Connexin 43 Induces Odontoblast Differentiation in Incisors of Rats With Dental Fluorosis

Objectives: Molecules of intercellular communication, such as connexin 43 (Cx43), are important during dentinogenesis since they control cellular growth and differentiation. Excessive intake of fluoride (F^-) during the phase of dental mineralization generates alterations in the structure and function of cells from different dental tissues. In previous works, we demonstrated that chronic intake of F^- through drinking water produced an increase in the activity of alkaline phosphatase and in the levels of mRNA of Cx43, osteocalcin and dentin sialophosphoprotein in pulp of rat's incisor. To study the effect of chronic exposure to F^- on the protein expression of Cx43 and morphological and molecular indicators of odontoblast differentiation.
Methods: Male Wistar rats (n=6 per group) drank water during 8 weeks, with different concentrations of F^- in the form of NaF: a) 0.3 mg/L (Control), b) 10 mg/L (Treated). Subsequently, all animals were euthanized; their mandibles were removed for histological processing and the upper maxilla to obtain incisor's pulp tissue. Protein expression of Cx43 was analyzed by immunohistochemistry. On digital microphotographs, histomorphometric parameters were analyzed: number of odontoblasts/μm^2, ratio nucleus/cytoplasm and predentin thickness. Total RNA was isolated from pulp tissue and gene expression of Hsp25, specific marker of odontoblast differentiation, was analyzed by RT-PCR. Data were analyzed by Student "*t*" test.
Results: Immunoreactivity of Cx43 was evident in odontoblasts and increased by exposure to F^- compared to controls. The F^- dose used in the treated group did not modify the number of odontoblasts/μm^2, although it increased odontoblast differentiation, evidenced by the decrease in the ratio nucleus/cytoplasm of odontoblasts and expression of the differentiation marker Hsp25.
Conclusions: Chronic exposure to elevated concentrations of F^- promotes odontoblast differentiation, mechanism probably mediated by connexin 43, which induces cells to express genes and proteins essential for mineralization process.

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