

Original Article

Study of Serum Calcium and Magnesium Levels in Reproductive Women Using Oral and Injectable Contraceptives

Rezwana Karim Roshny¹, M.A. Muttalib², Gazi Sharmin Sultana³, Farzana Akonzee Mishu⁴,
Md. Imran Khan Chayon⁵

Received: 10 May 2021

Accepted: 17 December 2021

doi: <https://doi.org/10.3329/jemc.v12i2.75780>

Abstract

Background: The oral and injectable contraceptives fulfill the human need for birth control with great effectiveness. These can effectively prevent pregnancy and alleviate menstrual disorder when used correctly. Many biochemical profiles of women taking oral and injectable contraceptives are disturbed due to metabolic alterations induced by its hormonal content. **Objective:** To find out the effects of oral and injectable contraceptives on serum calcium and magnesium levels. **Materials and Methods:** This cross-sectional comparative study was done in BIRDEM General Hospital, Shaheed Suhrawardy Medical College Hospital and Gandaria Family Planning Clinic of Nagar Shastho Kendro from July 2018 to June 2019. Study parameters- serum calcium and magnesium were estimated in each case. One hundred fifty women aged 18 to 45 were included according to the inclusion criteria. They were divided into three groups-50 oral contraceptive users as Group I, 50 injectable contraceptive users as Group II and 50 normal healthy controls as Group III. After taking the informed written consent from the study subjects, a structured questionnaire was filled in for each subject to collect data including personal identification, age, sex, chief complaints, duration of contraceptive use, socioeconomic status, demographic history, family history, genetic history, drug history, menstrual history and history of other systemic diseases. **Results:** The results of the study showed mean age and SD of the study subjects in Group I, Group II and Group III were 31.08±6.67, 31.60±7.83 and 36.74±6.27 years respectively. Mean (±SD) age was significantly higher in control group (Group III) than Group I and Group II ($p<0.001$). This study found that mean (±SD) serum calcium of the study subjects in Group I, Group II and Group III were 9.34±0.47, 9.20±0.40 and 9.14±0.49 mg/dL ($p<0.05$). The mean serum calcium was significantly higher in Group I compared to Group II and III. The mean value of magnesium in Group I, II and III were 0.82±0.09, 0.85±0.11 and 0.80±0.09 mmol/L respectively. There was significant increase in serum magnesium in injectable contraceptive users than oral contraceptive users and control group. **Conclusion:** This study concluded that oral contraceptives increased the serum calcium and injectable contraceptives increased the serum magnesium levels in comparison with control individuals and these were significant.

Key words: Oral contraceptives; Injectable contraceptives; Serum calcium; Serum magnesium

J Enam Med Col 2022; 12(2): 95–101

1. Lecturer, Department of Biochemistry, Enam Medical College, Savar, Dhaka
2. Professor, Department of Biochemistry, BIRDEM Academy, Dhaka
3. Associate Professor, Department of Biochemistry, BIRDEM Academy, Dhaka
4. Assistant Professor, Department of Biochemistry, BIRDEM Academy, Dhaka
5. Resident, Department of Nephrology, National Institute of Kidney Diseases & Urology (NIKDU)

Correspondence Rezwana Karim Roshny, Email: sabreenamohtarin@gmail.com

Introduction

Contraceptives are devices or techniques that prevent pregnancy. Among these most popular are oral contraceptive pills and injectable hormonal contraceptives.¹ Nearly 100 million women are using oral contraceptive pills (OCP) especially in recent years in around the world.² Current population of Bangladesh is 167,680,189. Contraceptive prevalence rate of Bangladesh is 62.3%.³ In Bangladesh among the available modern methods of contraceptives, oral contraceptives are used by about 30% couples.⁴

