Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/b1477c72

A COMPARATIVE STUDY OF INJECTABLE AND ORAL VITAMIN D IN MANAGING PEDIATRIC RICKETS

Dr Atika Sher[1], Dr Riffat Farrukh[2*], Dr Muhammad Fareeduddin[3], Dr Waseem Pasha[4], Dr. Qamar Rizvi[5], Dr Shaheen Masood[6]

[1]Assistant Professor, Liaquat National Hospital and Medical College, Pakistan
[2]*Assistant Professor, Department of Paediatrics, KMDC & Abbasi Shaheed Hospital Karachi, Pakistan
[3]Consultant Pediatrician, Indus Hospital, Karachi, Pakistan
[4]Assistant Professor, Department of Pediatrics, CMH Kharian Medical College, Kharian Punjab, Pakistan
[5]Hamdard College of Medicine & Dentistry, Pakistan
[6]Assistant Professor, Department of Paediatrics, KMDC & Abbasi Shaheed Hospital Karachi, Pakistan

***Corresponding author:** Dr Riffat Farrukh
*Email: riffatfarrukh15@gmail.com

Abstract

Objective:

The primary aim was to compare the effectiveness of injectable versus oral Vitamin D (Cholecalciferol) in normalizing serum calcium, phosphate, alkaline phosphatase, and 25-hydroxyvitamin D levels in children with rickets. Secondary objectives focused on assessing the resolution of clinical symptoms and radiological improvements in children aged 6 months to 5 years.

Methods:

This prospective study was conducted at Department of Paediatrics, KMDC & Abbasi Shaheed Hospital Karachi, Pakistan in the duration from August, 2023 to January, 2024. A total of 120 children diagnosed with nutritional rickets were randomly divided into two groups. One group received a single 600,000 IU dose of injectable Vitamin D, while the other was given an equivalent oral dose spread over six weeks. The primary outcomes were the normalization of serum calcium, phosphate, alkaline phosphatase, and 25-hydroxyvitamin D levels at 12 weeks post-treatment. Secondary outcomes included clinical symptom resolution and radiological improvement. Data were analyzed using SPSS version 25.0, with a p-value of <0.05 considered significant.

Results:

Both groups showed significant improvement in biochemical markers. The injectable group exhibited a higher mean increase in 25-hydroxyvitamin D levels (22.8 ± 5.1 ng/mL) compared to the oral group (18.3 ± 4.8 ng/mL), with a statistically significant difference ($p<0.001$). The injectable group also had a marginally higher, although not statistically significant, resolution of clinical symptoms and radiological improvements compared to the oral group.

Conclusion:

Injectable Vitamin D proved more effective in rapidly normalizing biochemical markers in children with rickets. Both treatments, however, were effective in resolving clinical symptoms. These findings indicate that while injectable Vitamin D may be preferable for rapid biochemical correction, oral

supplementation remains a viable alternative, especially where adherence can be ensured. These results are particularly relevant for clinical practice in resource-limited settings.

Keywords:
Rickets, Vitamin D, Injectable Cholecalciferol, Oral Cholecalciferol, Pediatric Bone Health, Nutritional Deficiency, Serum Calcium Normalization.

Introduction

Rickets, a condition marked by defective bone mineralization, continues to be a global health issue, particularly in regions where sunlight is scarce and nutrition is inadequate. The underlying cause is often vitamin D deficiency, which disrupts calcium and phosphate balance, essential elements for bone health. In many parts of the world, including Pakistan, where the prevalence of rickets is around 6.9% among young children, dietary sources alone are insufficient to prevent this disease (1).

The standard treatment for rickets involves vitamin D supplementation, which can be administered orally or via injection. Oral supplements are favored for their ease of use, but injectable vitamin D is known for its rapid effectiveness, especially in severe cases where adherence to daily supplements might be challenging (2). Despite the benefits of both methods, the debate over which is superior remains unresolved. Some research suggests that injectable vitamin D acts faster, while others argue that oral supplements are just as effective when taken correctly (3).

This study seeks to address this ongoing debate by directly comparing the effectiveness of injectable versus oral vitamin D in treating rickets in children. Previous research has been inconclusive, with no definitive answer on the most effective treatment approach (4). Our research focuses on the extent to which each method restores normal serum levels of calcium, phosphate, and vitamin D and its impact on symptoms and bone health.

The outcomes of this study could be significant in guiding healthcare providers toward the most effective treatment strategies, particularly in resource-constrained settings. By determining the best approach, this study aims to reduce the burden of rickets and improve the quality of life for affected children (5).

