



Original Research Article

Efficacy of Oral Vitamin B12 Therapy Versus Parenteral Vitamin B12 Therapy in Children with Nutritional Vitamin B12 Deficiency Macrocytic Anemia – A Prospective Observational Study

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Abstract: Background: -There is a proven role of oral vitamin B12 in nutritionally deficient conditions in adults but still there is not much literature and guidelines available for pediatric groups regarding oral Vitamin B12 therapy. In this study we have aimed to compare the efficacy of oral vitamin B12 therapy with the standard parenteral vitaminB12 therapy in improving vitamin B12 levels in children.

Method: This 1 year 4-month, hospital based Prospective observational Study was conducted at tertiary care institute. The sample size was calculated 50 in each group . Total 120 children were studied and divided in group A (56 children) parenteral and group B (64 children) oral between ages 6 months to 18 years with clinical features of anemia, peripheral smear showing macrocytic red blood cell or hyper segmented neutrophils and serum Vitamin B12 level <150 pg/mL. All children were followed up after three months of treatment for laboratory investigations, CBC, PBF and serum vitamin B12. **Result:** Out of included 120 children, most of the vitamin B12 deficiency was found in 6 months - 1 year age group followed by 10-18 years age group. We also found that vitamin B12 deficiency was more prevalent in socioeconomic status group, vegetarian group and in rural population. We found significant increment in hemoglobin; platelet count and vitamin b12 level in both parenteral and oral groups. Fall in MCV and WBC count is seen in both groups. **Conclusion:** We concluded that both oral and parenteral vitamin B 12 therapy are found efficacious. Although the Parenteral vitamin B 12 therapy is more efficacious in improving the vitamin B12 level and laboratory parameters, Oral therapy was also found efficient to normalize the vitamin B12 level and laboratory parameters.

Keywords: Vitamin B12, Parenteral therapy, Oral therapy, Nutritional deficiency, Macrocytic anemia, Laboratory parameters, Pediatric population

INTRODUCTION

B12 deficiency is recognized as a significant health issue, particularly among children, due to its detrimental effects on growth, development, and overall well-being Children are vulnerable to vitamin B12 deficiency due to factors such as inadequate dietary intake, malabsorption disorders, or exclusive vegetarian or vegan diets lacking in B12-rich foods. In pediatric populations, nutritional vitamin B12 deficiency can manifest in various ways, ranging from mild symptoms such as fatigue and weakness to severe complications including anemia, developmental delays, and neurological impairments. The mean corpuscular volume is greater than 100 fL, it is known as Macrocytosis.¹

The incidence and prevalence of vitamin B12 deficiency in the pediatric population vary depending on geographic

location, socioeconomic factors, dietary patterns, and underlying health conditions. Certain populations, such as infants exclusively breastfed by vitamin B12-deficient mothers or children with malabsorption disorders, may have a higher risk of deficiency.²

There is a proven role of oral vitamin B12 in nutritionally deficient conditions in adults but still there is not much literature and guidelines available for pediatric groups regarding oral Vitamin B12 therapy. Despite the widespread use of both oral and parenteral vitamin B12 therapy in clinical practice, there is a lack of consensus regarding their comparative efficacy, particularly in pediatric populations.

Parenteral administration, which includes intramuscular or subcutaneous injections of vitamin B12, bypasses potential absorption issues in the gut and ensures direct delivery of the vitamin into the bloodstream. Intramuscular (IM) injections are uncomfortable in infants, cause pain, lead to more complications and are not cost effective compared to oral therapy. Oral treatment is more relevant to children in developing countries where nutritional deficits account for clinical Vitamin B12 deficiency in most cases. It has already been proven that the oral regimen is more acceptable and cost effective.³

This Study aimed to address this gap by synthesizing existing literature, analyzing clinical studies, and examining empirical data to provide evidence-based insights into the most effective and feasible treatment approach for pediatric patients with this deficiency. So, in this study we have aimed to compare the efficacy of oral vitamin B12 therapy with the standard parenteral vitamin B12 therapy in improving vitamin B12 levels in children with nutritional macrocytic (megaloblastic and dimorphic) anemia, after three months of treatment.

