International Journal of Epidemiology

Vol. 24, No. 6
Printed in Great Britain

# Fluoride in Drinking Water and the Bone Mineral Density of Women in Taiwan

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Lan C-F (Graduate Institute of Public Health, National Yang-Ming University, 155 Li-Long St., Sec 2, Pei-Tou, Taipei 112, Taiwan ROC), Lin I-F and Wang S-J. Fluoride in drinking water and the bone mineral density of women in Taiwan. *International Journal of Epidemiology* 1995; **24:** 1182–1187.

*Background.* The current evidence on effect of fluoridation in drinking water on bone is inconsistent. This study was undertaken to assess the effect of fluoride concentration in drinking water on bone mineral density (BMD) in Taiwanese women.

*Methods.* The study subjects included 248 women aged ≥40 years who reside in naturally fluoridated and adjacent areas. The individual fluoride concentration of the drinking water and the BMD of the subjects' lumbar spines were assessed.

*Results.* Women aged 46–65 years living in areas which have fluoride levels <0.6 mg/l (mean = 0.18 mg/l; n = 130) had slightly lower bone densities than women living in areas with levels ≥0.6 mg/l (mean 0.98 mg/l, n = 118). Only the age groups 46–50 and 61–65 years proved to be statistically significant. After controlling for age and body mass index, the BMD of those who had a dose ≥1.0 mg/l is notably higher than the reference group (<0.6 mg/l). After stratification by menopausal status, fluoride appeared to have no association with bone density in postmenopausal women.

*Conclusions.* The BMD of the subjects from the area with a fluoride dose >1 mg/l were significantly higher than those from the reference group (fluoride <0.6 mg/l) for premenopausal women. There is no significant association between BMD and fluoride for postmenopausal women in Taiwan.

*Keywords*: bone mineral density, fluoridation

Drinking water, whether artificially fluoridated or not, can make an important contribution to the total daily fluoride intake.[1] For more than 30 years, the practice of adding fluoride to drinking water has been carried out in many areas of the world for the reduction of dental caries.[2–4] The effect of fluorides on bone tissue has also been shown in several studies, and the results were conflicting. Some researchers found that the incidence of bone fragility was less in fluoridated (1 mg/l) or high-fluoride (4–6 mg/l) areas than in low-fluoride areas;[5–7] some studies failed to detect an effect for fracture;[8,9] and most ecologic studies have shown an increased risk of fracture associated with fluoridation.[10–13]

In Taiwan, water fluoridation is a controversial issue, and the only fluoridation programme was terminated in 1984.[14,15] A large portion of the west coast of Taiwan is, however, naturally fluoridated with a high prevalence of mottled enamel among adolescents. This has lead to several studies on the effects of fluoride on teeth.[16–19] No study on the effects of fluoride in drinking water on bone has been reported in Taiwan. Our study was set up to find out if the dosage of fluoride sufficient to be associated with mottling of teeth has an effect on bone. Bone mass is the primary, although not the only, determinant of fracture risk. In this study we assessed the effect of fluoride in drinking water and related covariates on bone mineral densities (BMD) in Taiwanese women.

## MATERIALS AND METHODS

### *Study Population and Laboratory Measurements*

The study area, Longing Shiang, is rural and lies at the extension of the Chia-Nan coastal plain where the people are mainly of Fujien descent. This area can be divided into two parts, the coastal area and the hill area. According to our earlier survey fluoride concentration in drinking water is generally higher along the coast (0.771 ± 0.593 mg/l) and lower in the hills (0.105 ± 0.15 mg/l). Several studies on the relationship between dental mottling and fluoride in drinking water have been conducted in this area. In all, 35–42% of junior high students in Longing suffered from mottled teeth.[17,18]

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Most of the students affected were from the coastal area which has higher levels of natural fluoridation.

The subjects in this study were residents of the community aged >40 years, who participated from January to August 1990. Three 'Chuns' (the smaller unit of a rural district) out of 14 were selected. The selected Chuns included both coastal and hilly areas. Subjects were selected at random and then stratified by age group. Households were selected from the government's residents' list by a systematic random sampling procedure and a resident >40 years old was then chosen. If there was no eligible person or compliance could not be obtained, someone from the next door household was selected.