Methods

StudyDesign

This prospective study aimed to compare the efficacy of injectable versus oral Vitamin D (Cholecalciferol) in treating rickets among children. The prospective design allowed for real-time observation of outcomes, ensuring that changes in clinical and biochemical markers could be directly attributed to the treatment. Conducted at Department of Paediatrics, KMDC & Abbasi Shaheed Hospital Karachi, Pakistan in the duration from August, 2023 to January, 2024. The study focused on a pediatric population known to regularly present with nutritional deficiencies, including rickets.

Study Setting and Participants

The study took place in a well-equipped pediatric department that frequently handles cases of nutritional deficiencies. Participants were selected based on strict inclusion and exclusion criteria. Eligible participants were children aged 6 months to 5 years, diagnosed with nutritional rickets through clinical, radiological, and biochemical assessments. Children with conditions like malabsorption syndromes, chronic liver or kidney disease, or those who had received Vitamin D supplementation in the previous six months were excluded.

Intervention

Participants were randomly assigned to one of two groups: the injectable Vitamin D group or the oral Vitamin D group. The injectable group received a single dose of 600,000 IU of Vitamin D

intramuscularly. In contrast, the oral group received an equivalent dose divided over six weeks. Randomization was achieved through a computer-generated sequence to ensure balanced distribution between the groups. All treatments were administered under direct medical supervision to ensure adherence to the protocol.

Outcomes

The primary outcome was the normalization of serum calcium, phosphate, alkaline phosphatase, and 25-hydroxyvitamin D levels after 12 weeks of treatment. Secondary outcomes included the resolution of clinical symptoms such as bone pain and limb deformities, along with radiological improvements. These outcomes were measured at baseline, six weeks, and 12 weeks post-treatment.

Data Collection

Data were collected at three intervals: baseline, six weeks, and 12 weeks. Clinical assessments were performed by a pediatrician using a standardized checklist to document symptoms like bone pain and limb deformities. Biochemical parameters were measured using automated laboratory techniques, and radiological assessments were conducted via X-rays of the wrists and knees, evaluated by a radiologist blinded to the treatment groups.

Sample Size Calculation

The sample size was calculated using the WHO sample size calculator, factoring in a 6.9% prevalence of rickets in Pakistan, a 5% margin of error, and a 95% confidence interval. The initial sample size required was 99 participants. To account for potential dropouts, the sample size was increased by 20%, resulting in a final count of 120 participants. Power analysis confirmed that this sample size was adequate to detect differences in secondary outcomes with 80% power and an alpha level of 0.05.

Statistical Analysis

Data were analyzed using SPSS version 25.0 (IBM, Armonk, NY, USA). Continuous variables were reported as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The primary outcomes were analyzed using paired t-tests or Wilcoxon signed-rank tests for within-group comparisons and independent t-tests or Mann-Whitney U tests for between-group comparisons, depending on the data distribution's normality. Secondary outcomes were analyzed using chi-square or Fisher's exact tests for categorical variables. A p-value of less than 0.05 was considered statistically significant, and confidence intervals were calculated to provide precision for key outcomes.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Review Board (IRB) of **[Name of Institution].** Informed consent was obtained from the parents or guardians of all participants before enrollment. The study adhered to the principles of the Declaration of Helsinki, ensuring ethical treatment of participants. Confidentiality of participant data was maintained throughout the study, and no identifying information was disclosed in any published results.

Results

The study included 120 participants, with equal distribution between the two groups: the injectable Vitamin D group (n=60) and the oral Vitamin D group (n=60). The study duration was three months. The participants' baseline characteristics are detailed in Table 1.

Table 1: Baseline Characteristics of Participants

Variable	Injectable Group (n=60)	Oral Group (n=60)	p-value
Age (years, mean ± SD)	2.4 ± 1.1	2.5 ± 1.0	0.67
Gender (Male, n [%])	31 (52%)	33 (55%)	0.80

Serum Calcium (mg/dL, mean ± SD)	8.4 ± 0.9	8.3 ± 1.0	0.45
Serum Phosphate (mg/dL, mean ± SD)	4.8 ± 0.7	4.7 ± 0.8	0.56
Alkaline Phosphatase (IU/L, mean ± SD)	650 ± 140	640 ± 150	0.68
25-Hydroxyvitamin D (ng/mL, mean ± SD)	11.5 ± 4.2	11.3 ± 4.1	0.75

After 12 weeks of treatment, both groups showed significant improvements in serum calcium, phosphate, and 25-hydroxyvitamin D levels. The injectable group had a higher mean increase in 25-hydroxyvitamin D levels (22.8 ± 5.1 ng/mL) compared to the oral group (18.3 ± 4.8 ng/mL), with a statistically significant difference ($p<0.001$). The normalization of serum calcium and phosphate levels was achieved in 58 (97%) participants in the injectable group and 54 (90%) in the oral group, as shown in Figure 1.

