Dental effects of intravenous bisphosphonate when administered in early infancy

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Osteogenesis imperfecta (OI)

Characterized by abnormal bone development with low bone mass and increased bone fragility

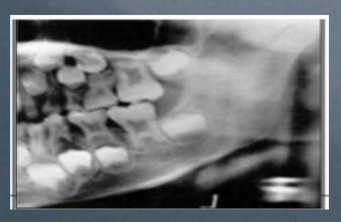
- **Dominant mutations** affect synthesis & structure of type 1 pro-collagen
- **Recessive mutations** affect post-translational processing or tracking of type 1 pro-collagen

Association with **dentinogenesis imperfecta type 1** with COL1A1 and COL1A2, SERPINH1, FKBP10 mutations

Primary and permanent dentitions both involved in DI type I

Primary dentition more severely affected

- Tooth discoloration
- Reduced enamel thickness
- Vertical enamel fracture
- associated short roots and bulbous crowns



Bisphosphonates

Primary action as osteoclast inhibitors

used for over 20 years in osteogenesis imperfecta

- increase bone hardness
- reduce fracture risk

To date

- No reports of any effect of bisphosphonates on tooth development in OI
- No reports of any adverse effects of bisphosphonates on incidence of osteonecrosis of jaw(ONJ) in children or adolescents

Patients and methods

3 Caucasian children with severe forms of OI

(Sillence classification type 3, more recently classified as Progressively Deforming OI with normal sclerae)

COL1A1/2 mutations

All presented with peri-natal multiple long bone fractures

Treatment

Zoledronic acid 0.04mg/kg/dose

All received intravenous zoledronic acid infusions

- 4 monthly from the first week of life
- Infusions administered to at least age 6-8 years
- Increasing intervals between treatment cycles based on improving bone mineral density

Dental examination

Primary dentition

Abnormal teeth

- brown discolouration of all teeth increased wear
- loss of dental height over 2-3 years
- increased rate of tooth loss

Results

Secondary dentition

almost white teeth

normal colour and appearance

no signs of reduced enamel or dentine

Mechanism of action of bisphosphonate on tooth formation ?

Possibly due to altered lamellation of collagen

?? within teeth exposed to bisphosphonate

Conclusions:

Very early treatment of dentinogenesis imperfecta associated with osteogenesis imperfecta can result in improved dental health and stronger teeth

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Bone & Mineral Metabolism

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