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Treatment of Perimenopausal Osteoporosis – Roll of HRT

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Menopause is a retrospective diagnosis characterized by stoppage of reproduction due to cessation of ovarian function. This leads to reduction in the levels of oestrogen and progesterone. This leads to some physiological changes which represent as mood changes, hot flushes, dry genital mucosa, night sweats, urinary symptoms and dysfunctional uterine bleeding.

The long term effects of these hormonal changes are on bones (osteoporosis) and cardiovascular system. Osteoporosis is a systemic disease characterized by low bone mass and micro-architectural deterioration of bone tissue resulting in fragile bones prone for fractures.

Osteoporotic fractures are four times more common than stroke and lead to permanent disablement. So the prevention of osteoporosis is the principle aim of management of the syndrome of MENOPAUSE.

Strategies for prevention are (1) calcium rich diet (2) exercise (3) sun exposure right from childhood. It has been shown that the calcium can be stored in the body up to the age of 32 yrs after which the body can not store the calcium. That means that the level of menopausal osteoporosis is determined by the level of calcium deposits by 32 yrs of age.

Treatment of osteoporosis consists of (1) Non-pharmacological methods like nutritional supplements and (2) Use of drugs. The indications for treatment are (a) post-menopausal women with low BMD (b) preventive treatment.

The drugs used commonly are –

- Oestrogens

  Bisphosphonates,
- SERMS (selective estrogen receptors modulators)
- STEAR (selective tissue estrogenic activity regulator)
- We will consider only hormone replacement therapy (HRT) in this write-up.

Estrogen

Prevents bone loss on recently menopausal women. Should be started at the earliest signs of menopause. The drug is available as tablets, gel, vaginal pessaries and skin patches. Sub-cutaneous slow release capsules are also available in some parts.

The treatment has to be started after careful evaluation by a gynaecologist and monitored to rule out the possibilities of Endometriosis and breast cancer. p/v bleeding sometimes warrants change or discontinuation of drug.

SERMS (Selective Estrogen Receptors Modulators)

These drugs have estrogene agonistic effect on bone and lipo-protein production. At the same time they have antagonistic effect on breast tissue and neutral effect on uterine mucosa (endometrium). These also have favourable cardio-vascular effects. These drugs get activated by transcriptional activation function. So they are preferred over oestrogen. The only drawback is these may aggrevate vasomotor

symptoms which is an important consideration in recent menopause candidate.

SERMS are available as,

1. First generation - Tamoxifene
2. Second generation - Raloxifene (designer's estrogene)
3. Third generation - Idoxifene

Of these Raloxifene is most widely used drug, approved by US FDA for prevention of osteoporosis. The mechanism of action is by gene transcription. It activates beta estrogenic receptors which are located in bone and blood vessels. It fails to activate

TAF 2 receptors present in endometrium and breast tissue and so chances of malignancies in these tissues are negligible.

It slows the rate of bone loss by binding to estrogen receptors and slows down bone resorption.

Clinical trials in MORE study done on 7705 post-menopausal women have shown that the SERMS(raloxifene) in the dose of 60mgs/da for a period of 36 months

1. Reduce the chances of vertebral fractures by 30%.
2. Reduce the chances of first fracture by 55%.
3. Increased the value of BMD by 2-3% in spine and hip.

Pharmaco-kinetics rapidly absorbed from GI tract and peak plasma levels are achieved in 6 hours. The dose advised is 60mgs/day with regard to meals. Nausea, myalgia and Insomnia are some troublesome complications. Occurrence of DVT is comparable to estrogen and should be watched for.

The drug should be with held 72 hrs pre operative and post operative period as it can increase the chances of thrombo-embolism.

ACOG (American college of ob and gy) recommendations for prescribing Raloxifene for Postmenopausal woman are

1. One or many risk factors for osteoporosis.
2. T-score of 2 or less.
3. Discontinuing HRT.
4. Family history of Ca of breast and or endometrium.
5. Established osteoporosis.

STEAR Selective Tissue Estrogenic Activity Regulator

This is a synthetic steroid having estrogenic, progesteronic and androgenic properties.

The drug is in use for last 2 decades for the treatment of menopausal symptoms.

Mechanism of action : The drug itself has no biological activity. Its effects are mediated bt its metabolites 3 alfa hydroxytibolone, 3 beta hydroxytibolone and d 4 isomer. 3-4 hydroxyl groups bind solely with estrogen receptors and isomer has affinity for both progesterone and androgen receptors but not estrogen receptors. The concentration of metabolites and hormonal activity very depending upon tissue type, thus conferring tibolone tissue specific action.

Tibolone has both central & peripheral hormonal effects.

Genital tract ; weak estrogenic action on vagina is useful in atrophic vaginitis and prevention of endometriosis.

Breast inhibits the formation of active estrogenes in tissue thus reducing the proliferation of breast tissue.

Lipids reduces the Triglycerides, VLDL & HDL. No effect on LDL.

Haemostasis increase in Hb and platelets count. Returns to normal after therapy. Androgenic effect causes increase in fibrinolytic activity.

Carbohydrate metabolism reduction in glucose tolerance.

Bones

Action on bone is stimulation of estrogen receptors.this reduces the bone turnover and improves trabecular bone quality. It thus reduces the levels of serum and urinary calcium. The serum concentration of phosphates is reduced.

In therapeutic doses the clinical trials show 8% improvement in lumber spine BMD at the end of 3 years as against bone loss at 2% per year in control group.

Six controlled trials compared the standard HRT with Tibolone in prevention of bone loss. The conclusion was Tibolone improves BMD significantly but there are no clinical trials available to back these findings.

Dose

2.5mg/day in women with established post-menopausal osteoporosis. It is rapidly absorbed and metabolized in liver and intestines. It is excreted in urine and faeces.

Nausea and breakthrough bleeding may occur in some patients. Breast tenderness and weight gain are not uncommon. Very rarely some androgenic effects are seen.

References

1. Menopause current concepts—Puandare, Khadilkar JAYPEE publishers 2004.

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Book Review

The book "BASICS OF ARTHRITIS" written by *Dr. Manoj Kondoi* is in its second edition. The exercise to have a comprehensive handbook giving essentials in symptomatology, diagnosis and management has made this book very useful for students and practitioners.

The book covers almost all varieties of arthritis and section peeping in to recent treatment modalities for rheumatoid arthritis has made the book interesting. The chapter on rhematological manifestation of HIV disease will be very useful in coming years.

The section of physiotherapy in the management with illustrations completes the book. The annexure outlining how to go about examining and diagnosing the problems of joint pain summarizes the contents of the book.

One thing which could have been avoided is spelling and grammatical mistakes.

Author : ***Dr. Manoj Kondoi.***

Published by : ***The National Book Depot.***

Pages : 268 Price Rs : 250/-

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