Ethinyl estradiol is the most frequently used estrogen in combined oral contraceptive pills.² This combination of estrogen and progestin is considered to be highly efficacious with a effectiveness of 97 to 98%.⁵ The prevalence of injectable contraceptives is 12.4%.⁶ Injectable contraceptives include depo-medroxyprogesterone acetate (DMPA), norethisterone enanthate (NET-EN) and combined injectable contraceptives of different combinations of estrogens and progestins that are given monthly. DMPA is used by approximately 3% of women of reproductive age. Medroxyprogesterone acetate (MPA) is a 17-acetoxyprogesterone compound. MPA is rapidly metabolized in humans to progesterone. MPAs primary mechanism of action is ovulation inhibition, but it works by increasing the cervical mucus viscosity and creating progestational changes in the endometrium wall.⁶

Calcium is the most abundant mineral in the body. About 98% of calcium in the adult is in the form of hydroxyapatite in the skeleton. Calcium, regulated by parathormone, calcitriol and thyrocalcitonin, has been implicated in virtually every metabolic function and is of major importance in bone formation, the blood clotting mechanisms, and in the activation of certain enzyme systems, e.g., adenylcyclase. A study showed the association between oral and injectable contraceptives with serum calcium levels.¹

Magnesium is an essential element in biological systems. Magnesium is a cofactor in more than 300

enzyme systems that regulate various biochemical reactions in the body, including protein synthesis, muscle and nerve functions. It also contributes to the structural development of bone.⁵ Serum magnesium levels was reduced by oral and injectable contraceptive use in some studies.⁴

Materials and Methods

It was a cross-sectional comparative study done in BIRDEM General Hospital, Shaheed Suhrawardy Medical College Hospital and Gandaria Family Planning Clinic of Nagar Shastho Kendro from July 2018 to June 2019. Study parameters serum calcium and magnesium were estimated in each case. According to the inclusion criteria, 150 women aged 18 to 45 were included in this study. They were divided into three groups—50 oral contraceptive users as group I, 50 injectable contraceptive users as group II and 50 normal healthy controls as group III. After taking informed written consent from the study subjects, a structured questionnaire was filled in for each subject to collect data including personal identification, age, sex, chief complaints, duration of contraceptive use, socioeconomic status, demographic history, family history, genetic history, drug history, menstrual history and history of other systemic diseases.

At first 5 mL blood specimens was collected from study subjects with aseptic precautions. 5 mL blood sample was delivered in a plain tube for serum calcium and magnesium estimation. Blood in plain tube was kept in standing position till clot formation. Serum and plasma were separated after centrifugation at 3000 rpm for 5 minutes. Then the study parameters were carried out at the clinical biochemistry section, Laboratory department, BIRDEM General Hospital. Then the serum was collected in microcentrifuge tube, labeled properly and stored in refrigerator at 2-8°C. Serum calcium was measured in Enzymatic method by BECKMAN COULTER Au-680 autoanalyzer. Serum magnesium was assessed in Enzymatic method by Abbott ARCHITECT PLUS C 8000 autoanalyzer. Collected data were checked, edited and processed with the help of SPSS (22.0). Continuous data were

analyzed by parametric test (student’s unpaired t-test, ANOVA test, chi-square test) and skewed data by nonparametric test.

Results

Baseline characteristics of the study subjects

The details of the socio-demographic characteristics of the study participants are shown in Table I. The total study subjects were 150. Among the participants 5.33% were ≤20 years of age, 37.33% were between 21-30 years of age, 41.33% were between 31-40 years of age and 16% were above 40 years of age. Among the total participants 25.3% were non-educated, 18.7% completed up to primary level education, 12% completed up to SSC, 12.7% up to HSC and 31.3% completed their graduation. Most of the participants (50.7%) were housewives, others were service holders (38.7%) and day labourers (10.7%). Among the participants 41.3% had low income, 2% had high income and the maximum (56.7%) were from middle class family. Most of the respondents (94%) were from urban areas and others were from rural areas (6%).

