Is sodium fluoride effective for advanced osteoporosis?

RUBIN C, PAK C, ADAMS-HUET B, ET AL. SUSTAINED-RELEASE SODIUM FLUORIDE IN THE TREATMENT OF THE ELDERLY WITH ESTABLISHED OSTEOPOROSIS. *ARCH INTERN MED.* 2001; 161:2325-2333.

BACKGROUND: We ascertained the safety and efficacy of fluoride in augmenting spinal bone mass and reducing spinal fractures in older women with established osteoporosis. We compared a combination of sustained-release sodium fluoride, calcium citrate, and cholecalciferol (SR-NaF group) with calcium and cholecalciferol alone (control group).

METHODS: Eighty-five ambulatory women aged 65 years or older with 1 or more nontraumatic vertebral compression fractures were enrolled in a 42-month, randomized, double-blind, placebo-controlled trial. Primary outcome measures were vertebral fracture rate, bone mass, and safety.

RESULTS: The vertebral fracture rate determined by means of computer assistance in the SR-NaF group was significantly lower than that in the control group (relative risk [RR], 0.32; 95% confidence interval [CI], 0.14-0.73; *P*=.007). Results of visual adjudicated inspection also confirmed a significant reduction in fracture rate (RR, 0.40; 95% CI, 0.17-0.95; *P*=.04). Bone mineral density in L2 through L4 increased significantly from baseline in the SR-NaF group by 5.4% (95% CI, 2.7%-8.2%; *P*<.001), and by 3.2% in the control group (95% CI, 0.8%-5.6%; *P*=.01). The between-group differences in bone mineral density were not significant. The femoral neck and total hip bone mineral density remained stable in the Sr-NaF group and was not significantly different from that of the control group. There were no significant differences in adverse effects between groups.

CONCLUSION: The SR-NaF group significantly decreased the risk for vertebral fractures and increased spinal bone mass without reducing bone mass at the femoral neck and total hip.

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EXPERT COMMENTARY: As our patient population continues to age, prevention of osteoporotic fractures presents an increasing challenge for Ob/Gyns. In the past, sodium fluoride was widely used to treat osteoporosis. However, side effects such as joint pain and swelling caused patients to abandon its use. Previous studies of women treated with high and/or continuous doses of fluoride also were discouraging. While increased bone mineral density was observed, the agent failed to lower the risk of vertebral fractures. Furthermore, the risk of nonvertebral fractures appeared to increase with continuous fluoride treatment.

In contrast, the study's authors found that the twice daily administration of low-dose sodium fluoride, combined with calcium citrate (945 mg/day) and vitamin D (600 IU/day), prevented recurrent vertebral fractures by stimulating new bone formation. (Sodium fluoride is known to spur mitosis of bone-forming cells while calcium and vitamin D suppress parathyroid function and reduce bone turnover.) No participants discontinued taking the sodium fluoride due to adverse effects. The key to this study's success was the intermittent dosing regimen, i.e., 12 months of therapy and then 2 months off, which may lessen side effects and prevent the accumulation of sodium fluoride in the bones.

THE BOTTOM LINE: Although anabolic agents such as sodium fluoride would be highly desirable for patients with severe osteoporosis, no such therapies have been approved by the FDA. However, if larger studies confirm these favorable findings, administering intermittent low doses of sodium fluoride may emerge as an important new treatment option for patients with advanced osteoporosis.

In the meantime, daily subcutaneous injections of parathyroid hormone are a promising alternative to bone-forming treatment.[1]

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REFERENCE

1. Neer RM, Arnaud CD, Zanchetta JR, et al. Effect of parathyroid hormone on fractures and bone mineral density in postmenopausal women with osteoporosis. *N Engl J Med.* 2001;344:1434-1441.