# Exfoliation of primary dentition in children with Osteogenesis Imperfecta medicated with bisphosphonates

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## Abstract

**Aim** To study root resorption of the primary dentition in children with osteogenesis imperfecta (OI) medicated with bisphosphonates (BPs) and compare the results with a control group of healthy patients.

**Study design and methods** A cross-sectional study was conducted analysing 20 panoramic radiographs belonging to children with OI with a mean age of 8.18 (±1.60), who had received BPs in a period equal to or greater than 1 year, comparing them to a control group of 367 panoramic radiographs belonging to healthy children with a mean age of 9.19 (±1.62). Children with tooth agenesis, caries or bilateral restorative treatments in the lower arch were excluded. Root resorption of primary teeth was examined with the *Haavikko* method and with the *PixelStick®* software. To indicate the presence of dentinogenesis imperfecta (DI), the radiographic characteristic of DI such as obliteration of the pulp chambers, bulbous crowns, and very narrow root walls, were taken into account. The cumulative dose of BPs was obtained by mathematically calculating the total dosage received (mg)/weight (kg) and multiplying the relative potency of the medication. The Mann-Whitney U test was used for comparisons, and $p < 0.05$ indicated statistical significance.

**Results** There was no difference in root resorption between children with DI or without DI in the study group. There was a delay in the exfoliation of the primary dentition ($p<0.05$) in the study group. The entire primary dentition of 108 children from the control group has been exfoliated, however, in the study group no children met this event. From 1.59mm to 1.95 mm delay in root resorption on mesial and distal root of the primary molars was described in the study group. According to gender, the root resorption was lower in males in the control group ($p<0.05$), in the study group the root resorption was lower in males but the differences were not significant.

**Conclusions** Not differences in root resorption was found between children with DI or without DI. BPs therapy was associated with delay in root resorption of the primary molars and delay in the exfoliation of primary dentition in children with OI. Delayed root resorption should be considered, particularly as it may increase the number of impacted teeth in children already suffering from dental disorders.

KEYWORDS Bisphosphonates, Osteogenesis Imperfecta, Panoramic radiograph, Root resorption, Dental exfoliation.

## Introduction

Osteogenesis imperfecta (OI) is an inherited disorder characterised by bone fragility and skeletal alterations [Rauch and Glorieux, 2004]. In the vast majority of cases, the cause is due to a mutation in one of the two genes that encode type I collagen (COL1A1 or COL1A2). In recent years, mutations have also been identified in other autosomal recessive, autosomal dominant and X-linked genes that could cause OI [Marini and Blissett, 2013; Forlino and Marini, 2016; Chetty et al., 2021]. Among all the clinical manifestations, multiple fractures and bone pain are especially relevant. In addition, clinical manifestations such as loss or decrease in hearing, joint hypermobility, and delays regarding development, among others, are also common. Regarding orofacial manifestations, dentinogenesis imperfecta (DI) is the most acknowledged, although oligodontia, alterations in dental development, are also described [Malmgren and Norgren 2002a; Rizkallah et al. 2013; Andersson et al. 2017, 2020; Malmgren et al. 2017, 2021]. The administration of bisphosphonates [BPs] in patients with OI reduces bone pain and decreased bone fragility in OI patients [Dwan et al. 2016]. The main mechanism of action of BPs is to inhibit osteoclast function and bone resorption [Aström and Söderhäll 2002; Phillipi et al. 2008; Russell 2011], which may alter physiological processes in which the action of the osteoclast is necessary. In the oral cavity of children with OI, during the period of growth and development, processes take place that require the action of osteoclasts. Dental eruption is carried out at the expense of the resorption of the alveolar bone for teeth that do not have ancestors and for those that do have them, at the expense of the root resorption of the temporary tooth. The osteoclast is responsible for the resorption during both processes [Wise 2009]. Studies in experimental animals indicate that antiresorptive agents can alter tooth eruption, root formation and induce dental malformations [Bradaschia-Correa et al. 2007, 2013; Hiraga et al. 2010]. There are few studies in humans that analyse the effect of antiresorptive agents on the exfoliation of primary dentition and the results are inconclusive [Vuorimies et al. 2017; Del Rio Cantero et al. 2024]. Therefore, the aim of this investigation is to study root resorption of the primary dentition in children with OI medicated with BPs and compare the results with a control group of healthy patients.