Samples of the drinking water for each subject were obtained by trained public health nurses. The samples were then sent to a local medical college laboratory for quantification of the fluoride concentration using the Electrode Method.[20]

The BMD of the lumbar spine region for each subject was measured by Dual-Photon Absorptiometry (DPA). The results of measurement of the second, third, and fourth lumbar vertebrae were expressed as grams of hydroxyapatite divided by the projected area of the vertebrae in square centimetres. Quality control was performed by scanning an aluminium reference rod daily and scanning a three-step phantom weekly. The measurements had an accuracy of 95% and a reproducibility of 97%. For serial measurements the position of the region of interest was carefully duplicated. Neither the subjects nor the technician knew the fluoride concentration until the end of the study. Data on the demography, dietary and exercise habits, existing disease and use of medication were collected using a structured questionnaire. One technician carried out the BMD measurements and questionnaire interviews in this study. Since the number of males who were willing to participate was insufficient to compare the stratified BMD to other covariates, this paper only includes the 248 females.

### *Statistical Analyses*

Since no significant linear trend was found between BMD and fluoride among subjects in the <0.6 mg/l group, we arbitrarily used 0.6 mg/l as the cutoff point. Less than 0.6 mg/l served as the reference group for comparing the bone density between the different fluoride concentration groups in the later analyses. The average fluoride concentration was 0.18 mg/l (SD = 0.17) in the <0.6 mg/l fluoride group (n = 130) and 0.98 mg/l (SD = 0.35) in the ≥0.6 mg/l fluoride group (n = 118). The two-sample t-test was used in the primary analysis which compared the difference between the two fluoride groups, stratified by 5-year age intervals.

The association between BMD and each of the selected non-fluoride variables were compared using Pearson's correlation coefficient for continuous variables and by ANOVA for categorical variables. Dietary data were originally scaled according to responses: every day, very frequently, occasionally (less than once per week), and never. The first two responses were then categorized as 'frequent' and coded as 1; the latter two as 'infrequent' and coded 0 in the analysis. If bivariate analysis indicated a factor to be associated with BMD, that factor was considered to be a potential confounder of the association between fluoride and BMD and they were assessed using the multivariate analyses.

To assess which level of concentration in the high fluoride group affected the mean BMD, given the low fluoride group as the baseline and after controlling for other important covariates, the subjects were further broken down into fluoride concentrations of 0.6–0.8, 0.8–1.0, and ≥1.0 mg/l. The multiple linear regression technique with dummy variables was used to compare the relative change of the mean BMD density among the different fluoride concentration groups after adjusting for selected variables. Interaction terms were examined in the process of regression analysis. All $P$ values were two sided. Statistical analyses were performed using the Statistical Analysis System Software Package (SAS Institute, Cary, North Carolina).

## RESULTS

The sociodemographic characteristics of the study subjects including age, body mass index (BMI), years of residence, tea consumption, seaweed diet, and occupation are shown in Table 1. Over 95% of the subjects living in this area have drunk ground water for more than 10 years. Our exploratory bivariate analysis showed that age was negatively ($r = -0.6$, $P = 0.0001$), and BMI was positively ($r = 0.272$, $P = 0.0001$), related to an increase in BMD at the lumbar spine region. Both of the above variables were considered to be potential confounders of the relationship between fluoride in the drinking water and BMD. No statistically significant differences in BMD were found in relation to the other four variables. In addition, over 99% were non-smokers, and 99% were non-alcohol drinkers. Only one woman claimed to have ever used oestrogen. These variables were not considered to be confounders.

Figure 1 shows the distribution of BMD in the lumbar spine by 5-year intervals of age and by fluoride concentration (0.6 mg/l as the cutoff point). The two-sample t-test identified a significant difference between

TABLE 1 *Selected characteristics of the Study Subjects in Longing Shiang, Taiwan (n = 248)*

