ASSESSMENT OF MENOPAUSAL SYMPTOMS AND ATTITUDE, AND INTERVENTION STUDY ON KNOWLEDGE OF HORMONE REPLACEMENT THERAPY AMONG PERI MENOPAUSAL WOMEN SEEN AT OUTPATIENT DEPARTMENT (KRK) & OBSTETRICS AND GYNAECOLOGY CLINIC (O&G), HUSM.

UNIVERSITI SAINS MALAYSIA
NOVEMBER 2001

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DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE (FAMILY MEDICINE)

Contents

ACKNOWLEDGEMENT

I wish to express my sincere thanks and appreciation to both of my supervisors:

i) Dr Shaiful Bahari Hj Ismail, Head of Family Medicine Unit, USM.

ii) Dr Nor Aliza Abdul Ghaffar , Lecturer in Obstetrics and Gynaecology, Department of Obstetrics & Gynaecology, USM.

iii) Dr Nik Hazlina Nik Hussain, Lecturer in Obstetrics and Gynaecology, Department of Obstetrics & Gynaecology, USM.

for their excellent guidance, overall comments and criticisms of the study.

My courteous thanks to all lecturers in Family Medicine Unit, Dr Amaluddin Ahmad, Dr Juwita Shaaban and Dr Sheikh Mohd Amin S. Mubarak for their general advice.

My special appreciation to Family Medicine Specialist at Klinik Kesihatan Kuala Besut, Dr Sukarno Mohd Saud, for his understanding and support given through out the preparation of this dissertation.

I also wish to thank Dr Rosli Abdullah for allowing me to conduct the study at Klinik Rawatan Keluarga (KRK). My sincere thanks to Sister Norhimah and all the staffs in Klinik Rawatan Keluarga for their tremendous support for the success of this project.

Thank you also to those who have been involved either directly or indirectly in the project.

Last but not least, my deepest regards to my family, both my parents and especially to my beloved husband, Major (Dr) Mazdy Haji Ismail for his patience, encouragement and understanding that make this study a success and worth while.

ABBREVIATIONS

AD	Alzheimer's Disease
BMD	Bone mineral density
BMU	Basic multicellular units
CAD	Coronary artery disease
CEE	Conjugated equine estrogen
CVD	Cardiovascular disease
ECG	Electrocardiograph
ERT	Estrogen replacement therapy
FSH	Follicle stimulating hormone
HDL	High density lipoprotein
HKB	Hospital Kota Bharu
HRT	Hormone replacement therapy
HUSM	Hospital Universiti Sains Malaysia
IHD	Ischaemic Heart Disease
KAP	Knowledge, Attitude and Practice
KRK	Klinik Rawatan Keluarga
LDL	Low density lipoprotein
LH	Luteinising hormone

O&G	Obstetrics and Gynaecology
OPD	Outpatient department
SERMs	Selective estrogen receptor modulator
SPSS	Statistical Package for Social Sciences
TG	Triglyceride
UTI	Urinary tract infection
WHI	Women's Health Initiative
WHO	World Health Organization
WHS	Women's Health Study

ABSTRACT

BAHASA MALAYSIA

OBJEKTIF:

Kajian ini adalah untuk memeriksa sikap dan pengetahuan pengguna tentang terapi penggantian hormon (TPH), mengenai alam putus haid, gejala putus haid, penggunaan TPH, dan juga membandingkan tahap pengetahuan asas sebelum dan selepas program intervensi kaunseling secara individu diberikan.