Table I: Baseline characteristics of the study subjects (n=150)

Variables	Frequency	Percentage
Age in years		
18-20	8	5.33
21-30	56	37.33
31-40	62	41.33
41-45	24	16.0
Residence		
Urban	141	94.0
Rural	9	6.0
Occupation		
Day labourer	16	10.7
Service holder	58	38.7
Housewife	76	50.7
Educational level		
Non educated	38	25.3

Primary education	28	18.7
SSC	18	12.0
HSC	19	12.7
Graduation	47	31.3
Monthly income		
Lower	62	41.3
Lower middle	16	10.7
Middle	68	45.3
Upper middle	1	0.7
High	3	2.0
Menstrual history		
Regular	81	54.0
Irregular	69	46.0

Table II shows the comparison of mean age among three groups. Mean (±SD) age of study subjects in Group I and Group III were 31.08±6.67 and 36.74±6.27 years respectively. Mean (±SD) age was significantly higher in Group III than that of Group I (p<0.001). In this study it was found that comparatively younger age group had taken oral combined pills for their contraception than older age group and it had significant difference. Table II also shows comparison of age group between Group II (injectable contraceptives users) and Group III (control group) in the study subjects. Mean (±SD) age of study subjects in Group II and Group III were 31.60 ± 7.83 and 36.74 ± 6.27 years respectively. Mean (±SD) age was significantly higher in Group III than that of Group II (p<0.001). In this study it was found that comparatively younger age group had taken injectable contraceptives for their contraception than older age group and it had significant difference.

Table III shows comparison of serum calcium and serum magnesium between Group I (OCP users) and Group III (control group) in the study subjects. Table IV shows comparison of serum calcium and serum magnesium between Group II (injectable contraceptives users) and Group III (control group) in the study subjects. Table V shows comparison of serum calcium and serum magnesium between Group

I (OCP users) and Group II (injectable contraceptives users) in the study subjects. Table VI shows comparison of serum calcium and serum magnesium among Group I (OCP users), Group II (injectable

contraceptives users) and Group III (control group) in the study subjects. Table VII shows correlation of serum calcium with serum magnesium among three groups.

Table II: Mean age of three groups

	Group I (n=50) Mean±SD	Group II (n=50) Mean±SD	Group III (n=50) Mean±SD	p value
Age in years	31.08±6.67	31.60±7.83	36.74±6.27	<0.001***

Group I: OCP users; Group II: Injectable contraceptives users; Group III: Control group

Table III: Comparison of different parameters between Group I and Group III

Parameters	Group I (n=50) Mean±SD	Group III (n=50) Mean±SD	p values
Serum calcium (mg/dL)	9.34±0.47	9.14±0.49	<0.05*
Serum magnesium (mmol/L)	0.82±0.09	0.80±0.09	>0.05

Group I: OCP users; Group III: Control group; *=significant

Table IV: Comparison of different parameters between Group II and Group III

Parameters	Group II (n=50) Mean±SD	Group III (n=50) Mean±SD	p values
Serum calcium (mg/dL)	9.20±0.40	9.14±0.49	>0.05
Serum magnesium (mmol/L)	0.85±0.11	0.80±0.09	<0.05*

Group II: Injectable contraceptives users; Group III: Control group ; *=significant

Table V: Comparison of different parameter between Group I and Group II

Parameter	Group I (n=50) Mean±SD	Group II (n=50) Mean±SD	p values
Serum calcium (mg/dL)	9.34±0.47	9.20±0.40	<0.05*
Serum magnesium (mmol/L)	0.82±0.09	0.85±0.11	>0.05

Group I: OCP users; Group II: Injectable contraceptives users; *=significant

Table VI: Comparison of different parameters among Groups I, II and III

Parameter	Group I (n=50) Mean±SD	Group II (n=50) Mean±SD	Group III (n=50) Mean±SD	p values
Serum calcium (mg/dL)	9.34±0.47	9.20±0.40	9.14±0.49	>0.05
Serum magnesium (mmol/L)	0.82±0.09	0.85±0.11	0.80±0.09	>0.05

Group I: OCP users; Group II: Injectable contraceptives users; Group III: Control group

Table VII: Correlation of serum calcium with serum magnesium among three groups (n=150)

Parameter	OCP users (n=50)		Injectable contraceptive users (n=50)		Control group (n=50)	
	r value	p value	r value	p value	r value	p value
Calcium	0.175	0.032*	-0.040	0.627	-0.135	0.099
Magnesium	-0.038	0.641	0.177	0.030	0.139	0.090

*=significant

Discussion

The present study was conducted in the department of Biochemistry & Molecular Biology of BIRDEM (Bangladesh Institute of Research & Rehabilitation for Diabetes, Endocrine & Metabolic Disorders) Academy from July 2018 to June 2019. According to inclusion and exclusion criteria 150 study subjects were taken in the study. Among them 50 normal healthy married women using oral contraceptive pills for at least last six months were taken as Group I, 50 normal healthy married women using injectable contraceptives for last six months were taken as Group II and 50 normal menstruating married women who were not using any oral or injectable contraceptives for last six months were taken as Group III.