MATERIALS AND METHOD

This hospital based Prospective observational Study was conducted at the Department of Pediatrics, Government Medical College and associated group of Hospitals, Kota, Rajasthan, from January 2023 to May 2024.

Assuming the minimum expected mean difference of vitamin B12 levels between oral and parenteral group as 250pg/mL according to reported literature and considering 5% level of significance, with a power of 80% and drop out of 10%, the required sample size was calculated after rounding off as 50 in each group (Total 100). The formula $2SD^2 (Z_{\alpha/2} + Z_{\beta/2})^2 / d^2$ was used to obtain sample size .4

SD- Standard deviation from previous studies or pilot studies (250 as above)

[here, $Z_{\alpha/2} - Z_{0.05/2} = Z_{0.025} = 1.96$ (From Z table) at type1 error of 5%, $Z_{\beta} = Z_{0.20} = 0.842$ (from Z table) at 80 power and d = effect size = assumed difference between mean values (considered 150)].

Child of age between 6 months to 18 years with clinical feature of anemia with peripheral smear showing macrocytic red blood cells (mean corpuscular volume >100 fL) or hyper segmented neutrophils with serum Vitamin B12 level <150 pg/mL were included. Pathological anemia or congenital anemia, chronic disease, patients on radiotherapy and chemotherapy and vitamin B12 therapy and blood transfusion in last 1 month were excluded from study.

The ethical clearance from the institute was taken prior to the study with order no. F.30 Acad/ethical clearance/batch2021/2022/ 62 dated 15/12/2022. Children coming to OPD or IPD and who were fit in inclusion and exclusion criteria, were enrolled in the study. After explaining the whole process of study to parents/guardians and patients, informed consent and assent was taken before study was initiated. All these included children will be divided into two groups, A and B. Group A was given parenteral and group B was given oral vitamin B12 therapy. All demographic details including age, sex and residential address were entered in the pre-designed proforma. Socioeconomic details of family of child were assessed by modified Kuppuswamy scale. The detailed history, general physical examination and systemic examination were done and recorded in the proforma.

In parenteral group A, 500 micrograms in <1-year children, 1000 micrograms of vitamin B12 was given to >1 year children IM after AST. Three doses in children less than ten years of age, whereas a total of five doses was given to those of 10-18 years of age at the time of admission. Subsequently, two more doses of similar strength were given per month, for three months.

In oral group B, Methyl cobalamin 1500 microgram, half tablet in less than two years of age and one tablet in 2 to18 year age child, was given daily for a total of 12 weeks. Folic acid, iron supplementation and proper dietary advice were given to both group in a similar way. Both the injectable and tablet of vitamin B12 was given to patients from the hospital supply free of cost under MNDY. All IM injections were given in the presence of observer at department of pediatrics at J K Lone, Kota. All children were followed up in pediatric outpatient department after three months of treatment and lood samples were withdrawn for laboratory investigations, CBC, PBF and serum vitamin B12.

1-2 ml of fresh blood was taken in EDTA vial for complete blood counts and peripheral blood smear. Peripheral smear was prepared using fresh blood with EDTA. The smear was stained by Leishman stain. The slides were studied under the microscope, first at scanner to rule out parasitic etiology, later, the slides were viewed under 40X for RBC morphology. 3-4ml of fresh blood was sent for serum vitamin B12 in plain vial and assessed by using CLIA (Chemiluminescence immunoassay, Roche Cobas E411 machine).

STATISTICAL ANALYSIS

All data collected was entered into Microsoft Excel. The results were evaluated after obtaining the distribution into software SPSS version 23. Descriptive statistics like proportions and percentages were employed for describing the qualitative data and quantitative data were expressed using mean and standard deviation. We used Student t test for comparison of distributed variables. P value that was less than 0.05, considered significant.

RESULTS

We have enrolled 150 children of 6 months to 18 years of age. Out of them 30 children were excluded or left out during study. So a total of 120 children studied who were divided into two groups. Group A was given parenteral therapy while group B was given oral vitamin B12 therapy for the next three months. Study flow of participants is shown in fig. 1. Demographic details and baseline clinical data are shown in table 1.