METHODA:

Di dalam kajian ini soalan yang telah dilengkapkan oleh 55 pengguna TPH daripada klinik menopos, HUSM dan 54 pesakit (bukan penggunaTPH) daripada Klinik Pesakit Luar, HUSM sebagai kontrol. Kajian ke atas dua kumpulan ini dijalankan serentak mulai 1hb Jun hingga 31 Disember 2000. Terdapat 40 soalan yang mana ianya diterjemahkan dan ditambah daripada soalan-soalan yang digunakan dalam kajian-kajian di London dan Scotland untuk disesuaikan dengan masyarakat tempatan. Soalan-soalan terdiri daripada gejala-gejala putus haid, pengetahuan dan sikap mengenai TPH. Soalan yang sama diberikan kepada bukan pengguna TPH. Intervensi kaunseling secara individu dilakukan kepada bukan pengguna mengenai alam

putus haid dan TPH. Lima belas soalan pengetahuan yang sama diberikan selepas lapan minggu sesi kaunseling. Pengetahuan asas yang dikaji seterusnya diberi markah dan tahap pengetahuan tersebut dinilaikan menggunakan skala Likert. Data yang diperolehi kemudiannya dianalisa menggunakan Statistical Package for Social Sciences (SPSS).

KEPUTUSAN:

Keputusan kajian menunjukkan tiada perbezaan antara umur, bangsa, taraf perkahwinan, pendapatan dan status penyakit. Tetapi terdapat perbezaan di antara pekerjaan dan taraf pendidikan di antara dua kumpulan tersebut. Kesan -kesan putus haid terutamanya kesan " klasikal/vasomotor" adalah yang paling dirasai. Walaupun di kalangan wanita tersebut mempunyai keseluruhan gejala putus haid, mereka tidak tampil meminta bantuan. Ini disebabkan oleh beberapa faktor iaitu kekurangan pengetahuan tentang TPH, mempunyai sikap yang negatif tentang alam putus haid dan TPH dan mereka adalah dari golongan yang kurang berpengetahuan. Dibandingkan pengetahuan pengguna dengan bukan pengguna, purata markah ialah 7.78 dan 5.07. Perbezaan purata markah di antara pengguna dan bukan pengguna TPH adalah signifikan. Keputusan juga menunjukkan perbezaan purata markah sebelum dan selepas

intervensi dimana purata markah sebelum dan selepas intervensi ialah 5.07 dan 10.26. Perbezaan purata sebelum dan selepas intervensi di antara kedua-dua kumpulan secara statistiknya adalah signifikan ($p<0.05$).

KESIMPULAN:

Pengetahuan secara keseluruhannya di antara pengguna TPH dan bukan pengguna TPH tidak memuaskan dan sikap bukan pengguna adalah negatif berbanding dengan pengguna TPH. Kebanyakan daripada mereka masih belum sedar tentang wujudnya TPH dan sekiranya mereka sedar, tahap pengetahuan yang salah adalah tinggi.

Kajian ini menunjukkan bahawa intervensi kaunseling secara individu telah meningkatkan pengetahuan mengenai TPH. Oleh itu, adalah tanggungjawab bersama pengamal perubatan untuk memberitahu dan menasihati wanita-wanita yang berdiam diri dan merana membakar diri.

ENGLISH

OBJECTIVES:

This study was designed to examine HRT users' attitudes and knowledge of menopause and HRT, their menopausal symptoms, comparing that with a control group (non HRT user) and to examine the effectiveness of counseling intervention in educating the non HRT user.

METHODS:

In this survey, a self administered questionnaire was completed by 55 patients of HRT users, taken from menopause clinic, HUSM and by 54 patients from outpatient department (OPD), HUSM as a control group (non HRT user). The study was started simultaneously in both groups in year 2000 from June, 1st to December 31st. The questionnaire consisted of forty questions which had been used in three surveys in London and Scotland tested on menopause symptoms, knowledge and attitude. Control patients were given a similar questionnaire. A counseling intervention was carried out in the control group (non HRT user), tuning towards menopause and HRT. A

similar fifteen questions on the knowledge aspects were tested post counseling. The knowledge studied were then scored based on Likert scale. The questions were modified, simplified, translated and new questions are added in order to suit our local population. All the data were analysed using Statistical Package For Social Sciences (SPSS).

