J. Cardiovasc Disease Res., 2020; 11(3): 80 – 84
A Multifaceted Peer Reviewed Journal in the field of Cardiology
www.jcdronline.org | www.journalonweb.com/jcdr
P – ISSN: 0975 – 3583 Online: 0976 – 2833

Selective Macro Minerals Study, Parathyroid Hormone and Lipid Profiles in Pre and Post-Menopausal Women Employees

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ABSTRACT

Menopause is a life phase when someone are going to stop their menstrual period. It is a common part of aging process and marks the end of your reproductive years. Menopause usually occurs in your late 40s to early 50s. Although, women who have surgery in their ovaries undergo surgical menopause "suddenly". Advances in medical care and treatment, large number of female population is expected to be in postmenopausal age group. Females are at greater risk of CVD after they attain menopause, when compared to men of similar age group, is a known fact. The exact reason is not known. But, estrogen deficiency and various other factors are said to play a role.

Keywords: Menopause, premenopause, women, post-menopause

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Submitted: 05-06-2020
Revision: 30-06-2020
Accepted Date: 20-07-2020

DOI: 10.31838/jcdr.2020.11.03.19

INTRODUCTION

Menopause means permanent stagnation of menstruation that occurs at the end of reproductive life due to loss of ovarian follicular activity[1]. This is the time when the last and last menstrual period occurs. Most women enter the menopausal transition during their late 40s. This is a physiologic change which occurs due to ovarian senescence and decline in estrogen.[2] The women experiences final menses averagely at 51.5 years, but this can take place at any time which is a result of ovarian failure. Older terms like climacteric and perimenopause indicate the late reproductive period. In majority of circumstances, these terms were used consistently. The more apt terminology for this phase of women's life is called as menopausal transition.[3] The initial systematized directives to classify female reproductive aging were given by the Stages of Reproductive Aging Workshop (STRAW, 2001).This staging has divided the reproductive and post reproductive life of women into life various stages. Final menstrual period (FMP) forms the main foundation of the staging system. There can be variation in age range and duration of each stage. Before FMP there are five stages and after it two stages. The group also summarized that older terminology like climacteric, etc should be used only in lay press or in connection to patients but not in articles to be published.[3] There are number of factors which speed the ovarian aging and in turn impact age of menopause like environment, genes and surgical causes. For example, smoking causes menopause to occur early by approximately 2 years. Apart from stopping of menses, in majority of women, no other symptoms are evident.[1] Common early symptoms are those caused by vasomotor instability, which include hot flashes, insomnia, and irritability mood disorders.

AIM AND OBJECTIVES

Aim of the study

To study selective macro-minerals, PTH, lipid profiles in pre and post- menopausal women employees at tertiary care hospital.

Objectives

To estimate calcium, phosphorus, magnesium, PTH in pre and postmenopausal women. To estimate lipid profile in pre and postmenopausal women.

REVIEW OF LITERATURE

The term menopause refers to the exact point of time following one year after the stoppage of menstruation. The post-menopause refers to period after this point. Average age of women experiencing her final menses is 51.5 years, but menstrual cessation due to ovarian failure can be seen at any point. Premature ovarian failure is end of menses before 40 years. This is accompanied by an elevated follicle stimulating hormone (FSH) level. Older terminologies such as, climacteric pertain to the late reproductive years. These terms are no longer preferred in scientific press and menopausal transition should be used.

In 2001, Stages of Reproductive aging workshop (STRAW) gave the standardized guidelines for classification reproductive aging in females. The STRAW report's purpose was to clarify the stages and nomenclature of normal reproductive aging. This staging system is for recommendation and not to be applied in diagnosis. Every stage may not occur in a given person and even it occurs there is no particular sequence for their occurrence. FMP is crux of the staging system with initial five stages and later having two stages.[3]

