e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(11); 1267-1273

Original Research Article

Effect of Pamidronate on Fracture Incidence and Bone Mineral Density in Children with Osteogenesis Imperfecta: A Prospective Observational Study Over 12 Months in a Tertiary Care Setting in West Bengal

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Received: 01-08-2025 Revised: 15-09-2025 / Accepted: 21-10-2025
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Conflict of interest: Nil

Abstract

Introduction: Osteogenesis Imperfecta (OI) is a rare genetic disorder characterized by increased bone fragility and frequent fractures. Bisphosphonates like Pamidronate have shown promise in improving bone mineral density (BMD) and reducing fracture incidence in affected individuals.

Objective: To evaluate the impact of intravenous Pamidronate therapy on fracture frequency and BMD in children with OI over a 12-month follow-up period.

Methodology: A prospective comparative observational study was conducted over 12 months at a tertiary care center. Fifty children with clinically diagnosed OI who received Pamidronate infusions formed the treatment group, while 50 age- and sex-matched OI patients not receiving bisphosphonates served as controls. Fracture history and BMD were assessed at baseline, 3, 6, and 12 months using structured clinical documentation and pediatric DEXA scans. Data were analyzed using JAMOVI version 2.6.44, and statistical significance was set at $p<0.05$.

Results: The Pamidronate group showed a significant reduction in fracture incidence and a consistent increase in BMD over the study period compared to controls. No serious adverse effects were observed.

Conclusion: Pamidronate therapy is effective in improving bone density and reducing fracture frequency in pediatric OI patients, supporting its use as a cornerstone in the management of this debilitating condition. Further long-term studies are warranted.

Keywords: Pamidronate, Bone Density, Osteogenesis Imperfecta, Fractures, Bone.

Introduction

Osteogenesis Imperfecta (OI) is a heterogeneous group of genetic disorders primarily affecting the connective tissue, characterized by bone fragility, low bone mass, and a propensity for fractures with minimal or no trauma. It is most commonly caused by mutations in the genes COL1A1 and COL1A2, which encode type I collagen, an essential component of the bone matrix [1].

The clinical presentation of OI varies significantly, ranging from perinatal lethality to relatively mild forms presenting with occasional fractures and minimal deformity. The Sillence classification remains a widely accepted system, dividing OI into four major types based on clinical severity and radiographic findings [2]. Children with OI often experience recurrent fractures, skeletal deformities, growth deficiency, and chronic pain, which substantially affect their quality of life and psychosocial development [3]. The mainstay of treatment has traditionally focused on fracture management, physiotherapy, orthopedic interventions, and rehabilitation. However, the advent of bisphosphonates, particularly Pamidronate, has significantly transformed the therapeutic landscape of OI [4].

Bisphosphonates are synthetic analogs of pyrophosphate that inhibit osteoclastic bone resorption, thereby increasing bone mineral density (BMD) and reducing the rate of bone turnover. Among them, intravenous Pamidronate has emerged as a preferred agent in pediatric patients due to its established safety profile and efficacy in increasing vertebral size, cortical thickness, and overall BMD [5,6]. Several studies have demonstrated that Pamidronate therapy leads to a significant reduction in fracture rates, improvement

in mobility, and better overall functional outcomes in children with moderate-to-severe OI [7].

Despite these promising results, the variability in clinical response, optimal dosing regimens, and long-term outcomes of bisphosphonate therapy continue to be areas of active investigation. Moreover, there is a paucity of controlled comparative studies assessing the impact of Pamidronate against untreated cohorts [8]. Hence, this study aims to evaluate the efficacy of Pamidronate in improving BMD and reducing fracture frequency over a 12-month period in children with OI, compared to a matched control group not receiving bisphosphonate therapy.