RESULTS:

The results showed no significant difference between the two groups with respect to age of respondents, ethnicity, marital status, income and medical status. However there was a significant difference in the level of education and occupation between the two groups. The menopausal symptoms especially the classical/vasomotor symptoms are widely experienced in both groups. The reason why these women do not use HRT are due to several confounding factors. They are unaware of HRT and were let down by poor level of education with negative attitudes towards menopause and HRT. Comparing the basic knowledge of menopause and HRT from both groups, they have poor basic knowledge (mean score of 7.78 in HRT user and 5.07 in non HRT user). The mean difference between the HRT user and non HRT user was significant. There was also a marked difference in the mean knowledge score

post-intervention programme in non user group. The mean score pre intervention is 5.07 as compared to 10.26 post intervention. The difference of means before and after intervention between the two is again statistically significant, $p < 0.05$.

CONCLUSIONS:

In conclusion, the overall knowledge of HRT users and non HRT users were poor and attitudes towards HRT were more negative among non users. Many of them are still not aware of the existence of HRT, but even if they do, misconceptions are still high.

This study showed that intervention by counseling improves the knowledge of menopause in the non user group, hence leads these women to make informed decisions to use HRT. Therefore, there was a need for health care providers to make an effort to inform and offer HRT to these women who are suffering in silence.

Chapter 1

INTRODUCTION

1.1 GENERAL INTRODUCTION

The menopause, which is the last menstrual period marks the end of the reproductive life in a woman. It is a landmark and is one of the few certainties in women's life. However this does not signal the end of the sexual and social activities.

In a study on the menopausal situation in Malaysia, the mean age of menopause was found to be 50.7 years (Nik Nasri , 1994). In a previous study several years ago, the mean age was 48.7 years (Hamid Arshat et al 1989). Both are within the range documented in most industrialized societies. A menopause which is a biological phenomenon, was not talked much before in Malaysia but is more frequently discussed now. The reason is due to better information available and more importantly it is attributed to the fact that the average life expectancy of the Malaysian women is increased, from 68 years in 1985 to 74 years in 1993 (Vital Statistics - Malaysia 1995) i.e women are spending one third of their lives in the post menopausal period, in a state of oestrogen deficiency.

Apart from the long recognized problems, vasomotor instability, uro-genital and psychological problem, there is also a concomitant and slow pathological deterioration in many other major organ systems. Osteoporosis, cardiovascular disease and Alzheimer's disease are all being increasingly linked to oestrogen deficiency and with growing awareness, more links are being established.

Menopause has led to the prescription of sex steroid hormones to replace the declining levels of natural sex steroid hormones from the "ageing ovaries" of these perimenopausal women (Datuk Sinnathuray, 1989).

The widespread beneficial effects of HRT in improving the health related quality of life of perimenopausal women are well documented. Unfortunately, despite all the beneficial effects, most women do not begin to use these exogenously administered sex steroid, or they may discontinued the use of these agents prematurely. Consequently the full benefits of the therapy will not be achieved.

Survey and audits of menopause and HRT has identified deficiencies. A population based survey on menopausal symptoms concluded that majority of them experienced the menopausal symptoms especially the classical symptoms but less percentage defined it as problematic. However a combination of classic, somatic and psychological symptoms might constitute a considerable problem (Maureen P et al 1996).

In terms of experiencing the menopausal symptoms, the Israelian women look upon menopause as normal, natural part of their lives in which it makes less likely to use HRT. Majority, 83.5% knew about HRT but only 6% use HRT (Blumberg et al 1996). This is in contrast to a survey done in Glasgow in 1989. With reference to their experience of the menopause, they stated that 50% expressed a need of treatment (Barlow et al 1989).

A population based survey in Grampian region of Scotland identified only 10% was on treatment. Majority of them did not consider treatment because 80% had never discussed with a doctor. The reason for low number of HRT users is not due to attitude among them (Hazel K et al 1993). A local study done by Nazimah Idris et al, 1996 illustrated that awareness of HRT

existence is very disappointing, the knowledge about benefits is unsatisfactory and misconception among study population is still high.

Despite the poor knowledge, Kristi J Ferguson concluded that positive effect regarding HRT use made by the physician, by simple communication between a women and her physician could significantly alter HRT use (Ferguson K 1989).

