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Research Article

ESTIMATION OF SERUM CALCIUM, MAGNESIUM AND PHOSPHORUS DURING DIFFERENT PHASES OF MENSTRUAL CYCLE

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ABSTRACT

Introduction: The menstrual cycle is unique to female human beings and a few nonhuman primates. It results from a complex interaction between the hypothalamus, anterior pituitary gland, ovaries and uterus.(1)The average menstrual cycle is of about 28 days (23-29days) and is divided into three phases-proliferative phase, secretory phase, menstrual phase. Thus the cyclic hormonal changes occurred during various phases of menstrual cycle, can affect a variety of physiological and biochemical processes affecting the levels of various minerals like calcium, magnesium and phosphorus present in the body.
Aims: The purpose of this study is to evaluate the changes in serum Calcium, Magnesium and Phosphorus levels during various phases of menstrual cycle in healthy normally menstruating female.
Materials and Methods: The 100 healthy female volunteers from M.B.B.S students participated as subjects in this study. Each subject has been explained about the procedure of the test to eliminate fear and apprehension. Informed Consent was taken from each subject. The subjects were selected on the basis of normal and regular menstrual cycle i.e (28+4) cycle. Those students having irregular menstrual cycle, distressing symptoms like severe abdominal pain, heavy or scanty menstrual blood loss are excluded from the study. The regular menstrual cycle of 28 days can be divided in to three phases. The blood sample was collected three times from each subject during their menstrual, proliferative and secretory phase. The blood sample was drawn in the morning hours between 8.00 a.m. to 9.00 a.m. during each phase of menstrual cycle. Estimation of serum calcium, magnesium and phosphorus was carried out on the same day of collection of blood sample.
Results: In the present study, we observed gradual increase in serum calcium level from menstrual to proliferative phase and gradual decrease from proliferative to secretory phase. Highest level of serum calcium was seen in proliferative phase. It further showed gradual decrease in serum magnesium level from menstrual to proliferative phase and then gradual increase from proliferative to secretory phase. Highest level of serum magnesium was seen in secretory phase. Study showed gradual decrease in serum phosphorus level from menstrual to proliferative phase and also from proliferative to secretory phase. Highest level of serum phosphorus was seen in menstrual phase.
Conclusions: Cyclic changes of serum calcium, magnesium and phosphorus are brought under the influence of ovarian hormones acting directly or indirectly. While interpreting the levels of serum calcium, magnesium and phosphorus for any reason, cyclic changes of serum calcium, magnesium and phosphorus were noted during different phases of menstrual cycle.

INTRODUCTION

The menstrual cycle is unique to female human beings and a few nonhuman primates. It results from a complex interaction between the hypothalamus, anterior pituitary gland, ovaries and uterus (Bayer and Decherney, 1993).

The average menstrual cycle is of about 28 days (23-29days) and is divided into three phases. The first phase is estrogen dominated phase that lasts up to the occurrence of ovulation, this phase is known as the proliferative phase or the follicular phase (Southan and Gezazo, 1965; Pavlik and Coulson, 1976). The second phase is due to an increase in the progesterone secretion, this phase is known as secretory or luteal phase.

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The last phase known as menstrual phase occur due to decrease in all the ovarian hormones which in turn decrease the production of all anterior pituitary reproductive hormones (Paula and Adams, 2002). Thus the cyclic hormonal changes occurred during various phases of menstrual cycle and it can affect a variety of physiological and biochemical processes affecting the levels of various minerals present in the body. Out of the many minerals calcium, magnesium and phosphorus are needed in large amount and are called major elements (API, 2008). It is known that regulation of calcium, magnesium and phosphorus are depend upon various hormones like parathyroid hormone calcitonin and cholecalciferol which are collectively called as calcitropic hormones (Textbook of Medical Physiology. Indu Khurana Endocrinal control of calcium metabolism and bone physiology. 1st Ed., p-725).