Methodology

This study is a hospital-based, prospective comparative observational study. It compares clinical outcomes between patients with Osteogenesis Imperfecta receiving Pamidronate therapy (exposure group) and those not receiving it (control group). The study was conducted at the Department of Orthopedics of a tertiary care referral hospital in West Bengal (KPC Medical College and Hospital, Kolkata), where comprehensive care for children with genetic and metabolic bone disorders is provided, including access to bone densitometry and pediatric endocrinology support. The study was carried out over a period of 24 months, from January 2023 to December 2024. This included recruitment, observation, follow-up, and final analysis. The study population consisted of diagnosed cases of Osteogenesis Imperfecta (types I–IV) in the pediatric age group (2–18 years), presenting to the hospital for routine care or newly diagnosed during the study period. A purposive sampling technique was used. Patients were grouped into the exposure (Pamidronate therapy) and control groups based on the treatment decision made by the treating physician, depending on clinical indication and parental consent.

The sample size was calculated based on the comparison of proportions (fracture incidence) between the two groups. Using the formula:

$$n = \frac{2(Z_{1-\alpha/2} + Z_{1-\beta})^2 \cdot p(1-p)}{(p_1 - p_2)^2}$$

Where $Z_{1-\alpha/2}$=1.96 for 95% confidence, $Z_{1-\beta}$=0.84 for 80% power, p1=0.70 (expected fracture incidence in control group), p2=0.40 (expected fracture incidence in treated group), p=(p1+p2)/2=0.55

$$n = \frac{2(1.96+0.84)^2 \cdot 0.55(1-0.55)}{(0.70-0.40)^2} = \frac{2 \cdot 7.84 \cdot 0.2475}{0.09} \approx 43.0$$

Therefore, a minimum of 43 patients per group (86 total) was required. A total of 50 patients in each group were included to account for attrition.

The Inclusion Criteria were Children aged 2–18 years diagnosed with Osteogenesis Imperfecta (Types I–IV), willingness of parents/guardians to participate and provide consent, and availability of at least 12 months of follow-up.

Exclusion Criteria included children with secondary causes of osteoporosis, patients already on any other bisphosphonate therapy and incomplete baseline data or loss to follow-up.

All eligible patients were assessed at baseline for clinical parameters and bone mineral density (BMD). The treatment group was chosen as those who received intravenous Pamidronate infusions at standardized doses (e.g., 1 mg/kg/day for 3 consecutive days every 3 months). The control group was chosen as those who received standard supportive care without bisphosphonates. Follow-ups were conducted at 3, 6, and 12 months with repeat clinical evaluations and BMD assessments. A structured clinical record form was used to record patient demographics, fracture history, functional status, dual-energy X-ray absorptiometry (DEXA) scan results, and adverse drug events (in the treatment group). The primary outcome of interest was the change in BMD over time between the two groups. Accordingly, the null hypothesis stated that there would be no significant difference in the change in BMD over time between children who received Pamidronate and those who did not. Conversely, the alternative hypothesis proposed that children who received Pamidronate would show a significantly greater increase in BMD over time compared to those in the control group. The secondary outcome was the incidence of fractures during the follow-up period. For this, the null hypothesis stated that there would be no significant difference in the reduction of fracture incidence between the treatment and control groups over time. In contrast, the alternative hypothesis suggested that Pamidronate-treated children would experience a significantly greater reduction in fracture incidence over time compared to untreated children.

Data was collected at four time points: baseline, 3 months, 6 months, and 12 months. Fracture events were documented clinically and radiologically. BMD was measured using pediatric DEXA scans.

Primary outcomes included change in the number of fractures over 12 months and change in BMD over 12 months compared to baseline. All data were entered in Microsoft Excel and analyzed using JAMOVI version 2.6.44. Descriptive statistics were calculated for baseline characteristics. Between-group comparisons were

performed using hic-square test for fracture incidence and repeated measures ANOVA for within-group BMD changes over time. Statistical significance was set at $p < 0.05$.

Data entry was cross-verified by two independent researchers. Instruments like DEXA were calibrated as per manufacturer's recommendations. Standardized protocols were followed for Pamidronate infusion and fracture documentation.

The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from parents or guardians of all participating children. Assent was obtained from children over 7 years. Confidentiality of patient data was strictly maintained. The study adhered to the principles of the Declaration of Helsinki.

