

## Comparison of Response of Oral Versus Injectable Vitamin D in Children Having Rickets

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### Abstract

Malnutrition is one of the major issues around the world. According to one estimation, it is stated that one of three children daily die from malnutrition in all over the world. Rickets is one of the most prevalent metabolic bone diseases in children. Proper diet and treatment can help in prevention of rickets. Rickets is a bone disorder due to deficiency of vitamin D. The level of vitamin D tells the severity of nutritional rickets as vitamin D is the major factor of this disease. There were no undesirable side effects observed in either group of children and both oral and injectable forms of treatment were well-tolerated. Cost of oral and injectable vitamin-D was almost same.

**Keywords:** Vitamin D; Calcium and phosphate; Malnutrition

### Introduction

Children are most sensitive to disease in the world. Proper vaccines and healthcare can help in decreasing childhood deaths in world. Malnutrition is one of the major issues around the world. According to one estimation, it is stated that one of three children daily die from malnutrition in all over the world. Malnutrition causes micronutrient and macronutrient deficiency among children. One of most prevalent micronutrient deficiency is vitamin D deficiency. Prolong Vitamin D deficiency leads to rickets in children and osteomalacia in adults.

Rickets is one of the most prevalent metabolic bone diseases in children. Proper diet and treatment can help in prevention of rickets. Rickets is a bone disorder due to deficiency of vitamin D, calcium and phosphate [1-9]. This disease causes faulty mineralization in growth plates of bones in children during childhood. Radiological and biochemical findings help in characterization of disease. Improper metabolism of calcium, vitamin D and phosphorous cause defective formation of bone in children that leads to bone abnormality and fracture [10-15]. Rickets is among the most incessant adolescence maladies in numerous developing nations. The prevalent cause is a vitamin D insufficiency, yet absence of sufficient calcium in the eating regimen may likewise prompt to rickets. In spite of the fact that it can occur in older people, the larger part of cases occurs in young children experiencing malnutrition, for the most part coming about because of starvation or starvation amid the early phases of adolescence. In developed nations, rickets is an uncommon disease (rate of under 1 in 200,000). Instances of rickets have been accounted among youngsters who are bolstered plant-based drain substitutes and not given supplemental vitamin D. It is a typical sickness in kids amid their adolescence i.e., 6 months to 3 years.

Nutritional rickets is a common health matter in numerous countries. It for the most part happens in babies who are exclusively breastfed without vitamin D supplementation. Nutritional rickets is essentially found in low wage nations in Asia, Africa, or the Middle

East exact prevalence in Pakistan is still not clear; despite the fact that its predominance in South East Asia is around 15-18%. Because of modern lifestyle and globalization, the recurrence of nutritional rickets is rising step by step in both developed and less developed nations Carol and Frank. It has been recommended that there are diverse variables and cofactors required in the commonness of sickness e.g., distinctive dietary intake, maternal intake, natural conditions, geological circulations. In 1930's some public activities were taken and prescribed vitamin D and cod liver oil for new-born children and kids as a wholesome supplement. Still rickets is predominant in less developed countries Bell. In industrialized nations, rickets is more pervasive among babies and kids because of numerous reasons. Nutritional rickets is getting much consideration of wellbeing experts and clinicians around the world. It remains a far-reaching issue in many developing countries [16-20].

According to a classification, Rickets has two types i.e., Calcipenic rickets and Phosphopenic rickets. Calcipenic rickets is mainly caused by deficiency of vitamin D, calcium or malabsorption of vitamin D or calcium. Phosphopenic rickets is not regular, but rather happens in exceptional circumstances like low phosphorous intake, prematurity/total parenteral nutrition, Renal phosphate wasting, Proximal renal tubular acidosis, Fibrous dysplasia, Oncogenic hypophosphataemic rickets and Hereditary hypophosphatemia rickets Megged and Karim.

Here our primary concern is nutritional rickets, sub kind of calcipenic rickets. Wholesome rickets is a typical issue in Pakistan as highlighted in various studies. Nutritional rickets remains a common health issue in numerous nations, regardless of dramatic decreases in the predominance of the disease in numerous developed nations since the revelations of vitamin D [21-26]. Vitamin D inadequacy as well as nutritional rickets stay predominant in developing areas of the world and rank among the 5 most prevalent diseases in children. Predominance of nutritional rickets in developed nations seems, by all accounts, to be rising. Proposed reasons in the writing for its re-emergence incorporate carelessness in strengthening nourishment, changing ways of life where youngsters invest a large portion of their energy inside on different types of innovation and globalization which

has brought about migration of various people groups to various geographic areas. Nutritional Rickets is unmistakable from different sorts of rickets in that it is just brought on by a straightforward insufficiency in vitamins and nourishment and consequently can be effectively revised if recognized early.

