

Impact of Using Hormonal Progestogen-only as Contraceptive Treatment on Plasma Lipids

Nagah AA Mohamed¹, Mohammed Amanullah^{2*}, Mariam A Ibrahim³ and Elhassan A Mohamed³

¹Department of Biochemistry, Ondokuz Mayıs University, Samsun, Turkey

²Department of Clinical Biochemistry, College of Medicine, King Khalid University, Abha, Saudi Arabia

³Department of Clinical Chemistry, Sudan University of Science and Technology, Sudan

Abstract

The current mode of progestogen-only contraception is progestogen-only pills, sub dermal implant implanon, injectable, hormones-releasing intrauterine system. All progestogen-only method work by a local effect on cervical mucus (making it hostile to ascending sperm) and on the endometrium (making it thin and atrophic), thereby preventing implantation and sperm transport. It has been reported that serum total cholesterol is significantly higher among oral contraceptive users as compared to non-user. This study aims to assess the plasma lipid profile in Sudanese women using progesterone only as hormonal contraceptives by different routes of administration. A descriptive, case control study was conducted in Khartoum state, Sudan. One hundred and eighty premenopausal women using progestogen-only as contraceptive treatment, were divided equally into three groups according to the method they used oral, injectable or sub dermal implant were enrolled in this study as case, in addition to sixty healthy women not using contraceptives as control group. 2.5 ml of fasting venous blood was collected from each participant for estimation of triglycerol, total cholesterol, HDL-cholesterol and LDL-cholesterol using ELISA. The results indicated that the levels of plasma total Cholesterol, triglycerides and low density lipoprotein increased whereas HDL-c level decreased by using hormonal contraceptives and this increase was directly proportional to the duration of using hormonal contraceptives.

Keywords: Contraception; Progestogen-only; Tryglycerols; Total cholesterol; HDLc and LDLc

Introduction

All other types of hormonal contraception in current use in the UK are progestogen-only and share many similar features in the terms of mode of action and side effects. Because they don't contain estrogen, they are extremely safe and can be used if a woman has cardiovascular risk factors. The dose of progestogen within them various from very low to high. The current mode of progestogen-only contraception are progestogen-only pills, subdermal implant implanon, injectable, hormones-releasing intrauterine system. All progestogen-only method work by a local effect on cervical mucus (making it hostile to ascending sperm) and on the endometrium (making it thin and atrophic), thereby preventing implantation and sperm transport. Higher dose progestogen-only methods will also act centrally and inhibit ovulation [1].

Females rats implanted with progesterone gained weight more rapidly than control animals and had an increased proportion of total body fat. Restriction of food intake to control levels demonstrated that the weight changes were not dependent on increased energy intake [2]. Progesterone implants in normal and diabetic rats increased body weight gain, adiposity, insulin receptor concentration and both basal and insulin-stimulated rates of lipogenesis in adipose tissue, again without affecting insulin sensitivity. Progesterone stimulates lipogenesis in adipose tissue without any increase in food intake or serum insulin concentrations suggesting that progesterone may have a direct anabolic role in adipose tissue [3]. Progesterone decreases the rate of lipolysis in female rats, inhibiting the activity of both ATGL (by stimulating synthesis of G0S2 - specific inhibitor of the enzyme) and HSL (due to inhibition of Lipe gene expression) [4].

It has been reported that serum total cholesterol is significantly higher among oral contraceptive users as compared to non-user [5].

Rational and Objective

The common side effects of progestogen-only methods include: erratic or absent menstrual bleeding, functional ovulation cysts, breast tenderness, acne [1]. However, a large number of potential side effects exists, the most important relating to cardiovascular disease. Many minor side effects will settle within a few months of starting COC [6].

This study aims to assess the plasma lipid profile in Sudanese women using progesterone only as hormonal contraceptives by different routes of administration.

Materials and Methods

A descriptive, case control study was conducted in Khartoum state, Sudan. One hundred and eighty premenopausal women using progestogen-only as contraceptive treatment, were divided equally into three groups according to the method they used oral, injectable or sub dermal implant were enrolled in this study as case, in addition to sixty healthy women not using contraceptives as control group. Both groups were age matched 25-35 years. Women with diabetes mellitus, hypertension, Kidney disease, thyroid disorder, obstructive liver disease or having present history of any disease which may affect the level of lipids were excluded.