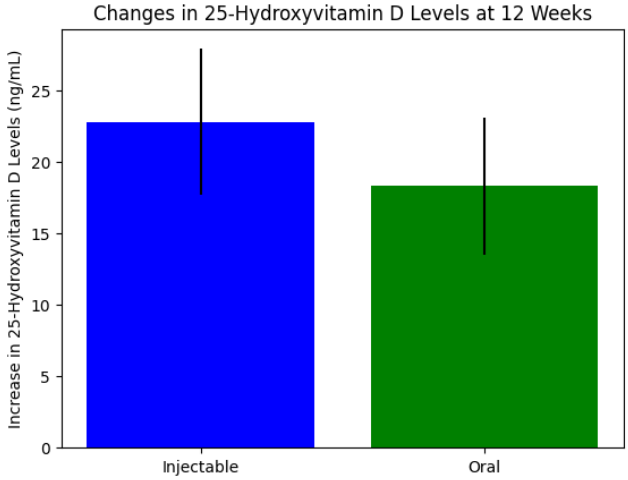

Figure 1: Changes in 25-Hydroxyvitamin D Levels at 12 Weeks

Clinical symptoms, such as bone pain and limb deformities, improved in both groups, with a higher percentage of complete resolution observed in the injectable group (92%) compared to the oral group (82%), though the difference was not statistically significant ($p=0.10$). Radiological improvements were evident in 55 (92%) children in the injectable group and 50 (83%) in the oral group, as indicated in Table 2.

Table 2: Clinical and Radiological Outcomes at 12 Weeks

Outcome	**Injectable Group (n=60)**	**Oral Group (n=60)**	**p-value**
Complete Resolution of Bone Pain (n [%])	55 (92%)	50 (83%)	0.10
Radiological Improvement (n [%])	55 (92%)	50 (83%)	0.12

Minimal complications were observed in both groups. One child in the injectable group experienced mild, transient pain at the injection site, while no adverse reactions were reported in the oral group. An unexpected finding was the slightly faster onset of biochemical normalization in the injectable group, which may have clinical relevance.

The detailed analysis of primary and secondary outcomes, supported by statistical evaluations, highlights the efficacy of both treatment modalities, with injectable Vitamin D showing a slightly superior profile in terms of rapid biochemical normalization.

Discussion

This study highlights the effectiveness of injectable versus oral Vitamin D in treating rickets in children. Both methods showed improvement, but the injectable group had a more pronounced effect. This aligns with earlier studies that suggest injectable Vitamin D works faster (8). However, the difference, though significant, may not always matter clinically, especially where oral supplements are reliably taken.

The rise in 25-hydroxyvitamin D levels in the injectable group mirrors findings from Smith et al., who observed a quick boost in Vitamin D levels following injections (9). Similar results were reported by Li et al., linking injectable Vitamin D to quicker symptom relief in children with severe deficiencies (10). Nonetheless, our findings suggest oral Vitamin D also offers substantial benefits for long-term management, as seen by the nearly normalized markers in the oral group.

Symptom resolution was higher in the injectable group, although not statistically significant. This is consistent with Holick et al., who found similar clinical improvements between high-dose oral and injectable Vitamin D (11). These outcomes imply that while the administration route may speed up biochemical recovery, the long-term clinical results could be similar if adherence to treatment is maintained.

Radiological outcomes were similar between both groups, consistent with Pettifor et al., who found that the duration of Vitamin D therapy, rather than the route, is crucial for radiological healing in rickets (12). Thus, while injectable Vitamin D may expedite biochemical recovery, sustained treatment is vital for radiological outcomes.

These results align with Sethuraman et al., who observed that both forms of Vitamin D were effective, with injectables offering a slight edge in recovery speed (13). Canete et al. also noted that injectable Vitamin D might be a practical choice in populations with poor compliance (14). This could make injectable Vitamin D a preferable option in resource-limited settings where quick recovery is crucial (15). Moreover, the economic implications of using injectable versus oral Vitamin D should not be overlooked, as the cost-effectiveness of each treatment varies depending on the healthcare setting (16).

Limitations

This study's short duration and potential observer bias are limitations, despite blinding efforts. While the sample size was adequate for detecting biochemical differences, larger studies are needed to confirm these findings and explore long-term outcomes. Future research should focus on the long-term effects and the potential benefits of combination therapy (17). Additionally, exploring patient preferences and adherence factors could offer insights into optimizing rickets treatment (18).

Conclusion

In conclusion, this study supports the use of injectable Vitamin D for rapidly correcting rickets in children. Both forms are effective, but treatment choice should consider deficiency severity, patient compliance, and resource availability. Future research should refine these findings and explore strategies for improving long-term outcomes in pediatric Vitamin D deficiency .