## Material and methods

The research was carried out at the Faculty of Dentistry of the Complutense University of Madrid (UCM), under the support of a collaboration agreement between the AHUCE Foundation and the UCM. A cross-sectional study has been designed. The study group consisted of 20 panoramic radiographs pertaining to children with OI between 6 and 11.9 years of age. Eleven males and 9 females; 14 of them had OI type I and 6 had OI type III-IV. The type of OI was classified according to Sillence et al. [1978]. The control group consisted of 367 panoramic radiographs pertaining to children between 6 and 11.9 years of age. 198 males and 169 females. The control group was similar to the study group in terms of age and gender to enable comparisons. The sample size of the control group was determined from the total number of

children who attended the Faculty of Dentistry of the Complutense University of Madrid between 2020 and 2024 using the Yamane´s formula, with a margin of error of 0.05 and a 95% confidence interval. The calculated sample size was 366.701 patients. As OI is a rare disease with an incidence ranging between 6 and 20 cases per 100,000 live births, a calculation of the needed sample size could not be carried out in the study group [Rauch and Glorieux, 2004]. A study conducted using a human sample was used as a reference. This study investigated the eruptive process in children with OI treated with BPs and included a sample of 25 children with OI [Vuorimies et al. 2017]. All primary teeth in the third quadrant have been studied. In the case of agenesis or restorative treatments in said quadrant, the fourth quadrant has been studied. The period of administration of the antiresorptive agent has been equal to or greater than 1 year. Pamidronate and zoledronic acid are the two types of BPs that patients have received. The different antiresorptive potencies of each antiresorptive agent have been taken into account, 100 for pamidronate and 10000 for zoledronic acid, and based on them, the cumulative dose of BPs for each patient was estimated by mathematical calculation of the total dose received (mg). /weight (kg) and the multiplication of the relative potency of the medication [Shaw and Bishop 2005; Vuorimies et al. 2017]. All participants have been informed and have signed an informed consent. The sample was classified based on gender and age. The study group was also classified based on the severity of the disease and according to the accumulated bisphosphonate dose.

### Radiographic analysis

A single blinded examiner from the Faculty of Dentistry of the Complutense University of Madrid evaluated all the medical records and panoramic radiographs, widely proven methodologies have been selected and used. The modified Haavikko method and the PixelStick® software were used. A maximum of 20 panoramic radiographs were evaluated per day to avoid operator fatigue. The operator was an experienced dentist previously trained in diagnosis X-ray. The measurement was made using digital X-ray with a computer. With the Haavikko method, the 5 temporary teeth of the III quadrant were studied. This method establishes four stages of root resorption according to root length. Each tooth was assigned the following score: 1: no root resorption; 2: ¼ part of the root is resorbed; 3: half of the root is resorbed; 4: ¾ of the root is resorbed or exfoliated [Haavikko, 1973]. As in most cases the roots of the primary molars are not resorbed symmetrically, this method was modified by separately studying both the mesial root and the distal root [Garcete Delvalle, Bruna Del Cojo, et al., 2025]. A maximum score of 28 could be obtained if all primary teeth have been exfoliated.

The mesial and distal root length of the lower left primary first molar (7.4) and the lower left primary second molar (7.5) were measured in mm with the PixelStick® software. First, the amelocemental line was located; it is the area where the convexity of the crown ends and the radio-opacity of the enamel is no longer observed. Once the amelocemental line and the occlusal plane were located, the information regarding the pixels from the radiographic images were acquired with the software. To obtain the desired measurement in mm it was essential to obtain the relationship between the pixel size and mm. This method was used previously by our team for studying the root resorption of the primary molar in panoramic radiographs [Garcete Delvalle, Bruna Del Cojo, et al., 2025].

To indicate the presence of DI, the radiographic characteristic of DI such as obliteration of the pulp chambers, bulbous crowns and very narrow root walls, were taken into account [Barron et al. 2008; Nguyen et al. 2021].

### Statistical analysis

The statistical analysis was carried out using IBM SPSS Statistics® version 25 (reference: IBM Corp. Released 2017. IBM SPSS Statistics v 25.0 for Windows; Armonk. NY. USA).

The Kolmogorov-Smirnov test was used for adjustment of normality. For the contrast between means of groups of independent subjects, the t-Student was applied, as well as scatter diagrams and Pearson coefficients, to study the relationship between quantitative variables. For the comparison of the means among groups of different subjects, the nonparametric alternative of the Mann-Whitney test was used since the variables did not meet normality criteria. p values $< 0.05$ were considered to indicate statistical significance. The ROC curve methodology was used to determine appropriate cut-off points based on sensitivity, positive predictive value, and Yuoden index values. The ethical principles of the Declaration of Helsinki have been followed, internal code: 21/418-0_M_OD. The study was approved by Ethics Committee of the San Carlos Hospital of Madrid.

