主論文の要旨

Hearing loss in humans drinking tube well water with high levels of iron in arsenic-polluted area

（ヒ素汚染地域において、高濃度の鉄を含む井戸水を摂取する人々の難聴）

名古屋大学大学院医学系研究科　総合医学専攻
社会生命科学講座　環境労働衛生学分野
（指導：加藤 昌志　教授）
何 婷超

【Background】

Well water for drinking that is contaminated with toxic elements including arsenic has been reported worldwide. High levels of iron as well as arsenic have been reported in drinking well water in some countries including Bangladesh, Vietnam and the United States. However, there is no information about the association between excessive exposure to iron in drinking water and hearing loss in humans, although oral exposure to arsenic has been shown to be associated with hearing loss in humans in our previous studies. In this study, we aimed to investigate whether exposure to iron is a risk factor for hearing loss in humans.

【Methods】

Participants were recruited from the control area (control group) and the arsenic-polluted area (exposure group) in Bangladesh by convenience sampling, a total of 145 subjects aged from 12 to 55 years including housewives, businessmen and students were included in our final analysis.

We measured hearing levels by pure tone audiometry (PTA) at 1, 4, 8 and 12 kHz to determine the auditory threshold of subjects at each frequency. We performed the test twice for both ears of each participant for repeatability of results and left ear of each subject was finally analyzed in multivariate analyses since hearing levels of both ears were comparable. In addition, hearing losses at 1, 4, 8 and 12 kHz were defined as ≥ 10 dB, ≥ 10 dB, ≥ 25 dB and ≥ 40 dB, respectively, according to previous studies.

Iron and arsenic levels in water and biological samples were measured by inductively coupled plasma mass spectrometry (ICP-MS). The Mann-Whitney *U* test was used to investigate differences of iron and hearing levels between the control and exposure groups. Finally, we used a logistic regression model to investigate the association between drinking tube well water and auditory threshold.

【Results】

The arsenic concentration in drinking well water (79.4 ± 82.8 μg/L) was significantly higher than that in piped supply water (0.6 ± 0.7 μg/L). The iron concentration in drinking well water (2,367.6 ± 2,094.7 μg/L) was also significantly higher than that in piped supply water (29.8 ± 27.1 μg/L).

The median iron concentrations in hair and toenail samples were 17.6 μg/g and 50.1 μg/g, respectively, in the control group and 50.0 μg/g and 262.6 μg/g, respectively, in the exposure group. The median concentrations of arsenic in hair and toenail samples were 0.05 μg/g and 0.4 μg/g, respectively, in the control group and 0.5 μg/g and 1.6 μg/g, respectively, in the exposure group. Both iron and arsenic levels in the exposure group were significantly higher than those in the control group for all biological samples

($P < 0.001$) (Figure 1).

In the univariate analysis, Fe level in hair showed positive correlation with hearing levels at 4 kHz (r = 0.25, p = 0.002), 8 kHz (r = 0.38, p < 0.0001) and 12 kHz (r = 0.36, p < 0.0001), Fe level in toenails showed positive correlation with hearing levels at 4 kHz (r = 0.38, p < 0.0001), 8 kHz (r = 0.53, p < 0.0001) and 12 kHz (r = 0.54, p < 0.0001). The median auditory thresholds at 4, 8, and 12 kHz in the exposure group were 10, 25, and 40 dB, respectively, and they were significantly higher than those in the control group, which is 5, 15 and 25 dB, respectively (Figure 2).

In the multivariate analysis, after adjustments for age, gender, BMI, smoking and arsenic levels, there were significant associations between the exposure group and hearing loss at 8 kHz (OR = 5.555; 95% CI: 1.440, 21.437; $P = 0.013$) and 12 kHz (OR = 3.928; 95% CI: 1.011, 15.261; $P = 0.048$) but not at 1kHz (OR = 0.675; 95% CI: 0.174, 2.612; P = 0.569) or 4 kHz (OR = 2.228; 95% CI: 0.599, 8.284; P = 0.232) in hair samples. Also, in the model, the exposure group was also associated with hearing loss at 4 kHz (OR = 4.860; 95% CI: 1.257, 18.785; P = 0.022), 8 kHz (OR = 8.301; 95% CI: 2.059, 33.457; P = 0.003) and 12 kHz (OR = 5.316; 95% CI: 1.376, 20.543; P = 0.015) but not at 1kHz (OR = 0.936; 95% CI: 0.226, 3.881; P = 0.927) in toenail samples (Table 1).

【Discussion】

In this study, iron and arsenic levels in drinking water in the arsenic-polluted area were significantly higher than those in the control area. The study also showed that the levels of iron and arsenic in hair and toenail samples from subjects in the exposure group were significantly higher than those in samples from subjects in the control group. In multivariate analysis with adjustments for age, sex, BMI, smoking and arsenic levels, significant associations between the exposure group and hearing loss were shown. Thus, this study suggested the risk of hearing loss in humans drinking tube well water with high levels of iron in an arsenic-polluted area.

It is possible that countries other than Bangladesh also have high concentrations of iron in drinking water, although iron concentrations in groundwater varied depending on geographical or aquifer features, the depth of the tube well and the sampling season. Iron levels in hair and toenails in this study were similar to those in previous studies, in which they ranged from 13.5 μg/g to 300 μg/g in hair and from 9.16 μg/g to 135 μg/g in nails. Further investigation is needed to determine the associations between hearing loss and exposure to iron via drinking well water worldwide.

Hearing levels at 4 kHz and 8 kHz are known to be important for daily conversation and examinations of noise-induced hearing loss and age-related loss, this study suggests that exposure to iron by drinking well water is may affects daily communications in humans.

The interaction effect of iron and arsenic levels in toenails and hair was also explored

to determine the synergistic influence of iron and arsenic on hearing loss. There were no significant interaction effects of iron and arsenic on hearing loss at least in the multivariate models. Therefore, it is not likely that there is synergistic influence of co-exposure to iron and arsenic on hearing loss in humans, although a previous study showed synergistic influence of co-exposure to iron and arsenic on carcinogenicity *in vitro*.

【Conclusion】

Our study provided epidemiological evidence that excessive exposure to iron by drinking well water is an independent risk of hearing loss in humans.