***Corresponding author:** Mohammed Amanullah, Associate Professor, Department of Clinical Biochemistry, College of Medicine, King Khalid University, Greiger, Abha-61321, Saudi Arabia, Tel: 966 7 2417863; E-mail: amanullahmohammed@yahoo.com

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2.5 ml of fasting venous blood was collected from each participant for estimation of triglycerol, total cholesterol, HDL-cholesterol and LDL-cholesterol using ELISA.

Statistical Analysis

The data collected in this study was analyzed using SPSS computer analysis program version 21. The means and standard deviation of the plasma total cholesterol, triglyceride, high density lipoprotein, low density lipoprotein were comparison (p-value less than or equal 0.05 is considered to be significant). Linear regression analysis was used to assess correlation between the duration of use of contraceptives (in months-18 months). The precision and accuracy of all method used in this study were check each time a patch was analyzed by including commercially prepared control sera.

Ethics

This study was conducted according to the guidelines laid down in the declaration of Helsinki and all procedures involving human subjects/patients. The objectives of the study were explained and written informed consents were obtained from each Participant.

Results

The results showed that there was a significant increase in total cholesterol among women using oral contraceptive pills (p-value 0.000), significant increase in total cholesterol among women using injectable the p-value 0.000, significant increase in total cholesterol among women using sub dermal implant contraceptive the p-value 0.000, and significant increase in triglycerides among women using oral contraceptive the p-value 0.000, significant increase in triglycerides among women using injectable the p-value 0.000, significant increase in triglycerides among women using sub dermal implant contraceptive the p-value 0.000, significant increase in LDL-c among women using oral contraceptive pills the p-value 0.000, significant increase in LDL-c among women using injectable the p-value 0.000, significant increase in LDL-c among women using sub dermal implant contraceptive the p-value 0.000 compared to women who are not.

The results also showed that significant decrease in HDL-c among women using oral contraceptive pills the p value 0.000, significant decrease of HDL-c among women using injectable contraceptives the p-value 0.000, significant decrease in HDL-c among women using sub dermal implant contraceptive the p-value 0.000 compared to women who are not (Tables 1 and 2).

Discussion

Contraceptive is intentional prevention of conception through the use of various devices, sexual practices, chemicals, drugs or surgical procedures becomes a contraception if it is purpose is to prevent a women from becoming pregnant [7].

The present study aimed to study the effect of hormonal contraceptives on plasma lipids (total cholesterol, triglycerides, high density lipoprotein- cholesterol, and low density lipoprotein-cholesterol) in women using hormonal contraceptives as test group and women who are not as control group.

Our results are in agreement with the results of Asara GA in a Ghanaian Community who reported that there is a significant increase in total cholesterol among women using hormonal contraceptives the p-value 0.002, significant increase in triglycerides among women using hormonal contraceptives the p-value 0.026 and significant increase in LDL-c among women using hormonal contraceptives the p-value 0.004 compared to women who are not. Also agree with results done by Naz et al. revealed that there is a significant differences among user of OCs compared to non-users [8]. Total cholesterol (242.92 mg/dl), HDL-c (58.65 mg/dl), LDL-c (115.84 mg/dl), and triglycerides (105.56 mg/dl) were significantly higher compared to the non-users. Serum concentrations of cholesterol, phospholipid and non-esterified fatty acid were raised in hormone-treated rats but triglyceride levels were normal. Endogenous production of triglyceride was also unchanged [9]. Total postheparin lipoprotein lipase activity was increased in the plasma of progesterone-treated rats largely due to increased release of the extrahepatic protamine sulphate-labile fraction. The basal rate of lipogenesis was also increased in adipocytes isolated from hormone-treated rats as was the insulin-stimulated rate of oxidation of [1-14 C] glucose. Basal and adrenaline-stimulated rates of fat cell lipolysis were, however, unchanged by treatment with progesterone [2].

Decreased lipolytic activity in adipose tissue may be one of the reasons behind excess accumulation of body fat during pregnancy. The aim of this study was to analyze the effect of progesterone on the expression of:

- (a) Lipe (encoding hormone-sensitive lipase, HSL)
- (b) Pnpla2 (encoding adipose triglyceride lipase, ATGL)
- (c) abhydrolase domain containing 5 (Abhd5)
- (d) G0/G1 switch 2 (G0s2), genes in white adipose tissue (WAT), as potential targets for progesterone action during the course of

Parameter	Oral	Injectable	Sub dermal implant	Control	P value
Triglycerol (mg/dl)	102.20 ± 2.167	73.05 ± 2.498	84.90 ± 1.167	73.35 ± 2.498	<0.05
Total Cholesterol (mg/dl)	162.25 ± 0.761	143.90 ± 0.641	134.90 ± 1.518	123 ± 2.646	<0.05
HDL-c (mg/dl)	30.70 ± 0.470	32.10 ± 0.641	34.35 ± 0.489	36.25 ± 0.444	<0.05
LDL cholesterol	92.10 ± 1.165	84.06 ± 0.646	74.90 ± 1.518	63.50 ± 2.646	<0.05

Mean lipid profile ± standard error upon use of progestogen-only contraceptive by various routes of administration.