## Results

During this investigation a total of 387 children have been studied, 367 from the control group and 20 from the study group. The study group has a mean age of 8.18 years with a standard deviation of +- 1.6 years; 11 are males and 9 are females; 70% of patients have OI type I and 30% have OI type III-IV. As for the control group, there are 367 children, with a mean age of 9.2 years with a standard deviation of +-1.62 years; 198% are males and 169 are females as described in Table 1 and 2.

### Haavikko method

The description of the root resorption values for the total sample of participants shows a marked asymmetry, with a high number of subjects at the highest value. The Kolmogórov-Smirnov test confirmed that this deviation is highly significant (P-value=.000 < .01), so we must affirm that this variable is not distributed according to statistical normality. The observed range is 8–28 (median 22), with 108 participants (27.9% of the total)

| | Total Sample (n=387) | Study Group (n=20) | Control Group (n=367) |
|---|---|---|---|
| Age | | | |
| Mean (S.D.) | 9.14 (±1.63) | 8.18 (±1.60) | 9.19 (±1.62) |
| Median (Range) | 9.24 (6-12) | 7.98 (6-12) | 9.33 (6-12) |
| Gender | | | |
| Males | 54.0% (209) | 55.0% (11) | 54.0% (198) |
| Females | 46.0% (178) | 45.0% (9) | 46.0% (169) |
| Severity of OI | | | |
| OI Type I | - | 70.0% (14) | - |
| OI Type III-IV | - | 30.0% (6) | - |
| Dentinogenesis Imperfecta (DI) | - | 30.0% (6) | - |

TABLE 1 Characteristics of the study group and the control group.

| | Study Group (n=20) | | Control group (n=367) | |
|---|---|---|---|---|
| Chronological age | Males (n=11) | Females (n=9) | Males (n=198) | Females (n=169) |
| 6 – 6.99 | 20.0% (4) | 5.0% (1) | 10.1% (37) | 1.4 % (5) |
| 7 – 7.99 | 15.0% (3) | 10.0% (2) | 8.2% (30) | 9.5% (35) |
| 8 – 8.99 | 10.0% (2) | 15.0% (3) | 9.0% (33) | 8.7% (32) |
| 9 – 9.99 | 5.0% (1) | 10.0% (2) | 8.7% (32) | 9.8% (36) |
| 10 – 10.99 | - | - | 8.4% (31) | 8.4% (31) |
| 11 – 11.99 | 5.0% (1) | 5.0% (1) | 9.5% (35) | 8.2% (30) |

TABLE 2 Characteristics of the study group and the control group according to age and gender.

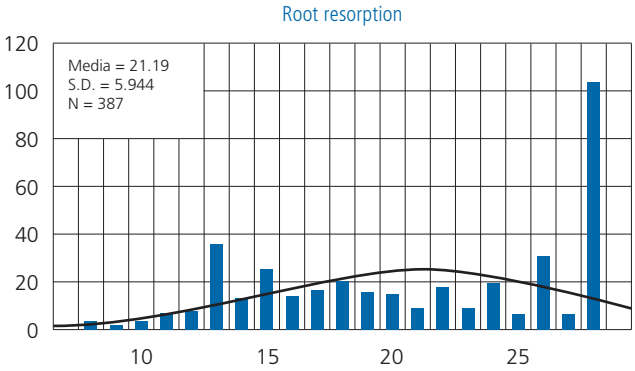



FIG. 1 Root Resorption of the primary dentition (N=387).

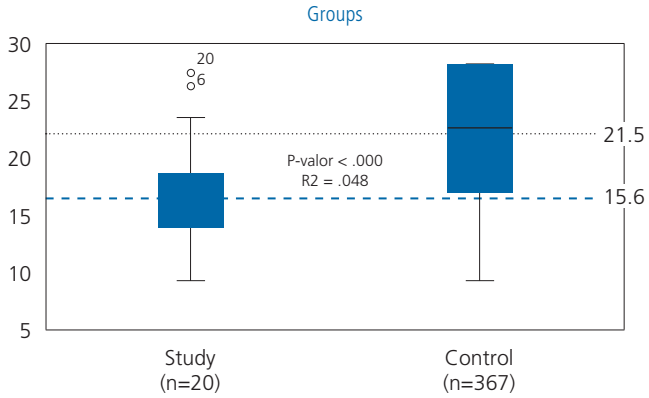



FIG. 2 Root resorption of the primary dentition. Comparison among both groups.

