

# Menopause

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Cessation of menstruation i.e. the menopause is the most striking feature during the period of transition from reproductive to non-reproductive stage of life. Menopause is defined as the permanent cessation of menstruation resulting from loss of ovarian follicular activity. Natural menopause can only be established in retrospect, after 12 consecutive months of amenorrhoea. The median age of menopause is about 50 years and about 1/3<sup>rd</sup> of the life span of women in developed countries is spent after menopause. As the longevity of life increases in developing countries we will also come across more problems related to menopause in future. It is therefore necessary that its physiopathology, symptoms and signs, short-term and long term problems as well as its management are well understood. Urbanisation, stress of life and lack of family support give a feeling of insecurity and makes the woman more vulnerable to the psychological and medical problems related to menopause. As women play an active role in professional and social areas, it is essential that they enjoy optimum health and continue to remain active and useful. The physical changes of menopause are often accompanied by changes in family and social environment which may have a profound influence on psychosocial functioning. The period of climacteric is the time around menopause and this may start as early as two years prior to menopause and effect may extend for many years after the menopause. This period may manifest short term symptoms and long term complications. There is a wide variation in frequency of different climacteric symptoms between different races and the need for treatment for short term symptoms such as vasomotor instability, hot flushes, night sweats, palpitations, etc. vary to great extent in different cultures. However, it is realised that many women go through this period without any treatment even if they suffer from urogenital complaints, psychological problems or vasomotor instability. It is therefore necessary that the gynaecologists makes the menopausal woman sufficiently comfortable to express her problems and demand treatment when required.

## Endocrinological changes during climacteric:

Menopause occurs due to ovarian senescence which is due to exhaustion of ovarian follicles. The ageing ovary reflects the decreasing capacity of the residual follicles to secrete estradiol. Over a period of time, she develops menstrual irregularities and increased number of anovulatory cycles, changes in circulatory levels of sex steroids, inhibin and pituitary gonadotrophins as wells as neuroendocrine changes of thermoregulation, influence on sleep, mood and behaviour. The estradiol decreases from 300-500pg/ml. To less than 25pg/ml. And this results in 10-20 fold increase in LH. A decline in serum prolactin levels of inhibin. The menstrual pattern during climacteric is influenced by the falling levels of estrogens leading to irregular menstrual periods and at times transient polymenorrhoea. Numerous neuroendocrine manifestations are observed as a part of the climacteric syndrome. Hot flushes, night sweats, sleep disturbances, mood changes and behavioral stress responses are some of these. The hot flushes represent a central dysfunction in thermoregulation. Changes in biological rhythms of both hormone secretion and neurotransmitter activity occur during middle age and may contribute to the cascade of interactive events leading to menopause.

## Urogenital Problems

The female genital tract and lower urinary tract is anatomically and embryologically closely related and are sensitive to estrogens. The declining estrogen levels cause atrophic changes such as thinning of the epithellium as well as supportive tissues and reduced vascularisation. This causes vaginal dryness, irritation, discharges, infection, pruritus, dyspareunia, postcoital bleeding and prolapse. This also leads to urinary symptoms varies from 50 to 85%. Genital atrophic changes are associated with decreased maturation of the vaginal epithelial cells and progressive decrease in vascularity in the surrounding tissue, accompanied by fragmentation of elastic tissues and hyalinization of collagen fibres. The glycogen

content of vaginal epithelial cells decreases, resulting in reduced colonization by pathogenic faecal coliforms and cocci. Besides, it leads to inadequate urethral closure and abnormal urinary flow pattern and stress urinary incontinence in some cases, due to decline in collagen in urogenital tissues. It needs good communication and empathy to understand the problems of menopausal women and it is important to give proper counselling so that the patients follow consistent and regular treatment and come for follow-up.

### **Psychological problems**

Psychological symptoms such as anxiety, irritability, and insomnia are most common just before the onset of menopause. These can be relieved considerably by a systemic estrogen therapy. However, some patients do need psychiatric help. Social factors and change in life circumstances contribute significantly to these problems.

### **Prevention of osteoporosis and cardiovascular disease.**

The incidence of osteoporosis and related fractures increase significantly in the menopausal women. Estrogen deficiency causes rapid bone loss particularly in cancellous bone such as spinal column and the ends of long bones and this process continues in the postmenopausal women for almost 2 decades. Osteoporosis is a disease characterised by low bone mass and a micro-architectural deterioration of bone tissue leading to fragility and increased risk of fracture. The osteoporotic peak bone mass is lower after menopause. Therefore there is a definite place for prophylactic treatment by hormone replacement therapy. The measurement of bone density is possible by dual energy X-ray absorptiometry (DEXA) or dual photon absorptiometry (DPA). Quantitative computed tomography (QCT) is the most accurate means of assessing bone density and can be useful in monitoring the effect of treatment. The ultrasound evaluation of bone does not expose the patient to ionising radiation but the assessment is less accurate.