Calcium

Calcium is the fifth most abundant element in the earth's crust, it is never found free in nature because it readily reacts with oxygen and water to form compounds. The average adult body contains about 1 kg or 25 mg of calcium, of which 99% is primarily in the form of hydroxyapatite extracellular crystals [Ca10(PO4) 6(OH) 2]. Naturally found fertilizers and calcium phosphate (Ca3 (PO4) 2) are the main substances found in bones and teeth. Extra fluid and soft tissues contain 1% of calcium in the rest of the organism.[4,10]

Distribution of calcium

99% is present in bones and teeth as calcium plus phosphorus salt in majority, while some amount is present as calcium citrate, calcium carbonate or calcium chloride. Physiologically, calcium can be classified as intracellular or extracellular. It is this intracellular calcium that plays important role in various physiologic functions. The calcium concentration in intracellular compartment of an unstimulated cell is around 0.1µmol/L, which is less than 1/10,000 of that in extracellular fluid. In blood, almost all calcium is present in plasma i.e. extracellular and the RBCs are devoid of any calcium. The normal plasma level is 8.6-10.3mg% or 2.15-2.57 mmol/L. Calcium is present in three forms in the blood as is present as free ionized form. Calcium is complexed with small diffusible inorganic and organic anions, including bicarbonate, lactate, phosphate, citrate, etc.[5]

Functions of calcium in body

Calcification of bones and teeth (99%). Coagulation of blood (factors 2, 7, 9 and 10 require calcium for their activation). Calcium helps in transmission of nerve impulse. Muscle contraction- both striated and cardiac muscles require calcium for their contraction. Calcium released from the sarcoplasmic reticulum binds to troponin C present on the actin containing thin filaments of myofibrils. This changes the structure of troponin and tropomyosin which is attached to it is rolled away from the myosin binding sites on the actin filaments that form the back-bone of the thin filaments. The actin filament slides on the myosin filament resulting in muscle contraction. The process is known sliding filament theory of muscle contraction. Normal excitability of heart is also dependent on calcium. It also prolongs systole in cardiac cycle. Calcium acts as a 2nd messenger for many hormones like adrenaline, nor-adrenaline, catecholamines, gastrin and glucagon. Occasionally also acts as a 3rd messenger for parathyroid hormone and anti- diuretic hormone. Helps in exocytosis and endocytosis Causes cell to cell binding. Curdling of milk requires calcium.

Phosphorus

An adult body contains approximately 700gms -1kg of phosphorus in inorganic and organic phosphates, of which 85% is in the skeleton and rest is mainly in the soft tissue.[5]

Distribution of phosphorus

Plasma contains both inorganic and organic phosphorus of which only inorganic phosphate is measured. The ratio of these two anions is pH dependent and varies from approximately 1:1 in acidosis to 1:4 at pH 7.4 and 1:9 in alkalosis.

Functions of phosphorus in the body

Phosphate is involved in the regulation of protein-mediated metabolism of lipids and carbohydrates, and in gene transcription and cell growth. Formation of bones and teeth (80%). It is present in phospholipids, phosphoroteins and nucleic acids. Formation of high energy compounds like Adenosine triphosphate(ATP), Guanosine triphosphate (GTP), creatine phosphate, etc. It is crucial element of coenzymes like nicotinamide adenine dinucleotide phosphate (NADP) and cyclic nucleotides like cyclic Adenosine Monophosphate (cAMP) and cyclic Guanosine Monophosphate (cGMP). Helps in activation of enzymes by phosphorylation. [4,5]

Magnesium

It is the fourth abundant cation in body and second most prevalent intracellular cation. The total content of magnesium in the body is about 24gms, of which about 55% resides in the skeleton. Total body content is approximately 20-25gms of which maximum is in the bones and teeth. Only 1% of the total amount of magnesium in the body.

Functions of magnesium

It is the cofactor for more than 300 enzymes in the body. It is required for the formation of substrates of enzymes and also acts as an allosteric activator of many enzyme systems. It is important in oxidative phosphorylation, glycolysis, cell replication, nucleotide metabolism and protein biosynthesis.