Results

The present study was designed to evaluate the impact of Pamidronate therapy on bone mineral density (BMD) and fracture incidence in children diagnosed with Osteogenesis Imperfecta. In this prospective cohort study, a total of 100 children diagnosed with Osteogenesis Imperfecta (OI) were followed over 12 months to assess the impact of intravenous Pamidronate therapy on bone health outcomes. The participants were divided into two cohorts: a treatment group (N = 50) who received Pamidronate and a non-exposed group (N = 50) who did not receive any bisphosphonate treatment. The mean age (Table 1) in the non-exposed cohort was 10.2 years (standard deviation = 0.0715), whereas in the exposed cohort it was slightly younger at 8.4 years (standard deviation = 0.0743). In terms of sex distribution, the non-exposed group included 27 males and 23 females (N = 50), while the exposed group consisted of 20 males and 30 females (N = 50), indicating a slight female predominance in the treatment group. Residential distribution was similar in both cohorts, with the non-exposed group comprising 42 urban and 8 rural participants (N = 50), and the exposed group including 43 urban and 7 rural children (N = 50).

Table 1: Demographic characteristics of study participants (N = 100)

Age	**Mean**	**Std. deviation**
Control (No Palmidronate)	10.2	0.0715
Treatment (Palmidronate)	8.4	0.0743
Sex		
Sex	**Group**	**Frequency**
Female	**Control (No Palmidronate)**	23
	Treatment (Palmidronate)	30
Male	**Control (No Palmidronate)**	27
	Treatment (Palmidronate)	20
Residence		
Residence	**Group**	**Frequency**
Urban	**Control (No Palmidronate)**	42
	Treatment (Palmidronate)	43
Rural	**Control (No Palmidronate)**	8
	Treatment (Palmidronate)	7

This table presents the baseline demographic data of children with Osteogenesis Imperfecta, comparing the Pamidronate-treated (exposed) and untreated (control) cohorts (N = 50 in each group). Variables include age (mean ± SD), sex distribution, and residential status.

Bone Mineral Density (BMD) was recorded at four intervals: baseline (prior to infusion), and at 3, 6, and 12 months post-infusion (Figure 1). At baseline, the mean BMD in the control group was 0.413 (standard deviation = 0.0715), while in the treatment group, it was 0.433 (standard deviation = 0.0743) (N = 50 in each group). At the 3-month follow-up, the control group had a mean BMD of 0.442 (standard deviation = 0.0762; 95% CI: 0.420–0.464), whereas the treatment group had a higher mean BMD of 0.477 (standard deviation = 0.0721; 95% CI: 0.457–0.498) (N = 50 in each group). At the 6-month mark, the control group showed a mean BMD of 0.446 (standard deviation = 0.0742; 95% CI: 0.425–0.467), and the treatment group recorded a mean BMD of 0.507 (standard deviation = 0.0765; 95% CI: 0.486–0.529) (N = 50 in each group).

After 12 months, the control group's mean BMD increased to 0.451 (standard deviation = 0.0644; 95% CI: 0.432–0.469), while the treatment group's mean BMD reached 0.541 (standard deviation = 0.0760; 95% CI: 0.519–0.562) (N = 50 in each group).