| Characteristics | Frequency (%) | Mean BMD | Mean BMDa[a] |
|---|---|---|---|
| Age (years) | | | |
| 40–45 | 33 (13.3) | 1.334 | |
| 46–50 | 38 (15.3) | 1.236 | |
| 51–55 | 45 (18.1) | 1.203 | |
| 56–60 | 46 (18.5) | 1.119 | |
| 61–65 | 37 (14.9) | 1.079 | |
| ≥65 | 49 (19.8) | 1.026 | |
| Body mass index (BMI) | | | |
| <22 | 43 (17.3) | 1.061 | 1.066 |
| ≥22, <25 | 89 (35.9) | 1.142 | 1.133 |
| ≥25, <27 | 42 (16.9) | 1.202 | 1.214 |
| ≥27 | 74 (29.8) | 1.204 | 1.204 |
| Years of residence | | | |
| <10 | 5 (2.0) | 1.141 | 1.155 |
| 10–30 | 61 (24.6) | 1.250 | 1.166 |
| >30 | 182 (73.4) | 1.126 | 1.153 |
| Tea consumption | | | |
| Frequent | 69 (27.8) | 1.150 | 1.135 |
| Infrequent | 179 (72.2) | 1.159 | 1.165 |
| Seaweed diet | | | |
| Frequent | 28 (11.3) | 1.165 | 1.153 |
| Infrequent | 220 (88.7) | 1.155 | 1.157 |
| Occupation | | | |
| Housewife | 163 (65.7) | 1.155 | 1.160 |
| Farming & fishing | 73 (29.4) | 1.139 | 1.140 |
| Others | 12 (4.8) | 1.287 | 1.212 |

[a] Mean BMD in different BMI groups was adjusted for age; the mean BMD of other variables were adjusted for age and BMI. Except for age and BMI, differences of BMD among levels of each of the other covariates were not statistically significant.

fluoride groups in the age groups 46–50 and 61–65. The Wilcoxon rank sum test also found similar results. The differences in BMD in the 51–55 and 56–60 years age groups were not statistically significant, although slight increases were observed in the ≥0.6 mg/l groups. The mean BMD were very similar between fluoride groups in both the 40–45 and >65 years age groups.

In Table 2, fluoride concentrations of ≥1 mg/l resulted in an 0.061 g/cm$^2$ increase in the mean BMD ($P$ = 0.0085) in the lumbar spine region while concentrations of 0.6–0.8, and 0.8–1.0 had almost no effect when compared to the reference group (<0.6 mg/l) after controlling for age and BMI. After stratification according to their menopausal status, these trends held true for perimenopausal women but there was no fluoride effect on BMD in postmenopausal women. There was no evidence of interactions among fluoride groups with other covariates because when interaction terms were added to the models, they were not found to be significant at $\alpha$ = 0.05 level.

## DISCUSSION

Our study indicates that fluoride has a slight positive effect on the mean BMD of the lumbar spine region among 46–65 year old women. If we compare the BMD of the women from Longing Shiang with those from Linkou Shiang, which is a township near the capital, Taipei, where the residents drink public tap water (fluoride concentration mean = 0.085, SD = 0.026, based on 30 sample points), the BMD from the higher fluoride group (fluoride concentration 0.98 ± 0.35 mg/l) were still slightly higher than the other two areas in the 46–65 year age group. The differences were not statistically significant (Table 3). There is now substantial evidence from pharmacological studies that fluoride at higher doses results in a marked increase in BMD in the lumbar spine at the expense of cortical bone density from peripheral sites.[21–24] Most of the studies reviewed the incidence of hip fractures and our study measured lumbar spine bone density which is predominantly cancellous bone.

A possible explanation for the statistically non-significant differences is that both fluoride groups have really low levels of fluoride (on average <2 mg/l) in the drinking water. The small sample sizes after stratifying the groups by age may also be a reason. According to a study in Linkou,[25] mean bone density in women reached its peak between ages of 40 and 45, declined significantly after 45, and the rate of change slowed down after age 65. As bone density does not change substantially at ages >65 or <40 years, from a statistical point of view, it is difficult for fluoride to play a significant role during this period.

In our study, most households had used private ground water for more than a decade. Fluoride levels may differ markedly from well to well, even among next-door neighbours. We do have individual data for fluoride concentration in drinking water available, i.e. the fluoride concentration has been measured for each subject. Dividing the subjects into two groups, >0.6 mg/l and <0.6 mg/l, instead of treating fluoride concentration as a continuous variable was done for two reasons. First, our data showed that the relationship between fluoride and BMD was not linear at this low level. Given the strong effects of age and BMI, it is hard to show this relationship with a two-dimensional scatter plot between fluoride and BMD. The correlation coefficient for fluoride concentration and BMD alone was r = 0.111, $P$-value = 0.08. Second, from the public health perspective, one of our major concerns was to determine if different fluoride concentrations (e.g. 0.6–0.8, 0.8–1.0, and >1.0 mg/l versus <0.6 mg/l fluoride concentration) have different effects on BMD rather than just looking at a unit change in fluoride concentration.