### **Cardiovascular and Metabolic changes :**

Studies have now shown that postmenopausal women are at an increased risk for arterial disease as compared to premenopausal. These include both cardiovascular problems such as angina, myocardial infarction and hypertension and cerebrovascular pathology. Coronary artery occlusion may be acute or chronic. Acute occlusion results in unstable angina, acute myocardial infarction and even ischaemic death from coronary spasm or from sudden disruption of an atherosclerotic plaque. Coronary artery stenosis is associated with negative oxygen balance and stable angina. There is increase in total cholesterol, low density lipoprotein cholesterol (LDL-C) and decrease in high density lipoprotein cholesterol (HDL-C) is seen at menopause. Hormone replacement therapy may prevent the cardiovascular problems to a significant extent if given prophylactically.

### **Carbohydrate Metabolism:**

There is a possible increase in insulin resistance and hyperinsulinaemia at menopause, since endogenous and exogenous sex steroids modulate glucose metabolism. Hyperglycaemia and hyperinsulinemia may damage the endothelium, allow the insulin to act on smooth muscle cells and thereby initiate or perpetuate atherothrombosis. Carbohydrate disorders are associated with platelet hyperactivity and hypercoagulability from increased fibrinogen and factor VII levels. Insulin also affects lipoprotein metabolism and stimulates hepatic synthesis of VLDL, resulting in hypertriglyceridemia.

The markers of clinical disease will therefore be, proatherogenic lipid factors such as total cholesterol, triglycerides and LDL as well as pro-coagulatory factors such as Fibrinogen & Factor VIIc. The other proatherogenic factors are insulin resistance, hyperinsulinemia, obesity, hypertension and diabetes.

### **Management of Menopause.**

A pretreatment assessment and counselling of patients who need HRT is essential for both symptomatic patients and those seeking long term health benefits. The aims of

HRT now go beyond offering short term relief of symptoms. Many menopausal or elderly women's clinics are established to act as referral centres for administering, and monitoring HRT and offer the guidance regarding diet, exercise and psychological support. A full medical history is essential, as women in this age group are likely to have problems such as hypertension, cardiac disease, obesity, diabetes and malignancy. A family history of diabetes, cardiovascular accidents, osteoporosis or breast carcinoma has to be obtained. A full general examination includes height, weight, blood pressure check up, cardiovascular and respiratory assessment. Breast examination and mammography are necessary before starting HRT. Gynaecological examination includes abdominal, bimanual and per speculum examination. A pap smear should be collected in every patient from the cervix and a lateral vaginal wall smear is also collected for the assessment of hormonal status. In most of the cases vaginal smear taken before starting HRT will indicate the initial hormonal status and the extent of estrogen deficiency. The response to HRT is assessment by FSH & E2 estimation is rarely required. This is necessary in women with premature menopause. The investigations include complete blood count, fasting and post lunch blood sugar, lipid profile, coagulation profile (optional), abdominal and transvaginal ultrasonography for endometrial thickness. Hormonal profile: FSH, LH, E2 and TSH as well as bone densitometry are optional investigations. Long term treatment is especially necessary for prevention of osteoporosis and coronary heart disease. Women with premature menopause should most certainly be treated by HRT.

### **Principles of HRT Administration**

HRT can be administered by oral and nonoral routes depending on several factors such as symptomatology, presence or absence of the uterus and the purpose and duration of the therapy. Oral route is commonly used and women who have undergone hysterectomy are given only estrogen as progesterone is unnecessary because endometrium does not exist. This does not apply to patients who have undergone endometrial ablation. In women who have an intact uterus, but have intolerance to proges-

terones, continuous estrogens can be offered with close monitoring by transvaginal sonography for endometrial thickness and endometrial aspiration for histopathology when necessary. However, a great deal of caution and counseling is necessary and progesterone administration for 12 days at least once in 3 months is desirable to rule out endometrial hyperplasia.

Cyclic Estrogen & Progesterone Therapy is the most frequently used regimen. Estrogen corrects the menopausal symptoms and progesterone added in the last 10-12 days of the cycle, prevents endometrial hyperplasia. The risk of endometrial cancer in unopposed estrogen users is certainly significant. There is more than 50% possibility of developing hyperplasia in women receiving unopposed estrogen. Progesterone supplementation for 12 days in each cycle rules out this disadvantage. However, about 50% of patients are likely to get withdrawal bleeding which may be mild or moderate. Continuous regimen, progestogen HRT is used for some women when withdrawal bleeding is unacceptable. This combined continuous regimen improves the compliance. Only progesterone may be used in perimenopausal women where estrogen are contraindicated. Testosterone Androgen HRT can be offered to women, who do not improve with estrogen alone.

Tibolone (Livial), a gonadomimetic preparation has a weak estrogenic, androgenic and progestogenic activity. Besides the prevention of osteoporosis, it improves the mood and libido and does not cause endometrial proliferation. It is given in a daily dose of 2.5 mg orally. Although extremely good for elderly menopausal patients, it has to be affordable.

### **Summary**

Menopause should be managed by a multidisciplinary team where gynaecologist, orthopaedic surgeon, cardiologist, psychiatrist and a counsellor are involved when necessary to give the optimum benefits to the women. Laboratory facilities, sonography and mammography have important roles. A caring husband, loving children and happy atmosphere at work at home are most essential.