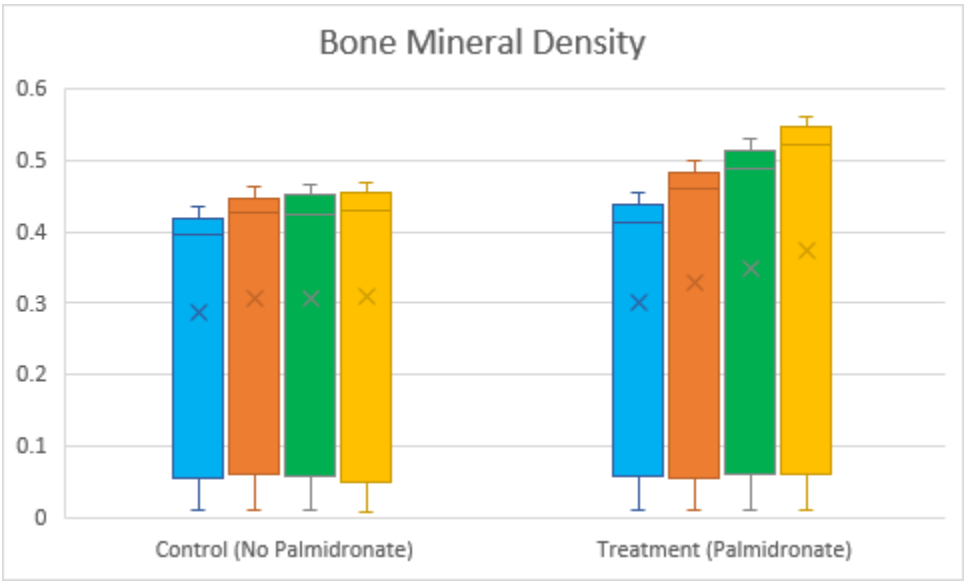

Figure 1: Longitudinal changes in Bone Mineral Density (BMD) over 12 months in control and Pamidronate groups (N = 50 each)

The figure shows BMD values (mean, standard deviation, standard error, and 95% confidence intervals) at baseline and at 3, 6, and 12 months post-infusion for both groups.

Repeated measures ANOVA was performed to assess the significance of changes in BMD over time (Figure 2). The within-subjects effect for BMD was statistically significant with a sum of squares of 0.2856, degrees of freedom (df) = 3, mean square = 0.0952, F = 1000, and $p < 0.001$. The interaction between BMD and treatment group was also significant with a sum of squares of 0.0712, df = 3, mean square = 0.0237, F = 249, and $p < 0.001$. Residual error was 0.028 with df = 294. The between-subjects effect comparing the two groups showed a sum of squares of 0.2652, df = 1, mean square = 0.2652, F = 12.5, and $p < 0.001$.

Residual between-subjects error was 2.076 with df = 98, and mean square = 0.0212. These results indicate a statistically significant improvement in BMD over time, with the effect significantly more pronounced in the Pamidronate group.

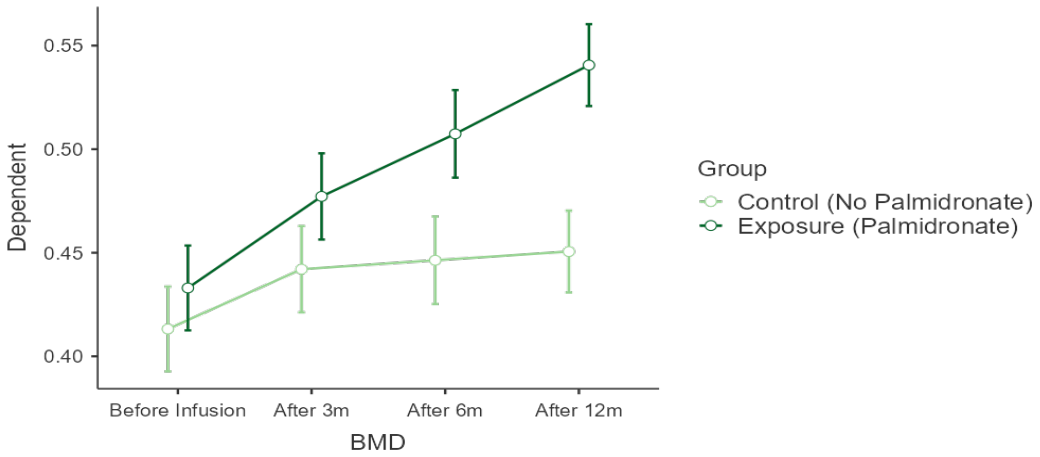

Figure 2: Repeated Measures and Between-Group ANOVA for Bone Mineral Density (BMD) Over 12 Months (N = 100)

This figure summarizes the results of repeated measures ANOVA conducted to evaluate the change in Bone Mineral Density (BMD) over four time points (baseline, 3 months, 6 months, and 12 months) in children with Osteogenesis Imperfecta. The within-subjects effect tests whether BMD changed significantly over time. The BMD × Group interaction term tests whether the change in BMD differed significantly between the Pamidronate-treated and control cohorts. The between-subjects effect tests for overall differences in BMD between the two groups, regardless of time. Results are presented as sum of squares (SS), degrees of freedom (df), mean square (MS), F-

statistic, and p-value, with statistical significance set at $p < 0.05$.