In 1991, the special Menopause clinic was set up in Malaysia through family planning clinic. Various forms of HRT are available - oral tablets, skin patches, gel, cream and implant. According to the patient's wishes, HRT is tailored to be cyclical with regular withdrawal bleeding or continuous with no withdrawal bleeding.

The service for menopause women are available at primary care level, under the care of family physician at present. Primary care physicians are to be responsible for initial recognition and management of these patients. HRT represents one of the most significant advances in preventive medicine in this century and may be used safely by most women provided they do so under medical supervision.

To properly implement HRT among the perimenopausal women who would benefit most, we have to go to the source, the women themselves. We wanted to assess how women feel about menopause in general, whether they think it as a deficiency disease. We also wanted to assess about HRT and its benefit. Therefore this study will assess the menopause symptoms among perimenopausal women with the objectives to determine the level of knowledge, attitude, practice and misconception among study population and to evaluate the influence of counseling of these women.

1.2 LITERATURE REVIEW

Definition of menopause

The term menopause is derived from the Greek words for month and end, and refers to the cessation of menstrual periods. Menopause which is the last menstrual period marks the end of the reproductive life in a woman. The premenopause period begins several years before any signs of climacteric occur. It usually begins at about 40 and its end is determined by the menopause. The transitional period towards the menopause has two phases, the climacteric and the perimenopause. The climacteric usually begins around the age of 45 years, and according to the definition of Senium, ends at the age of 65. Perimenopause also begins with the onset of the climacteric symptoms. It is a period of time around the menopause and ends one year after the menopause. While the postmenopause period usually refers to the period at least 1-2 years after the menopause (Jaszmann 1976) - refer Figure 1.

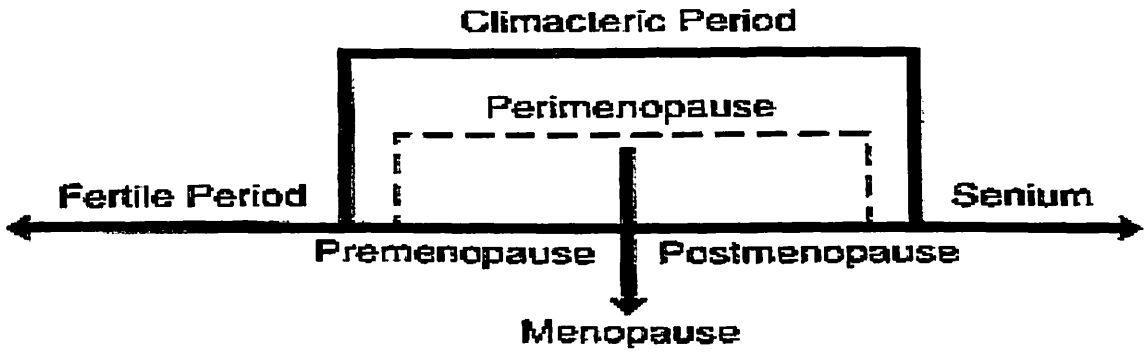

Figure 1 The climacteric period (Jaszmann LJB)

Evidence to support the idea that the climacteric, which by definition is transition period from reproductive to non reproductive, is an endocrinopathy, is based on the demonstration of four classic sequential steps. First there must be morphologic changes in the ovary, an endocrine gland. Second, an alteration in the endocrine mileau must occur, that changes in sex hormone concentrations are measurable. Third, changes in estrogen receptor target tissue must be evident and finally women must seek medical help with complaint preceeding changes in ovaries, sex steroid hormone and target tissue responses (Ann M Voda 1992).