It is also noted that osteoporosis causing a reduction in bone mass consisting various minerals are more common in post-menopausal woman (Harrison's Principles of Internal Medicine. International Ed. Isselbacher KJ. Endocrinology and Metabolism- Metabolic Bone Disease (Osteoporosis), 1994). Further the withdrawal of estrogen is reported to cause a significant loss of bone calcium. This decreased calcium input contributes to a declining bone mass and the increased risk of fracture in the aged due to osteoporosis. It is also observed that basal metabolic rate (BMR) varies significantly with menstrual cycle. This BMR is associated with increased carbohydrate utilization and requires magnesium ions (Christiansen and Riss, 1990; Czaja, 1978). Also the rapid fall in serum phosphorus concentration was observed to be associated with rise in serum calcium concentration after parathyroid hormone administration (Guyton and Hall, 2006). The purpose of this study is to evaluate the changes in serum calcium, magnesium and phosphorus levels during various phases of menstrual cycle in healthy normally menstruating female.

MATERIALS AND METHODS

The 100 healthy female volunteers from M.B.B.S students participated as subjects in this study. Each subject has been explained about the procedure of the test to eliminate fear and apprehension. Informed Consent was taken from each subject. The subjects were selected on the basis of normal and regular menstrual cycle i.e (28+4) cycle. Those students having irregular menstrual cycle, distressing symptoms like severe abdominal pain, heavy or scanty menstrual blood loss are excluded from the study.

Determination of different phases of menstrual cycle

The regular menstrual cycle of 28 days can be divided in to three phases as per the day of menstrual cycle as follow.

Menstrual phase from 1st to 5th day.
Proliferative phase from 6th to 14th day
Secretory phase from 15th to 28th day (Textbook of Medical Physiology. Indu Khurana. Endocrinal control of calcium metabolism and bone physiology. 1st Ed., p-725; Dokuz Eylu, 1994; Pandya *et al*., 1995)

Collection of blood sample

The blood sample was collected three times from each subject during their menstrual, proliferative and secretory phase. The blood sample was drawn in the morning hours between 8.00 a.m to 9.00 a.m during each phase of menstrual cycle. About 3 ml of blood sample was drawn from the anticubital vein collected in plane bulb; blood sample was taken on 2nd, 10th and 22nd days of menstrual cycle. Serum gets separated and used for estimation of following biochemical parameters.

- Serum Calcium
- Serum Magnesium
- Serum Phosphorus

Estimation of serum calcium, magnesium and phosphorus was carried out on the same day of collection of blood sample.

Estimation of serum Calcium

Serum calcium was estimated by Modified Arsenazo method (Indu Khurana ?). It is the photometric method. Calcium present in the sample react with reagent Arsenazo in a slightly alkaline medium to form purple coloured Calcium-Arsenazo complex which absorbs at 650 nm. The intensity of colour of the formed complex is measured using spectrophotometer which is proportional to the amount of calcium present in the sample.

Estimation of serum Magnesium

Serum magnesium was estimated by Xylidyl blue method (Chromy and Svoboda, 1973). It is also the photometric method. Here magnesium present in the sample combines with reagent Xylidyl blue in alkaline solution to produce a red coloured Xylidyl blue magnesium complex. The intensity of colour of the formed complex is measured using spectrophotometer which is proportional to the amount of magnesium present in the sample.

Estimation of serum Phosphorus

Serum phosphorus was estimated by Ammonium Molybdate method (Young, 1975). It is also photometric method. Here phosphorus present in the sample combines with reagent Ammonium Molybdate in presence of strong acids to formed phosphomolybdate is measured using spectrophotometer which proportional to the amount of phosphorus present in the sample.

Statistical Analysis

For each parameter i.e. for the levels of serum calcium, magnesium and phosphorus, mean and standard deviations (S.D) were calculated during menstrual, proliferative and secretory phase. Then find out the difference, the comparison was made for each parameter between menstrual and proliferative phase, between proliferative and secretory phase and between menstrual and secretory phase. The significance of the difference was tested by paired't'test. The significance was noted at $p<=0.05$ (Park, 2001).

RESULTS

Levels of serum calcium estimated during different phases of menstrual cycle are shown in the Table 1A. Table 1B showed gradual increase in serum calcium level from menstrual to proliferative phase and then gradual decrease from proliferative to secretory phase. Also the difference in levels of serum calcium was statistically analysed using paired't' test between menstrual and proliferative phase, between proliferative and secretory phase and between menstrual and secretory phase and it is found to be significant with each other. Levels of serum magnesium estimated during different phases of menstrual cycle are shown in the Table 2A. Table 2B showed gradual decrease in serum magnesium level from menstrual to proliferative phase and then gradual increase from proliferative to secretory phase. Also the difference in levels of serum magnesium was statistically analysed using paired't' test between menstrual and proliferative phase, between proliferative and secretory phase and between menstrual and secretory phase and it is found to be significant with each other.