Fracture incidence was also assessed at the same intervals (Table 4). At baseline (before infusion), fracture count distributions showed that in the control group, most children reported between 2 and 4 fractures: 8 had 2 fractures, 14 had 3, 10 had 4, 6 had 5, 5 had 6, and 6 had 7 fractures, while only 1 child had a single fracture (N = 50). In the treatment group, fracture distributions were comparable with 13, 12, and 13 children falling into categories of 2, 3, and 4 fractures, respectively, with only one child reporting 8 fractures (N = 50). The chi-square test comparing both groups yielded a value of $\chi^2 = 7.42$ with df = 7 and a p-value of 0.387, indicating no significant difference in fracture frequency between groups before treatment.

At 3 months post-infusion, fracture incidence began to diverge. In the control group, children still exhibited a wide distribution: 7 had 1 fracture, 11 had 2, 10 had 3, 7 had 4, and 8 had 5 fractures, with 4 having 8 fractures (N = 50). In contrast, the treatment group showed improvement: 13 had only 1 fracture, 13 had 2, and 14 had 3 fractures, with no children reporting more than 4 fractures (N = 50). The chi-square test gave a value of $\chi^2 = 10.7$, df = 7, and a p-value of 0.154, indicating that although the trend favored the treatment group, the difference was not statistically significant at 3 months. The 6-month post-treatment data displayed a more distinct pattern. In the control group, children still reported higher fracture counts, with 6 having 1 fracture, 9 having 2, 18 having 3, 5 having 4, 6 having 5, and 4 having 8 fractures (N = 50). Conversely, the treatment group showed remarkable reduction: 26 had only 1 fracture, 14 had 2, 5 had 3, and 5 had 4 fractures, with no child reporting more than 4 (N = 50). The chi-square test showed a statistically significant difference with a value of $\chi^2 = 32.9$, df = 7, and $p < 0.001$. At 12 months, the control group remained dispersed across fracture categories with 8 children having 0 fractures, 5 having 1, 11 having 2, 6 having 3, 12 having 4, 3 having 5, 4 having 6, and 1 having 7 fractures (N = 50). In the treatment group, outcomes were significantly better: 13 had 0 fractures, 27 had 1, and only 10 children had more than 1 fracture, with none exceeding 3 fractures (N = 50). The chi-square value here was $\chi^2 = 38.7$, df = 7, and $p < 0.001$, confirming a highly significant reduction in fracture frequency in the treatment group at 12 months.

Table 2: Repeated Measures ANOVA for BMD and Between-Group Effects (N = 100)

Group	**Fracture incidence Before Infusion**									**χ^2 Tests**		
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Total**	**Value**	**df**	**p**
Control (No Palmidronate)	1	8	14	10	6	5	6	0	50	7.42	7	0.387
Treatment (Palmidronate)	0	13	12	13	6	4	1	1	50			
Total	1	21	26	23	12	9	7	1	100			
Group	**Incidence 3m post infusion**									**χ^2 Tests**		
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Total**	**Value**	**df**	**p**
Control (No Palmidronate)	7	11	10	7	8	2	1	4	50	10.7	7	0.154
Treatment (Palmidronate)	13	13	14	5	5	0	0	0	50			
Total	20	24	24	12	13	2	1	4	100			
Group	**Incidence 6m post infusion**									**χ^2 Tests**		
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**Total**	**Value**	**df**	**p**
Control (No Palmidronate)	6	9	18	5	6	1	1	4	50	32.9	7	**<.001**
Treatment (Palmidronate)	26	14	5	5	0	0	0	0	50			
Total	32	23	23	10	6	1	1	4	100			
Group	**Incidence 12m post infusion**									**χ^2 Tests**		
	0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**Total**	**Value**	**df**	**p**
Control (No Palmidronate)	8	5	11	6	12	3	4	1	50	38.7	7	**<.001**
Treatment (Palmidronate)	13	27	5	5	0	0	0	0	50			
Total	21	32	16	11	12	3	4	1	100			

This table provides statistical output from repeated measures ANOVA evaluating within-subjects effect (change in BMD over time), interaction effect (BMD × Group), and between-subjects effect (difference between groups).