The myth of menopause as an estrogen deficiency disease was first proposed by Robert Wilson, a New York Gynaecologist in 1960s. Wilson believed that a woman's destiny after menopause without estrogen replacement was to spend that period of live in living decay. Therefore in the 1970's estrogen

hormone primarily estrone was used in treating the menopausal symptoms. Besides the beneficial effects of estrogen for treating menopausal symptoms, Wilson also proclaimed that the hormone would protect against osteoporosis, heart disease, and cancer of breast and uterus (Wilson R 1963). In his book, Feminine Forever, a compelling word of picture was painted by Wilson about the horrors of living through the post menopausal years in a body without estrogen (Wilson R 1966). After the widespread publicity that estrogen caused rather than prevented uterine cancer, treatment of menopause women diminished, decrease to 40%. A concerted effort to rehabilitate estrogen therapy was undertaken. A major step toward rehabilitation resulted when progestin was added to the estrogen to minimize the treatment of menstrual cycle and to transform the rapidly proliferating uterine endometrium into a secretory organ (Ann M Voda 1992).

There was a major difference between Wilson's and Uttian's definition of menopause. While Wilson's described it as a deficiency disorder, Uttian's definition of climacteric was constructed to represent a subset of menopausal women whom the changes were viewed as outside of context of

normality. Therefore, Uttian argued some form of hormone replacement in appropriately selected women only (Uttian WH 1987).

Physiology of menopause

At the time of menopause, a shift to a state of hypoestrogenecity accelerates. The ovaries of women become depleted of oocytes as well as their complementary granulose cells, the estrogen progestogen producing cells of ovary.

Ovulation occurs less frequently prior to the menopause and the Graafian follicles become increasingly insensitive to gonadotrophin stimulation. Inadequate follicular maturation leads to low estrogen production and eventually, cessation of menstruation.

After menopause, much of the major source of estrogen, primarily estrone, are derived from the aromatization of androstenedione in body fat, the amount of aromatization of androstenedione to estrone and testosterone to estradiol more than doubles in postmenopausal women and relates directly to the amount of body fat (Gupta & Kenney 1997).

The biochemical diagnosis of menopause rests on an elevated serum follicle stimulating hormone (FSH) of greater than 40 IU/l and low estrogen levels of less than 80 pmol/l. FSH and LH (luteinising hormone) levels rise steadily during the first 12 months after menopause and then they either level off or decrease. The stromata of the ovaries continue to produce androgens throughout life.

Although the depletion of estrogen and progesterone producing cells is a gradual 40 to 50-year long process, the last menstrual period can be abrupt in a small percentage of women. In most women, however the menopause is preceeded by irregular or oligomenorrheic menstrual cycles. The last two years before natural menopause may consequently be associated with the symptoms of menopause or climacteric. This perimenopausal interval prior to menopause can be a time of rising FSH levels, rising and falling estradiol levels and vasomotor symptoms (Morton & Hall - Health Care for Older Women).

Age at menopause

According to historic literature, the average age of menopause has not changed for the last 2000 years. In industrialized countries, menopause usually occurs between the age of 45 to 55 years with the median age at 51 years (Brambilla & McKinlay 1989). In a study on the menopausal situation in Malaysia, the mean age of menopause was found to be 50.7 years (Nik Nasri, 1994). However in the earlier study by Hamid Arshat, the overall average age of menopause was slightly lowered, reported at 48.7 years (Hamid Arshat 1989). Both of the ages in the study fall within the range documented in industrialized societies.

Serum oestrogen concentrations have a pronounced impact on the estimation of age in perimenopause period (Ludwig et al 1999). The age of onset is however by far and large an individual experience.

Factors influencing age of onset

The Massachusetts Women's Health Study (Sonja McKinlay et al 1985), large scale prospective trial conducted in the United States, found that cigarette smoking was the only factor among those examined that affected age of menopause, producing a shift of 1.5 years. There appears to be a dose related trend, where women who smoke greater number of cigarettes for longer periods are more likely to experience the greatest reduction in age at menopause. Even women who have stopped smoking are still likely to undergo menopause at an earlier age than their counterparts who never smoked. Socioeconomic status, marital status, age at marriage, number of pregnancies, body height and racial heritage were the other factors investigated in this study. These were not found to have any clear correlation with the age of the menopause.