Table 1A. Showing levels of Serum Calcium during different phases of menstrual cycle

Phases of menstrual cycle	Levels of Serum Calcium (mg./ dl.)	
	Mean	S.D.
Menstrual Phase	9.003	0.278
Proliferative Phase	9.723	0.407
Secretory Phase	8.547	0.296

Table 1B. Showing statistical analysis of Serum Calcium levels during different phases of menstrual cycle

Phases of menstrual cycle compared	Change observed	p value	Remark
Menstrual to Proliferative Phase	Increased	<0.001	Highly significant
Proliferative to Secretory Phase	Decreased	<0.001	Highly significant
Menstrual to Secretory Phase	Decreased	<0.001	Highly significant

Table 2A. Showing levels of Serum Magnesium during different phases of menstrual cycle

Phases of menstrual cycle	Levels of Serum Magnesium (mg./ dl.)	
	Mean	S.D.
Menstrual Phase	1.777	0.291
Proliferative Phase	1.447	0.254
Secretory Phase	2.220	0.318

Table 2B. Showing statistical analysis of Serum Magnesium levels during different phases of menstrual cycle

Phases of menstrual cycle compared	Change observed	p value	Remark
Menstrual to Proliferative Phase	Decreased	<0.001	Highly significant
Proliferative to Secretory Phase	Increased	<0.001	Highly significant
Menstrual to Secretory Phase	Increased	<0.001	Highly significant

Levels of serum phosphorus estimated during different phases of menstrual cycle are shown in the Table 3A. Table 3B showed gradual decrease in serum phosphorus level from menstrual to proliferative phase and also from proliferative to secretory phase. Also the difference in levels of serum phosphorus was statistically analyzed using paired't' test between menstrual and proliferative phase, between proliferative and secretory phase and between menstrual and secretory phase and it is found to be significant with each other.

Table 3A. Showing levels of Serum Phosphorus during different phases of menstrual cycle

Phases of menstrual cycle	Levels of Serum Phosphorus (mg./ dl.)	
	Mean	S.D.
Menstrual Phase	4.123	0.261
Proliferative Phase	3.307	0.692
Secretory Phase	2.853	0.578

Table. 3B. Showing statistical analysis of Serum Phosphorus levels during different phases of menstrual cycle

Phases of menstrual cycle compared	Change observed	p value	Remark
Menstrual to Proliferative Phase	Decreased	<0.001	Highly significant
Proliferative to Secretory Phase	Decreased	<0.001	Highly significant
Menstrual to Secretory Phase	Decreased	<0.001	Highly significant

DISCUSSION

Minerals are inorganic substances that are widely found in and on earth. There are 92 elements found in nature. They are required by the body for variety of functions such as formation of bones and teeth, certain components of various body tissues, body fluids and enzyme system and also for performing normal functions of nerves. Some of minerals such as calcium, magnesium are needed by body in large quantity (API, 2008). The menstrual cycle is the most extensively studied rhythm in women. The hormonal changes during the normal menstrual cycle are well established and these hormonal changes are commonly associated with fluctuations in the state of physiological functions and subjective feeling in women. An extensive literature search has revealed very scanty data for the changes in serum calcium, magnesium and phosphorus levels in the various phases of menstrual cycle.

