Strontium Ranelate Has Durable Bone Protection

Ten years of use gives one the chance to return bone turnover to premenopause levels.

BY MITCHEL L. ZOLER

FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

LONDON – Strontium ranelate continued to safely and effectively prevent vertebral and nonvertebral fractures in postmenopausal women with osteoporosis during 5-10 years of continuous treatment, in a "modified" case-control study that included 233 women who maintained daily 2-g/day strontium dosing for 10 years.

"Strontium ranelate should not be considered a second-line alternative to bisphosphonates or to any other [osteoporosis] treatment," Dr. Jean-Yves Reginster said at the meeting.

Treatment with strontium ranelate "gives you a chance to bring bone turnover back to premenopausal values," said Dr. Reginster, professor of epidemiology and chairman of the department of public health at the University of Liège in Belgium.

The ability of strontium ranelate to maintain a reduced rate of both vertebral and nonvertebral fractures over 10 years of continuous use in this study marks the first reported evidence of an antiosteoporotic drug exerting an unequivocal antifracture benefit for such a prolonged period.

The only other report on 10-year treatment came from the Fracture Intervention Trial Long Term Extension, which included 1,099 women randomized to alendronate or placebo for 10 years (JAMA 2006;296:2927-38).

Those results showed that 5-10 years of extended alendronate treatment did not result in a reduction of all clinical fractures or nonvertebral fracture, compared with women maintained on placebo during years 5-10, but extended alendronate did reduce the clinical vertebral fracture rate, compared with placebo.

"In our study [of strontium ranelate], we had no placebo group, but we showed that you can reduce fractures over 10 years with this drug."

VITALS

Major Finding: During the 5- to 10-year period of extended, continuous treatment with strontium ranelate, postmenopausal women with osteoporosis at baseline had a 21% rate of vertebral fractures and a 14% rate of nonvertebral fractures, significantly less than the 28% and 20% rates, respectively, of fractures in a matched placebo group.

Data Source: Cohort of 233 postmenopausal women with osteoporosis maintained on 2 g/day strontium ranelate for 10 years, compared with a matched control group of 458 women drawn from a pivotal trial of strontium ranelate.

Disclosures: The SOTI and TROPOS trials were funded by Servier, which markets strontium ranelate (Protelos). Dr. Reginster reported financial relationships with Amgen, Analis, Bristol-Myers Squibb, Ebewe, Genévrier, GlaxoSmith-Kline, IBSA, Eli Lilly, Merck Sharp & Dohme, Merckle, Negma, Novartis, Novo Nordisk, NPS Pharmaceuticals, Nycomed, Roche, Rottapharm, Servier, Teijin, Teva, Theramex, Wyeth, UCB, and Zodiac.

Strontium maintained its efficacy over 10 years "probably because of its mechanism of action, a dual action," Dr. Reginster said in an interview.

"With bisphosphonates you reduce bone resorption. With strontium ranelate you reduce bone resorption by 20%-25%, and you increase bone formation by 20%-25%, so you bring the bone back to what you see in younger women. I think it is a more physiologic approach" than treatment with a bisphosphonate.

In addition, "safety is most important to me when you treat for 10 years. One of the biggest advantages of strontium ranelate is that it is a very safe drug, with little risk of adverse effects over time. I think that calculating the risk/benefit ratio of a drug over time is very important."

In his report, Dr. Reginster emphasized that the women maintained on the drug for 10 years did not have a single episode of atypical fracture, osteonecrosis of the jaw, or atrial fibrillation, and their adverse-event profile showed better safety than in the original, pivotal trials of strontium ranelate.

He also noted that while the extension included only 233 women on the drug, registry data on about one million patients who have taken the drug also show no reported cases of atypical fracture, osteonecrosis of the jaw, or atrial fibrillation.

The 233 women followed for 10 years on continuous strontium ranelate treatment came from either of the two pivotal, 5-year trials of the drug: the Treatment of Peripheral Osteoporosis Study (TROPOS) (J. Clin. Endocrinol. Met. 2005;90:2816-22), and the Spinal Osteoporosis Therapeutic Intervention (SOTI) trial (New. Engl. J. Med. 2004;350:459-68).