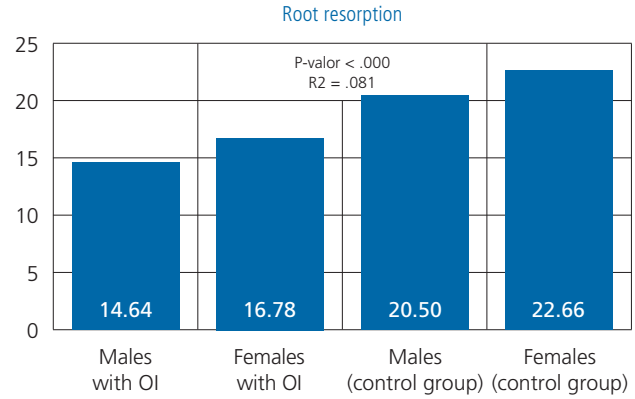



FIG. 3 Root resorption of the primary dentition values. Comparison among subgroups.

at the maximum score (28 units). Despite the asymmetry and the lack of normality, the total mean value: 21.19 units (95% CI: 20.60–21.79; with a standard deviation of ±5.99) was similar to that of the median as described in Figure 1. The root resorption in the study group was found to be lower than in the control group (15.60 vs 21.50), this difference being significant with The Mann-Whitney U test ($p<0.001$) as described in figure 2. Within the study group, females have accelerated root resorption compared to males (16.78 vs 14.64), although without reaching statistical significance. This may be an indication that root resorption is more advanced in girls or delayed in boys with OI. This difference (22.66 vs 20.50) is also observed in the control group and is significant $p<0.001$. These results indicate that, regardless of the group, there is an advance in root resorption in females or a delay in root resorption in males among both groups as described in Figure 3. There is a clear trend towards a direct linear association between the resorption of the primary dentition and chronological age in all groups, such that greater chronological age is associated with greater resorption of the primary dentition as described in Figure 4 and 5. In 29.4% of the children in the control group (108 children) the entire primary dentition has been exfoliated, however, in the study group no patient met this event. The minimum and maximum age at which cases of complete exfoliation of the primary dentition are found was sought, and 3 cutting interval ages were located: at 8.5; 9.5 and 10.5 years. At 10.5 years we found a positive predictive value (PPV) of 85.5%. Therefore, we conclude that at 10.5 years is the point in time at which the entire primary dentition could be exfoliated. As 4.5% of the cases had been found to have some temporary dentition at that age, the maximum

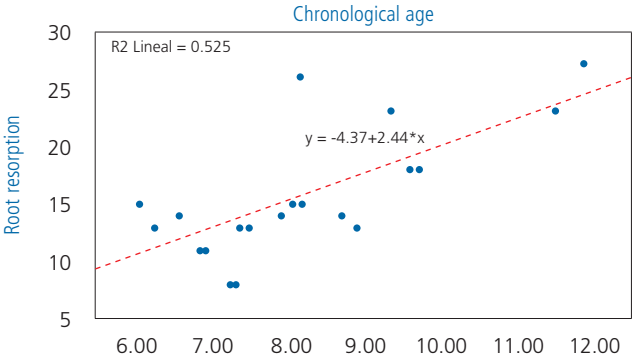



FIG. 4 Association between the resorption of the primary dentition and chronological age. Study group

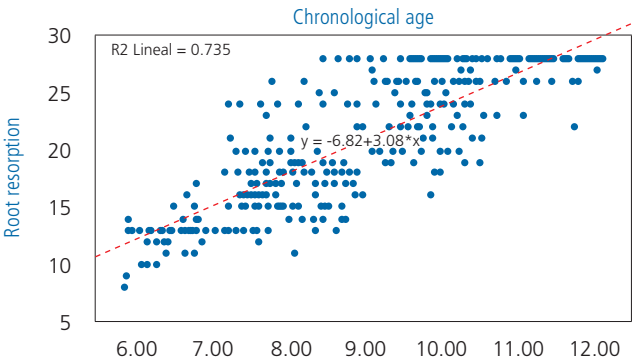
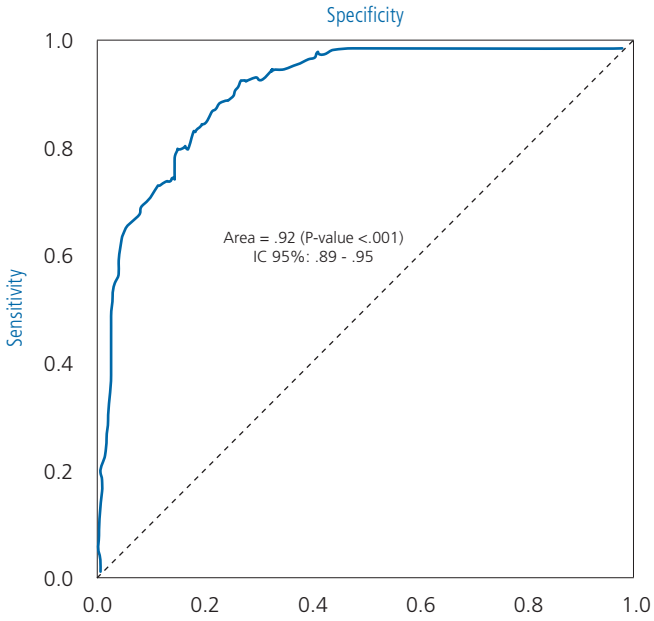



