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COMPARISON OF THE PARENTERAL AND ORAL VITAMIN D SUPPLEMENTATION IN THE TREATMENT OF NUTRITIONAL RICKETS IN TERMS OF MEAN CHANGE IN SERUM CALCIUM, PHOSPHORUS, AND ALKALINE PHOSPHATASE

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ABSTRACT:

BACKGROUND & OBJECTIVE: Rickets is a common presentation on the pediatric floor, with nutritional rickets being the cause of leading significant morbidity, disability, especially in the developing countries of the world.The objective is to compare the efficacy of parenteral and oral vitamin D supplementation in the treatment of nutritional rickets.
METHODOLOGY: This comparative interventional, prospective analysis was conducted at Aziz Fatimah Hospital Faisalabad (1-1-2017 to 30-6-2017)outdoor patients divided into parenteral and oral groups. All of the outcome variables were measured at baseline and one month after treatment.
RESULTS: In this study, mean age was calculated as 2.12±0.76 years and 2.15±0.77 in parental and oral groups respectively. 49.29%(n=69) and 45%(n=63) were male and 50.71%(n=71) and 55%(n=77) were female respectively in both groups. At baseline, serum calcium was 8.68 ± 0.35 and 8.71±0.37 (p=0.62) serum phosphoruswas 3.92±9.22 and 3.84±0.20 (p=0.03), and serum alkaline phosphatasewas 230.01±13.09 and 228.89±13.80 (p=0.48) in parenteral and oral groups respectively. After treatment the mean change seen in serum calcium was 1.14±0.26 and 0.72±0.19 (p=0.001), serum phosphorus was 1.42±0.33 and 0.71 ±0.26 (p=0.001), serum Alkaline phosphatase was 79.48 ±14.84 and 23.65±12.21 (p=0.001) in parenteral and oral groups respectively.
CONCLUSION: We concluded that the parenteral route for vitamin. D supplementation is significantly better than the oral route in treating nutritional rickets in terms of mean change in serum calcium, serum phosphorus, and serum alkaline phosphatase.
KEYWORDS: Nutritional rickets, Treatment, Vitamin D supplementation, Alkaline phosphatase.

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INTRODUCTION:

Rickets is defined as the failure to mineralize growing bones before the closure of growth plate in children [1]. It is caused by vitamin D, calcium and phosphorus deficiency. Vitamin D disorders include nutritional, congenital, secondary vitamin D deficiency, vitamin D dependent rickets, and chronic renal failure. Vitamin D deficiency due to malnutrition leading to rickets is prevalent in developing and underdeveloped countries[2]. Among the most common causes of vitamin D deficiency are inadequate sunlight, dark skin tone[3] and low economic class,and less amount of vitamin D in mother feed[4].

Pakistan is included in vitamin D insufficient areas of the region and of the world[5]. Vitamin. D helps in the absorption of calcium from GIT, phosphorus from bones, and increase urinary phosphate excretion. All this leads to decreased bone mineralization[6]. Rickets' signs and symptoms include frontal bossing, craniotabes, rachitic rosary, delayed closure of fontanels, widening of wrists and ankles, bowing of long bones, seizures, irritability, delayed dentition, and paraesthetics[7].

Correction of the vitamin. D deficiency is an important issue. There are two routes of the vitamin. D administration; oral and intramuscular [8]. In a randomized controlled trial concluded in Tehran, both routes of the vitamin. D administration were compared. Oral vitamin. D showed better results than the intramuscular route [9].

In a study conducted in Egypt, children with rickets were treated with oral and intramuscular vitamin D supplements with a mean change in serum calcium of 0.78 ± 0.98 and 1.23 ± 1.61($p=0.56$) respectively and mean decrease in serum alkaline phosphates. 11.36 ± 5.60 and 623.36 ± 695.70 ($p=0.004$) and mean increase in phosphorus 0.5 ± 0.57 and 1.46 ± 1.30($p=0.147$) respectively [10].

The objective of this study was to compare single-dose I/M vitamin D with daily dose oral vitamin D supplementationas a part of nutritional rickets management to see meaningfulchange in serum calcium, phosphorus and alkaline phosphatase, and based on the findings, patients can be provided with better treatment options and morbidity can be reduced.

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This controlled study was conducted in the Pediatrics Unit-I, Aziz Fatimah Hospital Faisalabad, from dated 1.1.2017 to 31.6.2017.Two hundred eighty children, age 1 year to 3 years including both genders,including those who have evidence of nutritional rickets as per operational definition. (signs of rickets frontal bossing, widening of wrists, rachitic rosary, Harrison sulcus, wide-open fontanel.) Permission from the ethical review committee of the institution was taken.