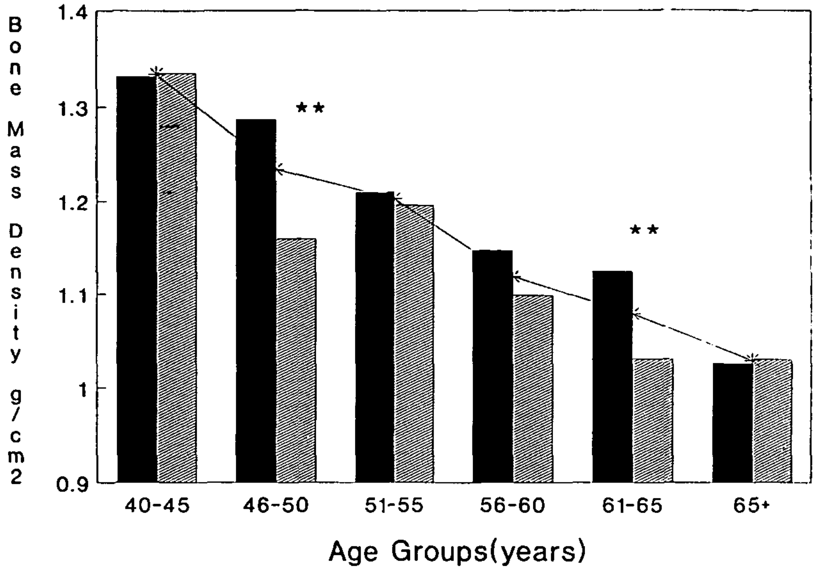


FIGURE 1 *Distribution of mean bone mineral density by age group and fluoride concentration among 248 women in Longing Shiang.*

Fluoride 0.98 ± 0.35 mg/l;
Fluoride 0.18 ± 0.17 mg/l;
—✱— Overall;
** $P < 0.05$

Fluoride impact on bone may vary not only according to dose, but also according to climate (temperature).[26,27] One of the limitations of this study is that daily water consumption was not precisely quantified. Our study area (Middle Taiwan) is subtropical while other studies of fluoride and fractures based on a comparison of geographical areas with various levels of fluoride in their water supplies have been conducted in temperate areas. The optimal concentration to prevent dental caries in western countries is 1 mg/l while in middle Taiwan it is 0.6 mg/l for artificial fluoridation in drinking water.[14] When one compares the results with those of other studies, the fluoride concentration 0.98 mg/l (average dosage in higher fluoride area) in our study could actually have a greater impact than the dose suggests.

Another limitation regarding the level of exposure to fluoride is duration of residence. Although the duration of residence was obtained, no information was available on fluoride intake prior to moving into the area for any recent immigrants. However, the majority of study subjects (98%) have resided in the same area for more than 10 years (Table 1) with a strong correlation between years of residence and age ($r = 0.52$, $P$-value = 0.0001). Fluoride concentration in the drinking water was assumed to be unchanged over recent decades in this cross-sectional study.

Hypo-oestrogenism following menopause can reduce bone mass and is the most common cause of osteoporosis. It has been suggested that ovarian failure is associated with increased movement of calcium into and out of the skeleton and that the increase in calcium loss exceeds accrual, leading to a net loss of bone.[28–31] We found that the fluoride effect (≥1 mg/l versus the reference <0.6 mg/l) on BMD was non-significant for postmenopausal women. Also fluoride has the strongest effect on lumbar bone density in the 46–50 year age group. The fluoride dosage is considered as a 'weak association'. Stronger associations for prevention of disease are usually well demonstrated in high-risk populations.[32] The association between fluoride and bone density was stronger in perimenopausal women where bone density may change through other mechanisms such as an oestrogen effect. The two most dominant factors contributing to variable bone density are age (years since menopause) and BMI in postmenopausal women. Fluoride concentration ≥1 mg/l does not play an important role for postmenopausal women in our study.