FIG. 5 Association between the resorption of the primary dentition and chronological age. Control Group.




| Cutting interval | S | E | Yuoden Index | PPV | NPV |
|---|---|---|---|---|---|
| 5 years | 1.00 | .00 | 1.00 | | |
| 6 years | 1.00 | .00 | 1.00 | | |
| 7 years | 1.00 | .17 | 1.17 | | |
| 8 years | 1.00 | .42 | 1.42 | | |
| 8.5 years | 1.00 | .55 | 1.55 | 47.6% | 100% |
| 9 years | .96 | .66 | 1.62 | | |
| 9.5 years | .94 | .73 | 1.67 | 58.0% | 96.4% |
| 10 years | .80 | .85 | 1.65 | | |
| 10.5 years | .66 | .95 | 1.61 | 85.5% | 87.0% |
| 11 years | .55 | .97 | 1.53 | | |
| 11.5 years | .31 | .98 | 1.29 | | |
| 12 years | .01 | 1.00 | 1.01 | | |
| S= Sensitivity; E= Specificity; PPV & NPV= Positive and Negative Predictive Value | | | | | |

FIG. 6 ROC curve, relationship between exfoliation of the primary dentition (root resorption=28) with chronological age. (N=367 subjects in the control group)

cut-off age was set at 11.9 years. In the study group there was no case in which the entire primary dentition has been exfoliated at any of the previously mentioned cutting intervals, as described in Figure 6.

### The PixelStick® software method

After analysing the root resorption of the primary molars (7.4 and 7.5), we found children with OI presented a delayed in root resorption (around 1.59 to 1.95 mm) or an advanced in root resorption in the control group, this difference reach statistical significance (p<.05), as shown in tables 3 the mesial radicular length (MRL) and the distal radicular length (DRL) of the primary molars. A delayed of 1.83mm in the MRL and a delayed of 1.72mm in the DRL in the root reabsorption of the primary molar; and in the second primary molar a delayed of 1.95mm in the MRL and 1.59mm in the DRL was found, as shown in Tables 3. Comparing by gender, females had a higher degree of root resorption than males, reaching statistical significance in the control group, although not in the study group. It has also been observed that as age increases the trend is for root length to decrease until reaching values of 0mm. However, in the study group we did not reach this value indicating a delay in root resorption, as shown in tables 4, 5, 6 and 7. While 7.4 had exfoliated in 38.4% of the cases and 7.5 had exfoliated in 27.2% of the cases in the control group, neither 7.4 nor 7.5 exfoliated in any case in the study group. We located 3 cutting interval ages at which 7.4 could be exfoliated: at ages 8.5; 9.5 and at 10 years. In addition, three cutting interval ages were located for the possible exfoliation of 7.5. The maximum age was 10.5 years with a PPV value of 85.5%. Studying the root resorption and the severity of the disease, a slight difference has been found in children with OI type III-IV. We could argue that the greater the severity of the disease, the greater the delay in root resorption, but this difference did not reach statistical significance (p>.05). It was found that the mean value for type I (15.29 ± 5.77) was slightly lower than the mean value for the other types (16.33 ± 4.80), although this difference did not reach statistical significance (Mann-Whitney test: ZU = 0.96; P = .353), and the effect size was almost zero (0.1%). There is no statistical evidence to accept that the root resorption varies according to the type of OI, although there is a trend. Regarding the accumulated doses of BPs, they are distributed between 48.27 and 12818.75 units. The root

| | Median | | Mann-Whitney Test | | |
|---|---|---|---|---|---|
| | Study Group (n=20) | Control Group (n=367) | Values | P-value | Effect size: $R^2$ |
| MRL 7.4 | 3.88 mm (±1.69) | 2.05 mm (±1.89) | 4.01 (**) | .000 | .044 |
| DRL 7.4 | 3.84 mm (±1.48) | 2.12 mm (±1.92) | 3.82 (**) | .000 | .039 |
| MRL 7.5 | 5.18 mm (±1.49) | 3.23 mm (±2.27) | 3.78 (**) | .000 | .036 |
| DRL 7.5 | 5.54 mm (±1.79) | 3.95 mm (±2.66) | 2.04 (**) | .009 | .018 |
| (**) = high stadistical significance | | | | | |