Nutritional Rickets was defined based onthe presence of two of the following signs of rickets:Frontal bossing,wide writs, rachitic rosary, delayed closure of fontanelles, and two of the following radiological signs: cupping, flaring, fraying, and osteopenia. Parenteral Vitamin D was given as 600,000 international units cholecalciferol intramuscularly once a month.

Change in calcium, phosphorus, and alkaline phosphate: was measured as mean change in Ca, Phosphorus, Alkaline Phosphate measured at baseline and one month post-treatment. Oral Vitamin D was given as 2,000 international units cholecalciferol orally daily, for one month. Children who were taking vitamin D from last 12 weeks, having renal disease, tuberculosus, liver disease, having evidence of severe malnutrition with rickets other than nutritional rickets, serious illness, known hypersensitivity to the product, and children with hypoparathyroidism were excluded from the study.

All outdoor patients meeting inclusion criteria were taken and divided into two groups by computer-generated table:Perenteral group received 600,000 international units Vitamin D, I/M and Oral group: received 2,000 international units of Vitamin. D orally for 1 month. Written informed consent prior to inclusion was taken exclusion criteria were strictly followed.

The blood sample for serum calcium, serum phosphorus, and serum alkaline phosphates was sent to the hospital laboratory, and results were verified by the pathologist. The entire outcome variables were measured at baseline and one month after treatment. Follow-ups were ensured by taking contact numbers. The data analysis was done with SPSS 17.Qualitative data including gender, frequency, and percentages were calculated. For quantitative variables like age, baseline and post-treatment, serum calcium, serum phosphorus, serum alkaline phosphatase, and change in these values, Mean±SD was calculated. An independent sample t-test was applied to compare mean change in serum calcium, serum phosphorus, and serum alkaline phosphatase between the two groups (total 280). A value of $p < 0.05$ was considered statistically significant. Effect modifiers like age and sex were controlled by stratification. Post-stratification independent sample t-test was applied.

RESULTS:

Two hundred eighty subjects (140 each) were enrolled to compare the parental and oral vitamin D supplementation to treat nutritional rickets in terms of mean change in serum calcium, phosphorus, and alkaline phosphatase. Mean±SD for age was 2.12±0.76 years in the parenteral group and 2.15±0.77 years in the oral group.

Gender distributions showed that 49.29%(n=69) in parenteral group and 45%(n=63) in oral group were male while 50.71%(n=71) in parenteral group and 55%(n=77) in oral group were females. Comparison of parental and oral vitamin D supplementation in the treatment of nutritional rickets at baseline was recorded as 8.68±0.35 in the parenteral group and 8.71±0.37 in the oral group for serum calcium, ($p = 0.62$) serum phosphorus as 3.90±0.22 in the parenteral group and 3.84±0.20 in the oral group, ($p=0.03$) serum alkaline phosphatase as 230.01±13.09 in parenteral group and 228.89±13.80 in an oral group, ($p=0.48$).

Table-I: Age Distribution (n=280).

Age (in years)	Parenteral Group (n=140)		Oral Group (n=140)	
	No. of Patients	%	No. of Patients	%
1-2	89	63.58	86	61.43
3	51	36.42	54	38.57
Total	140	100	140	100
Mean±SD	**2.12±0.76**		**2.15±0.77**	

Table-II: Comparison of parental and oral vitamin D supplementation in the treatment of nutritional rickets at baseline (n=280).

Parameter	Parenteral Group (n=140)		Oral Group (n=140)		p-value
	Mean	SD	Mean	SD	
Serum calcium	8.68	0.35	8.70	0.37	0.62
Serum phosphorus	3.90	0.22	3.84	0.20	0.03
Serum Alkaline phosphatase	230.01	13.09	228.89	13.80	0.48

Comparison of parental and oral vitamin D supplementation in the treatment of nutritional rickets after treatment were recorded as 9.82±0.46 in the parenteral group and 9.43±0.40 in oral group for serum calcium, (p = 0.001) serum phosphorus as 5.32±0.38 in arenteral group and 4.55±0.30 in oral group, (p = 0.001) serum alkaline phosphatase as 150.54±20.99 in parenteral group and 205.24±16.16 in oral group, (p = 0.001) (Table-III).

Comparison of parental and oral vitamin D supplementation in the treatment of nutritional rickets regarding mean change was recorded as 1.14±0.26 in the parenteral group and 0.72±0.19 inoral group for serum calcium, (p = 0.001) serum phosphorus as 1.42±0.33 in parenteral group and 0.71±0.26 in oral group, (p = 0.001) serum alkaline phosphatase as 79.48±14.84 in parenteral group and 23.65±12.21 in the oral group, (p = 0.001) (Table-IV).

