INFLUENCE OF AGE AND MENOPAUSE ON SERUM LIPIDS AND LIPOPROTEINS IN HEALTHY WOMEN

N. Sharma ● K. Sharma ● V K. Malhotra ● P Chada ● S. Sardana

SUMMARY

Sex hormone deficiency is associated with an increased risk of coronary heart disease (CHD) in postmenopausal women. We measured fasting serum lipids and lipoprotein concentrations in a group of 215 healthy non-obese pre and post menopausal women (aged 20-96 yrs.) Menopause was associated with high concentration of total cholesterol, triglycerides and low density lipoprotein (LDL) cholesterol concentration whereas high density lipoprotein (HDL) cholesterol concentrations fell slightly. These changes were independent of age and BML. From this study, we conclude that menopause is associated with potential adverse changes in lipid and lipoprotein independent of any effect of ageing. These changes in part explain the increased incidence of CHD seen in postmenopausal women.

INTRODUCTION

Coronary heart disease (CHD) is one of the major causes of death in postmenopausal women. It is well established that premenopausal women have much less incidence of CHD than men of the similar age, however the prevalence of CHD appears to increase constantly in women throughout life (Heller et al 1978). Although

Dept. of Obst & Gyn & Biochemistry, L.N.Hospital & M.A. Medical College and Dept of Biostatistics, I.C.P.O (I.C.M.R)., M.A. Medical College, New Delhi.

exogenous sex steroids may have profound effects on lipid risk markers for CHD there is controversy as to whether endogenous female sex steroids influence lipid metabolism (Godsland et al 1987). Many previous studies have shown that serum cholesterol levels, triglycerides and cardiodeleterious LDL-Cholesterol levels are significantly higher in postmenopausal women than in age matched premenopausal women (Ginsberg, 1991, Ushiroyama, 1993). The dramatic decline in the circulating oestrogen levels after menopause results in decreased levels of cardioprotective HDL Cholesterol (Longscope et al 1986).

To study the possible independent influence of aging and oestrogen deficiency 215 women aged between 20-96 yrs were included in this study. The lipid profile was analysed and their menopausal status was carefully determined.

MATERIAL AND METHODS

This study was carried out on women attending the out patient gynaecology clinic at L.N.Hospital of M A.M C., New Delhi. Out of a total of 165 women in normal physical and mental health, 83 women had undergone spontaneous menopause as demonstrated by amenorrhoea. Eighty-two women were premenopausal as shown by regular menstrual cycle and lack of menopausal symptoms. We excluded all obese women (Qutelet index >28) to minimise this confounding effect on lipid & lipoprotein concentrations. We also excluded women who had undergone a premature menopause (<45 yrs) and surgical menopause. None of the patients had undergone a premature menopause (<45 yrs) and surgical menopause. None of the patients was taking any medication including sex steroids known to influence lipid metabolism. Fifty young healthy women aged between 20-30 yrs were included as control.

Following a 12 hrs. overnight fast, a blood sample of 5ml was drawn from the cubital vein in an autoclaved plain vial with a disposable syringe without the use of any anticoagulant. The samples were centrifuged at 4000 rpm for 15 mts The serum was separated and analysed Total Cholesterol (TC), Triglycerides Low Density Lipoprotein Cholesterol (LDL Cholesterol), and High Density Lipoprotein Cholesterol (HDL Cholesterol) were assessed with enzymatic determination as described by Richmond 1973, Bucolo et al 1973, Wieland et al 1983, Lopex-Virefila 1977 respectively, on an autoanalyser Genesis 21, a discrete, microprocessor controlled total-access chemistry analyser by one of the authors (V K.M.) Body mass index (BMI) was calculated as weight/height 2 (quetelet index).

STATISTICAL ANALYSIS

Multiple linear regression analysis was performed separately for the premenopausal and postmenopausal women, with lipid and lipoprotein measurements as independent variables Linear regression analysis was then

used to examine the relationship between age or BMI and the independent variables. For the analysis of the effect of menopause status, age and BMI were included as independent variables in the regression.

