, Rabbi SF. Lipid profile in women receiving depot medroxyprogesterone acetate as contraceptive. Mymensingh medical journal: MMJ. 2014 Jan;23(1):114-20.

8. Asare GA, Santa S, Ngala RA, Asiedu B, Afriyie D, Amoah AG. Effect of hormonal contraceptives on lipid profile and the risk indices for cardiovascular disease in a Ghanaian community. International journal of women's health. 2014; 6:597.

9. Faddah L, Al-Rehany M, Abdel-Hamid N, Bakeet A. Oxidative stress, lipid profile and liver functions in average Egyptian long-term depo medroxy progesterone acetate (DMPA) users. Molecules. 2005 Sep;10(9):1145-52.

10. Berenson AB, Rahman M, Wilkinson G. Effect of injectable and oral contraceptives on serum lipids. Obstetrics and gynecology. 2009 Oct;114(4):786.

11. Lizarelli PM, Martins WP, Vieira CS, Soares GM, Franceschini SA, Ferriani RA, Patta MC. Both a combined oral contraceptive and depot medroxyprogesterone acetate impair endothelial function in young women. Contraception. 2009 Jan 1;79(1):35-40.

12. Jamil S, Siddiq A. Comparison of CVD risk associated with the long term use of contraceptives in young females. Journal of Applied Pharmaceutical Science. 2012 Nov 1;2(11):62.