Although good correlation exists between bone mass and bone strength, increased bone mass is not necessarily translated into a reduction in fracture incidence. In this study, lumbar spine bone density alone was measured. In the large Mayo Clinic study,[21] there was a

TABLE 2 *Comparisons of mean bone mineral density (BMD) according to fluoride concentration in drinking water in Longing Shiang, Taiwan*

| | Fluoride concentration (mg/l) | Sample size | Mean BMD | Mean BMDa[a] | *P*-value[b] |
|---|---|---|---|---|---|
| All ages | <0.6 | 130 | 1.133 | 1.144 | (reference) |
| (n = 248) | ≥0.6, <0.8 | 47 | 1.143 | 1.145 | 0.9719 |
| | ≥0.8, <1.0 | 30 | 1.202 | 1.163 | 0.4761 |
| | ≥1.0 | 41 | 1.212 | 1.205 | 0.0085 |
| Premenopause | <0.6 | 43 | 1.233 | 1.222 | (reference) |
| (n = 98) | ≥0.6, <0.8 | 20 | 1.213 | 1.243 | 0.5903 |
| | ≥0.8, <1.0 | 19 | 1.276 | 1.276 | 0.1819 |
| | ≥1.0 | 16 | 1.342 | 1.335 | 0.0090 |
| Postmenopause | <0.6 | 87 | 1.084 | 1.088 | (reference) |
| (n = 150) | ≥0.6, <0.8 | 27 | 1.092 | 1.076 | 0.9175 |
| | ≥0.8, <1.0 | 11 | 1.074 | 1.088 | 0.7562 |
| | ≥1.0 | 25 | 1.129 | 1.122 | 0.1957 |

[a] Adjusted for age and BMI.

[b] Three dummy variables served for fluoride concentration 0.6–0.8, 0.8–1.0, and ≥1.0 mg/l groups respectively as compared with the referent group (fluoride concentration <0.6 mg/l)

TABLE 3 *Comparison of bone mineral density by age group among Longing and Linkou Shiang*

| Age | Longing Shiang | | | | | | Linkou Shiang | | |
|---|---|---|---|---|---|---|---|---|---|
| | Higher fluoride 0.98 ± 0.35 mg/l | | | Lower fluoride 0.18 ± 0.17 mg/l | | | Public supplied water 0.085 ± 0.026 mg/l | | |
| | n | mean | SD | n | mean | SD | n | mean | SD |
| 40–45 | 14 | 1.322 | 0.098 | 19 | 1.335 | 0.153 | 25 | 1.323 | 0.157 |
| 46–50 | 22 | 1.288 | 0.163 | 16 | 1.159 | 0.165 | 26 | 1.199 | 0.178 |
| 51–55 | 23 | 1.210 | 0.165 | 22 | 1.196 | 0.154 | 32 | 1.177 | 0.152 |
| 56–60 | 19 | 1.147 | 0.146 | 27 | 1.099 | 0.156 | 30 | 1.068 | 0.147 |
| 61–65 | 19 | 1.125 | 0.140 | 18 | 1.031 | 0.112 | 28 | 1.081 | 0.172 |
| >65 | 21 | 1.026 | 0.070 | 28 | 1.030 | 0.093 | 22 | 0.974 | 0.152 |

30% increase in lumbar spine bone density among a group of patients who were treated with 75 mg of sodium fluoride daily, but there was no apparent change in their vertebral fracture incidence rate. This study collected a number of self-reported fractures in the women during the past 5 years. The proportions of fracture at all sites between fluoride groups did not show any significant differences (6.15% for lower and 7.64% for higher fluoride groups; $P = 0.651$). The fracture data, however, were only collected incidentally and details of the mechanism and severity of fractures were not available. The effect of fluoride at the low concentration (<2 mg/l) prevalent in Taiwan should be further studied.

Although no natural fluoridation programme is in progress in Taiwan, a large portion of the west coast is naturally fluoridated. Our study is a valuable exploration into the effects of fluoride in the drinking water as well as other important factors relating to BMD in women in Taiwan. Further studies, especially of a longitudinal nature, are still required.

## ACKNOWLEDGEMENTS

This study was supported by a grant from Ching-Ling Medical Foundation (CI-78-30). We thank the Longing Shiang Health Station of Taichung County and Jin-Jing Wu of Department of Public Health of China Medical

College for their assistance. We also thank Ms Virginia Lan of University of Michigan for her valuable suggestions.

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*(Revised version received April 1995)*