Novel therapeutic strategies for osteoporosis

This has reference to the article on the Molecules of the Millennium, entitled ‘Novel agents in osteoporosis’ published in the Indian Journal of Pharmacology, 2004;36:48-9. The article is very informative and interesting. The mechanism of the actions of selective estrogen receptor modulators (SERMs) in relation to regulation of the growth factor beta cytokines and the induction of osteoblasts with inhibition of osteoclasts, is well explained. However, there are few more novel SERMs having therapeutic advantages over raloxifene.

Ospemifene, a derivative of foremifene with estrogen receptor (ER) blocking action on breast tissue and ER partial agonistic actions on bone and cardiovascular system, is being investigated for the treatment and prevention of osteoporosis. It has $C_{\text{max}}$ (maximum concentration) of 43 µg/L, $t_{\text{max}}$ (time to achieve $C_{\text{max}}$) of 1-4 h, $t_{1/2}$ of 24 h after a single 50 mg dose per day. Various Phase I and Phase II clinical trials have demonstrated better results with ospemifene than raloxifene. It has the additional advantage of having an LDL lowering effect and a positive effect on vaginal dryness (ER agonist effect on the vagina). Moreover, no effect has been reported with its use, on blood clotting, hot flushes and insomnia.

Arzoxifene is another benzothiophene derivative related to raloxifene with ER blocking effect on the breast and uterine tissue and ER partial agonistic effect on bone and cardiovascular system. However, various in vitro and in vivo studies have demonstrated the superiority of arzoxifene over tamoxifen in breast cancer. It has $t_{1/2}$ of 30-35 h, $C_{\text{max}}$ of 4.67 µg/L, and $t_{\text{max}}$ of 2-6 h after a 50 mg single dose. It is also a potential candidate for the treatment and prevention of osteoporosis. However, the common side effects reported with its use are rash, pruritis, constipation, headache, nausea, vomiting, stomatitis and rarely, it can cause pulmonary embolus and deep vein thrombosis.

HMGCoA reductase inhibitor is another class of drug that is being investigated for its potential role in osteoporosis. Statins like lovastatin and simvastatin have demonstrated an increase in bone volume and rate of bone formation after oral therapy. Soy-derived isoflavones are also being investigated as potential therapeutic agents in the prevention and treatment of osteoporosis.

If the efficacy of these agents is proved, then there will be novel additions to the armamentarium of the physician against osteoporosis, especially in post-menopausal women.

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References