Values reported include sum of squares, degrees of freedom, mean square, F-statistic, and p-values.

Discussion

The results of this study provide compelling evidence for the efficacy of Pamidronate therapy in improving bone health outcomes among children diagnosed with Osteogenesis Imperfecta (OI). In the present cohort of 100 children, divided equally into a treatment group receiving Pamidronate and a control group receiving no bisphosphonates (N = 50 each), a significant and consistent increase in bone mineral density (BMD) was observed in the

treatment group across all follow-up periods. The baseline mean BMD in the Pamidronate group (0.433 ± 0.0743) was slightly higher than in the control group (0.413 ± 0.0715), but by 3, 6, and 12 months, the difference became increasingly significant. By 12 months, the mean BMD in the treatment group had risen to 0.541, compared to only 0.451 in the control group, with all statistical comparisons showing p-values < 0.001, indicating robust treatment effects.

These findings align with several previous studies that have established the role of bisphosphonates in enhancing BMD in pediatric OI patients. Rauch et al. reported that cyclic intravenous Pamidronate therapy leads to marked increases in BMD and vertebral reshaping in children with moderate-to-severe OI [9]. Another longitudinal study by Glorieux et al. demonstrated a significant gain in lumbar spine BMD and reduced incidence of vertebral fractures in children treated with Pamidronate, confirming its skeletal benefits [5]. Our repeated measures ANOVA supports these observations, showing a highly significant interaction between time and treatment ($F = 249$, $p < 0.001$), and a significant main effect of the treatment group ($F = 12.5$, $p < 0.001$), underscoring the superior performance of Pamidronate over non-treatment.

Fracture incidence—a key clinical outcome in OI—also declined sharply in the Pamidronate group compared to the control group over the 12-month follow-up. Initially, there was no statistically significant difference in fracture frequency at baseline ($\chi^2 = 7.42$, $p = 0.387$), indicating comparable disease severity across groups.

However, by the 6-month interval, the fracture incidence in the Pamidronate group dropped substantially, with most children experiencing one or two fractures at most, whereas the control group continued to exhibit a broader and higher distribution of fracture counts ($\chi^2 = 32.9$, $p < 0.001$). This trend persisted and intensified at 12 months, where the majority of the treated children had either no fractures or only one, while the control group continued to experience higher fracture burdens ($\chi^2 = 38.7$, $p < 0.001$).

These results are consistent with previous clinical trials. Plotkin et al. reported a significant reduction in fracture rate among children with severe OI receiving cyclic Pamidronate therapy, along with improved mobility and quality of life [10]. Similarly, Biggins et al. found a reduction in fracture incidence and improved cortical bone architecture following long-term bisphosphonate treatment [11]. The observed improvements in both BMD and fracture outcomes are biologically plausible. Pamidronate, a nitrogen-containing bisphosphonate, acts by inhibiting farnesyl pyrophosphate synthase in osteoclasts, leading to reduced bone resorption and increased bone mass [12]. The therapy is particularly beneficial in pediatric populations with OI, where bone fragility and recurrent fractures significantly impair growth and development. Importantly, the benefits were seen as early as 3 months post-infusion and were sustained through 12 months, indicating both short- and long-term skeletal benefits. It is also noteworthy that our sample maintained demographic balance between the two groups in terms of sex and residential background, ruling out potential confounding effects from these variables. Although the treatment group had a slightly younger mean age (8.4 years vs. 10.2 years in the control), the difference was not large enough to substantially affect treatment outcomes, especially considering the strong effect sizes and statistical significance.

