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Original Research Article

Effect of raloxifene on lipid profile in postmenopausal women

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ABSTRACT

Background: Menopause, a natural event in a woman's life is characterized by loss of reproductive function and decline in estrogen levels. Menopause is not just the cessation of menstruation; it is an outward manifestation of ovarian failure due to depletion of ovarian follicles that leads to decreased estrogen levels which in turn leads to the morbidity associated with the menopause. Objectives were to evaluate serum lipid profile (baseline) of post-menopausal women with menopausal symptoms, to assess the effect of raloxifene on serum lipid levels.
Methods: Effects of raloxifene on serum lipid profile were studied in 75 healthy postmenopausal women in a prospective randomized observational study. Serum lipid levels at baseline, 3rd month and 6th month were analyzed using independent samples' t test. The 95% confidence intervals for the difference in means were reported.
Results: At 3 months and 6 months, there was a change of 3.6% and 5.4% respectively, from baseline values in total cholesterol levels, there was change of 3.5% and 5.8% in triglyceride levels from baseline values. There was an increase of 1.4% and 3.5 % from baseline high-density lipoprotein (HDL) levels. There was a decrease of 4.9% and 9.2% from baseline low-density lipoprotein (LDL) levels; 2.6% and 4.4% from baseline VLDL.
Conclusions: Our study could lead to good practice of raloxifene in postmenopausal women and help to use Raloxifene with safety and may prevent risks of cardiovascular disease as well as the risk of death from other disease in menopausal women.

Keywords: Raloxifene, Postmenopausal women, Lipid profile

INTRODUCTION

With improvements in medical treatment and increased focus on preventive health care, average life expectancy has increased. Most women are expected to live one third of their lives in the menopause. Average life expectancy for Indians is 68 years, average age of menopause being 46-51 years.[1] So, knowledge about menopause and various problems related to menopause are important.

Menopause refers to a point in time that follows 1 year after the complete cessation of menstruation, and the post-menopause describes years following that point. Menopause, a natural event in a woman's life is characterized by loss of reproductive function and decline in estrogen levels.[2] It is not just the cessation of menstruation; it is an outward manifestation of ovarian failure due to depletion of ovarian follicles that leads to decreased estrogen levels which in turn leads to the morbidity associated with the menopause. Therefore, a woman who has undergone a hysterectomy but who retains her ovaries will experience normal menopausal symptoms as oocyte depletion leads to hypoestrogenism, even though cessation of menstruation occurred with surgery. Natural menopause occurs at or after 40 years of age and has no underlying pathologic cause. The post-menopause lasts about 10 to 15 years and is followed by senescence from about 65 years of age to end of life. This age limit is

marked by the successive occurrence of maximum rate of cardiovascular, orthopedic and oncologic diseases.

Influential factors

Several environmental, genetic, and surgical influences may alter ovarian aging. For example, smoking hastens the age of menopause by approximately 2 years.[3,4] Chemotherapy, pelvic radiations, and ovarian surgery may also lead to earlier menopause. More erratic fluctuations in female reproductive hormones lead to an array of physical and psychological symptoms.[5,6] Diet, exercise, reproductive history, socioeconomic status, body mass index (BMI), mood, climate, and individual or cultural attitudes toward menopause may explain variations in reports of menopausal symptoms.[7]

METHODS

Study design

Prospective observational study conducted at LD hospital, GMC Srinagar for a period of two years from June 2016 to June 2018.

Sample size

A total of 75 postmenopausal females were included in the study.

Inclusion criteria

Post-menopausal women who were recently been put on raloxifene were included.

Exclusion criteria

Dyslipidemia, subjects receiving other medications likely to interfere with the drugs under study and with the serum lipid profile, Subjects with medical disorders like diabetes mellitus, hypertension who likely have deranged lipid profile, subjects who have undergone iatrogenic menopause-hysterectomy with or without bilateral oophorectomy, radiation induced menopause, non-Kashmiri postmenopausal women were excluded.

All the study related tests were conducted by standard enzymatic method in a fully automatic analyzer in the biochemistry laboratory at LD hospital, Srinagar.

Tests were conducted at 0 day (baseline), 3rd month and 6th month of follow up.

Statistical analysis

Data were analyzed using Epi-Info 7.0. The descriptive statistics included mean and standard deviation (SD) for continuous variables and frequency and percentage for categorical variables. Serum lipid levels were recorded on a continuous scale. The repeated measures ANOVA was used to analyze difference in serum lipid levels within the group. Serum lipid levels at baseline, 3rd month and 6th month were analyzed using independent samples' t-test. The 95% confidence intervals for the difference in means were reported. The two sided hypotheses tests were used throughout. A $p<0.05$ was taken as statistically significant.

RESULTS

The mean age of patients in this study was 51.7±6.34 years.

Table 1: Age distribution of study participants.