RESULTS

The mean age of 83 menopausal women was 53.96 yrs + 8.28 yrs, range 45-96 yrs. The mean age of 82 premenopausal women 37.27 + 3.75 yrs, range 29-44 yrs. Fifty young healthy women aged between 20-30 yrs were included as control. There was no significant difference in the weight between the pre and postmenopausal group of women. The concentrations of lipids and lipoproteins for each 5-year's age group are shown in Fig. 1. Total cholesterol, LDL cholesterol and triglycerides concentration showed positive association with age, whilst a significant negative association was observed between age and HDL Cholesterol concentration.

The standardised mean values of lipids and lipoproteins in premenopausal and postmenopausal women are shown in fig 2 and Table 1. The changes in the LDL cholesterol levels are significant ($p<0.05$) the changes in the other parameters are apparent but not significant. The percentage of premenopausal and postmenopausal women with hyperlipidemia are shown in Table II. The rise in triglycerides and LDL concentration in postmenopausal women was in 53% and 24.5% women respectively as compared to 43.9% and 20.4% premenopausal women. Similarly total Cholesterol was found raised in 18.1% of postmenopausal women and in 17.1% of premenopausal women. While HDL Cholesterol declined in 75.6% of premenopausal

TABLE I
THE STANDARDISED MEAN VALUES OF LIPID & LIPOPROTEIN IN PRE AND POST MENOPAUSAL WOMEN IN Mg/dl

	Total Cholesterol >250	Triglycerides >140	LDL Cholesterol >150	HDL Cholesterol <45
Premenopausal (n = 82)	288.6 +20.79	213.4 +20.79	193.2 +31.92	38 + 33.68
Postmenopausal (n = 83)	294.8 +42.74	217.1	192.4 +64.86 p<0.05 (significant)	32.94 + 7.2 +26.19

TABLE II
PERCENTAGE OF PRE & POSTMENOPAUSAL WOMEN WITH HYPERLIPIDEMIA

Variable	Premenopausal (n = 82) Percentage	Postmenopausal (n = 83) Percentage
T.Chol > 250 mg./dl.	17.1%	18.1%
Trig > 140 mg/dl.	43.9%	53.0%
LDL > 150 mg/dl.	20.4%	24.5%
HDL < 45mg/dl.	63.9%	75.6%

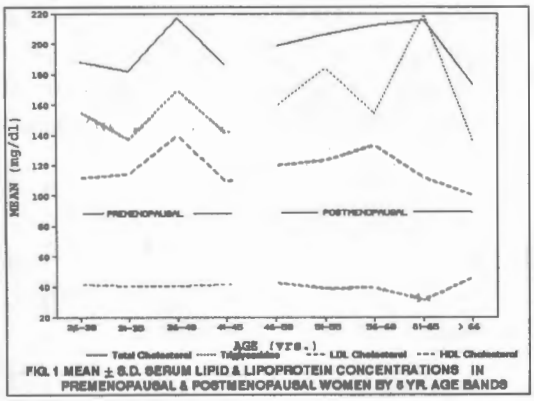

Fig 1. Mean ± S.D. Serum Lipid & Lipoprotein concentrations in premenopausal & women by 5 yr. age bands

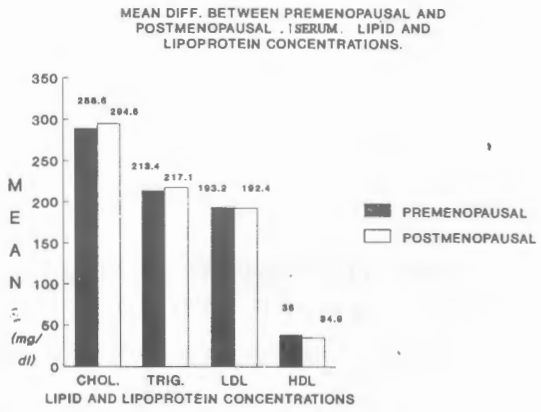

Fig. 2. Lipid and Lipoprotein Concentrations

women and in 63.9% of postmenopausal women. The control group had all levels of lipids and lipoproteins within normal limits.