Figure 1. Flowchart of Patient

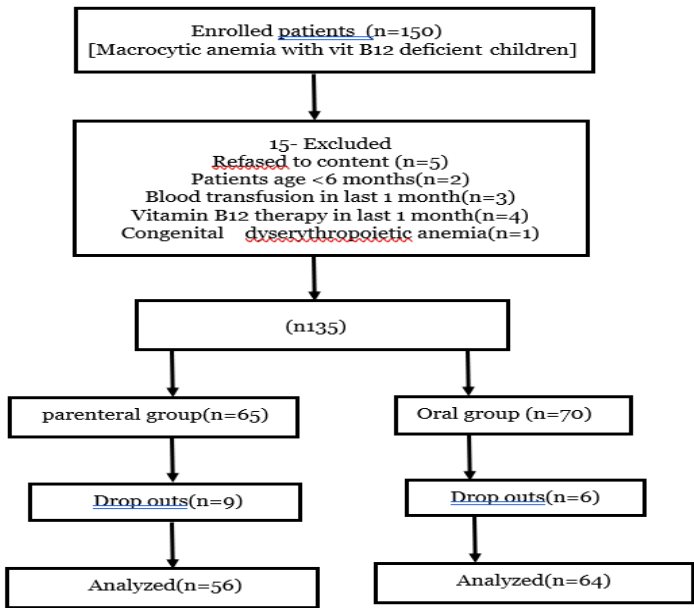


Table no. 1 Demographic indices

		Parenteral (n=56)	Oral (64)
AGE	Mean Age(months)	44.12	79.45
GENDER	Male	33(59%)	32(50%)
	Female	23(41%)	32(50%)
Kuppuswamy socioeconomic scale	I	0(0%)	0(0%)
	II	2(4%)	3(5%)
	III	25(45%)	25(39%)
	IV	26(46%)	22(34%)
	V	3(5%)	14(22%)
Diet type	Only Breast Feeding	14(25%)	15(23%)
	Mixed	2(4%)	11(17%)
	Vegetarian	40(71%)	38(60%)
Anthropometric Parameters	Mean Weight (in kg)	13.52	20.64
	Mean Height (in cm)	83.72	100.65
	Weight for height (age 6m-5y)>-3SD	21(50%)	13(37%)
	Weight for height (age 6m-5y) -3SD to-2SD	9(22%)	11(32%)
	Body Mass Index (in 5- 8 years)	16.44	17.64
Nutritional status	Severe undernutrition	20(38%)	21(33%)
	Undernutrition	10(18%)	16(25%)
Locality	Urban	22(39%)	28(44%)
	Rural	34(61%)	36(56%)

Presenting Complaints	Anorexia	8(14%)	7(11%)
	Developmental delay	2(4%)	2(3%)
	Diarrhea	6(11%)	4(6%)
	Fatigue	4(7%)	19(30%)
	Fever	23(41%)	18(28%)
	Irritability	8(14%)	4(6%)
	Respiratory distress	5(9%)	10(16%)

Table no. 2 showing Change in mean Laboratory parameters in parenteral and oral group at the time of admission and after 3 months. It shows significant increment in hemoglobin; platelet count and vitamin b12 level in both parenteral and oral group. Fall in MCV and WBC count is seen in both groups.

Table: - 2 Mean Laboratory parameters at admission and after 3 months of treatment

Laboratory parameters	Parenteral (n=56)			Oral (64)		
	Pretreatment	Post treatment	p value*	Pretreatment	Post treatment	P value*
Hb(g/dL)	7.01	13.48	0.0001	8.14	13.64	0.0001
MCV (fL)	104.27	78.76	0.0001	101.63	77.22	0.0001
WBC($\times 10^3$ /uL)	7.9	4.45	0.0001	8.5	4.54	0.0161
Platelet Count ($\times 10^3$ /	184.08	273.48	0.0001	171.49	264.9	0.0001
Vitamin B12(pg/ml)	85.69	737.1	0.0001	94.18	628.09	0.001

*Student's paired t-test

DISCUSSION

Vitamin B12 deficiency is treated with parenteral therapy by intramuscular route injection. This study aimed to compare the efficacy of oral vitamin B12 therapy with the standard parenteral vitamin B12 therapy in improving vitamin B12 level in children with nutritional macrocytic anemia.

