ABSTRACTS

NEUROLOGICAL EFFECTS IN ANIMALS

SUBCHRONIC FLUORIDE INTAKE INDUCES IMPAIRMENT IN HABITUATION AND ACTIVE AVOIDANCE TASKS IN RATS

Since clinical case reports suggest that sodium fluoride (NaF) intoxication may impair learning and memory, the objective of the present study was to evaluate the effects of NaF on two memory tasks: open-field habituation and two-way active avoidance. Adult male rats were exposed to NaF in drinking at three concentrations for 30 days: 1.54 (control, tap water), 50, and 100 ppm NaF, corresponding to an intake of 0.1±0.005, 5.15±0.14, and 10.77±0.39 mg NaF/kg bw, respectively). At day 30, the rats were placed in an open-field and retested after 24 hr (test session) to measure habituation. In the two-way active avoidance task, another three groups of rats were trained in a 30-day trial training session and tested again 24 hr later (test session). Dental fluorosis was also evaluated. Habituation was impaired by 50 and 100 ppm but not by 1.54 ppm NaF. Moreover, 100 ppm NaF reduced the number of avoidance responses in the active avoidance task. No locomotor impairment was observed. Mild dental fluorosis in rat incisor teeth was found in the 50 and 100 ppm F groups. Overall, these results suggest that moderate fluoride intoxication has potentially deleterious effects on learning and memory.

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DENTAL EFFECTS

EFFECTS OF FLUORIDE ON THE INTERACTIONS BETWEEN AMELOGENIN AND APATITE CRYSTALS

Fluorosed enamel is more porous and less mineralized, possibly related to altered amelogenin-modulated crystal growth. The purpose of this study was to examine the role of fluoride in interactions between amelogenin and apatite crystals. Recombinant human amelogenin (rh174) was bound to carbonated hydroxyapatite containing various amounts of fluoride, and analyzed by protein assay, SDS PAGE, and AFM. Interactions between rh174 and fluoride were assayed by isothermal titration calorimetry (ITC). The initial binding rate of rh174, as well as total amount of rh174 bound to fluoride-containing carbonated hydroxyapatite, was greater than that in the control carbonated hydroxyapatite. Fluoride in solution at physiologic (5.3 micromolar, or 0.1 ppm) concentrations showed no significant effect on binding, but higher fluoride levels significantly decreased protein binding. ITC showed no interactions between fluoride and rh174. These results suggest that fluoride incorporation into the crystal lattice alters the crystal surface to enhance amelogenin binding, with no direct interactions between fluoride and amelogenin.

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HEALTH/BIOLOGICAL EFFECTS IN HUMANS

EFFECTS OF TREATMENT WITH FLUORIDE ON BONE MINERAL DENSITY AND FRACTURE RISK – A META-ANALYSIS.

Fluoride has fallen into discredit due to the absence of an anti-fracture effect. However, in this meta-analysis, a fracture reducing potential was seen at low fluoride doses [</=20 mg fluoride equivalents (152 mg monofluorophosphate/44 mg sodium fluoride)]: OR= 0.3, 95% CI: 0.1-0.9 for vertebral and OR = 0.5, 95% CI: 0.3-0.8 for non-vertebral fractures. INTRODUCTION: Fluoride is incorporated into bone mineral and has an anabolic effect. However, the biomechanical competence of the newly formed bone may be reduced. METHODS: A systematic search of PubMed, Embase, and ISI Web of Science yielded 2,028 references. RESULTS: Twenty-five eligible studies were identified. Spine BMD increased 7.9%, 95% CI: 5.4-10.5%, and hip BMD 2.1%, 95% CI: 0.9-3.4%. A meta-regress ion showed increasing spine BMD with increasing treatment duration (5.04+/- 2.16%/year of treatment). Overall there was no significant effect on the risk of vertebral (OR = 0.8, 95% CI: 0.5-1.5) or non-vertebral fracture (OR = 0.8, 95% CI: 0.5-1.4). With a daily dose of </=20 mg fluoride equivalents (152 mg monofluorophosphate/44mg sodium fluoride), there was a statistically significant reduction in vertebral (OR = 0.3, 95% CI: 0.1-0.9) and non-vertebral (OR =0.5, 95% CI: 0.3-0.8) fracture risk. With a daily dose >20 mg fluoride equivalents, there was no significant reduction in

