**THERAPEUTICS**

**Strontium ranelate reduced the risk of vertebral fractures in postmenopausal women with osteoporosis**


Clinical impact ratings GP/FP/Primary care ★★★★★★ Geriatrics ★★★★★★ Rheumatology ★★★★★★

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In postmenopausal women with osteoporosis, is strontium ranelate more effective than placebo for reducing the risk of vertebral fractures?

**METHODS**

- **Design**: randomised controlled trial.
- **Allocation**: unclear.*
- **Blinding**: blinded (patients and healthcare providers)*
- **Follow up period**: 3 years.
- **Setting**: 72 centres in 11 European countries and Australia.
- **Patients**: 1649 women who were ≥50 years of age (mean age 69 y) and had been postmenopausal for ≥5 years, had ≥1 fracture confirmed by spinal radiography, and had a lumbar spine bone mineral density (BMD) < 0.840 g/cm². Exclusion criteria were severe diseases or conditions that could interfere with bone metabolism or use of antosteoporotic treatments (fluoride salts and bisphosphonates, oestrogen, calcium, or calcitonin).
- **Intervention**: all patients received daily calcium supplements (< 1000 mg, depending on dietary intake) at lunchtime to maintain a daily intake ≥1500 mg, and vitamin D (400–800 IU, depending on baseline serum concentration of 25-hydroxyvitamin D). After a run in period of 2–24 weeks, patients were allocated to strontium ranelate, 2 g/day (powder mixed with water) (n = 828) or placebo powder (n = 821) for 3 years.
- **Outcomes**: new vertebral fractures (a vertebral score change > 1 cm), non-vertebral fractures, and bone mineral density (BMD) at the lumbar spine and proximal femur.
- **Patient follow up**: 87% (intention to treat analysis).

**MAIN RESULTS**

Fewer patients who received strontium ranelate had new vertebral fractures and vertebral height loss of >1 cm than patients who received placebo (table). Patients in the treatment group also had increased BMD at the lumbar spine, femoral neck, and total hip (mean percent change from baseline 14.4%, 8.3%, and 9.8%, respectively; p<0.001). The groups did not differ for non-vertebral fracture (table) or adverse events.

**CONCLUSION**

In postmenopausal women with osteoporosis, strontium ranelate reduced the risk of vertebral fractures.

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<table>
<thead>
<tr>
<th>Outcomes at 3 years</th>
<th>Strontium</th>
<th>Placebo</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New vertebral fracture</td>
<td>21%</td>
<td>33%</td>
<td>36% (24 to 47)</td>
<td>9 (7 to 14)</td>
</tr>
<tr>
<td>Vertebral height loss &gt;1 cm</td>
<td>30%</td>
<td>37.5%</td>
<td>20% (7 to 31)</td>
<td>14 (9 to 40)</td>
</tr>
<tr>
<td>Non-vertebral fracture</td>
<td>16%</td>
<td>17%</td>
<td>8% (17 to 27)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article.

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**Commentary**

Strontium was originally identified in lead mines near Strontian, Scotland in the late 1700s. It was used to treat osteoporosis in the 1950s but was found to cause unacceptable mineralisation defects due to the high doses used at the time.

A renewed interest now exists in strontium ranelate, which increases bone formation and decreases bone resorption. 4 major trials have examined strontium ranelate for the treatment of postmenopausal osteoporosis. 2 dose finding trials, PREVOS1 and SOTI2 (with a total sample of >500 women), showed that strontium ranelate increased corrected lumbar spine BMD in a dose dependent manner over 2 years (BMD must be corrected because strontium causes a false elevation in BMD as measured by DEXA).

The current 3 year trial by Meunier et al showed that 2 g daily of oral strontium ranelate reduced morphometric vertebral fractures by 47% (number needed to treat [NNT] = 17) at 1 year and by 36% (NNT = 9) by 3 years. These results indicate efficacy that is comparable to but not remarkably better than currently available osteoporosis agents. A large ongoing trial is examining the efficacy of strontium ranelate in preventing hip fractures in postmenopausal women with osteoporosis, and preliminary results are promising.3

Potential side effects of strontium ranelate include diarrhoea and asymptomatic transient increase in creatine kinase. However, before strontium can become an attractive treatment option for osteoporosis, studies of its long term safety, effectiveness, and cost effectiveness relative to other agents are needed.

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