Similar to our Study, previous literatures also reported that vitamin B12 deficiency was more prevalent in lower socioeconomic group. Vitamin B12 is exclusively dietary vitamins which are acquired from exogenous diet or supplements. Family belonging to low-income class and with low education levels were not met the requirements due to inaccessibility and in affordability.

Indian breastfeeding women accounting for lower vitamin B12 levels and later inadequate complementary feeding, further pushes the young children towards malnutrition during the crucial time of brain development. The adolescent age group becomes the other vulnerable group as they are in a state of constant growth, having high

requirements of nutrients, deficient diets, junk food consumption, leading to Vitamin B12 deficiency in them.

Vitamin b12 is mainly obtained from animal-based products (non-vegetarian diet/mixed diet). In our study we found that 89% cases were on either breastfeeding or on a vegetarian diet. Similar trends were also observed by study Tandon R et al (2022)⁵ and Kumar K et al (2021)⁶.

Concerning the change in the laboratory parameters, there were significant and positive changes found in our study in both the groups. The findings of our study are compared with different studies as mentioned below in table 3. The more increment/changes in different parameters, noted in our study is probably due to enrollment of more severe anemic patients as compared to other studies. Similar changes were seen in Bolaman et al (2003)⁷. Initial higher value of WBC was due to possibly associated sepsis at the time of admission.

Table 3:- Comparison of change in different lab parameters (mean values) with previous studies

STUDIES	Hb (g/dl)		MCV (fL)		WBC count (x10 ³ µ/l)		PLATELET (x10 ³ µ/l)		VIT B12(pg/dL)	
	O*	P**	O*	P**	O*	P**	O*	P**	O*	P**
Bolaman et al (2003)⁷	5.4	4.7	-25.4	-28.1	2.5	2.3	139	115	140.9	155.3
Tugba-kartal et al(2020)⁸	1.3	1.7	-3	-1.7	0.526	1.698	8.03	-18	417.8	454.5
Tandon R et al (2021)⁵	1	-5	-5	-11	0.3	0.3	10	-44	394	568
Parihar S et al (2023)⁹	0.3	2.5	6.3	8.5	0	402	-8	-30	397	600
In Present study	5.5	-24.4	-24.4	-25.51	-3.85	-3.44	93.41	89.39	534.08	651.41

O*-Oral, P**-. Parenteral

More increments in Hb and Vit B12 level were seen in parenteral group as compared to oral therapy. It was possibly due to bypassing liver metabolism, strict adherence to treatment and less subjectivity in parenteral therapy. In oral therapy adherence was solely dependent on history given by parents and children which is more subjective. The chances of missing the dose were more in oral therapy. Despite all this oral therapy has also shown significant and required improvement in vit B12 levels. Oral therapy is simple, convenient, economical and painless. It is free from the anxiety for prickling needle, associated sepsis and hypersensitivity reaction. All these advantages will make oral therapy more acceptable in the pediatric population.

Main strength of this Study was that we have included vast variety of age group criteria covering from 6 months to 18 years of age group. We have

also tried to compare socioeconomic status, locality, age and sex wise distribution of vitamin b12 deficiency.

However, the present study is also not perfect. The actual percentage of vitamin B12 deficiency in pediatric population in general may be different than that shown in our study due to limited sample size. The two-group allocations were not randomized. Population based surveys may show better reflection of accuracy in pediatric population. Further we have not done methylmalonic acid, homocysteine and iron level in our subjects. Although iron folic was given to all participants. Furthermore, no assessment was made for participant’s mental status or satisfaction level of their parents. Vitamin B12 has a longer half-life, so long-term follow-up should be done for finalizing an effective regimen.



CONCLUSION

We concluded that both oral and parenteral vitamin B 12 therapy are efficacious in improving the vitamin B12 level and hematological parameters in children with nutritional macrocytic vitamin B 12 deficiency anemia. Although the result revealed that the Parenteral vitamin B 12 therapy is more efficacious in improving the vitamin B12 level and laboratory parameters yet Oral therapy was also found efficient to normalize the vitamin B12 level and laboratory parameters. Most of the vitamin B12 deficiency was found in 6 months - 1 year age group followed by 10–18-year age group. We also found that vitamin B12 deficiency was more prevalent in socioeconomic status group.

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