In contrast to earlier studies that often lacked control groups or used historical controls, our prospective design with a well-matched control group provides more rigorous evidence of efficacy. The use of repeated measures ANOVA allowed for a robust assessment of intra-subject changes over time and inter-group differences, accounting for both within- and between-subject variability. Limitations of our study include the relatively short follow-up period of 12 months and the sample size, although adequate for detecting statistically significant differences, might limit generalizability to all OI subtypes. Moreover, other important outcomes such as pain, functional mobility, and quality of life were not assessed and should be considered in future studies.

Conclusion

Children receiving Pamidronate demonstrated a significantly greater improvement in bone mineral density over 12 months when compared to controls, with consistent increases at each follow-up point. Fracture frequency in the treatment group decreased significantly from baseline to 6 and 12 months, while the control group showed minimal changes. Statistical analyses confirmed the robustness of these findings, with repeated measures ANOVA and chi-square tests supporting the efficacy of Pamidronate therapy in reducing morbidity and improving skeletal outcomes in pediatric OI.

This study, involving $N = 50$ in each group, contributes to the growing evidence supporting the use of bisphosphonates as a cornerstone of OI management in children.

References

1. Rauch F, Glorieux FH. Osteogenesis imperfecta. Lancet. 2004;363(9418):1377–85. doi: 10.1016/S0140-6736(04)16051-0.

2. Sillence DO, Senn A, Danks DM. Genetic heterogeneity in osteogenesis imperfecta. J Med Genet. 1979;16(2):101–16. doi: 10.1136/jmg.16.2.101.
3. Monti E, Mottes M, Fraschini P, et al. Current and emerging treatments for the management of osteogenesis imperfecta. Ther Clin Risk Manag. 2010;6:367–81. doi: 10.2147/tcrm.s5932.
4. Bishop N, Adami S, Ahmed SF, et al. Risedronate in children with osteogenesis imperfecta: a randomised, double-blind, placebo-controlled trial. Lancet. 2013;382(9902):1424–32. doi: 10.1016/S0140-6736(13)61091-0.
5. Glorieux FH, Bishop NJ, Plotkin H, et al. Cyclic administration of pamidronate in children with severe osteogenesis imperfecta. N Engl J Med. 1998;339(14):947–52. doi: 10.1056/NEJM199810013391402.
6. Rauch F, Plotkin H, Travers R, Glorieux FH. Osteogenesis imperfecta types I, III, and IV: effect of pamidronate therapy on bone and mineral metabolism. J Clin Endocrinol Metab. 2003;88(3):986–92. doi: 10.1210/jc.2002-021371.
7. Ward LM, Rauch F, Whyte MP, et al. Alendronate for the treatment of pediatric osteogenesis imperfecta: a randomized placebo-controlled study. J Clin Endocrinol Metab. 2011;96(2):355–64. doi: 10.1210/jc.2010-0636.
8. Esposito P, Plotkin H. Surgical treatment of osteogenesis imperfecta: current concepts. Curr Opin Pediatr. 2008;20(1):52–7. doi: 10.1097/MOP.0b013e3282f35f03.
9. Rauch F, Munns CF, Land C, Glorieux FH. Pamidronate treatment of children and adolescents with osteogenesis imperfecta: effect of treatment discontinuation. J Clin Endocrinol Metab. 2006;91(4):1268–1274. doi: 10.1210/jc.2005-2413.
10. Plotkin H, Rauch F, Bishop NJ, Montpetit K, Ruck-Gibis J, Travers R, et al. Pamidronate treatment of severe osteogenesis imperfecta in children under 3 years of age. J Clin Endocrinol Metab. 2000;85(5):1846–1850. doi: 10.1210/jcem.85.5.6584.
11. Biggin A, Munns CF. Long-term bisphosphonate therapy in osteogenesis imperfecta. Curr Osteoporos Rep. 2017;15(5):412–8. doi:10.1007/s11914-017-0401-0.
12. Russell RG, Watts NB, Ebetino FH, Rogers MJ. Mechanisms of action of bisphosphonates: similarities and differences and their potential influence on clinical efficacy. Osteoporos Int. 2008;19(6):733–759. doi.org/10.1007/s00198-007-0540-8