This study showed majority (41.33%) of the respondents were between age group 31 to 40 years. Women of age 21 to 30 years were second highest in percentage (37.33%) among the study population. Respondents of age group ≤ 20 years were very few (5.33%) and women of age above 40 years were 16%. Mean age of study subjects in Group I and Group III were 31.08 ± 6.67 and 36.74 ± 6.27 years respectively. Mean age was significantly higher in Group III than Group I ($p < 0.001$). Mean age of study subjects in Group II and Group III were 31.60 ± 7.83 and 36.74 ± 6.27 years respectively. Mean age was significantly higher in Group III than Group II ($p < 0.001$). Mean age of study subjects in Group I and Group II were 31.08 ± 6.67 and 31.60 ± 7.83 years respectively. No significant differences were found between the two groups ($p > 0.05$). Mean age and SD of the study subjects in Group I, Group II and Group III were 31.08 ± 6.67 , 31.60 ± 7.83 and 36.74 ± 6.27 years respectively. Mean age was significantly higher in control group (Group III) than Group I and Group II ($p < 0.001$). Rahman and

coworkers found the highest number of women using contraceptives in late twenties and early thirties.⁷

Current study showed that 25.3% participants were non-educated, 18.7% completed up to primary level education, 12% completed up to SSC, 12.7% up to HSC and 31.3% completed their graduation. It was revealed that among the respondents educated women were predominant.

Long time use of hormones such as oral and injectable contraceptives can affect various metabolic pathways to such an extent that would cause detectable clinical abnormality due to the alteration of concentrations of serum trace elements.⁴

Serum calcium

The present study showed that those on oral contraceptives had significantly increased serum calcium levels over the control group while serum calcium levels in injectable users did not differ significantly from those of the control group. This study found that mean calcium was significantly higher in Group I compared to Group III (9.34 ± 0.47 vs 9.14 ± 0.49 mg/dL; $p < 0.05$). This study also found that mean value of serum calcium in Group II was 9.20 ± 0.40 mg/dL whereas mean value of serum calcium in Group III was 9.14 ± 0.49 mg/dL. The calcium levels showed no significant difference between Group II and Group III.

Similar significant increase in calcium level was observed in oral contraceptive participants as reported by Akinloye et al¹ It was possible that the use of oral contraceptives is most often associated with increased absorption of calcium. Apart from increased absorption of calcium, it is also possible that oral contraceptives play a role in calcium homeostasis which brings about a net effect of increased calcium mobilization from

the bone leading to bone demineralization. This may predispose individuals of these contraceptives to osteoporosis.

Akinloye et al¹ reported that serum calcium showed no significant correlation with the duration of contraception in the combined contraceptive participants (oral and injectable contraceptive groups). Dietary habit, socioeconomic conditions, free from any disease condition, dosages and formulation of contraceptives may be responsible for these findings. A significant increase in the serum calcium levels in women on oral contraceptives in respect to women on injectable contraceptives was also described in another study.⁸

Increased level of serum calcium was found in oral contraceptive users compared to non-oral contraceptive users in a study conducted on Indian and European population.⁹ No significant difference of serum calcium between oral contraceptive and control groups was observed ($p>0.05$) in one study by Hasanat et al⁴ which was in disagreement with present study. However, Akinloye et al¹ also showed that there was a little decrease in serum calcium level in oral contraceptive therapy, but these changes were not significant.

