

WATERBORNE FLUORIDE AND BONE FRACTURES

Although the relationship between fluoride in drinking water and bone fractures in humans has been studied for many years, our knowledge of the subject, especially at lower levels of intake, is still far from complete.¹ In this issue of *Fluoride* are reports of three new, large-scale investigations of this relationship in three different countries:

- (1) In Mexico, a cross-sectional representative survey of the 418,504 residents of the Guadiana Valley in the State of Durango disclosed higher rates of bone fractures in both children and adults that were associated with the prevalence and severity of dental fluorosis as well as increasing levels of fluoride in the drinking water.²
- (2) In China, an investigation that included 8266 men and women age 50 and over residing in six different localities revealed a significantly lower bone fracture (but not hip fracture) rate connected with 1.00-1.06 ppm fluoride in the drinking water.³ Below 0.34 ppm and above 4.32 ppm fluoride, the overall fracture rate was higher. Between 1.75 and 4.6 ppm, the hip fracture rate doubled, and between 4.6 and 7.97 ppm it tripled.
- (3) In the United States, a study compared bone mineral density and risk of bone fracture among 7129 elderly white women who had resided continuously for at least 20 years in a fluoridated, a non-fluoridated, or a partially fluoridated community.⁴ In this study, but only after multivariable adjustments of the data, fluoridation was concluded to be associated with a significant lowering of hip fracture rates and an almost significant trend toward increased risk of wrist fracture.

Since bone fractures often cause serious disablement, especially among the elderly, all three of these reports deserve careful study. The first two basically agree in their findings, and they raise concern about what appears to be a direct connection between increased risk of bone fracture and higher levels of fluoride in drinking water. The report from Mexico, moreover, presents new data showing that bone fracture rates are also higher in children with dental fluorosis due to early intake of toxic levels of fluoride.

The third report by Kathy R Phipps *et al.*,⁴ is one of the various studies on fluoride and hip fractures that I examined last year as part of my peer evaluation of the University of York Review of Water Fluoridation.⁵ As reported in the York Review and independently in another recent review,⁶ about half of the known studies purport to indicate increases in rates of hip

fracture while the other half claim decreases. The Phipps findings fall into the latter category, and they included a wide range of multivariable adjustments that were considered by the York team in their meta-analysis of bone fracture data. I understand Dr Phipps also gave testimony in person to the panel. Therefore it may not be coincidental that her paper appeared in the same 7 October 2000 issue of the *British Medical Journal* in which a summary of the York review also appeared.⁷

Unlike many previous investigations, the Phipps study included bone density measurements. Using data “adjusted for age and other variables,” it showed that women with continuous exposure to fluoridated water for at least 20 years had “significantly higher bone density of the lumbar spine, femoral neck, and trochanter, but significantly lower density of the [distal] radius” compared to women with no history of exposure to fluoridated water. Although bone fluoride levels were not determined, higher bone mineral density, which is often (but not always) the result of increased fluoride intake, does not necessarily mean stronger bones. Under certain conditions fluoride produces abnormal, weaker bones that may have increased compression strength but not tensile or torsional strength.^{1,8}

In the Phipps study, using only age adjustment, the hip fracture rate, although down by 15% in the continuously exposed fluoride group, was not significantly lower than in the nonexposed group ($P = 0.287$). The age-adjusted wrist fracture rate, on the other hand, was 36% higher in the continuously exposed group, which was statistically significant ($P = 0.012$). However, when multivariable adjustments for a dozen other factors besides age were applied, the hip fracture rate was then 31% lower and statistically significant in the continuously exposed group ($P = 0.028$ with a confidence interval of 0.50 to 0.96), while the wrist fracture rate became almost, but not quite, formally significant as its increase was reduced from 36 to 32% ($P = 0.051$ with a confidence interval of 1.00 to 1.71). Curiously, in the York Review, this interval, based on what the panel had received from Dr Phipps, was given as 1.02-1.71, which *is* statistically significant.

Among the individual characteristics that were considered, many of them favored lower fracture rates among women in the continuous exposure group, thereby making adjustments for them tenuous and uncertain. These characteristics of the 3218 women in this group, in comparison to the 2563 women with no history of exposure to fluoridated water, included the following statistically significant differences in the final tabulation: mean age (73.9 vs 74.5 years); (b) mean body weight (66.5 vs 68.5 kg); (c) education beyond the 12th grade (45.1 vs 33.0%); (d) grip strength (21.5 vs 21.0 kg); (e) surgical menopause (11.5 vs 15.2%); and mean calcium intake (5189 vs 4733 mg/week or 9.6% higher). Current estrogen use, which retards bone loss, was also greater, but not statistically so, among the fluoride-exposed

women (20.4 vs 18.8%). Pre-menopausal exposure, which could also affect the results,¹ was not considered.

With respect to estrogen use, the Phipps study, like so many other similar surveys, did not determine or even consider non-protein-bound progesterone as one of the key factors for optimal bone strength in women. Sufficient circulating levels of “free”, bioavailable progesterone in women (and testosterone in men) are not only important for increasing the sensitivity of estrogen receptors to retard bone loss but also for stimulating normal bone growth.¹

In contrast to the Phipps study, the subjects of the surveys in both Mexico² and China³ were relatively homogeneous demographically and geographically. In the Phipps study, however, they were drawn from widely separated regions of the United States: Portland, Oregon for the nonfluoridated group; Minneapolis, Minnesota, and Baltimore, Maryland for the continuously fluoridated group; and the Monongahela Valley in Pennsylvania for the partially or mixed fluoridated group. Since dental surveys have shown there are significant differences in caries rates among these regions quite apart from their fluoride status, the likelihood of similar nonfluoride-related differences in bone fracture rates must be recognized. Even in the study by Li *et al.*,³ the selection of the six particular localities for comparisons, unless all relevant variables were nearly identical, might in part account for their finding of the lowest overall fracture rate in association with 1.00-1.06 ppm fluoride in the drinking water. As already noted, however, the Li study did find progressively higher hip fracture rates as water fluoride levels increased from 1.5 to 8.0 ppm, but this fact was not cited in the York Review.⁵

Finally, one must be concerned about evidence of underlying bias in the Phipps report. Although hip fractures are a very serious, major medical problem, the trend toward increased wrist fractures in the continuously exposed fluoride group after multivariable adjustments was so close to being statistically significant that its importance should not have been minimized. Moreover, it is clear in both the Introduction and the Conclusion of the Phipps report that the authors did not acknowledge the existence of strong and substantial evidence, recognized by the York Review⁵ (but not in its official summary⁷), that water fluoridation is relatively ineffective in reducing dental caries and that various aspects of its medical safety remain seriously in question.

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