Effects of hormonal contraceptives on serum glucose, lipid profile and some liver function test

Isam Hamo Mahmood, Israa Mohammid Jaber
Department of Pharmacology and Toxicology, College of Pharmacy, University of Mosul, Mosul, Iraq.
Correspondence: israa.albanaa@gmail.com

Received 30.7.2013 Accepted 11.11.2013

ABSTRACT

Objective: To investigate the effects of hormonal contraceptives on serum glucose, lipid profile and some liver function tests.

Patients and Methods: One hundred and three women participated in this study. They were taken hormonal contraceptives including oral contraceptive pills or injection for a period not less than 6 months up to 12 years . Another group consisting of one hundred non contraceptive users taken from the same population participated in the study as a control group. Blood samples were taken from the individual and sera were used for the determination of serum glucose, lipid profile and some liver function tests which include alkaline phosphatase (ALP), aspartate amino transaminase (AST) and alanine amino transaminase (ALT).

Results: A highly significant values of serum glucose concentrations, total cholesterol, triglycerides and LDL- cholesterol were obtained in contraceptive users as compared with contraceptive non users. Whereas a non significant values of ALP, AST, ALT and HDL cholesterol were obtained.

Conclusion: The use of hormonal contraceptives was associated with undesirable effects on serum glucose and lipid profile. Care should be taken when using hormonal contraceptives in women having diabetes mellitus or cardiovascular diseases.

Key Words: Hormonal contraceptives, ALP, AST, ALT, lipid profile.

الخلاصة

الهدف: للبحث في تاثير موانع الحمل الهرمونية على تركيز السكر في المصل و على واجهة الدهون و على بعض فحوصات وظائف الكبد.

المرضى و طرائق العمل: شارك في الدراسة مائة و ثلاثة امراة استعملن حبوب منع الحمل عن طريق الفم او الحقن لمدة لاتقل عن 6 أشهر. وقد شارك في الدراسة مجموعة اخرى لا تستعمل موانع الحمل و تتكون من مائة امرأة. وقد تم أخذ نمودج من الدم من جميع النساء و تم قياس تركيز السكر وصفحة الدهون و على بعض فحوصات وظائف الكبد.

النتائج: اظهرت النتائج ارتفاع معنوي لتركيز السكر في المصل و الكولسترول الكلي والكلسترول الواطئ الكثافة والدهون الثلاثية في النساء الدين يستعملون موانع الحمل.و لم تضهر النتائج اي فرق معنوي بين انزيمات الكبد و الكلسترول العالي الكثافة بين النساء الدين يستعملون مانع الحمل والدين لا يستعملون موانع الحمل.

الاستنتاج: ان استخدام موانع الحمل يؤدي الى بعض التأثيرات الغير مرغوب فيها على تركيز السكر و اجهة الدهون. و لهدا يجب الانتباه عند استخدام موانع الحمل في النساء الدين يعانون من مرض السكري و من امراض القلب و الاوعية الدموية.

Hormonal contraceptives are widely used for the prevention of pregnancy in women. They are available in many forms including oral combined pills which are made of a combination of estrogen and progesterone, progesterone only pills,

progesterone only injection or implant and progesterone intrauterine system[1].

Unlike other commonly prescribed drugs, oral contraceptives pills are taken by healthy women for long period of time[2]. Oral combined contraceptive pills contain one of 2 synthetic estrogens (Mestranol or ethyl estradiol) and one of the following semisynthetic progestogens (norethindrone, norethynodrel, levonorgestrel, ethynodioldiacetate, desogestrel, norgestimate, gestodene)[3]. The combination of estrogen and progestogens exert their contraceptive effect largely through selective inhibition of pituitary function that results in inhibition of ovulation[4].

Regarding progestogen only injection, 2 preparations are available for long term use, including medroxyprogesterone acetate 150 mg given every 3 months and norethisteroneoenathate 200 mg given every 2 months[1]. The contraceptive action of progestogen injection occurs primarily at the level of the pituitary and the hypothalamus. As with oral combined contraceptives, medroxyprogesteroneacetate interrupts the usual hormonal messages sent from the brain to the ovary that lead to ovulation. Specifically, it prevents the mid cycle surge of LH, which is necessary for ovulation[5].

Long term use of hormonal contraceptives was associated with some adverse metabolic effects including effects on serum glucose وbody weight, BP, liver enzymes, and lipid profile. Review of literature showed different results.Al-chalabi and Al-sulevany[6] reported that there was a significant effect of oral contraceptives on serum triglycerides, total cholesterol, LDL and VLDL levels.In contrast, Skoubyet al.[7] showed no effect on plasma triglycerides and decreasing effects on total cholesterol.

The present study aimed to investigate the effects of oral contraceptive and injectable hormonalcontraceptives on body weight, serum glucose concentrations and lipid profile.

