HORMONE REPLACEMENT THERAPY (HRT)

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Introduction

The HRT is indicated in menopausal women to overcome the short-term and long-term consequences of estrogen deficiency.

Indication of Hormone Replacement Therapy

- i. Relief of menopausal symptoms
  ii. Prevention of osteoporosis
  iii. To maintain the quality of life in menopausal years.
- ***Special group of women to whom HRT should be prescribed:***
  •.Premature ovarian failure
  •.Gonadal dysgenesis
  •.Surgical or radiation menopause

BENEFITS OF HORMONE REPLACEMENT THERAPY (HRT)

- Improvement of vasomotor symptoms (70-80%)
- Improvement urogenital atrophy
- Increase in bone mineral density (2-5%)
- Decreased risk in vertebral and hip fractures(25-50%)
- Reduction in colorectal cancer (20%)
- Possibly cardioprotectio

HRT and Osteoporosis

- HRT prevents bone loss and stimulate new bone formation. HRT increases BMD by 2–5% and reduces the risk of vertebral and hip fracture (25–50%). Estrogen is found to play a direct role, as receptors have been found in the osteoblasts.

- Women receiving HRT should supplement their diet with an extra 500 mg of calcium daily.
- Total daily requirement of calcium in postmenopausal women is1.5 g.
- *HRT is thought to be cardiovascular protective*

LDL on oxidation produces vascular endothelial injury and foam cell (macrophage) formation. These endothelial changes ultimately lead to intimal smooth muscle proliferation and atherosclerosis. Estrogen prevents oxidation of LDL, as it has got antioxidant properties

RISKS OF HORMONE REPLACEMENT THERAPY

- **Endometrial cancer:** When estrogen is given alone to a woman with intact uterus, it causes endometrial proliferation, hyperplasia and carcinoma. It is therefore advised that a progestogen should be added to ERT to counter balance such risks.

- ***Breast cancer:***
- Combined estrogen and progestin replacement therapy, increases the risk of breast cancer slightly (RR 1.26). Adverse effects of hormone therapy are related to the dose and duration of therapy.

- **Venous thromboembolic (VTE) disease** has been found to be increased with the use of combined oral estrogen and progestin . Transdermal estrogen use does not have the same risk compared to oral estrogen.

  Coronary heart disease (CHD)

- Combined HRT therapy shows a relative hazard of CHD. Hypertension has not been observed to be a risk of HRT.

- **Lipid metabolism:**
- An increased incidence of gallbladder disease has been observed following ERT due to rise in cholesterol (in bile).
  Dementia, Alzheimer disease are increased.

AVAILABLE PREPARATIONS FOR HORMONE REPLACEMENT THERAPY

- The principal hormone used in HRT is estrogen. This is ideal for a woman who had her uterus removed (hysterectomy) already. But in a woman with an intact uterus, only estrogen therapy leads to endometrial hyperplasia and even endometrial carcinoma.
- Addition of progestins for last 12–14 days each month can prevent this problem

- Commonly used estrogens are conjugated estrogen (0.625–1.25 mg/day) ormicronized estradiol (1–2 mg/day). Progestins used are medroxyprogesterone acetate (2.5–5 mg/day), micronized progesterone (100–300 mg/day) or dydrogesterone (5–10 mg/day).

- **Considering the risks, hormone therapy should be used with the lowest effective dose and for a short period of time.**

- Low dose oral conjugated estrogen 0.3 mg daily is effective and has got minimal side effects.
- Dose interval may be modified as daily for initial 2–3 months then it may be changed to every other day for another 2–3 months and then every third day for the next 2–3 months. It may be stopped thereafter if symptoms are controlled

- **Oral estrogen regime:** Estrogen—conjugated equine estrogen 0.3 mg or 0.625 mg is given daily for woman who had hysterectomy.
  Estrogen and cyclic progestin: For a woman with
  intact uterus estrogen is given continuously for 25
  days and progestin is added for last 12–14 days.
  Continuous estrogen and progestin therapy
  Continued combined therapy can prevent endometrial hyperplasia. There may be irregular bleeding with this regimen.

