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Therapy - Antifracture Efficacy of Pharmacological Interventions

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THERAPY – ANTIFRACTURE EFFICACY OF PHARMACOLOGICAL INTERVENTIONS

There is plenty evidence that pharmacological interventions can reduce the risk of fracture and improve the quality of life among postmenopausal women with osteoporosis. Currently, several options are available (Fig. 1), and these can be classified according to their mechanism of action (Tab. 1). The two main classes of drugs used to treat osteoporosis are anticatabolic agents, and anabolic agents. Anticatabolic agents primarily inhibit bone resorption by inhibiting osteoclast activity and/or decreasing osteoclast number. However, at the same time, also bone formation is inhibited, although to a smaller extent. In contrast, bone anabolic agents primarily promote bone formation by stimulating bone forming activity of osteoblasts and also by increasing osteoblast number. However, these drugs also increase bone resorption, although this increase clearly remains behind the increase in bone formation. Recently, a third mode of action called "dual" has been proposed, which particularly refers to strontium ranelate. This drug has been shown to inhibit bone resorption while maintaining or even improving bone formation.

H. P. Dimai

ANTICATABOLIC DRUGS

A classical representative of anticatabolic drugs are bisphosphonates. Bisphosphonates currently are the first-line drugs for treating postmenopausal women with osteoporosis. Particularly alendronate and risedronate have been shown to reduce the risk of vertebral and non-vertebral fractures, including the risk of hip fractures, if taken once daily. However, both alendronate and risedronate also are available as once-weekly formulations, and these account for more than 90 % of the total prescriptions regarding alendronate and risedronate in many countries worldwide. These formulations have been developed to increase the patient's compliance and adherence to the therapy. However, it should be noted that currently there is only indirect evidence for antifracture efficacy of these once-weekly formulations.

Ibandronate, another bisphosphonate, has also been shown to reduce the risk of vertebral fractures, either orally taken or intravenously administered. However, there are no adequately designed studies available showing that ibandronate could also reduce the risk of non-vertebral fractures.

In some countries, but not worldwide, another bisphosphonate, etidronate, is still available for treatment of postmenopausal osteoporosis. There is some evidence that this bisphosphonate also could reduce the risk of vertebral fractures.

The selective estrogen-receptor modulator (SERM) raloxifene is often considered in postmenopausal women with low bone mass or younger postmenopausal women with osteoporosis who are at greater risk of spine fracture than hip fracture. Raloxifene has been shown to prevent bone loss and to reduce the risk of vertebral fractures. However, its effectiveness in reducing other fractures is uncertain. Extraskeletal risks and benefits are important when considering raloxifene therapy.

Calcitonin is not a first-line drug for postmenopausal osteoporosis treatment, as it has been shown that its

Figure 1: Compounds available for the treatment of postmenopausal osteoporosis.

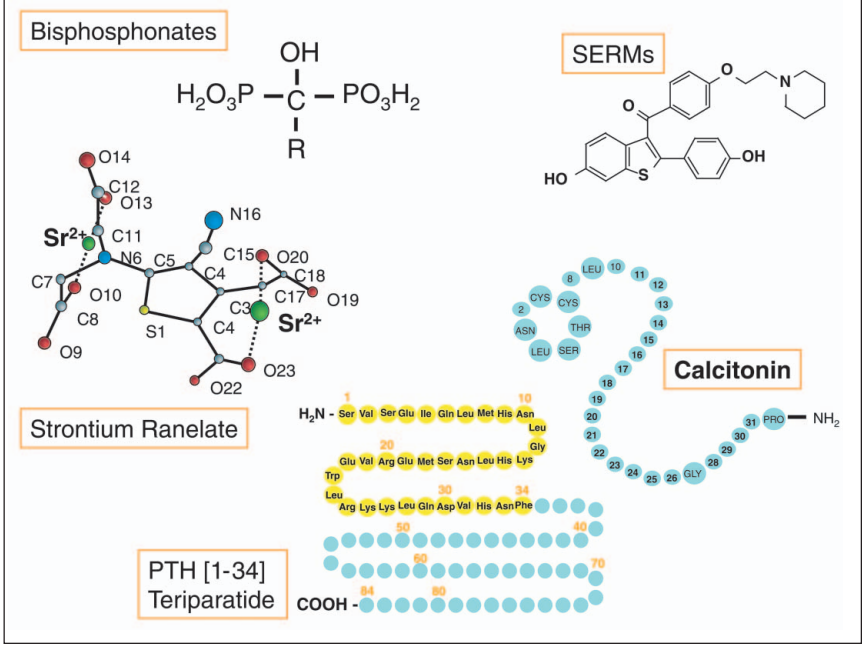

Table 1: Anti-fracture efficacy of pharmacological interventions for postmenopausal osteoporosis (evidence-based).

Intervention	Vertebral	Non-vertebral	Hip
Alendronate	+	+	+
Risedronate	+	+	+
Strontium Ranelate	+	+	+
Teriparatide	+	+	–
Raloxifene	+	–	–
Ibandronate	+	–	–
Etidronate	+	–	–
Calcitonin	+	–	–

efficacy to prevent vertebral fractures is not very strong. Also, currently there is no evidence for a potency to reduce non-vertebral fracture risk. Also its BMD effects are less than those of other agents. However, it may be an option for women with osteoporosis who are more than 5 years beyond menopause experiencing bone pain from acute vertebral compression fractures.

Estrogen has been shown to reduce or stop the annual bone loss after menopause. However, currently no data from adequately designed randomized, controlled clinical trials are available providing clear evidence that estrogens or a combination of estrogens and progestins could sufficiently reduce the risk of vertebral and/or non-vertebral fractures.

Anabolic drugs

The recombinant human parathyroid hormone fragment teriparatide (PTH 1-34) currently is the only anabolic agent approved for treatment of postmenopausal osteoporosis. It is mainly reserved for treating women at high risk of fracture, including those with very low BMD (T-score worse than –3.0) with a previous vertebral fracture or those who developed an osteoporotic fracture during therapy with anticatabolic drugs. PTH has been shown to improve BMD and to reduce the risk of new vertebral and non-vertebral fractures.

Dual acting drugs

Recently, strontium ranelate has been approved for the treatment of postmenopausal osteoporosis in Europe and many other countries worldwide. Strontium ranelate consists of two stable strontium atoms and the organic moiety ranelic acid. Strontium ranelate has been shown to reduce the risk of vertebral and non-vertebral fractures. Also, in a subgroup of patients with high fracture risk, strontium ranelate has been shown to reduce the risk of hip fractures.

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