Patients and Methods

One hundred and three women participated in this study. They were taken hormonal contraceptives (contraceptive users) including oral contraceptive pills (microgynon which contains levonorgestrel 0.15 mg +ethinyl estradiol 0.03 mg) or injection (depoprovera which contains medroxyprogesterone 150 mg) for a period not less than 6 months up to 12 years. Another group consisting of one hundred non contraceptive users taken from the same population participated in the study as a control group. Inclusion criteria involved apparently healthy women taking microgynon (which contains levonorgestrel 0.15 mg +ethinyl estradiol 0.03 mg) or depoprovera (which contains medroxyprogesteron 150 mg), free from chronic diseases such as diabetes, hyperlipidemia and hypertension, not taking any medications which affect the outcome of the research.

Blood samples were withdrawn from each contraceptive and non contraceptive user. The separated sera were used for the determination of serum glucose, lipid profile and liver enzyme activities. Serum glucose was measured by glucose-oxidase-peroxidase spectrophotometric method by using a kit supplied by BIOCON (Germany).Serum triglycerides concentration was measured by enzymatic method using a kit supplied from BIOCON (Germany). Serum total cholesterol concentration and serum HDL concentration were determined by using kits provided from BIOCON (Germany). Serum

LDL concentration was calculated by Friedewaldequation8.

Determination of alkaline phosphatase activity (ALP)in serum was done by using a kit supplied by BIOMERIEUX laboratory reagents, Marcy L'Eoile, France.Alanine Amino Transaminase (ALT) and Aspartate Amino Transaminase (AST) activities were determined by using spectophotometeric test using a kit CTM, TECH medical company (UK). Body mass index (BMI) was calculated as the weight in kilograms divided by the squared height in meters (kg/m2). The effects of drugs on the measured parameters were determined by comparing the results obtained from contraceptive users and users.

Statistical Methods: Comparison between the parameters of the contraceptive users and non users was done by using Z-test. Level of significance is ≤ 0.05.

Results

Table 1 shows contraceptive users and non users characteristics. The 2 groups were matched regarding age and Body Mass Index (BMI) as evident by a non significant difference between the 2 groups.

Table 2 shows the comparison between the measured parameters of the 2 groups. Highly significant values of Fasting Blood Sugar (FBS), total cholesterol, triglycerides and Light Density Lipoprotein(LDL- cholesterol) were obtained in contraceptive users as compared with contraceptive non users. Whereas a non significant values of ALP, AST, ALT and HDL cholesterol were obtained.

Table 1. Contraceptive users and non users characteristics (Mean + SD).

Parameter	Non contraceptives users (N=100)	Contraceptive users (N=103)	P-value
Age (year)	31.9±7.71	31.98±5.68	NS
BMI (k/m^2)	25.31±5.32	26.09±5.79	NS
Duration of using the contraceptives (Year)	-----	2.96±2.2	

Table 2. Comparison between the measured parameters of the contraceptive users and non-users (Mean+SD).

Parameter	Contraceptive non users N=100	Contraceptive users N=103	P-value
FBS (mmol/L)	3.89±0.74	5.0±0.72	≥ 0.0001
ALP (U/L)	50.51±15.66	53.91±18.26	NS
AST (U/L)	8.24±2.62	8.42±3.11	NS
ALT (U/L)	9.73±3.53	10.44±3.95	NS
Total Cholesterol (mmol/L)	4.4±0.6	5.2±1.51	≥ 0.0001
Triglycerides (mmol/L)	1.2±0.41	1.63±0.81	≥ 0.001
HDL-cholesterol (mmol/L)	1.1±0.35	1.15±0.29	NS
LDL-cholesterol(mmol/L)	2.77±0.69	3.31±1.36	≥ 0.01

Discussion

Since the introduction of oral contraceptives in the early 1960s, repeated attention has been focused on possible harmful side effects. Also the putative association between oral contraceptive use and risk factors for heart disease, for example, blood pressure and serum lipids have been subject of many investigations. The results of these studies, however, have been equivocal. Thus the present study was undertaken to evaluate the effects of contraceptives on serum glucose, lipid profile and some liver function tests in number of women using hormonal contraceptives and compared with a number of women who did not use hormonal contraceptives.

The present study revealed a highly significant elevation of serum glucose concentrations in contraceptive user's individuals as compared with contraceptive non user's individuals indicating an effect of hormonal contraceptives on the metabolism of glucose.

Review of literature showed different results regarding the effects of hormonal contraceptives on serum glucose concentrations.Simon et al.9 reported that in comparison between oral contraceptive users and non users, fasting serum glucose was not significantly different. Likewise Reismanet al.10 reported the same results. Other studies 11,12reported higher concentrations of glucose concentrations in contraceptive users as compared with contraceptive non users which were in agreement with the present study.