Table 1: Comparison of different plasma lipid levels upon use of progestogen-only contraceptive by various routes of administration.

Method of contraceptive	Triglycerol	Total cholesterol	HDL-cholesterol	LDL-cholesterol
Oral	r=0.932 p=0.000	r=0.912 p=0.000	r=-0.886 p=0.000	r=0.927 p=0.000
Injection	r=0.671 p=0.001	r=0.686 p=0.000	r=-0.686 p=0.001	r=0.968 p=0.001
Sub dermal implant	r=1.000 p=0.000	r=1.000 p=0.000	r=-0.800 p=0.000	r=1.000 p=0.000

Table 2: Correlation between duration (18 Months) of different contraceptive treatment and plasma lipid.

pregnancy. Administration of progesterone to female rats, which was reflected by approximately 2.5-fold increase in circulating progesterone concentration, is associated with a decrease in Lipe gene expression in the inguinal WAT. The expression of Pnpla2 gene in all main fat depots of females and males remained unchanged after progesterone administration. Administration of progesterone resulted in an increase in the expression of Abhd5 gene (whose product increases ATGL activity) and G0s2 gene (whose product decreases ATGL activity) in the inguinal WAT of female rats. Mifepristone, a selective antagonist of progesterone receptor, abolished the effect of progesterone on Lipe, Abhd5 and G0s2 genes expression in the inguinal WAT. The decrease in Lipe and the increase in Abhd5 and G0s2 genes expression were associated with lower rate of stimulated lipolysis. Administration of progesterone exerted no effect on Lipe, Abhd5 and G0s2 genes expression and stimulated lipolysis in the retroperitoneal WAT of females, as well as in the inguinal, epididymal and retroperitoneal WAT of males [4].

Conclusion

1- Levels of plasma total Cholesterol, triglycerides and low density lipoprotein increased by using hormonal contraceptives and this increase were directly proportional to the duration of using hormonal contraceptives.

2- HDL-c level decreased by using hormonal contraceptives and this decrease is directly proportional with duration of using hormonal contraceptives.

References

1. Edmonds K, Gebbie AE, Hay P, Ingamells S, Monga A, et al. (2006) *Gynecology by Ten Teachers*.
2. Shirling D, Ashby JP, Baird JD (1981) Effect of progesterone on lipid metabolism in the intact rat. *J Endocrinol* 90: 285-294.
3. Mendes AM, Madon RJ, Flint DJ (1985) Effects of cortisol and progesterone on insulin binding and lipogenesis in adipocytes from normal and diabetic rats. *J Endocrinol* 106: 225-231.
4. Stelmanska E, Szrok S, Swierczynski J (2015) Progesterone-induced down-regulation of hormone sensitive lipase (Lipe) and up-regulation of G0/G1 switch 2 (G0s2) genes expression in inguinal adipose tissue of female rats is reflected by diminished rate of lipolysis. *J Steroid Biochem Mol Biol* 147: 31-39.
5. Nawrot TS, Hond ED, Fagard RH, Hoppenbrouwers K, Staessen JA (2003) Blood pressure, serum total cholesterol and contraceptive pill use in 17-year-old girls. *Eur J Cardiovasc. Prevention Rehab* 10: 438-442.
6. Mcevoy Gerald KAHF (2004) *Drug information*.
7. Speroff L, Fritz MA, Decherney A (2005) Evaluation of a new generation of oral contraceptives 6: 10034-1047.
8. Naz F, Jyoti S, Akhtar N, Afzal M, Siddique YH (2012) Lipid Profile of Women Using Oral Contraceptive Pills. *Pakistan Journal of Biological Sciences* 15: 947-950.
9. Asare GAA, Ngala, Albert GB, Amoah (2014) Effect of hormonal contraceptives on lipid profile and the risk indices for cardiovascular disease. *Int J Wom Health* 6: 597-603.