

Serum Calcium and Risk of Cardio Vascular Diseases with Menopause in North Indian Women

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Abstract

Menopause is a natural transition but has inconvenient effects on ageing women due to lack of health/ treatment awareness. Calcium supplements, which are commonly recommended to elderly people, particularly post menopausal women. Recent evidence warns that taking calcium supplements might increase myocardial infarction (MI) risk. We aimed to evaluate the relation of different biochemical and anthropometric parameters with baseline characteristic of postmenopausal women, related to risk of cardio vascular diseases (CVD). Correlation between fasting serum lipid profile [serum total cholesterol, serum triglyceride, serum HDL, (AIP; logTG/HDL)] with serum calcium and different anthropometric parameters in 200 menopausal women aged 45-56 years was studied retrospectively. All biochemical parameters were measured on fully automated analyser using standard reagent kits. History was taken through questionnaires from subjects with complains regarding menopause after taking verbal consent. In menopausal women between age 45-48 years when serum total cholesterol and serum triglyceride were in higher range and statically significant, at the same atherogenic index of plasma (AIP) was not significant, while above 48 years in age when serum calcium found to be in the normal range (8.7-11.0 mg/dl), atherogenic index of plasma (AIP) and serum lipid parameters show a statically significant relation to risk of CVD, and most of our subjects were unaware about menopausal symptoms and it's treatment because of illiteracy. The counseling activity should go on complained regarding menopause with all anthropometric and biochemical parameters.

Keywords: Menopause; CVD; Serum calcium; AIP (atherogenic index of plasma); Total cholesterol

Introduction

Menopause is a normal part of ageing for woman and literally means "last period". Menopause is generally considered complete when a woman has not had a period for an year. When the monthly growth of endometrium is stopped due to failure of enough hormone secretion by the ovaries, which is necessary to stimulate the endometrium, stops period permanently and menopause occurs [1]. In women between the ages of 45-55 years, level of estrogen and progesterone decline naturally, and menstrual cycle stops. There are three type of menopause- Natural, Premature and Artificial menopause. Sometimes due to any disease or genetic defect, menopause occurs before 40 years of age, known as premature menopause. In some cases, cancer treatment or removal of both ovaries drop the level of estrogen and progesterone, which stop the period permanently, known as artificial menopause [2].

The intensity and frequency of menopause symptoms varies from woman to woman [3]. In menopause, changes in the physical and psychological symptoms are presented as: Change in bleeding patterns, change in the time between periods, or sometimes missed period or period may become heavier or lighter [1]. The average length of time for menopause symptoms to be experienced is three to five years. In some woman these are very mild while in others they are more severe [3]. Various factors like parity, body mass index, age at menarche, socio-economic factors, etc. are associated with menopause apart from genetic factors and smoking [4,5].

Cardiovascular disease is the single leading cause of death for women instead of breast cancer [6]. After menopause, a woman's risk of CVD increases. In women who have undergone early menopause (before age 50) or surgical menopause, the risk of CVD is also higher, especially when combined with other risk factors. This is partly due to higher rates of obesity and diabetes in the some races [6]. In

the menopausal women at the age of 50-52 (about the age of natural menopause), the risk of heart disease increases dramatically. At age between 50- 70 and beyond, men and women are equally at risk.

Changes in the level of lipids in the build-up of plaque and blood clot contribute to heart attack and stroke. Calcium supplements, which are commonly recommended to elderly women, particularly post-menopause, to maintain their bone health, have also been suggested as beneficial agents to improve serum cholesterol profile and to control hypertension [7-9]. However, no strong epidemiological evidence suggests that calcium supplementation might provide cardio vascular benefits [7,10-12]. But a study was done, which suggested that there were higher risk of CVD (86%) in women who used calcium supplements in comparison to women who used vitamin and mineral supplements [13]. After menopause, cardiovascular disease becomes more of a risk for women because of the reduce level of estrogen. Hormone replacement therapy (HRT) may be used short-term to treat menopause symptoms; long-term use is discouraged because the risk of heart-attack, stroke and breast cancer, increases when HRT is used in longer terms [6].

In view of aforementioned controversial literature, we were aimed to evaluate the different biochemical parameters related to risk of CVD/ CHD and serum calcium, in the post menopausal women.

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Materials and Methods

This study was conducted at the Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly (India) on two hundreds subjects between November 2012 and April 2013 who were non-diabetic and aged between 45 and 56 years were included in this retrospectively study. The Body mass index (BMI) was calculated as weight in kilograms divided by square of height in meter. In this study overweight was defined as a BMI of 25 to <30, and a BMI of a ≥ 30 was defined as obese. The subjects were tested for various biochemical parameters, including fasting blood glucose and fasting lipid profile, serum calcium, in the hospital's clinical biochemistry laboratory. Questionnaires were included for subjects with complaints regarding menopause after taking verbal consent from the subjects. Patients were divided into three groups. Between ages 45-48 years Group A, Group B between 49-52 years and Group C between 53-56 years. Exclusion criteria were artificial menopausal and premature menopausal women and women who were not taking proper calcium supplements.