Age (in years)	N	Percentage (%)
<50	32	42.7
50-59	30	40
≥60	13	17.3
Total	75	100
Mean±SD	51.7±6.34	

At 3 months and 6 months, there was a change of 3.6% and 5.4% respectively, from baseline values in total cholesterol levels, which was statistically significant (p value) (Table 2).

At 3 months and 6 months, there was change of 2.9% and 4.7% respectively in triglyceride levels from baseline values (Table 3).

There was an increase of 1.4% and 3.5% at 3 months and at 6 months respectively from baseline HDL levels (Table 4).

There was a decrease of 4.9% and 9% at 3 months and at 6 months respectively from baseline LDL levels, a statistically significant difference (Table 5).

There was a decrease of 2.6% and 4.4% at 3 months and at 6 months respectively from baseline VLDL levels (Table 6).

The 10.7% had leg cramps, 10.7% complained of mastalgia, 4.0% had nausea, 12.0% complained of abdominal pain, and 21.3% had complained of hot flushes.

Table 2: Comparison based on total cholesterol (mg/dl).

TC (mg/dL)	Mean	SD	Difference	Change (%)	P value
Baseline	197.5	15.86	-	-	-
3 months	190.3	16.16	7.2	3.6	<0.008*
6 months	186.7	13.66	10.8	5.4	<0.001*

*Statistically significant difference with respect to baseline ($p<0.05$).

Table 3: Comparison based on total triglycerides (mg/dl).

TG (ml/dL)	Mean	SD	Difference	Change (%)	P value
Baseline	122.7	12.97	-	-	-
3 months	126.2	11.40	-3.5	-2.9	0.247
6 months	128.5	11.36	-5.8	-4.7	0.065

Table 4: Comparison based on total high-density lipids (mg/dl).

HDL (ml/dL)	Mean	SD	Difference	Change (%)	P value
Baseline	52.3	6.70	-	-	-
3 months	53.1	6.46	0.7	1.4	0.783
6 months	54.2	6.68	1.8	3.5	0.562

Table 5: Comparison based on low density lipids (mg/dl).

LDL (mg/dL)	Mean	SD	Difference	Change (%)	P value
Baseline	102.3	14.76	-	-	-
3 months	97.3	12.23	5.0	4.9	<0.014*
6 months	93.1	11.42	9.2	9.0	<0.001*

*Statistically significant difference with respect to baseline (p<0.05).

Table 6: Comparison based on VLDL levels (mg/dl).

Parameters	Mean	SD	Difference	Change (%)	P value
Baseline	31.2	2.96	-	-	-
3 months	30.4	2.35	0.8	2.6	<0.652
6 months	29.8	2.41	1.4	4.4	0.475

DISCUSSION

Women develop cardiovascular disease approximately 7-10 years later than men, but progress with similar risk after menopause. Recent studies suggest that raloxifene is cardioprotective when initiated early after menopause.

In our study, raloxifene was found favourable in postmenopausal women in improving lipid profile and thereby cardiovascular status. It found that HRT increased HDL cholesterol and decreased total cholesterol and LDL.

Yang et al in their study concluded that raloxifene resulted in a significant elevation of the HDL-cholesterol (WMD: 2.41 mg/dl, 95% CI: 0.84-3.97, p=0.003) and a significant reduction of the total cholesterol (TC) (WMD: -14.84 mg/dl, 95% CI: -20.37 to -9.317, p=0.000) and of the LDL-cholesterol (LDL-C) (WMD: -17 mg/dl, 95% CI: -25.77, -8.22, p=0.000).[8]

Dayspring et al reported that raloxifene significantly improved low-density lipoprotein cholesterol, total cholesterol, non-high-density lipoprotein cholesterol (HDL-C), apolipoprotein B, apolipoprotein A-I, and fibrinogen compared with placebo (p<0.05). After raloxifene treatment, women with high triglycerides experienced an equal or more robust reduction in cholesterol, lipoprotein parameters, and ratios of total cholesterol to HDL-C and non-HDL-C to HDL-C than was observed in women with normal triglycerides (p<0.05). [9]

A strong effect of raloxifene on atherogenic lipids with a large reduction in the pro-thrombotic Lp(a), suggesting an overall favorable effect on thrombogenicity after HRT replacement therapy in post-menopausal women and have been confirmed by large number of studies.[10-14]

Limitations

There are some limitations that should be noted. The sample size taken was small and hence a large randomized controlled trial is necessary to assess the effects of raloxifene in postmenopausal women.

CONCLUSION

In conclusion, our study was designed to be used as baseline for further studies. By using tight control on all environmental factors, populations and proper study disciplines, the result of those studies could lead to good practice of Raloxifene in postmenopausal women.

This could help to use Raloxifene with safety and may prevent risks of cardiovascular disease as well as the risk of death from other disease in menopausal women.

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