Serum magnesium

In the present study it was found that there was no significant difference in serum magnesium levels between oral contraceptive and control groups. The mean value of magnesium in Group I was 0.82 ± 0.09 mmol/L whereas mean value of magnesium in Group III was 0.80 ± 0.09 mmol/L. But there was significant increase in serum magnesium in injectable contraceptive users than in control group. The mean magnesium was significantly higher in Group II compared to Group III (0.85 ± 0.11 vs 0.80 ± 0.09 mmol/L; $p<0.05$). It may explain resistance of young women to heart disease and osteoporosis, as well as increased prevalence of these diseases when estrogen secretion ceases. However, estrogen-induced shifts of magnesium can be deleterious when estrogen levels are high and magnesium intake is suboptimal. The resultant lowering of blood magnesium can increase the Ca/Mg ratio, thus favoring coagulation. Akinloye

et al¹ and Hasanat et al⁴ and almerly et al⁵ found highly significant decrease in serum magnesium level in oral contraceptive user women when compared with non-oral contraceptive user women. A significant decrease in serum magnesium levels in oral contraceptive users was also found in other study.¹⁰ This is also in agreement with the study of Hameed et al¹¹.

In this study, significantly higher serum calcium was observed in women taking oral contraceptives in comparison with control individuals who were not taking any hormonal contraceptives. Serum magnesium was significantly higher in women taking injectable contraceptives in comparison with control individuals. In the present study there was significantly positive correlation of serum calcium with OCP users. There was negative correlation of serum magnesium with OCP users which was not significant. There was significantly positive correlation of serum magnesium with injectable contraceptive users. The present study also showed negative correlation of serum calcium with injectable contraceptive users which was not significant.

References

1. Akinloye O, Adebayo TO, Oguntibeju OO, Oparinde DP, Ogunyemi EO. Effects of contraceptives on serum trace elements, calcium and phosphorus levels. *West Indian Med J* 2011; 308–315.
2. Huda FA, Robertson Y, Chowdhuri S, Sarker BK, Reichenbach L, Somrongthong R. Contraceptive practices among married women of reproductive age in Bangladesh: a review of the evidence. *Reproductive health* 2017; 14: 1–9.
3. Kamal M, Islam A. Prevalence and socioeconomic correlates of unintended pregnancy among women in rural Bangladesh. *Salud publica de Mexico* 2011; 53: 108–115.
4. Hasanat F, Chakroborty PK, Nahar DN, Bishwash S, Hena KN, Mollika R. Status of serum calcium and magnesium in women taking oral contraceptive. *Bangladesh Journal of Medical Biochemistry* 2017; 10(2): 64–68.
5. Palmery M, Saraceno A, Vaiarelli A, Carlomagno G. Oral contraceptives and changes in nutritional

- requirements. *European Review for Medical & Pharmacological Sciences*. 2013; 17: 1804–1813.
6. Berenson AB, Van Den Berg P, Williams KJ, Rahman M. Effect of injectable and oral contraceptives on glucose and insulin levels. *Obstetrics & Gynecology* 2011; 117(1): 41–47.
 7. Rahman J, Sultana N, Nazneen K, Wahab F, Wazed F, Begum HA. Pattern of contraceptive use among women of different ages: a hospital based study. *Journal of Dhaka Medical College* 2014; 23(1): 109–113.
 8. Di Carlo C, Gargano V, Sparice S, Tommaselli GA, Bifulco G, Schettino D et al. Short-term effects of an oral contraceptive containing oestradiol valerate and dienogest on bone metabolism and bone mineral density: an observational, preliminary study. *The European Journal of Contraception & Reproductive Health Care* 2013; 18(5): 388–393.
 9. Gipson JD, Hindin MJ. The effect of husbands' and wives' fertility preferences on the likelihood of a subsequent pregnancy, Bangladesh 1998–2003. *Population Studies* 2009; 63(2): 135–146.
 10. Haroon S, Naveed AK. Effect of hormonal contraceptives on serum electrolytes and blood pressure. *Journal of Postgraduate Medical Institute* 2014; 28(4): 409–413.
 11. Hameed A, Majeed T, Rauf S, Ashraf M, Jalil MA, Ullah N et al. Effect of oral and injectable contraceptives on serum calcium, magnesium and phosphorus in women. *Journal of Ayub Medical College Abbottabad* 2001; 13(3): 24–25.