Parathyroid Hormone (PTH)

The hormone is secreted by the parathyroid gland cells and its main target cells are located in the bones and kidneys. Another hormone, the parathyroid-related enzyme, attaches to the same receptor as the parathyroid hormone and has significant developmental consequences. Parathyroid hormone is secreted as a linear protein containing 84 amino acids. As any other protein hormones, parathyroid hormones are synthesized as preprohormones. After intracellular treatment, the mature hormone is packaged inside the Golgi into secretive vesicles, which are secreted into the blood by exocytosis.

Functions of PTH

It maintains calcium and phosphate homeostasis directly by its actions on both bones and kidneys and indirectly by acting on the intestine through vit D. In kidneys it increases production of 1,25(OH)2D3 by stimulating 1α- hydroxylase, increases calcium reabsorption in the distal convoluted tubule(DCT), decreases phosphate reabsorption in proximal tubule and inhibits Na+-H+ antiporter activity. It has both catabolic and anabolic effect on the bone, but receptors are found only at 2 places, i.e., the osteoblasts and bone marrow stromal cells in vicinity. PTH (1-34) is used as a drug for treatment of osteoporosis under the name teriparatide, because of its anabolic effect on the bone.

Cholesterol

In healthy individuals, levels of total plasma cholesterol vary between 150- 200mg/dl. They vary according to age, gender and genetics of an individual. Plasma cholesterol starts rising in men after fourth decade and after menopause in women. Cholesterol is usually associated with different lipoproteins (LDL, VLDL and HDL), due to its relative insolubility in water. Still it has various functions in the body helps in formation of cell membrane and intracellular membranes. Important constituent of brain, central nervous system (CNS) & myelin sheath Helps in transport of non-polar lipids by taking part in formation of lipoproteins. It assists in free fatty acids transfer and precursor for vitamin

D and steroid hormones synthesis. Formation of bile acids occurs through cholesterol catabolism.

Triglycerides / Lipids in general

Measurement of serum triglycerides in addition to cholesterol is useful in detecting certain genetic and other types of metabolic disorders, as well as in characterizing the risk of CVD. It is also used in estimation of LDL cholesterol by Friedewald equation. [6,7]

MATERIALS AND METHODS

Women working in a tertiary care hospital between the age group of 30-60 years, classified into two groups as pre and post-menopausal based on the history of attaining menopause were voluntarily recruited in the study.

Place

The department of biochemistry, KIMS, Karad.

Sample size

Calculated by Open Epi software using related article. Premenopausal women in the age group of 30-60 years (Group A) – 60 Postmenopausal women in the age group of 30-60 years (Group B) – 60. Both these groups were classified according to the history of occurrence of menopause.

Sampling method

Simple random sampling by lottery method

Methodology

Written consent was taken after proper explanation of need of study from all the participants and a proforma was used to collect the baseline data. A detailed medical and obstratic history was taken from all the participants who voluntarily enrolled for the study. Details on the occurrence of menopause, whether natural or not, were ascertained.

OBSERVATION AND RESULTS

Table 1: Age wise distribution of premenopausal and postmenopausal women

Group	No. of participants	Age in years Limits	Mean+SD
Premenopausal women	60	30-0	39.2 + 6.4
Postmenopausal women	60	43-60	51.6 + 4.5
Total	120		

Out of 120 participants, half (60, 50%) were premenopausal women and other half (60, 50%) were postmenopausal women. Premenopausal women were between the age group of 30-40 years with mean 39.2 years and SD 6.5 years, while postmenopausal women were between 43 to 60 years with mean 51.6 years and SD 4.5 years.

Table 2: Comparison of serum calcium in premenopausal and postmenopausal women

Study Parameter	Calcium	
	Premenopausal women	Postmenopausal women
Mean	9.41	8.93
Standard deviation (SD)	0.77	0.65
Minimum	8.2	8
Maximum	11.2	10.6
p-value	0.0004**	

**Highly Significant when P<0.005

*Significant when P<0.05

In comparison to postmenopausal women, the serum calcium in premenopausal women was significantly high. (t= 3.622, P= 0.0004) In premenopausal women, mean serum calcium was 9.41 mg/dl with SD 0.77 mg/dl, while in postmenopausal women it was 8.93 mg/dl with SD 0.65 mg/dl.