They continued to receive 2 g/day strontium ranelate, and 73% of the women completed the full extension period. Their average duration of drug use was 9.8 years, and their average compliance with the regimen was 89%.

During their additional 5 years on the drug, average lumbar spine bone mineral density continued to rise, increasing from about 20% above baseline at the start of the extension to about 27% above baseline at 10 years.

To assess the efficacy of treatment for preventing vertebral and nonvertebral fractures, Dr. Reginster and his associates "rebuilt" a control population by selecting placebo patients from the TROPOS trial who matched the 233 extended-treatment women based on their baseline Fracture Risk Assessment scores.

The researchers matched two TROPOS placebo-group women with each woman in the extension study, assembling a total of 458 controls.

The incidence of vertebral fractures during years 5-10 in the women on strontium ranelate was 21%, compared with a 28% rate in the rebuilt control group, a statistically significant difference.

In addition, the 21% reduction during the 5 to 10-year period was statistically similar to the 19% vertebral fracture rate among women treated during 0-5 years in SOTI.

The incidence of nonvertebral fractures during years 5-10 with strontium ranelate was 14%, significantly less than the 20% rate in the derived placebo group and statistically similar to the 13% rate seen in TROPOS, Dr. Reginster reported. ■

Gastric Bypass May Increase Long-Term Fracture Risk

BY KERRI WACHTER

FROM THE ANNUAL MEETING OF THE ENDOCRINE SOCIETY

BOSTON – Gastric bypass surgery appears to be linked to increased long-term fracture risk, based on a retrospective study of 258 bariatric surgery patients.

"Bariatric surgery results in an increased risk of fractures. We think the important take-home point here is that we need to start looking at the skeleton as one of those key areas for long-term follow-up," Dr. Kurt Kennel said at the meeting.

The fracture risk for bariatric surgery patients in this study was 2.3 times greater than that for individuals who did not have bariatric surgery, reported Dr. Kennel of the endocrinology department at the Mayo Clinic in Rochester, Minn.

"We have questions about what this means in the long term," said Dr. Kennel. In this study, the mean time to first fracture was 6 years, with a mean follow-up of 9 years. However, in much of the current literature on bariatric surgery, patients are followed only 1-2 years and the only issues addressed are related to surgery or weight.

"Some issues – like bone, for example – may not show the manifestations of these effects for many years and therefore we may be missing some of those effects," said Dr. Kennel.

VITALS

Major Finding: The fracture risk for gastric bypass surgery patients was 2.3-fold greater than that for the general population.

Data Source: A retrospective study of 258 patients who underwent bariatric surgery between 1985 and 2004.

Disclosures: Dr. Kennel reported that he and his coinvestigators have no significant financial relationships to report.

The researchers used data from the Rochester Epidemiology Project to conduct a retrospective study of fracture incidence. REP connects medical records from the Mayo Clinic, local hospitals, and local private practices. The study included data from 258 patients, who underwent a first bariatric surgery between 1985 and 2004 at the Mayo Clinic.

Fractures were expressed in standardized incidence ratios that compare the number of observed fractures to the number of expected fractures by skeletal site.

Expected fracture data were derived by applying age- and sex-specific incidence rates from the local population to the age- and sex-specific person-years of follow-up.

The average age of the bariatric surgery patients was 44 years and most (83%) were female. Following bariatric surgery, 79 patients experienced 132 fractures.

Bariatric surgery patients had an increased risk of fracture at nearly all of the skeletal sites studied, not just in weight-bearing bones.

Also of note, 94% of these patients had undergone gastric bypass procedures. Dr. Kennel attributed this to the time frame used in the study.

Other bariatric surgical procedures – such as adjustable gastric banding and sleeve gastrectomy – are more recent developments. Dr. Kennel acknowledged that different bariatric procedures might yield different fracture risks.

The increased rate of fractures "suggests that structural and biochemical changes in bone that are observed after bariatric surgery are clinically important.

Clinicians should discuss bone health with patients who have undergone or are considering bariatric surgery." ■