TABLE 3 Comparison of root resorption of the mesial and distal roots of primary molars between both groups.

| Chronological age (years-old) | OI study group (n=20) | | Control group (n=367) | |
|---|---|---|---|---|
| | Males (n=11) | Females (n=9) | Males (n=198) | Females (n=169) |
| 6 – 6.99 | 4.58 (3.10/5.65) | 5.68 (5.68/5.68) | 4.58 (2.76/6.47) | 5.02 (3.71/5.83) |
| 7 – 7.99 | 5.37 (4.15/7.43) | 4.17 (3.14/5.20) | 3.59 (1.14/7.03) | 3.07 (0.64/5.61) |
| 8 – 8.99 | 4.46 (3.42/5.49) | 3.02 (1.49/4.68) | 3.46 (0.00/6.02) | 2.41 (0.00/4.53) |
| 9 – 9.99 | 4.00 (4.00/4.00) | 2.18 (1.45/2.91) | 1.81 (0.00/4.20) | 1.13 (0.00/4.54) |
| 10 – 10.99 | - | - | 1.22 (0.00/4.86) | 0.38 (0.00/3.72) |
| 11 – 11.99 | 0.81 (0.81/0.81) | 1.94 (1.94/1.94) | 0.08 (0.00/2.92) | 0.00 (0.00/0.00) |

TABLE 4 Comparison of root resorption of the mesial and distal roots of primary molars between both groups.

| Chronological age (years-old) | OI study group (n=20) | | Control group (n=367) | |
|---|---|---|---|---|
| | Males (n=11) | Females (n=9) | Males (n=198) | Females (n=169) |
| 6 – 6.99 | 4.58 (3.10/5.65) | 5.68 (5.68/5.68) | 4.58 (2.76/6.47) | 5.02 (3.71/5.83) |
| 7 – 7.99 | 5.37 (4.15/7.43) | 4.17 (3.14/5.20) | 3.59 (1.14/7.03) | 3.07 (0.64/5.61) |
| 8 – 8.99 | 4.46 (3.42/5.49) | 3.02 (1.49/4.68) | 3.46 (0.00/6.02) | 2.41 (0.00/4.53) |
| 9 – 9.99 | 4.00 (4.00/4.00) | 2.18 (1.45/2.91) | 1.81 (0.00/4.20) | 1.13 (0.00/4.54) |
| 10 – 10.99 | - | - | 1.22 (0.00/4.86) | 0.38 (0.00/3.72) |
| 11 – 11.99 | 0.81 (0.81/0.81) | 1.94 (1.94/1.94) | 0.08 (0.00/2.92) | 0.00 (0.00/0.00) |

TABLE 5 Root Resorption values belonging to the distal root of 7.4 (mean and range) within each group and gender, according to chronological age.

| Chronological age (years-old) | OI study group (n=20) | | Control group (n=367) | |
|---|---|---|---|---|
| | Males (n=11) | Females (n=9) | Males (n=198) | Females (n=169) |
| 6 – 6.99 | 4.65 (3.56/5.65) | 5.88 (5.88/5.88) | 5.41 (3.14/7.32) | 6.92 (4.00/8.54) |
| 7 – 7.99 | 5.50 (4.22/7.22) | 5.00 (3.45/6.54) | 4.79 (2.64/7.13) | 4.53 (1.17/6.64) |
| 8 – 8.99 | 5.81 (5.68/5.93) | 4.99 (3.43/7.41) | 4.76 (0.00/3.96) | 3.84 (0.00/6.49) |
| 9 – 9.99 | 4.85 (4.85/4.85) | 6.66 (6.47/6.85) | 3.71 (0.00/6.37) | 2.60 (0.00/6.39) |
| 10 – 10.99 | - | - | 2.94 (0.00/6.60) | 1.43 (0.00/5.00) |
| 11 – 11.99 | 1.69 (1.69/1.69) | 6.11 (6.11/6.11) | 0.57 (0.00/4.27) | 0.03 (0.00/0.98) |