Regarding lipid profile, the present study reported a significant increase in total-cholesterol, triglyceride and LDL-cholesterol and a non significant change in HDL-cholesterol in the contraceptive users as compared with the contraceptive non users. These results were in agreement with the results reported by other researchers. Al-chalabi and Al-sulevany6 reported a significant effect of oral contraceptive on serum

triglycerides, total-cholesterol, LDL-cholesterol and VLDL-cholesterol levels while no significant effect on serum HDL-cholesterol. Plasma triglycerides level was significantly higher in women taking oral contraceptive pills compared with non users13. Another study reported thatserum LDL-cholesterol was significantly higher in the oral contraceptive users thannon-users14.

Data obtained in this study showed non significant differences between liver enzyme activities of the contraceptive users and non users. Review of literature cleared that the effect of hormonal contraceptives on liver enzyme activities were controversial. Tagyet al.15 and Schiele et al.16 reported anon significant effects of hormonal contraceptives on liver enzyme activities which were in agreement with our results. In contrast, other studies 17,18 reported a reduction in liver enzyme activities.

Conclusion: The use of hormonal contraceptives was associated with undesirable effects on serum glucose and lipid profile. Care should be taken when using hormonal contraceptives in women having diabetes mellitus or cardiovascular diseases.

References

1- Miller WF, Hanretty KP, Callander R, Ramsden I. Hormonal contraceptives. In: Obstetrics Illustrated. 5th edition, Churchill Livingstone, London 1997:400-415.

2- Miller KE. Oral contraceptives are safe and effective. FertilStewril 1999; 71:S1-S6.

3- Carr BR, Bradshow KD. Disorders of the ovary and female reproductive tract. In: Harrison's Principles of Internal Medicine.14th edition, McGraw-Hill, New York 1998: 2097-2115.

4- Chrousos GP, Zoumakis E, Gravanis A. Gonadal Hormone. In: Basic and Clinical Pharmacology. Katzing BG. 8th edition. McGraw-Hill, New York 2001: 679-710.

5- Mishell DR. Effect of 6-methyl-17 hydroxyprogesterone on urinary excretion of luteinizing hormone. Am J Obestet Gynecol 1976; 99: 86-90.

6- Al-chalabiSD, Al-sulevany BK. The effect of contraceptive pills on plasma lipids and blood pressure. Ann Coll Med Mosul 2002; 28: 69-73.

7- Skouby SO, Wagner HH, Andersen O. The short term effects of a low dose oral contraceptive on glucose metabolism, plasma lipids and blood clotting factors. Contraceptive 1983; 28: 489-499.

8- FriedwaldWT ,Levy RJ and Fredrickson DS 1972. Estimation of the concentration of LDL-C in plasma without use of the preparative ultracentrifuge. Clin Chem 1972; 18:499-502

9- Simon D, Senan C, Garnier P, et al. Effects of oral contraceptives on carbohydrate and lipid metabolism in a healthy population. Am J Obstet Gynecol 1990;163:382-387.

10- Reisman H, Marein D, Gast MJ. Amulticenter randomized comparison of cycle control and laboratory findings with oral contraceptive agents containing 100 µg levonorgestrel with 20µg ethinylestradiol or triphasicn-orethindrone with ethinylestradiol. Am J Obstet Gynecol 1999;18:54-52.

11- GodslandIF, Crook D, Devenport M,et al. Relationships between blood pressure, oral contraceptives use and metabolic risk markers for cardiovascular disease. Contraception 1995; 52: 143-149.

12- Spellacy WN, Tsibris JCM, Ellingson AB. Carbohydrate metabolic studies in women using a levonorgestrel/ethinylestradiol contain-ing triphasic oral contracetive for eighteen months. Int J Gynecol Obstet 1991;35:69-71.

13- Straznicky NE, Barrington VE, BranleyP,et al. A study of the interactive effects of oral contraceptives use and dietary fat intake on blood pressure, cardiovascular reactivity and glucose tolerance in normotensive women. J hyperten 1998;16:357-368.

14- Oyelola OO. Fasting plasma lipids, lipoproteins, and apolipoproteins in Nigerian women using combined oral and progestin only inhestable contraceptives. Contraception 1993; 47:445-454.

15- Tagy AHF, Saker ME, Moussa AA, et al. The effect of low dose combined oral contraceptives pills versus injectable contraceptive of women on liver function tests of women with compensated bilharzial liver fibrosis. Contraception 2001;64: 173-176.

16- Schiele F, Vincent-Viry M, Fournier B, et al. Biological effects of eleven combined oral contraceptives on serum triglycerides, gamagluitamyl-transferase, alkaline phosphatase, bilirubin, and other biochemical variables. Clin Chem Lab Med 1998; 36:871-878.

17- Loke DF, Ng CS, HolckS, et al. Lipid and biochemical changes after low dose oral contraception. Contraception 1992;227-241.

18- Cowan LD,Wallce RB, Barrett-Connor E, et al. Alterations in clinical chemistry measures associated with oral contraceptive and estrogen use. J Repord Med 1982;27:275-282.