The mechanisms by which cigarette smoking affect hormonal changes is not fully understood. Smoking accelerates the hepatic metabolism of oestrogens and decrease the bioavailability of oestrogen (Sonja McKinlay et al 1985).

Menopause symptoms

The climacteric women faces a variety of clinical problems that are thought to be associated with the decline in estrogen production and function that follows menopause. These include vasomotor symptoms, genitourinary symptoms, physical symptoms and as well as psychological symptoms.

Cultural influences, biologic variability among different races, psychological factors and sociologic factors all can have an enormous impact on the meaning, experience and symptomatology of menopause (McNagny, 1999).

Vasomotor symptoms

Vasomotor symptoms are the predominant symptoms and most characteristic manifestations of climacteric and menopause. The symptoms include hotflush, night sweat and palpitation. The vasomotor symptoms of menopause appear attributable to a dysfunction of the brain's thermoregulatory center in the hypothalamus, with a sudden downward setting of the hypothalamic thermostat. The physiological changes that accompany this menopausal central thermal dysfunction include an acute rise in skin temperature, peripheral vasodilatation, a transient increase in heart rate, fluctuations in

the electrocardiograph (ECG) baseline, and a pronounced clearance in skin resistance (Sturdee et al 1978).

The physiological changes of sweating and vasoconstriction result from different peripheral sympathetic function; sympathetic cholinergic fibers excite sweat glands, while tonic alpha adrenergic neurons control peripheral vasoconstriction. Both of these responses lower core temperature during hot flush (Mulley G et al 1997).

The hot flushes have been known for several milleania, described first in ancient Egypt. Hot flushes are described as transient periods of intense sensation, flushing, profuse sweating primarily on the chest, neck and head (Kronenberg & Downey 1987).

For most of these women, hot flush means an occasional sensation of warmth and discomfort, others 10 - 15% experience hourly waves of heat sensation and drenching sweats that disrupt daily activities and wreak havoc on sleep. Hot flushes generally subside spontaneously within about a year, however this can persist for 10, 20 or even 40 years (Kronenberg 1990). These

episodes can be physically and emotionally draining and can seriously interfere with work, family and social relationship.

Urogenital symptoms

The urogenital tissues are embryonically same and are estrogen dependant. Declining estrogen levels lead to atrophy of the urogenital tissues and vaginal thinning and shortening. Vaginal dryness and atrophy can result and lead to atrophic vaginitis, urethral irritation, dyspareunia in 20 - 30% of postmenopausal women. In addition urinary tract infection and urinary incontinence may develop because of tissue thinning, laxity, decreased urethral apposition and alteration of vaginal flora (Toni M Cutson 2000).

Most of these changes can be treated with estrogen replacement therapy (ERT). With ERT the vagina mucosa thickens, the pH of the vagina decreases and there is a decrease in vaginal dryness. ERT either delivered vaginally or orally has same efficacy. A dosage of 0.3mg /day of conjugated equine estrogen (CEE) produces therapeutic result in women with vaginal mucosal atrophy, 0.1 to 0.2 mg of estradiol in vaginal cream is also effective (Toni M. Cutson 2000).

Similarly ERT has a beneficial effect on urinary tract. A meta-analysis of estrogen treatment (oral or intravaginal) for urinary incontinence revealed a significant improvement in subjective symptoms but no improvement in objective measures such as urodynamic testing (Fant et al 1996).

Psychological symptoms

It is during the declining estrogen level that susceptible women begin to have problems related to insomnia, irritability and mood disturbances. Vasomotor symptoms tend to occur with the onset of rapid eye movement sleep, thus disrupting normal sleep architecture. These women may also report difficulty not only in falling asleep but also maintaining sleep as well as early morning awakening. This resulted in daytime fatigue, poor concentration and dysphoria which may be difficult to differentiate from the somatic symptoms associated with depression (Toni M Cutson 2000).

Insomnia has been shown to be estrogen dependant, however brain mechanisms remain unclear. Estrogens seem to have direct effect on sleep regularity areas of the hypothalamus, preoptical area and hippocampus (Halbreich 1997). Estrogen therapy however improves mood and dysphoria,

possibly by affecting the metabolism of serotonin in the central nervous system or due to indirect effect of improved sleep mechanism (Sherwin 1996).