Blood Sampling and Routine Biochemical Analysis

As per our clinical laboratory procedure, serum was separated from venous blood of fasting subjects and analyzed within two hours of collection. Serum glucose, serum triglyceride and serum total cholesterol were analyzed spectrophotometrically by GOD-PAP, GPO-PAP and CHOD-PAP methods respectively by employing reagent kits on a fully automated analyzer of the mind ray series. Serum HDL-C was measured using reagent kit (Accurex, Mumbai) on semiautoanalyser-BTR-830 (Biosystems SA, Spain). This uses the supernatant for HDL-C assay by the same enzymatic method used for TC analysis, after the other lipoproteins are precipitated by phosphotungstate and Mg^{2+} . Atherogenic index of plasma was calculated as $\log(TG/HDL-C)$ with TG and HDL-C expressed in molar concentrations [14]. It has been suggested that AIP value of -0.3 to 0.1 is associated with low CAD risk, 0.1 to 0.24 medium and above 0.24 high risks [15]. Serum calcium level was analyzed by Arsenazo III method kits [16].

Results are presented as mean \pm SD. A p value < 0.05 was considered significant. Statistical analysis was performed using GraphPad Prism version 5.00 for Windows (GraphPad software, San Diego California USA, www.graphpad.com).

Results

Table 1 showed different anthropometric parameters in menopausal women. 200 subjects were studied, only 10% (20/200) cases were presented between age group (A) 45-48 years, while 75% (150/200) were presented in age group (B) 49-52 years, 15% (30/200) were presented in the age group (C) 52-56 years. In these entire groups, 86% (172/200, 86%), 5.5% (11/200, 5.5%) and 8.5% (17/200, 8.5%) were normal, overweight and obese respectively. In group A 15 (15/20, 75%), 2 (2/20, 10%), 3 (3/20, 15%) were Normal, overweight and obese respectively. Similarly, in group B and C 135 (135/150, 90%), 5 (5/150, 3.3%), 10 (10/150, 6.6%) and 22 (22/30, 73.33%), 4 (4/30, 13.33%), 4 (4/30, 13.33%) were normal, overweight and obese respectively. In all groups only 20.06% [2 (2/20, 10%), 1(1/150, 0.6%), 3 (3/30, 10%), respectively] were current smokers, while 11.66% [1(1/20, 5%), 0 (0/150, 0%), 2 (2/30, 6.66%) respectively] were past smokers. In all 200 subjects, 31% (62/200, 31%), 57% (114/200, 57%) and 12% (24/200, 12%) were Nil, Primary and Graduates in field of education. In the cases of family history of CVD/CHD, in all 200 subjects 73.5% (147/200), 14.5% (29/200) and 12% (24/200) had no family history, MI and Angina, respectively.

Parameters	45-48 years (Group A)	49-52 years (Group B)	53-56 years (Group C)
Frequency of cases	20 (10%)	150 (75%)	30 (15%)
BMI			
Normal weight(<25 kg/m ²)	15 (75%)	135 (90%)	22 (73.33%)
Over weight(25-<30 kg/m ²)	2 (10%)	5 (3.35%)	4 (13.33%)
Obese (≥ 30 kg/m ²)	3 (15%)	10 (6.6%)	4 (13.33%)
Smoking			
Present smoker	2 (10%)	1 (0.6%)	3 (10%)
Past smoker	1 (5%)	0 (0%)	2 (6.66%)
Education			
Nil	4 (2%)	40 (20%)	18 (9%)
Primary	4 (2%)	100 (50%)	10 (5%)
Graduation	12 (6%)	10 (5%)	2 (1%)
Family history of CVD/CHD			
No- History	12 (60%)	120 (80%)	15 (50%)
MI	6 (30%)	18 (12%)	5 (16.66%)
Angina	2 (10%)	12 (8%)	10 (33.33%)

BMI=body mass index, CVD=cardio vascular disease, CHD=coronary heart disease

Table 1: Comparisons of different anthropometric and baseline parameter in menopausal subjects

Complain	Frequency	Percentage
Mood change	50	25%
Urinary complain	70	35%
Post- bleeding	20	10%
Body ache	20	10%
Hot flushes	10	5%
Utero vaginal prolapsed	30	15%

Table 2: Complain regarding menopause.

Table 2 showed different complained regarding menopause in the post menopausal subjects. Most of the subjects had the problems (35%, 70/200) of urinary tract infection and (25%, 50/200) mood change or change in normal behavioral pattern.