DISCUSSION

The results of this study demonstrates that the menopause has profound effect on lipid and lipoprotein concentrations independent of any effects of the aging process and body mass index changes. The major effects seen with the changes from premenopausal to postmenopausal status were increase

in total cholesterol, LDL cholesterol and Triglycerides with striking reduction in HDL cholesterol as also observed in earlier studies. (Ushiroyama et al 1993) Our data suggests that these differences in lipids and lipoproteins are due either directly or indirectly to oestrogen defeciency resulting from the loss of ovarian function. Oestrogens appear to have direct effect on LDL by up regulation of apo B100, receptors (Kovanen et al 1979). Both oral and parentral oestrogen administration to hormone deficient women reverses the change in total and LDL cholesterol as described above (Godsland et al 1987). Oral oestrogen replacement has also been shown to increase HDL cholesterol (Tikkanen et al 1982) and the lower concentration of HDL Cholesterol observed with the onset of oestrogen deficiency in the present study would be in keeping with this observation. Again the precise mode of action for this effect is not known but it may involve reduced hepatic lipase activity (Tikkanen et al 1982) and increased HDL synthesis (Schaefer et al 1983).

Our findings are in agreement with those of others who compared pre and post menopausal women of similar age (Kannel 1976, Jensen et al 1990) Further an increase in LDL cholesterol and Triglycerides together with a decrease in HDL concentration following menopause as observed in the present study should be regarded as being potentially adverse in terms of risk for CHD as also reported in earlier study (Stevensen et al 1993) There is evidence that both surgical and natural menopause increases CHD incidence (Oliver and Boyd 1959 , Gordon et al 1978) independent of age while replacement of oestrogen may reduce this incidence (Knopp 1988). It is obvious that several factors are involved in the pathogenesis of CHD, nevertheless the changes in lipids and lipoprotein following menopause as demonstrated in the present study are likely to explain in part this increased CHD incidence Oestrogen replacement therapy regimens should aim to mimic the physiological effects of oestrogens on these lipids and lipoprotein cardiovascular factors.

REFERENCES

1 *Bucolo G and David M : Clin Chem 19 76, 1973*
2 *Ginsberg J : In: Burger H, Boulet M, eds A portrait of the menopause New Jersy Parthenon Publishing, 15, 1991*
3 *Godsland IF, Wynn V, Crook D Miller NE . Am Heart J 114 1467, 1987.*
4. *Gordon T, Kannel WB, Hjortland MC, McNamara PM : Ann Intern Med 89: 157, 1978*
5. *Heller RF and Jacobs HS. Brit Med J 1: 172, 1978*
6. *Jensen J, Nilas L, Christiansen C : Maturitas 12 : 321, 1990*
7 *Kannel WB, Hjortland MC, McNamara PM, Gordon T . Ann Inter Med 85: 447, 1976*
8 *Knopp RH . Obstet Gynaecol. 72 238, 1988*
9. *Kovanen PT, Brown MS, Goldstein JL . J Biol Chem 254: 11367, 1979.*
10 *Longscope C, Granz C, Morello C, Baker R, Johnston Jr, cc : Maturitas 8 189, 1986*
11 *Lopez-virefila m f Clin Chem 23 882, 1977.*

12. *Oliver MF and Boyd GS : Lancet ii : 690, 1959*
13. *Richmond N : C;om Chem 19 : 1350, 1973*
14. *Schaefer EJ, Foster DM, Zech LA : J Clin Endocrinol Metab 57: 262, 1983.*
15. *StevensonJC, CrookD, GodslandIF : Atherosc. 98: 83, 1993.*
16. *Tikkanen MJ, Nikkila EA, Kuusi T, Sipinen S : J Clin Endocrinol Metab 54 : 1113, 1982.*
17. *Ushiroyama T, Okamoto Y, Sugimoto : Acta Obstet Gynec. Scand 72: 428, 1993.*
18. *Wieland H, Seidel D : J Lipid Res 24 : 904, 1983.*