Reports are inconsistent about association between menopause and depressed mood. Studies from clinic based endorse depression as part of the menopause, community based populations do not. It appears that women are more tolerant of the physical changes associated with menopause but seek care for mood symptoms. Like other community based studies, the Massachusette Women Health Study conducted by Avis did not show an increase in depression associated with menopause (Avis et al 1997).

EFFECTS OF MENOPAUSE

A) Menopause and Cardiovascular Disease

Cardiovascular disease kills 500,000 American women each year making it the leading cause of death in women in the US (American Heart Association 1997). It is responsible for more female deaths than all other diseases combined. The picture is similar in other developed countries and in many

developing countries. In Malaysia, 29% of female deaths are directly attributable to cardiovascular disease (Vital Statistic Malaysia 1995).

There are clear differences in the pattern of disease between men and women. Men have 3.5 times the lifetime risk of developing coronary heart disease (CHD) (Prashat et al 1999). The Framingham study demonstrates age specific differences :The female /male risk ratio for CHD is 1:7 in the third decade of life and increases progressively to reach parity only after the seventh decade. This escalation of risk is pronounced after the menopause: a recent estimate suggests a threefold rise in risk is directly attributable to the menopause (Kannel et al 1976). Despite the disappearance of gender differences after the menopause, overall, women are protected from coronary heart disease. They lag behind men in the incidence of CHD by 10 years and of myocardial infarction by 20 years (Kannel et al 1976). CHD alone accounts for 40% of the difference in mortality between the sexes.

A complex interplay of factors leads to the development of postmenopausal cardiovascular disease. While many of these, such as genetic predisposition, cigarette smoking, dyslipidaemia, hypertension and diabetes for both sexes,

women have to contend with the profound effects of oestrogen withdrawal (The Writing Group for the PEPI Trial 1995). Indirect evidence of the effects of this hypo-oestrogenaemia comes from prospective studies. The 1991 Nurses Health Study report assessed 48,470 postmenopausal women who did not have cardiovascular disease at baseline and followed this cohort for 10 years. There was a relative risk of 0.53 (95%CI 0.31 to 0.91) (Stampfer M et al 1991). Current oestrogen use was associated with both reduced incidence and mortality from CHD, independent of other risk factors.

Dyslipidaemia contributes a major role in coronary heart disease. During their reproductive years, women have higher level of high density lipoprotein cholesterol (HDL) and lower level of low density lipoprotein (LDL) and total cholesterol levels than their male counterparts. The HDL continues to be higher even after menopause, although after age 70 it begins to equalize. Overall therefore, the menopause is associated with increased total cholesterol (5%), LDL (11%), and TG (8%) and decreased HDL (6%) (Matthews 1989).

Epidemiological studies have confirmed the protective effect of HDL and established that among all the lipids, HDL level seems to be the most powerful predictor of CHD. The largest of these is the Framingham study which demonstrated a 40 - 50 % decrease in incidence for every 10 mg/dL (0.24 mmol/L) increase in HDL (Castelli 1992).

In evaluating the impact of HRT in reducing cardiovascular disease, population studies show a consistent benefit. Meta - analysis of existing observational studies confirmed that the post menopausal oestrogen replacement reduces cardiovascular risk by as much as 40 - 50% (Grodstein F et al 1996).

B) Osteoporosis

Osteoporosis is defined as a systemic skeletal disease characterized by low bone mass and micro architectural deterioration of bone tissue leading to increased bone fragility and susceptibility to fracture (Consensus Development Conference 1993). The skeleton consists of discrete microscopic units called basic multicellular units (BMUs). BMUs have osteoclasts (bone resorbing cells) and osteoblasts (bone forming cells) along

with their respective precursors, for remodelling of the skeleton. The aim of remodeling being to maintain the integrity of the skeleton.