TABLE 6 Root Resorption values belonging to the mesial root of 7.5 (mean and range) within each group and gender, according to chronological age.

| Chronological age (years-old) | OI study group (n=20) | | Control group (n=367) | |
|---|---|---|---|---|
| | Males (n=11) | Females (n=9) | Males (n=198) | Females (n=169) |
| 6 – 6.99 | 5.14 (4.19/6.59) | 6.96 (6.96/6.96) | 6.26 (4.78/7.81) | 7.75 (7.54/7.96) |
| 7 – 7.99 | 6.01 (3.94/8.58) | 6.54 (4.45/8.64) | 5.81 (3.39/7.81) | 5.56 (0.96/7.68) |
| 8 – 8.99 | 6.09 (4.96/7.22) | 5.61 (4.35/8.07) | 5.74 (0.00/7.60) | 4.59 (0.00/8.00) |
| 9 – 9.99 | 5.88 (5.88/5.88) | 5.44 (5.29/5.58) | 5.11 (0.00/7.09) | 3.54 (0.00/7.37) |
| 10 – 10.99 | - | - | 3.47 (0.00/6.96) | 1.50 (0.00/5.48) |
| 11 – 11.99 | 1.14 (1.14/1.14) | 5.29 (5.29/5.29) | 0.83 (0.00/5.92) | 0.03 (0.00/0.98) |

TABLE 7 Root Resorption values belonging to the distal root of 7.5 (mean and range) within each group and gender, according to chronological age.

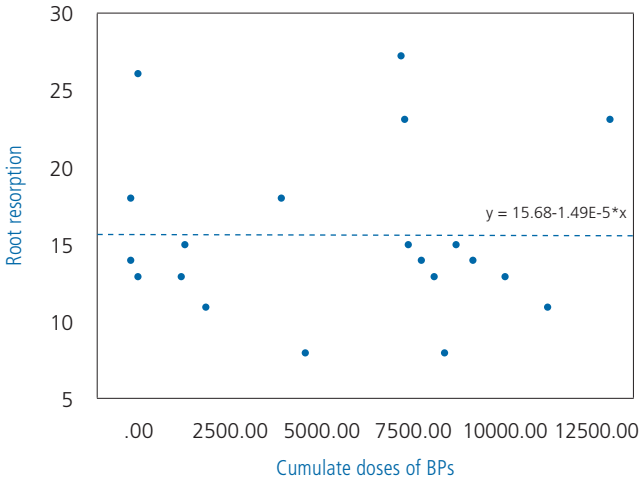



FIG. 7 Association of RR with cumulative BFS dose. Study group (N=20)

resorption was correlated with these doses. First, the scatter plot figure 7 shows a cloud of points that clearly does not represent a relationship between the variables (neither linear nor otherwise). This visual impression is confirmed by the value of the correlation coefficient obtained, which does not reach statistical significance at $p > 0.05$ ($r = -.14$; P value = .555). There is no evidence of the existence of a relationship between the root resorption and the dose of BPs, although this could be influenced by the small sample of the study group. Two groups were analysed based on the number of cumulative doses of the antiresorptive agent, a group with less than 2000 cumulative doses of BPs and a second group with a cumulative dose of BPs greater than 2000. The root resorption is accelerated in cases with a dose less than 2000 compared to cases with doses greater than 2000. This difference does not reach statistical significance, although it does show that patients with a cumulative dose greater than 2000 have a greater delay in exfoliation of temporary dentition. This finding indicates that the higher the cumulative dose of BPs, the greater the delay in the resorption of the primary dentition, although without reaching statistical significance.

### Dentinogenesis Imperfecta

Thirty percent of children with OI have DI as shown in figures 8 pulp obliteration, short roots, bulbous crowns, cervical constriction in panoramic radiography. It was analysed whether DI could affect the root resorption of the temporary dentition in the study group, the results was very similar between the subgroups (15.83 ±50.4 vs 15.50 ±5.72).

## Discussion

The results of this investigations with the two methods indicates that children with OI medicated with BPs tend to have difficulty in exfoliating the primary dentition. With the Haavikko method, in the control group the entire primary dentition of 108 patients has been exfoliated, however, in the study group no patient met this event. With the PixelStick® software method, we found children with OI presented a

FIG. 8 A female patient with 8.14 years old from the study group with DI. The 5 temporary teeth of the III quadrant were studied. Root resorption score =26. OI type III, has received 22 cycles of Pamidronate.

delayed in root resorption of the primary molars (around 1.59 to 1.95 mm) or an advanced in root resorption in the control group, these differences reach statistical significance (p<.05). This results agree with ours previous work, we found from 1mm to 1.25mm delayed in root resorption of the primary molars in children with OI medicated with BPs [Garcete Delvalle, De Nova García, et al. 2025]. This results agree with several authors who have shown that this alteration is caused by the antiresorptive medication that these patients receive [Vuorimies et al. 2017; Del Rio Cantero et al. 2024].

