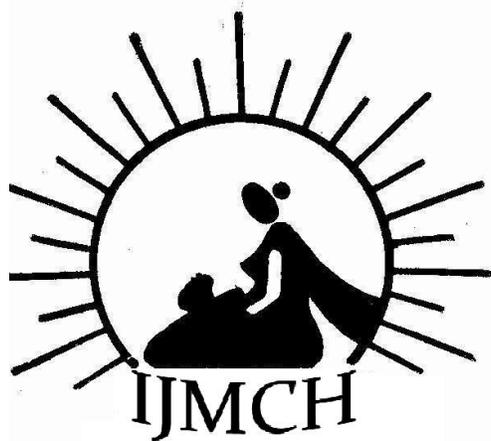


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Effect of Hormone Replacement Therapy on Lipid Profile in Women after Surgical Menopause

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Abstract

Objective: Women who are at higher risk for cardio vascular disease after menopause, can they be protected by hormone replacement therapy (HRT). So the effect of HRT was studied on lipid profile in women after surgical menopause.

Material and Methods: The study was done on 100 women (age 30-40 years) undergoing total abdominal hysterectomy with bilateral salpingo oophorectomy. Overnight fasting lipid profile was done on Multichannel Auto analyzer (Hitachi-911), before and after one month of hysterectomy. After one month of hysterectomy, patients were divided into two groups of 50 each. Group 1 did not receive HRT. Group II was put on two types of HRT for 3 months and classified as IIa and IIb (25 patients each). Group IIa received conjugated equine estrogen (CEE) 0.625mg/day, orally. Group IIb received CEE 0.625mg/day, orally combined with 2.5mg/day of medroxy progesterone acetate for last 10 days of each cycle. All patients were followed up for postmenopausal symptoms. After three months of HRT, fasting lipid profile was done in all the patients. The data collected was statistically analyzed.

Results and Discussion: There was marked improvement in post menopausal symptoms after HRT whereas symptoms increased significantly in patients not receiving HRT (control group I). The mean levels of total lipids, cholesterol, triglycerides, LDL-C increased after one month and continued to increase significantly ($p < 0.001$) in control group while this trend was reversed in HRT groups. After three months of HRT, total lipids levels in group IIa and IIb (620.72+108.45, 700.40 +102.67 respectively) were significantly decreased as compared to group I (without HRT) and even pre hysterectomy levels (677.48+160.28). HDL-C remains almost same in control group and increased only in group IIb. HDL/LDL ratio decreased in controls from 0.38 to 0.3 but increased significantly in both HRT groups (from 0.3 to 0.46) which indicate similar cardio-protection by two regimes of HRT.

Conclusion: Both mono and combined therapy has similar effect in decreasing vasomotor symptoms as well as lipid fractions after surgical menopause.

Keywords: HRT, surgical menopause, lipid profile.

Introduction

Menopause is a universal event, marks the cessation of menstrual cycle and ovarian functions, resulting in estrogen deficiency. It can be natural or surgically induced due to some uterine or ovarian disease, before attaining menopausal age. During natural menopause, changes in hormone levels and metabolism occur gradually whereas after surgical menopause, hormonal changes are abrupt and patients suffer from severe climacteric symptoms. After menopause, fall in estrogen levels results in deranged functioning of not only reproductive system but many other systems also like cardiovascular, central nervous, immune and skeletal system. It has been reported that incidence of coronary artery disease (CAD) is lower in women compared to men in younger age group but after menopause it is almost same in both the gender. This protection is given by estrogen, present in menstruating women. Changes in lipid profile and CAD risk associated with changes in estrogen level would be expected to be apparent with onset of menopause. Lipid profile is significantly altered and becomes more atherogenic in post menopausal years. Raised levels of cholesterol, triglycerides and lower levels of HDL-C have been reported in bilateral oophorectomised women.¹⁻² Replacing hormones in menopausal women not only relieves the climacteric symptoms but also prevents bone changes and reverses some of the adverse changes in lipid profile.³⁻⁴

In India, very few reports are available, where women undergoing surgical menopause have been given supplemental estrogen or estrogen progestin therapy for amelioration of menopausal symptoms for fear of their adverse effects. Hence the present study was undertaken to evaluate the effects of hormone replacement therapy (HRT) on lipid profile in women undergoing surgical menopause. Role of mono therapy (estrogen alone) and combination therapy (estrogen- progesterone) was also compared after short duration of three months HRT.