The peak bone mass which is the maximum density of the bone is usually built by the age of 25-30 years. Bone loss occurs inevitably after this. Imbalance between the amount of bone resorbed and bone forming form the basis of age related and menopause related bone loss. Once a woman reaches about 40 years of age, resorption begins to exceed formation by about 0.5% per year. When menopause begins, the amount of bone being resorbed increases sharply, while the amount being formed increases moderately. Consequently, each year losses of 1% to 3% of cortical bone and up to 5% of trabecular bone occur. The accelerated erosion of bone lasts about 10-15 years, after which bone losses considerably diminished. Bone loss may actually stop after the eighth decade.

Menopause-related bone loss results in a total of 15% to 30% decrease in trabecular bone and a 10% to 15% reduction in cortical bone. Therefore estrogen deficiency is responsible for one third to one half of the bone lost during a woman's lifetime (Ettinger B 1985). Hence, maintaining adequate

estrogen levels remains the most important way of maintaining adequate bone density in women (Ravn P et al 1999).

Estrogens have been shown to regulate different aspects of remodeling process. On the bone it exerts its action on the osteoblasts and osteoclasts. At the tissue the main action is to reduce bone turnover. For the benefit of these women, all women with decreased bone density should be offered estrogen replacement therapy (ERT) unless contraindications exist. Conjugated estrogens in dosages of 0.625 mg per day and transdermal estrogen (a weekly patch containing 0.05 mg) are equally effective in reducing bone loss in postmenopausal women (Lindsay R et al 1984).

In relation to the type of HRT used, Cauley et al found that bone mineral density (BMD) was similar in women using unopposed estrogen or estrogen plus progestin (Cauley et al 1995). This is in contrast to The Postmenopausal Estrogen Progestogen Intervention Trial (PEPI Trial). The PEPI trial a 3 year longitudinal study, showed significant benefits of 0.625 mg of conjugated equine estradiol in the maintenance of bone density at the spine and the femoral neck. Constant compliance can produce a 5% and 2% increase in bone

mineral density (BMD) in the spine and the femoral neck, respectively. The addition of continuous progestin resulted in a significantly higher BMD than with cyclic therapy (The Writing Group For PEPI Trial 1996).

The sooner estrogen is started after menopause the more protective effect on the bone. Studies have been made on the effect of the timing of initiation and duration of postmenopausal estrogen therapy on bone mineral density. Studies by Cauley JA et al, 1995 and Schneider DL et al, 1997 concluded that current users who started ERT at menopause had the highest BMD levels, which were significantly higher than "never" users or "past" users who started at menopause and continued it for at least 10 years (Cauley et al 1995 & Schneider et al 1997).

Current users who started ERT within five years of menopause had a decreased risk of hip, wrist and all nonspinal fractures compared with those who never used estrogen. Cauley et al also found long term users who initiated therapy five years after menopause had no significant reduction in risk for all non spinal fractures, despite an average duration of use of 16 years (Cauley et al 1995). This is supported by the Rancho Bernando Study

that current users who started after 60 years and continued for nine years had the same BMD of 7-19% (Schneider et al 1997). Therefore early initiation of ERT with respect to menopause may be more important than the total duration of use. Estrogen initiated early in menopause and continued into late life appears to be associated with the highest bone density.

As compared with HRT to antiresoptive therapies, bisphosphonates, calcitonin, Selective Estrogen Receptor Modulator (SERMs) - raloxifene, estrogen was found to be more superior in increasing BMD. This was shown in Lindsay study, alendronate increased spinal BMD by 3.5% and 1.9% at the spine and the hip, while the response to estrogen was 1-2% higher than this at both sites (Lindsay R et al 1998). A synergistic action has also been shown with alendronate in combination with estrogen replacement after one year of treatment from this study. When raloxifene was compared to estrogen, the latter proved to be slightly more efficient in long term in suppressing bone turnover (Heaney & Draper 1997).

As bone loss in later life is inevitable, thus peak bone mass should be built up adequately in the first 20-30 years of one's life to cope with the loss that