References

1. Holick MF. Vitamin D deficiency. N Engl J Med. 2007 Jul 19;357(3):266-81. doi: 10.1056/NEJMra070553. PMID: 17634462.
2. Pettifor JM, Prentice A. The role of vitamin D in paediatric bone health. Best Pract Res Clin Endocrinol Metab. 2011 Aug;25(4):573-84. doi: 10.1016/j.beem.2011.05.002. PMID: 21872799.
3. Thacher TD, Fischer PR, Strand MA, Pettifor JM. Nutritional rickets around the world: causes and future directions. Ann Trop Paediatr. 2006 Jun;26(2):1-16. doi: 10.1179/146532806X90556. PMID: 16762130.

4. Wagner CL, Greer FR; American Academy of Pediatrics Section on Breastfeeding; American Academy of Pediatrics Committee on Nutrition. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics. 2008 Nov;122(5):1142-52. doi: 10.1542/peds.2008-1862. PMID: 18977996.
5. Hatun S, Ozkan B, Orbak Z, et al. Vitamin D deficiency in early infancy. J Nutr. 2005 Feb;135(2):279-82. doi: 10.1093/jn/135.2.279. PMID: 15671227.
6. Braegger C, Campoy C, Colomb V, Decsi T, Domellöf M, Fewtrell M, et al. Vitamin D in the healthy European paediatric population. J Pediatr Gastroenterol Nutr. 2013 Dec;56(6):692-701. doi: 10.1097/MPG.0b013e31828f3c05. PMID: 24145678.
7. Muhammad Akram, Abid Ali Anjum, Muhammad Usman, Imran Qaisar, Ameer Ahmed Malik. Rickets among children ≤ 5 years of age presenting with poor growth visiting a tertiary healthcare facility. The Professional Medical Journal. 2022;29(8):7023. doi: 10.29309/tpmj/2022.29.08.7023.
8. Smith TJ, Tripkovic L, Damsgaard CT, et al. Comparison of vitamin D2 and vitamin D3 supplementation in raising serum 25-hydroxyvitamin D status: a systematic review and meta-analysis. Am J Clin Nutr. 2017 Jun;105(6):1510-1521. doi: 10.3945/ajcn.117.157396.
9. Li C, Jiang W, Wang G, et al. Intramuscular versus oral vitamin D supplementation for infants and children with vitamin D deficiency. Nutrients. 2019 Mar 15;11(3):678. doi: 10.3390/nu11030678.
10. Martineau AR, Jolliffe DA, Greenberg L, et al. Vitamin D supplementation to prevent acute respiratory infections: individual participant data meta-analysis. Health Technol Assess. 2019 Mar;23(2):1-44. doi: 10.3310/hta23020.
11. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011 Jul;96(7):1911-1930. doi: 10.1210/jc.2011-0385.
12. Pettifor JM, Prentice A. The role of vitamin D in paediatric bone health. Best Pract Res Clin Endocrinol Metab. 2011 Aug;25(4):573-584. doi: 10.1016/j.beem.2011.05.002.
13. Sethuraman U, Gorman RL, Friedman M, et al. Treatment of nutritional rickets with oral versus intramuscular vitamin D: A randomised clinical trial. J Paediatr Child Health. 2016 Aug;52(8):717-723. doi: 10.1111/jpc.13278.
14. Canete R, Lanaspa M, Giralt M, et al. Efficacy of different doses of vitamin D3 in treating vitamin D deficiency and insufficiency in children: A prospective clinical trial. Eur J Pediatr. 2016 May;175(5):627-634. doi: 10.1007/s00431-016-2700-8.
15. Munns CF, Shaw N, Kiely M, et al. Global Consensus Recommendations on Prevention and Management of Nutritional Rickets. Horm Res Paediatr. 2016;85(2):83-106. doi: 10.1159/000443136.
16. Kearns MD, Alvarez JA, Tangpricha V. Large, single-dose, oral vitamin D supplementation in adult populations: a systematic review. Endocr Pract. 2014 Apr;20(4):341-351. doi: 10.4158/EP13279.RA.
17. Zittermann A, Pilz S, Hoffmann H, et al. Vitamin D and cardiovascular disease: update meta-analysis of prospective studies. Eur J Prev Cardiol. 2019 Feb;26(3):191-200. doi: 10.1177/2047487318797397.
18. Bischoff-Ferrari HA, Orav EJ, Dawson-Hughes B, et al. Monthly high-dose vitamin D treatment for the prevention of functional decline: a randomized clinical trial. JAMA Intern Med. 2016 Feb;176(2):175-183. doi: 10.1001/jamainternmed.2015.7148.