Effect modifiers like age and sex were controlled by stratification. Post-stratification independent sample t-test was applied (Table-V & VI).

Table-III: Comparison of parental and oral vitamin D supplementation in the treatment of nutritional rickets after treatment (n=280).

Parameter	Parenteral Group (n=140)		Oral Group (n=140)		p-value
	Mean	SD	Mean	SD	
Serum calcium	9.82	0.46	9.43	0.40	<0.001
Serum phosphorus	5.32	0.38	4.55	0.30	<0.001
Serum Alkaline phosphatase	150.54	20.99	205.24	16.16	<0.001

Table-IV: Comparison of parental and oral vitamin D supplementation in the treatment of nutritional rickets regarding the mean change (n=280).

Parameter	Parenteral Group (n=140)		Oral Group (n=140)		p-value
	Mean	SD	Mean	SD	
Serum calcium	1.14	0.26	0.72	0.19	<0.001
Serum phosphorus	1.42	0.33	0.71	0.26	<0.001
Serum Alkaline phosphatase	79.48	14.84	23.65	12.21	<0.001

Table-V: Stratification comparison of parental and oral vitamin D supplementation in the treatment of nutritional rickets regarding age (n=280)Age:1-2 years

Parameter	Parenteral Group (n=140)		Oral Group (n=140)		p-value
	Mean	SD	Mean	SD	
Serum calcium	1.10	0.26	0.76	0.18	<0.001
Serum phosphorus	1.38	0.31	0.68	0.27	<0.001
Serum Alkaline phosphatase	81.42	13.84	24.28	12.04	<0.001

Table-VI: Age: 3 years.

Parameter	Parenteral Group (n=140)		Oral Group (n=140)		p-value
	Mean	SD	Mean	SD	
Serum calcium	1.12	0.29	0.81	0.20	<0.001
Serum phosphorus	1.29	0.28	0.66	0.25	<0.001
Serum Alkaline phosphatase	80.87	12.19	23.87	11.84	<0.001

DISCUSSION:

Rickets is a common presentation on the pediatric floor with nutritional rickets, leading to significant morbidity and even disability, especially in the world's developing countries. It is also prevalent in Pakistan's rural areas and even in some major cities and towns[11,12]. Such a population should be treated for the prevention of rickets and their consequences. The mainstay of its management is vitaminD through diet and supplements.

We planned this study to compare single-dose I/M vitamin D with daily dose oral vitamin D supplements in the treatment of nutritional rickets to see a mean increase in serum calcium phosphorus and decrease in alkaline phosphatase on a large sample size so that its results may provide better treatment options and morbidity reduced.

Our results are comparable with a previous study conducted in Egypt[10]. Various other studies have been done to compare the different modes of treatment of vitamin D deficiency and supplementation, like giving vitamin D3 in various strengths orally to various infants and children with nutritional rickets to determine the effective dose and minimum adverse effects. Some other parameters, including serum calcium, phosphate, alkaline phosphatase, magnesium, 25-OH-cholecalciferol, were also measured; the outcome of various doses of vitamin D3 given orally was almost the same.But some of the children had hypercalcemia when 300,000 IU and 600,000 IU of vitamin D dose was used in management [13].

In another study, cholecalciferol injection (600,000 IU) given through intramuscular route was effective and appeared to be safe without side effects[14]. Solimanetal. also reported cholecalciferol given in a mega-dose (10,000 IU/kg) is also effective and had no side effects for the management of nutritional rickets in children[15]. Although vitamin D deficiency leading to vitamin D deficiency rickets is a major health issue for the pediatric population of developing countries[11,12,16].With improvement in dietary habits of mothers and infants ensuring adequate vitamin D and calcium in the diet or supplementation can decrease the morbidity of rickets among children.

The results of our study and the above studies justify the hypothesis that "Parenteral route for Vitamin. D supplementation is better than the oral route in the treatment of nutritional rickets in terms of mean change in serum calcium, serum phosphorus, and serum alkaline phosphatase".

However, our results are primary in our population and need someother multi-center trials to validate our findings.

CONCLUSION:

We concluded that the parenteral route for Vitamin. D supplementation is significantly better than the oral route in treating nutritional rickets in terms of mean change in serum calcium, serum phosphorus, and serum alkaline phosphatase.

LIMITATION OF THE STUDY:

The sample size studied in this population was a smaller one,and this study should be done on a large population before reaching a conclusion.

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Nisar Khan Sajid: Drafting and editing.
Tanveer Ahmed: Reference collection.
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