Changes in these irons are, however, reported to be mainly due to changes in the hormonal levels during the different phases of the menstrual cycle (Textbook of Medical Physiology Indu Khurana. Endocrinal control of calcium metabolism and bone physiology. 1st Ed., p-725; Harrison's, 1994; Christiansen and Riss, 1990). In the present study, the mean serum calcium level was 9.003mg/dl during menstrual phase, 9.723 mg/dl during proliferative phase and 8.547 mg/dl. during secretory phase. All these levels were within the normal reference range (API, 2008). In the present study the mean serum calcium levels increased in the proliferative phase as compared to the menstrual phase and decreased in the secretory phase. Earlier research shows that the increase serum calcium levels during the proliferative phase could be due to the effect of oestrogen on parathyroid glands and the higher levels of progesterone compared to oestrogen during the secretory phase could be responsible for these low serum calcium (Pandya *et al*., 1995; Young, 1975). In the present study, the mean serum magnesium level was 1.777 mg/dl during menstrual phase, 1.477 mg/dl during proliferative phase and 2.220 mg/dl during secretory phase. All these levels were within the normal reference range (API, 2008). In 1994 Dokuz E *et al* found that the mean serum magnesium level significantly lower in women suffering from premenstrual syndrome than in the control group. They also found that serum magnesium level was diminished significantly during the proliferative phase compared to the secretory phase in women with premenstrual syndrome (Dokuz Eylul, 1994).

In 1995 Pandya AK *et al*investigated serum calcium, magnesium and phosphorus levels serially during menstrual, proliferative and secretory phases of menstrual cycle. Serum calcium level was highest during proliferative phase and lowest during secretory phase. Exactly opposite result was observed for serum magnesium levels. It was highest during secretory phase and lowest during proliferative phase. However, for serum phosphorus, the highest level was seen during menstrual phase and lowest during the secretory phase. They stated that these changes are probably brought about under the influence of cyclic variations of the ovarian hormones (Pandya *et al*., 1995). We have found the decrease serum magnesium levels in the proliferative phase as compared to the menstrual phase and increase in the secretory phase as compared to the menstrual phase. Thus, the levels of serum magnesium were highest during the secretory phase and lowest during the proliferative phase. These results are in agreement with the observations of Pandya *et al* (Czaja, 1978). The raised oestrogen levels could possibly be acting on the parathyroid gland, due to which serum magnesium levels dropped during the proliferative phase as reported by Pitkin *et al*. Pitkin and co-workers further stated that clinical hyperparathyroidism could deplete the body stores of magnesium (Young, 1975). It has been reported that magnesium irons and oxidative enzymes are needed for carbohydrate utilization which increases significantly during the secretory phase (Young, 1975).

Increased serum calcium levels during the proliferative phase may also contribute to the decreased magnesium levels by exerting an effect on the cell permeability (Chromy and Svoboda, 1973; Young, 1975). In the present study, the mean serum phosphorus level was 4.123 mg/dl during menstrual phase, 3.307 mg/dl during proliferative phase and 2.853 mg/dl. during secretory phase. All these levels were within the normal reference range (API, 2008). The study showed the serum phosphorus level decreased in the proliferative and secretory phases as compared to the menstrual phase. This pattern is consistent with an earlier report in which serum phosphorus levels were found to be higher during the menstrual phase than in the other two phases (Czaja, 1978). The present study also compares well with an earlier observation that high estrogen production can lead to a decrease in serum inorganic phosphorus levels (Young, 1975).

SUMMARY AND CONCLUSION

The comparisons were made for each of these between menstrual and proliferative phase, between proliferative and secretory phase and between menstrual and secretory phase. Significance of the difference was tested by paired‘t’ test. The significance was noted at the level of p=0.05.In the present study, we observed gradual increase in serum calcium level from menstrual to proliferative phase and gradual decrease from proliferative to secretory phase. Highest level of serum calcium was seen in proliferative phase. It further showed gradual decrease in serum magnesium level from menstrual to proliferative phase and then gradual increase from proliferative to secretory phase. Highest level of serum magnesium was seen in secretory phase. And it also showed gradual decrease in serum phosphorus level from menstrual to proliferative phase and also from proliferative to secretory phase. Highest level of serum phosphorus was seen in menstrual phase.

Thus, in short, cyclic changes were noted in the levels of serum calcium, magnesium and phosphorus during different phases of menstrual cycle. Still, all these serum calcium, magnesium and phosphorus levels found to be within physiological limits i.e. in their normal range. So it was concluded that these changes are probably brought under the influence of cyclic variations of ovarian hormones acting directly or indirectly. Further it was suggested that while interpreting the levels of serum calcium, magnesium or phosphorus for any reason, one should keep in mind their cyclic variation during different phases of menstrual cycle.

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