vertebral (OR = 1.3, 95% CI: 0.8-2.0) and non-vertebral (OR = 1.5,95% CI: 0.8-2.8) fracture risk. CONCLUSIONS: Fluoride treatment increases spine and hip BMD, depending on treatment duration. Overall, there was no effect on hip or spine fracture risk. However, in subgroup analyses a low fluoride dose (</=20 mg/day of fluoride equivalents) was associated with a significant reduction in fracture risk.

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RECOVERY FROM SKELETAL FLUOROSIS (AN ENIGMATIC, AMERICAN CASE).

A 52-year-old man presented with severe neck immobility and radiographic osteosclerosis. Elevated fluoride levels in serum, urine, and iliac crest bone revealed skeletal fluorosis. Nearly a decade of detailed follow-up documented considerable correction of the disorder after removal of the putative source of fluoride (toothpaste). INTRODUCTION: Skeletal fluorosis, a crippling bone disorder, is rare in the United States, but affects millions worldwide. There are no data regarding its reversibility. MATERIALS AND METHODS: A white man presented in 1996 with neck immobility and worsening joint pains of 7-year duration. Radiographs revealed axial osteosclerosis. Bone markers were distinctly elevated. DXA of lumbar spine (LS), femoral neck (FN), and distal one-third radius showed Z scores of +14.3, +6.6, and -0.6, respectively. Transiliac crest biopsy revealed cancellous volume 4.5 times the reference mean, cortical width 3.2 times the reference mean, osteoid thickness 25 times the reference mean, and wide and diffuse tetracycline uptake documenting osteomalacia. Fluoride (F) was elevated in serum (0.34and 0.29 mg/liter [reference range: <0.20]), urine (26 mg/liter [reference range: 0.2-1.1 mg/liter]), and iliac crest (1.8%[reference range: <0.1%]). Tap and bottled water were negative for F. Surreptitious ingestion of toothpaste was the most plausible F source. RESULTS: Monitoring for a decade showed that within 3 months of removal of F toothpaste, urine F dropped from 26 to 16 mg/liter (reference range: 0.2-1.1 mg/liter), to 3.9 at 14 months, and was normal (1.2 mg/liter) after 9 years. Serum F normalized within 8months. Markers corrected by 14 months. Serum creatinine increased gradually from 1.0 (1997) to 1.3 mg/dl (2006; reference range:0.5-1.4 mg/dl). Radiographs, after 9 years, showed decreased sclerosis of trabeculae and some decrease of sacrospinous ligament ossification. DXA, after 9 years, revealed 23.6% and 15.1% reduction in LS and FN BMD with Z scores of +9.3 and +4.8, respectively. Iliac crest, after 8.5 years, had normal osteoid surface and thickness with distinct double labels. Bone F, after 8.5 years, was 1.15% (reference range, <0.1), which was a 36% reduction (still 10 times the reference value). All arthralgias resolved within 2 years, and he never fractured, but new-onset nephrolithiasis occurred within 9 months and became a chronic problem. CONCLUSIONS: With removal of F exposure, skeletal fluorosis is reversible, but likely impacts for decades. Patients should be monitored for impending nephrolithiasis.

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SUBMITTING MANUSCRIPTS TO *FLUORIDE*

GUIDELINES FOR AUTHORS

Authors are advised that, for timely processing of their submissions, all instructions for submitting manuscripts must be followed *exactly* as directed in FLUORIDE 2007;40(1):77-88 (also available online at www.fluorideresearch.org). For more efficient processing of submissions, and because far more manuscripts are being received than there is space to publish without a huge increase in the cost of the journal, manuscripts should be written as concisely as possible without unnecessary extraneous information or undocumented claims.