Primary driver of nutritional rickets is inadequacy of vitamin D. Vitamin D is a fat-soluble hormone imperative for calcium assimilation and bone mineralization. Its main function is maintenance of serum calcium and phosphorous level in the typical range by increasing the efficiency of the small intestine to digest these minerals from the diet. DeLuca, Reichel. Vitamin D advances calcium retention in the gut and keeps up sufficient serum calcium and phosphate levels to maintain typical mineralization of bone and to prevent hypercalcaemic tetany [27-35]. It is likewise required for bone development and bone redesigning by osteoblasts and osteoclasts. Without adequate vitamin D, bones can turn out to be thin, weak, or misshapen. It has been concurred that serious and long lasted vitamin D lack can cause rickets in children and osteomalacia in older persons. Low level (ordinarily <5 ng/mL) of 25-hydroxyvitamin D [25(OH)D] and disabled intestinal calcium ingestion are imperative markers of vitamin d deficiency rickets.

Sunlight exposure is the major vitamin D source. Sunlight radiations vary with season and latitudes. Every country has different duration of sunlight exposure. Some countries having small duration of sunlight exposure will have less amount of vitamin D. Naturally a small number of foods contains vitamin D like oily fish (salmon, mackerel etc) fish oils or COD liver oils. According to researches, it is stated that wild salmon contains greater amount of vitamin D than farmed salmon. The reason is that vitamin D is abundant in food chain of wild salmon than in foods given to farmed one. Some countries have launched vitamin D fortified foods i.e., juices, yogurts, cheeses etc.

Indications of rickets can cause pain or weakness in the bone of arms, legs, pelvis or spine. It likewise causes hindered growth, short stature, bone fracture, muscle cramps, tooth disfigurements and skeletal deformities. Tooth distortions incorporates deferred tooth formation, holes in the enamel, abscesses, defects in the tooth structure and an expanded number of cavities. Skeletal deformations include a strangely moulded skull, bowlegs, or legs that bow out, bumps in the ribcage, a projecting breastbone, a bended spine, pelvic distortions [21].

Treatment of rickets varies with type of rickets. Here we will examine just nutritional rickets. The analysis of nutritional rickets is made on the premise of history, physical examination, and biochemical testing, and is affirmed by radiographs. Basic treatment of nutritional rickets is to fulfil the deficiency of vitamin D. If there will be proper required quantity of vitamin D in body then there will be no chance of getting nutritional rickets [36-40]. The deficiency of vitamin D can be fulfilled by two ways either by supplements or by injections.

Keeping in view the severity of the issue, the present research work is designed to address the increasing incidence of vitamin D deficiency in children affected with rickets. Purposely, children with reported incidence of rickets will be administered with cholecalciferol (both oral and injectable) in the subjects for a period of 90 days. The comparison of efficiency between the oral administration and injectable doses is the limelight of the present research work.

## Material and Methods

The study was conducted in Children Hospital Lahore and Fatima Memorial Hospital from May 2016 to September 2016. 100 children were selected randomly. Children having age between 6 months to 3 years and having biochemical, clinical and radiological evidence of nutritional rickets were selected after taking informed consent from parents. Children having chronic disease or severe serious condition were not included. The details of each child were recorded in prescribed Performa. Clinical, biochemical and x-ray of wrist were done and their findings were recorded in Performa. The children were divided into two groups i.e., Oral (group A) and Injectable (group B). Children included in group A were given vitamin D (Cholecalciferol) i.e., 200,000 IU orally on 0 visit and children of group B were given vitamin D through intramuscular injection. All children were requested to come for two further follow-up visits. At each visit, the children were subjected to biochemical, clinical and radiological examination and findings were recorded.

For statistical analysis, ANOVA was used. Means were compared through LSD. Level of significance was defined as  $\leq 0.05$ .

## Results

After data analysis, following observations were recorded at the end of study. 100 children were included in the record. 50 in group A (oral) and 50 in group B (injectable) according to prescribed inclusion criteria. 94 % of children from Group A and 98% from group B completed full study.

Basic characteristics like age, gender, weight and height are shown in Tables 1 and 2. Weight gain are statistically significant in group B and increase in height is statistically significant in group B.