Table 3: Comparison of serum phosphorus in premenopausal and postmenopausal women

Study Parameter	Phosphorus	
	Premenopausal women	Postmenopausal women
Mean	3.65	3.72
Standard deviation (SD)	0.49	0.46
Minimum	2.6	3
Maximum	5.01	5.18
p-value	0.4138	

The difference between the levels of serum phosphorus in both the groups was not statistically significant. The mean serum phosphorus in the premenopausal women was 3.65 mg/dl with SD 0.49 mg/dl while, in postmenopausal women it was 3.72 mg/dl with SD 0.46 mg/dl.

Table 4: Comparison of serum magnesium in premenopausal and postmenopausal women

Study Parameter	Magnesium	
	Premenopausal women	Postmenopausal women
Mean	2.69	1.56
Standard deviation (SD)	0.69	0.31
Minimum	1.24	1.46
Maximum	4.71	2.93
p-value	<0.0001**	

In comparison to postmenopausal women, the serum magnesium in premenopausal women was significantly high. (t= 11.434, P <0.0001) In premenopausal women, the mean serum magnesium was 2.69 mg/dl with SD 0.69 mg/dl, while in postmenopausal women it was 1.56 mg/dl with SD 0.31 mg/dl.

DISCUSSION

In postmenopausal women, coronary artery disease (CAD) is one of the main reasons of death. In fact, these women have a four to eight times higher risk of death due to CAD than any other disease.[8] Postmenopausal women also frequently face the problem of osteoporosis for which they tend to take supplements. Calcium supplements are important for bones of older people and menopausal mothers. Although, there is apprehension that there may be a possible interrelation with the occurrence of cardiovascular disease.[9,10] This study was conducted for finding and comparing the relationship between selective macro-minerals, PTH and parameters of lipid profile in pre and postmenopausal women employees at tertiary care hospital, aged between 30-60 years, during the period from December 2016 to June 2018. An observational cross sectional method of research was employed.

Estrogen is known to act on intestinal cells through estrogen receptors ERα and ERβ. Studies have shown that decreased estrogen lowers the expression of intestinal apical calcium channels (transient receptor potential cation channels TRPV5, TRPV6), calcium binding proteins (calbindin CBD28K) and basolateral channels (PMCA, NCX). This causes decreased calcium absorption from intestine.[11] This is corroborated by our study. In postmenopausal women, we found significantly low levels of serum calcium (Table 2). This can be due to reduced intestinal absorption of calcium, secondary to decreased estrogen associated with aging.[12]

CONCLUSION

This study was done to find an association between calcium, phosphorus, magnesium, PTH and lipid profile in pre and post menopausal women. Significant difference between the levels of calcium, phosphorus, magnesium and PTH was found in both premenopausal and postmenopausal women suggesting the increased bone turnover in the postmenopausal women. Also, significant difference between the lipid profiles in both the groups with TC, TG, LDL and VLDL increased in postmenopausal women was found. While significant decrease in HDL was found in the postmenopausal women, suggesting the protective role of estrogen in the premenopausal women. Due to positive correlation among calcium, phosphorus and lipid profile, calcium phosphate supplementation should be done with great care, at least in the postmenopausal women by closely monitoring the lipid profile. As low magnesium is associated with bad lipids, foods rich in Mg (such as nuts, green vegetables, soya beans, dark chocolates and whole grains) may provide protection against heart disease and hence can be advised. Customary high intake of the Mg might well be contributory in the prevention and treatment of the adverse cardiovascular effects.

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Cite this article: Ajit V. Sontakke Selective Macro Minerals Study, Parathyroid Hormone and Lipid Profiles in Pre and Post – Menopausal Women Employees. J. Cardiovascular Disease Res. 2020; 11 (3): 80 – 84