Material and Methods

The present prospective study was done on 100 women (age 30-40 years) who underwent total abdominal hysterectomy with bilateral salpingo oophorectomy for benign conditions of internal genitalia before attaining menopause, in the department of Obstetrics and Gynecology of tertiary care hospital. The patients with liver, gallbladder, thyroid diseases, past history of breast tumor or malignancy were excluded from the study.

Haemogram, RBS, RFT, LFT, urine routine, x-ray chest, ECG, ultra-sound of whole abdomen was done in all the patients. Overnight fasting samples were collected for lipid profile before and after one month of hysterectomy. Total cholesterol, HDL-C and triglycerides were estimated on multichannel autoanalyser (Hitachi-911). Total lipids were estimated by Randox kits. LDL-C was done by Boehringer Mannheim kits.

After one month of hysterectomy, patients were divided into two groups of 50 each. Group I did not receive any HRT and served as control. Group II was put on two types of HRT and classified as IIa and IIb (25 patients each). Group IIa received conjugated equine estrogen (CEE) 0.625mg/day, orally for three months. Group IIb received CEE 0.625mg/day, orally for three months combined with 2.5mg/day of medroxy progesterone acetate for last 10 days of each cycle.

Postoperatively, all patients were followed up with special reference to postmenopausal symptoms or any other complications at monthly intervals for four months. At each follow up visit, they were enquired regarding appearance, persistence and complete/incomplete

relief of post menopausal symptoms, any complication of HRT with particular reference to breast examination. After three months of HRT, fasting lipid profile and ultrasound for liver and gallbladder evaluation was done in both the group patients.

Ethical clearance was obtained from Institutional Ethical Committee prior to start of the study. Informed consent was taken from all patients.

The data collected in respect to various parameters was statistically analyzed. Mean and standard deviation were computed. ANOVA technique was used to compare the groups. P-value <0.05 was considered as significant. The analysis was done by using statistical software SPSS 12.5 version.

Results

The common post menopausal symptoms were hot flushes, sweating, depression, palpitations, fatigue and irritability. After one month of hysterectomy hot flushes and sweating was experienced by 29-32% of patients and 7-11% patients showed other symptoms like depression, irritability and fatigue. There was significant increase in number of patients having hot flushes and sweating after four months of surgery (without HRT) compared to one month (62-66% vs 29-32%). Similar increase was noted in other symptoms as well, Table 1. But there was significant decrease in number of patients experiencing these symptoms in group IIa and IIb, after receiving HRT (4-16% only). We further noted that addition of progesterone (group II b) did not show any additional benefit in improvement of symptoms. We also observed that number of patients without post menopausal symptoms decrease from initial 30% to 10% in control group whereas in both the HRT groups approximately 50% of the patients were without any post menopausal symptoms at end of study period (Table 1).

Mean levels of total lipids, cholesterol, triglycerides and LDL-C increased after one month of hysterectomy in all the patients, these levels further increased significantly ($p < 0.001$), after four months of surgery. But no change in HDL-C levels (37 mg%) was observed after one month and rather it decreased to 35.6mg% in control group after four month (Table 2). Estrogen therapy (group IIa) showed significant decrease in all lipid fractions as compared to control group I ($p < 0.05$) except HDL-C which remained almost same. Similarly HRT in group IIb resulted in decrease in lipid levels but not significant, but it had beneficial effect on HDL-C levels, which increased significantly to 41.90 mg% (Table 3).

Table 1: Percentage of women having post menopausal symptoms

Post-menopausal symptoms	Without HRT		After three month HRT	
	After 1 month Group I (n=100)	After 4 month Group I (n=50)	Group IIa (n=25)	Group IIb (n=25)
Hot flushes	32	66#	08***	04***
Sweating	29	62#	08***	04***
Depression	09	16#	12	08*
Irritation	07	10#	04*	-
Fatigue	11	18#	16	04*
No symptoms	30	10#	48*	52*

without HRT one month vs four month

* Group I 4 month vs Group IIa & IIb

#* $p < 0.05$, *** $p < 0.001$

Table 2: Pre and Post-hysterectomy - Lipid profile

Lipid profile	Pre-hysterectomy (n=100)	Post-hysterectomy 1 month (n=100)	Post-hysterectomy 4 month (n=50)
Total Lipids (mg/dl)	677.48±160.28	720.94±198.63**	776.02±195.59**##
T-Cholesterol (mg/dl)	166.88±46.37	174.74±50.76	186.14±46.94*#
Triglyceride (mg/dl)	172.50±67.74	197.72±98.89*	197.76±95.04*
LDL-C (mg/dl)	96.76±33.27	102.78±37.75	121.06±39.77*#
HDL-C (mg/dl)	37.12±4.84	37.60±6.49	35.62±6.09
HDL/LDL	0.38	0.36	0.30#