Table 3 showed different biochemical parameters in these groups. All subjects were in non diabetic range (91.16 ± 7.01 , 108.71 ± 7.22 , 107.06 ± 5.55 , blood fasting glucose in group A, B, C respectively). While changes in the serum total cholesterol and serum TG were statically significant in all groups. Changes in serum calcium level in these subjects were also statically significant, with the change in atherogenic index of plasma (AIP).

Discussion

In our study all subjects were in post menopausal phase of life. In all these subjects, 86% had normal weight or 73.5% had no family history of CVD/CHD. 32.72% (20.06% current, 11.66% past) were smokers. All subjects were taking good calcium diet with calcium supplements. Serum Calcium level were also in normal range (8.7-11.0 mg/dl). After that there were higher risk of CVD/CHD in these subjects, in all subjects there were higher level of Serum cholesterol and Serum lipid profile, which was statically significant and higher values of atherogenic index of plasma. With this, Serum calcium levels were also statically significant in these subjects. This also suggested that calcium supplements were beneficial agents to improve cholesterol profile [7,8]. Epidemiological studies have consistently reported inverse association between dietary calcium intake and the risk of hypertension, obesity and type-2 diabetes, suggesting that a reasonably higher intake of this mineral might ultimately decrease the occurrences of cardiovascular

Parameters	Group A mean \pm sd	SEM	Group B mean \pm sd	SEM	Group C Mean \pm sd	SEM	P value between A&B	P value between B&C	p value between A&C
Blood Glucose	91.16 \pm 7.01	0.4957	108.71 \pm 7.22	0.51	107.06 \pm 5.55	0.39	0.0001*	0.0108*	0.0001*
Serum TC	220.55 \pm 42.22	2.98	255.52 \pm 48.64	3.43	272.28 \pm 48.64	2.98	0.0001*	0.0006*	0.0001*
Serum TG	110.19 \pm 65.48	4.63	131.25 \pm 69.49	4.91	147.70 \pm 79.73	5.63	0.0019*	0.0284*	0.0001*
Serum HDL	62 \pm 15.05	1.06	64.63 \pm 16.60	1.17	64.47 \pm 16.60	1.17	0.0977	0.09233	0.1198
Serum Calcium	9.22 \pm 0.39	0.027	9.48 \pm 0.43	0.030	9.7 \pm 0.44	0.031	0.0001*	0.0001*	0.0001*
AIP	-0.110 \pm 0.279	0.019	-0.052 \pm 0.62	0.04	0.123 \pm 0.321	0.022	0.0225	0.0004*	0.0001*

*statistically significant, TC= serum total cholesterol, TG= serum triglyceride, HDL high density lipoprotein, AIP= atherogenic index of plasma, Group A= age between 45-48 years, Group B= age between 49-52 years, Group C= age between 53-56 years.

Table 3: Comparison of different biochemical parameters in menopausal women.

events [17,18]. Dietary calcium intake was significantly inversely associated with the ischemic stroke risk [19,20]. Several studies have observed a positive association between serum calcium levels and vascular calcification [21,22]. Too much calcium in serum might cause this pathological change by influencing calcification modulators such as pyrophosphate and binding to the calcium- sensing receptors on vascular smooth muscle cell [23].

In our study, 88% (31%, 57%) subjects were nil or primary in the field of education. They were had no positive attitude towards the menopause. While 12% (24/200) women were consider menopause as a natural transition and cling to positive approach about it. All women experience menopause transition in their old [24]. Approach to menopause also affects the severity of particular menopausal symptoms and negative approaches are more linked to more frequent complaints [25]. Negative attitude toward the menopause connected with depressing attitudes towards the menopausal transition. This finding was similar to upsetting symptoms like mood instability, body-ache, urogenital symptoms etc. [26] Numerous factors like socio-economic class, education, physical and emotional health may alter women's concept and understanding about menopause [27,28]. A study was done in Taiwan found the educated women had more problems with menopause when compared to less educated women [25]. Whereas another study indicated that well educated women hold a more positive attitude regardless of being from an eastern or western culture [29]. Owing to lack of estrogen, women during menopause may experience compromised physical wellbeing and climacteric symptoms such as mucosal dryness, hot flushes, night sweats and emotional fluctuations [11].

Our study was reported positive relation in post menopausal women with serum calcium level and some predictive biomarkers of CVD/CHD, such as fasting lipid parameters and atherogenic index of plasma (AIP) [30]. In the subjects who were between age group 49 to 56 years, serum calcium level were slightly increased (while this was in normal range) with this there were higher level of atherogenic index of plasma. While between 45-48 years age there were no Change. Our study was suggested that the counseling activity should go on regarding menopause but many factors, i.e. past experiences, BMI, education, complain regarding menopause and different biochemical parameters may influence this practice.

Conclusions

According to the educational status we were found that Most of subjects were unaware about menopausal symptoms and its treatment; they had a desire for learning about this phase. Add to counseling activities to their satisfaction for healthy living with this transition. We will be reduced the risk of CVD/CHD in these women for having a better health.

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