In this study all children have started treatment with BPs before reaching one year of life. The half-life of bisphosphonates is a decade, so the effects persist in the child during the ages at which the exfoliation of the primary dentition and the eruption of the permanent teeth occur [Forlino and Marini 2016]. Since dental eruption involves the resorption of the primary dentition and bone formation, osteoclasts are important for the eruptive process to develop [Wise 2009]. Many studies support the results that we had found in this study [Kamoun-Goldrat et al. 2008; Vuorimies et al. 2017; Malmgren et al. 2020; Del Rio Cantero et al. 2024; Garcete Delvalle et al. 2024], but we do not have a control group of children with OI without medication since patients with OI in Spain, by medical protocol, in most cases receive cycles of BPs at very early ages. This means that we cannot know if the delay in root resorption is due to the medication or whether it is due to the disease. The root resorption has been analysed on the basis of the accumulate dose of BPs and a greater delay in root was found in children with a higher dose of BPs, although the difference has not reached statistical significance. Scandinavian studies with a control group of children with OI with and without medication support our results that BPs therapy in OI seems to lower tooth eruption and the root resorption of the primary dentition [Vuorimies et al. 2017; Malmgren et al. 2020]. We have found that children with OI type III-IV have a greater delay in root resorption than children with OI type I, so we could say that the greater the severity of the disease, the greater the delay in exfoliation, but this difference does not reach statistical significance. These values could be biased due to the small number of the sample. There are cases in which patients with OI type III-IV are considered OI type I due to the positive effect of the measurement, so currently analysing by type of OI is complicated and could create confusion. Thanks to the medication, severe forms of OI transition to milder forms. In addition, 30% of children with OI present DI in the study group, a high figure although it could have been much higher since of the initial 51 patients we had, 31 patients had to be excluded due to caries and restorative treatments, and many of those patients were diagnosed with DI. Other authors indicate an incidence of 42% (Malmgren and Norgren 2002b] and others even up to 80% [O'Connell and Marini 1999]. The presence of DI is a predictor of caries [Ma et al. 2019]. We did not find difference in this study between patients with DI and without DI in root resorption, like other authors [Kamoun-Goldrat et al. 2008; Malmgren et al. 2020]. When we studied root resorption in males and females with the group, we found that males in the control group were delayed compared to females. However, in the study group, we found no differences between genders. We found the same results as in a previous study [Garcete Delvalle, De Nova García, et al. 2025]. This could be because the disease or the medication could have a homogenising effect on root resorption in females and males with OI. According to another authors, no significance differences was found in eruption in females and males with OI who had been medicated with BPs compared with those who have not [Malmgren et al. 2020]. We excluded children with caries, obturations, orthodontic treatment, and dental agenesis in the lower arch so all the patients started with similar conditions and only the physiological process of root resorption on the primary dentition could be measured, in order to limit the potential bias/errors.

### Limitations

The study design is cross-sectional and only association can be established. The effect of medication on this delay leaves the door open for future research, since although we have observed a greater alteration in patients who have received greater amounts of the medication, no statistical significance was found. The study group was represented by a small sample as OI is a rare disease and the control group was 1.01 years older than the study group, which is why the reliability of these results could be compromised. To limit the potential bias/errors associated with measurement tools, images with distortion/or irregular apex were excluded. Qualitative and quantitative methods were used to study root resorption of the primary dentition in children with OI. Both methods showed delayed in root resorption of the primary dentition in children with OI.

## Conclusions

Not differences in root resorption was found between children with DI or without DI. BPs therapy was associated with delay in root resorption of the primary molars and delay in the exfoliation of primary dentition in children with OI. Delayed root resorption should be considered, particularly as it may increase the number of impacted teeth in children already suffering from dental disorders.

*Abbreviations*

- 74: Lower left first temporary molar
- 75: Lower left second temporary molar
- LMR: Length of the mesial root
- LDR: Length of the distal root
- OI: Osteogenesis Imperfecta
- DI: Dentinogenesis Imperfecta
- BPs: Bisphosphonates

- PPV: Positive Predictive Value
- PNV: Negative Predictive Value

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