* pre-hysterectomy vs post-hysterectomy after 1 month

post-hysterectomy- 1month vs 4 month

*#p< 0.05, **## p< 0.005, *** p<0.001

Table 3: Comparison of lipid profile after three months of HRT

Lipid profile	Group I (n=50)	Group IIa (n=25)	Group IIb (n=25)
Total Lipids (mg/dl)	776.02±195.59	620.72±108.45***#	700.40±102.67*
T-Cholesterol (mg/dl)	186.14±46.94	147.20±46.73*#	161.72±41.02*
Triglyceride (mg/dl)	197.76±95.04	135.24±58.67*#	193.20±46.84
LDL-C (mg/dl)	121.06±39.77	84.60±21.65*	92.24±20.35*
HDL-C (mg/dl)	35.62±6.09	37.72±4.04	41.90±3.85
HDL/LDL	0.30	0.45**	0.46**

* group I vs group IIa and IIb

group IIa vs group IIb

* #p< 0.05, ** p< 0.005, *** p<0.001

On comparing both the HRT groups (IIa and IIb) it was found that estrogen therapy alone was sufficient in lowering all the lipid fractions. This group IIa had significantly lower values of all the lipids compared to group IIb. But addition of progesterone was helpful in increasing protective cholesterol HDL-C. On the other hand HDL-C/LDL-C ratio was higher (0.45 and 0.46) in both the treated groups showing similar and significant cardio-protection as compared to control group (p<0.005), where it was decreased from 0.38 to 0.30 after four month of hysterectomy (Table 3).

In the present study no untoward side effect of HRT were observed and hence there was no drop out during our study period.

Discussion

This study was conducted to evaluate and compare the effect of estrogen and estrogen-progesterone combined treatment on lipid profile in women who had undergone surgical menopause. Post menopausal symptoms improved significantly after HRT whereas in control group I these symptoms increased significantly. Our results are consistent with previous studies which showed similar trends but variable results.5-6

There was continuous increase in all the lipid fractions except HDL-C, after hysterectomy in group I, because protective effect of estrogen is lost after surgical menopause. The increased LDL-C and decreased HDL-C indicate more atherogenic profile in menopause women. So, they are at greater risk of cardio vascular disease at this stage and are likely to

be benefited from hormone therapy. Hormone supplementation reduces LDL-C and increases HDL-C in post menopausal women. The reduction of LDL-C is probably a result of accelerated conversion of hepatic cholesterol to bile acids and increased expression of LDL receptors resulting in faster LDL clearance from the plasma. Increase in HDL levels is due to increased production of apo lipoprotein A-1 and decreased hepatic lipase activity. HDL is considered protective cholesterol since it is responsible for reverse cholesterol transport. The favorable effect of estrogen on lipoprotein fractions could reduce the progression of atherosclerosis. 7-9

Estrogen alone or in combination has been shown to reduce LDL-C and increase HDL-C in dose and duration dependent fashion.^{7,10-12} In the present study it is also found that ratio of HDL-C/LDL-C, anti-atherogenic factor, significantly increased in treated groups as compared to control group. This indicates that both mono as well as combination therapy has similar cardio-protective effect. Women, if not treated with HRT at all, are at risk of CAD as HDL/LDL ratio decreased after one month and continued to decrease even after four months. Previous studies have shown that progesterone protects uterus from some of the harmful effects caused due to estrogen therapy.^{10, 13} Moreover, both HRT regimes did not show any adverse effects during our study period.

Conclusions

It has been observed that both the therapies were helpful in decreasing vasomotor symptoms as well as lipid fractions. Combined therapy showed similar cardio-protection as estrogen alone. So, HRT is recommended in surgically induced menopausal women but more extensive study in larger population and long term follow up is needed, before giving final verdict.

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