REVIEW

Salmon Calcitonin Nasal Spray

An Effective Alternative to Estrogen Therapy in Select Postmenopausal Women

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The efficacy and safety of estrogen replacement therapy (ERT) and salmon calcitonin in the treatment of postmenopausal osteoporosis are reviewed with special consideration given to patients for whom ERT, the primary antiresorptive therapy for osteoporosis, is not indicated, tolerable, or is refused. The various formulations of estrogen and salmon calcitonin, for which the nasal spray formulation was recently approved for use in the United States, are reviewed in depth with reference to dose ranges, side effects, and convenience. Data regarding increases in bone mineral density (BMD) produced by each agent are presented. Specifically, the range of increases in BMD induced by ERT and salmon calcitonin are comparable. Given the substantial public health consequences of postmenopausal osteoporosis and osteoporotic fractures, the primary care physician is increasingly faced with the need to educate and recruit postmenopausal patients to appropriate therapy with the optimal agent for that particular patient. In the many patients who are unable or unwilling to accept, initiate, and comply with prescribed ERT, alternative therapeutic options are necessary. Based on the established safety profile of salmon calcitonin, ease of administration, an uncomplicated dosing regimen, no reported drug interactions, and the lack of uterine bleeding associated with ERT or gastrointestinal adverse effects of other agents used to treat osteoporosis, salmon calcitonin nasal spray is an appropriate alternative approach for the treatment of postmenopausal bone loss.

Key Words: Estrogen replacement therapy; salmon calcitonin; postmenopausal osteoporosis.
osteoarthritis within the United States was 5–6 million; corresponding figures for osteopenia were 10–15 million women. Melton (1995) reported 1995 estimates of 9.4 million and 16.8 million for osteoporosis and osteopenia, respectively, in white postmenopausal women in the United States. He further estimated that 4.8 million women (51% of the osteoporotic women and 16% of all white women ≥50 yr) have established osteoporosis, noting that this figure is probably an underestimate since most fractures in elderly women are related at least in part to low BMD. Based on these figures, the total population of white women in the United States at risk of fracture secondary to osteopenia or osteoporosis is 26.2 million.

The Consequences of Osteoporosis

Often called “the silent thief” (World Health Organization, 1994) because of its covert early progression, osteoporosis is associated with substantial disability and increased morbidity and mortality with advancing age, as the overt manifestations of the disease—osteoporotic fractures—occur at a markedly increased rate. In the United States, approx 1.5 million fractures attributable to osteoporosis occur each year (Peck et al., 1988; Riggs, 1991). The most common fracture sites include the vertebrae (650,000), the hip (250,000), and the distal forearm (200,000). The consequences of hip fracture are often particularly severe: In the first year after a hip fracture, the mortality rate is approx 12–20% higher than that in persons of similar age and gender without hip fracture in the general population (Miller, 1978; Gallagher et al., 1980; Lewinnek et al., 1980; Cummings et al., 1985); the excess mortality occurs primarily in the first 4–6 mo after the hip fracture (Miller, 1978; Gallagher et al., 1980; Nevitt, 1994). Of the patients who survive hip fractures, at least 50% of those who could walk before sustaining the fracture are unable to walk unassisted afterward. In addition, up to 50% of all patients with hip fracture cannot live independently following the fracture (Melton, 1993). Specifically, according to Phillips et al., hip fractures in the United States result in approx 61,000 nursing home admissions per year among white women (Phillips et al., 1988).

No less devastating are the financial costs of osteoporosis care in American women: In 1986, the total cost of treating osteoporosis—including inpatient, outpatient, and nursing home care—were approx $5.2 billion (Phillips et al., 1988). Recently reported estimated total care costs have nearly doubled and are reported to be at least $10 billion (Riggs and Melton, 1992). The enormous public health impact of osteoporotic fractures and the burden to the community and the healthcare system indicate the urgent need for prevention and necessitate that the primary care physician be able to identify appropriate patients for preventative and therapeutic treatment of osteoporosis and then select the most appropriate therapy for those patients.

Estrogen Replacement Therapy

Mechanism of the Antiresorptive Action of Estrogen

Menopause is often associated with a relatively sudden cessation of endocrine function of the ovary that significantly alters skeletal homeostasis, resulting in loss of bone tissue. Prior to menopause, the predominant estrogen is 17β estradiol, which is secreted by the ovary (Lindsay, 1993). Postmenopause, there is a marked decline in estradiol, as well as in estrone and progesterone, producing a significant decrease in total circulating estrogen levels, which has been shown to correlate with the rate of bone loss (Lindsay, 1993).

The relatively marked decrease in total estrogen levels is thought to result in increased activation of bone remodeling and the number of bone remodeling sites, resulting in a proposed increase in the activity and number of osteoclasts and possibly altered osteoblast function (Lindsay, 1991, 1993; Compston, 1993; Lindsay et al., 1993). The net effect is a significant negative imbalance between bone resorption and bone formation at each remodeling cycle (Lindsay, 1991, 1993). An independent, age-related factor contributing to the increase in bone loss is also thought to exist in addition to an estrogen deficiency mechanism of action (Lindsay, 1993).

The reintroduction of estrogen via estrogen-replacement therapy (ERT) reverses the effects of ovarian failure (Lindsay, 1991). The minimum effective dose for conjugated equine estrogen is 0.625 mg/d, and for percutaneous estradiol, 50 µg via transdermal patch appears to achieve these levels (Lindsay, 1993).

Review of Prospective Clinical Trial Data

Two decades of prospective clinical trial results stand in support of the efficacy of ERT in the prevention and treatment of estrogen-deficient osteoporotic syndrome. These results, though frequently difficult to compare owing to inconsistencies in study design and methodology, have established the therapeutic role of estrogen in stopping and/or reversing bone resorption in the axial and appendicular skeleton.

The results of controlled studies conducted in the past 5 yr continue to corroborate the well-documented efficacy of ERT in preventing and/or minimizing bone loss and in increasing BMD in estrogen-deficient women. Of equal importance, these therapeutic effects on BMD have been clearly shown to decrease the risk of fractures in early postmenopausal women and in those with established osteoporosis. As a result, estrogen is the agent of first choice in most women for the prevention of skeletal bone loss and for the long-term treatment of primary and established osteoporosis.

The salutary effects of estrogen on bone resorption and mineral density were noted anecdotally for many years and...