Subdermal implants:

Implants are inserted subcutaneously over the anterior abdominal wall using local anesthesia.

17 β estradiol implants 25 mg, 50 mg or 100 mg are available and can be kept for 6 months. This method is suitable in patients after hysterectomy. Implants maintain physiological E2 to E1 ratio

Percutaneous estrogen gel: 1 g applicator of gel, delivering 1 mg of estradiol daily, is to be applied onto the skin over the anterior abdominal wall or thighs. Effective blood level of oestradiol (90–120 pg/mL) can be maintained.

Transdermal patch: It contains 3.2 mg of 17β estradiol, releasing about 50 µg of estradiol in 24 hours. Physiological level of E2 to E1 is maintained.

It should be applied below the waist line and changed twice a week. Skin reaction, irritation and itching have been noted with their use.

Vaginal cream: Conjugated equine vaginal estrogen cream 1.25 mg daily is very effective specially when associated with atrophic vaginitis.

It also reduces urinary frequency, urgency and recurrent infection. Women with symptoms of urogenital atrophy and urinary symptoms and who do not like to have systemic HRT, are suitable for such treatment.

Progestins: In patients with history of breast carcinoma, or endometrial carcinoma, progestins may be used. It may be effective in suppressing hot flushes and it prevents osteoporosis. Medroxyprogesterone acetate 2.5–5 mg/day can be used.

LEVONORGESTREN INTRAUTERINE SYSTEM with daily release of 10 microgram (see below) of levonorgestrel per 24 hours, it protects the endometrium from hyperplasia and cancer. At the same time it has got no systemic progestin side effects. Estrogen can be given by any route. It can serve as contraception and HRT when given in a perimenopausal women.

Tibolone:

Tibolone is a steroid (19 nortestosterone derivative) having weakly estrogenic, progestogenic and androgenic properties. It prevents osteoporosis, atrophic changes of vagina and hot flushes. It increases libido. Endometrium is atrophic. A dose of 2.5 mg per day is given.

Duration of HRT Use

- Generally, use of HRT for a short period of 3–5 years have been advised. Reduction of dosage should be done as soon as possible. Menopausal women should maintain optimum nutrition, ideal body weight and perform regular exercise.

- **Individual woman should be given informed choice as regard the relative merits and possible risks of continuing HRT.**

MONITORING PRIOR TO AND DURING HRT

A base level parameter of the following and their subsequent check up (at least annually) are mandatory.

- Physical examination including pelvic examination.
- Blood pressure recording.
- Breast examination and Mammography
- Cervical cytology

- Pelvic ultrasonography (TVS) to measure endometrial thickness (normal <5 mm)
- Any irregular bleeding should be investigated thoroughly (endometrial biopsy, hysteroscopy)
- Ideal serum level of estradiol should be 100 pg/Ml during HRT therapy. Serum level of estradiol is useful to monitor the HRT therapy rather than that of serum FSH.

CONTRAINDICATIONS TO HRT

- Undiagnosed genital tract bleeding
- Estrogen dependent neoplasm in the body
- History of venous thromboembolism
- Active liver disease
- Gallbladder disease
- Known , Suspeceted or history of Breast cancer

PROGRESS IN HORMONE REPLACEMENT THERAPY

- **Low Dose HRT:**

  Women with intact uterus with 0.3 mg conjugated equine estrogen (CEE) and Medroxy Progesterone acetate (MPA) 1.5 mg is found effective to control the vasomotor symptoms. Similarly 1 mg of estradiol and norethisterone acetate 0.5 mg orally, are also effective and have significant bone sparing effect. Progestogen is added in the HRT to minimize the adverse effects of estrogen.

THANK YOU