Characteristics	Group A(oral)	F-value	Group B(Injectable)	F-value
Age (months)				
Mean	21.7		20	
Gender				
Male	22		28	
Female	25		21	
Weight (Kg)				
Day 1	7.5596		8.0062	
Day 30	7.9149	45.88	8.4854	177.12
Day 90	8.2234		9.0021	
Height (cm)				
Day 1	65.572		68.406	
Day 30	72.368	307.81	72.344	93.85
Day 90	76.823		75.371	

**Table 1:** Basal characteristics of groups.

Signs and symptoms	Oral (Group A)	Injectable (Group B)
Bow legs	51.00%	59.10%
Frontal Bossing	59.50%	65.30%
Wide wrist	57.40%	59.10%

**Table 2:** Signs and Symptoms.

Table 3 shows the comparison of biochemical findings between two groups. The level of Alkaline Phosphatase becomes normal in both groups but rapid improvement was seen in group B (injectable). The serum Calcium level increased to normal level in both levels in both groups but increase was obvious in group B as compare to group A. The level of serum Phosphorous becomes normal in both groups but rapid improvement was seen in group B than group A. The level of 25 hydroxyvitamin D increased to normal level in both groups but rapid increase was in group B.

	Group A(oral)	F-value	Group B(injectable)	F-value
	Mean ± S.D		Mean ± S.D	
I. Serum Calcium				
Day 1	8.3		8.0563	
Day 30	8.6	11.41	8.6687	69.35
Day 90	8.7		8.7646	
II. Serum Phosphorus				
Day 1	4.7		4.3625	
Day 30	5.2	10.44	4.1937	38.03
Day 90	5.0		3.4083	
III. Alkaline Phosphatase				
Day 1	627.89		668.81	
Day 30	423.43	324.79	466.17	829.35
Day 90	303.96		251.46	
IV. Vitamin D				
Day 1	12.7		13.625	
Day 30	41.1	5003.73	56.946	9078.78
Day 90	58.0		72.635	

**Table 3:** Biochemical values.

Radiologically, the healing of rickets and decreasing of width in growth plate was obvious in children of injectable group. The parents preferred the injectable route over oral one there were no side effects seen in children of both groups.

## Discussion

The comparison of clinical efficiency of injectable and oral form of cholecalciferol was done in this study. Children having symptoms of nutritional rickets. Each group had 50 children.

Average age in this study was  $21.7 \pm 9.2$  months in group A and  $20.8 \pm 8.1$  months in group B. A study from Karachi included children having age between 2 months to 36 months having clinical manifestations of rickets. Nutritional rickets mostly occurs in children during age between 3 months to 18 months. A study done in Hyderabad included children having age less than 5 years. According to study done in Rawalpindi, vitamin D deficiency mostly occurs in children having age range of 9 months to 12 months. Age of rickets children range from 6 to 11 months in local study from Lahore [41-44]. According to the nutritional rickets mostly occur in children having age less than 1 year.

This study included 50% males and 46% females. Another study included 47% males and 52% females. Mostly studies shows that there is more percentage of rickets effective males than females i.e., a study from Karachi included 62% males and a study included 62% males done in Peshawar. Male gender is risk factor for nutritional rickets in local study from Lahore.

Children Hospital is government hospital and covers almost treatment of poor and lower-class children at an affordable cost. The majority of population who visit this hospital is not well nourished and not aware of importance of vitamin D or sunlight. The women and children wear the local dress shalwar kameez, which covers most of the skin surfaces except face and hands.

Nutritional rickets also effects the growth of children. It is obvious from results that height and weight of affected children are not in recommended normal range in first visit and it becomes gradually normal after vitamin D introduction in preceding visits in both groups (injectable and oral). But obvious change was seen in injectable group as compare to oral group. Vitamin D deficiency affects the height and weight of children. Vitamin D deficiency cause improper skeletal growth in children as oddly shaped skull, bow legs, protruding abdomen etc.

Previous studies show that level of Alkaline Phosphatase increase abnormally in nutritional rickets. Results of this study also show that value of Alkaline Phosphatase is high in both groups on first visit. The decrease in Alkaline Phosphatase level after vitamin D doses was obvious in preceding visits in both groups but decrease was rapid in injectable group as compare to oral group.

Nutritional Rickets decrease the level of calcium and phosphorous as discussed in previous studies. Results of this study show that calcium and phosphorous levels were low on first day. Calcium and phosphorous becomes normal after vitamin D dosage in preceding visits. But rapid increase in Calcium and Phosphorous level was in injectable group as compare to oral group.

Vitamin D levels are biomarker of nutritional rickets. The level of vitamin D tells the severity of nutritional rickets as vitamin D is the major factor of this disease. The vitamin D level was low in both groups on first day. After vitamin D dosage, it increases to normal level in both groups in preceding visits.

X-rays of wrists and knees are mostly taken for the diagnosis of nutritional rickets as mentioned in previous studies. Wrist and knee x-rays of children were taken on every visit. The x-ray reports showed

improvement in healing in subsequent visits prior to first visit. There was little bit difference between the groups. Injectable group showed rapid healing as compare to oral one.

There were no undesirable side effects observed in either group of children and both oral and injectable forms of treatment were well-tolerated. Cost of oral and injectable vitamin-D was almost same. Regarding route of administration of cholecalciferol, the parents preferred intramuscular route.

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