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ASSESSING THE EFFICACY OF ORAL VITAMIN B12 TO PARENTERAL VITAMIN B12 IN TREATING CHILD SUBJECTS WITH NUTRITIONAL MACROCYTIC ANEMIA

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ABSTRACT

Background: The literature data is scarce concerning the efficacy of various routes for administering vitamin B12 in child subjects with macrocytic-megaloblastic anemia and vitamin B12 deficiency.

Aim: The present study aimed to comparatively assess the efficacy of Oral vitamin B 12 to parenteral vitamin B12 in treating child subjects with nutritional macrocytic anemia.

Methods: The study assessed 160 child subjects in the age range of 3 months to 18 years with laboratory and clinical findings suggestive of megaloblastic macrocytic anemia. All subjects were given 1000µg vitamin B12 in a single parenteral dose. The subjects were then divided into 2 groups randomly where Group I was given oral vitamin B12 daily for 3 months in 1500µg dose (500µg in subjects aged < 2 years) and Group II was given intramuscular 1000µg B12 in 3 and 5 doses alternate days for <10 and >10 years respectively followed by 2 doses of 1000µg. Iron and folic acid were given to both groups. Hemoglobin and serum vitamin B12 were compared after 3 months.

Results: A significant improvement was seen in levels of vitamin B12 in group II with p=0.01. Also, a significant improvement in Group II was seen for hemoglobin levels with p=0.001.

Conclusion: The study concluded that a significant improvement in hemoglobin and serum vitamin B12 levels is seen in child subjects with macrocytic anemia with parenteral vitamin B12 compared to oral Vitamin B12.

Keywords: Knuckle Pigmentation, Megaloblastic Anemia, Macrocytic Anemia, Methylcobalamin.

INTRODUCTION

Anemia is a highly prevalent condition globally including in India. Anemia affects all the subjects from all age ranges with a significant effect on the child subjects. A deficiency of folate/vitamin B12 is considered to be a significant contributor to nearly one-third of cases of anemia reported in Indian subjects. Vitamin B12 or folate deficiency is the second major cause of anemia followed by iron deficiency anemia in adolescents and child subjects of age 5-9 years.[1]

Various treatment options are available to treat the deficiency of Vitamin B12 in both children and adults including oral therapy and parenteral therapy where both therapies have proven to be effective with results showing marked improvement with oral as well as parenteral vitamin B12 therapy.[2] However, the literature data is scarce and clear indications and guidelines are lacking for the use of these therapies in child subjects concerning the hematologic manifestations, particularly in Indian subjects.[3]

In child subjects, needle phobia is prevalent and injection intake is painful along with the need for trained personnel and the cost of the injection. In adult subjects, treating macrocytic anemia with oral vitamin B12 has shown equal efficacy as with the parenteral vitamin B12. However, owing to its absorption mechanism, vitamin B12 is rarely prescribed in the oral dosage form.[4]

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The present study aimed to comparatively assess the efficacy of oral vitamin B12 to parenteral vitamin B12 in improving the vitamin B12 status and treating child subjects with nutritional megaloblastic macrocytic anemia following 3 months of therapy.

MATERIALS AND METHODS

The present clinical study aimed to comparatively assess the efficacy of oral vitamin B12 to parenteral vitamin B12 in improving the vitamin B12 status and treating child subjects with nutritional megaloblastic macrocytic anemia following 3 months of therapy. The study population was from the Department of Pediatrics of the institute. Informed consent in written format and verbally was taken from the parents of study subjects.

The study screened 280 subjects within the age range of 3 months to 18 years where 160 subjects were enrolled based on the inclusion and exclusion criteria. The inclusion criteria for the study were child subjects in the age range of 3 months to 18 years with a minimum of one laboratory parameter from the following: vitamin B12 level <150pg/mL, MCV (mean corpuscular volume) >110 fL, and all three in peripheral blood smear including thrombocytopenia, hyper segmented neutrophils, and macrocytic red blood cells. The exclusion criteria for the study were subjects with neurological conditions, and nutritional anemia, who received vitamin B12 therapy within the past 1 month, subjects who had a blood transfusion in the past month, and the study subject whom informed consent was not given.

The study assessed 160 child subjects from both genders in the age range of 3 months to 18 years with clinical and laboratory parameters suggestive of megaloblastic macrocytic anemia. After final inclusion, detailed demographic data were recorded for all the subjects along with history, laboratory data concerning anemia, anthropometry, nutritional assessment, and clinical presentation at baseline.

After inclusion, all 160 study subjects were given an initial single intravenous or intramuscular B12 dose of 1000µg. The subjects were then randomly divided into two groups where Group I was given oral vitamin B12 and Group II was given parenteral vitamin B12. In Group I (oral), 1500 µg oral Methylcobalamin was given by the name of Nurokind OD from Mankind Pharma Ltd. It was given as one tablet in subjects aged 2-18 years and half a tablet to subjects of age <2 years for 12 weeks. In Group II (parenteral), intravenous/intramuscular 1000µg vitamin B12 was given to subjects with a platelet count of <50×109/L in three and 5 doses respectively for subjects of age <10 and 10-18 years. Also, two more doses of the same strength were given at the end of 1st and 2nd month of follow-up.

Age-appropriate nutritional and dietary advice was given to all the subjects of both groups along with 5mg folic acid tablet supplementation. All the subjects were recalled weekly for the initial 4 weeks followed by monthly assessments till the end of 3rd month. After 3 months, all laboratory evaluations were reperformed and analyzed along with clinical parameters including adverse drug reactions, mood alterations, general health and well-being, tingling sensation, knuckle pigmentation, and pallor.

The data gathered were assessed and statistically analyzed using SPSS software version 21.0 with Mann Whitney U and student t-test. The significance level was kept at $p<0.05$.

RESULTS

The present clinical study aimed to comparatively assess the efficacy of oral vitamin B12 to parenteral vitamin B12 in improving the vitamin B12 status and treating child subjects with nutritional megaloblastic macrocytic anemia following 3 months of therapy. The study assessed 160 child subjects from both genders in the age range of 3 months to 18 years with clinical and laboratory parameters suggestive of megaloblastic macrocytic anemia. The demographic data of the study subjects are listed in Table 1. The mean age of the study subjects in Group I and II was 13.2±2.4 and 11.4±1.8 years. There were 52.5% (n=42) and 75% (n=60) of study subjects in Group I and II respectively. Iron therapy was done in 75% (n=60) and 62.5% (n=50) study subjects respectively in Group I and II. In Group I, breastfeeding, mixed, and vegetarian diet were reported in 17.5% (n=14), 12.5% (n=10), and 70% (n=56) study subjects respectively, whereas, in Group II, breastfeeding, mixed, and vegetarian diet was taken by 20% (n=16), 15% (n=12), and 65% (n=52) study subjects respectively. The nutritional state

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was overweight in 15% (n=12), undernutrition in 27.5% (n=22), and normal in 57.5% (n=46) subjects in Group I and 7.5% (n=6), 40% (n=32), and 52.5% (n=42) subjects from Group II respectively.

On assessing the clinical features in the two groups of study subjects, jaundice, knuckle pigmentation, tremors, apathy, irritability, and pallor were seen in 17.5% (n=14), 95% (n=76), 7.5% (n=6), 2.5% (n=2), 15% (n=12), and 65% (n=52) study subjects respectively. In Group II where parenteral vitamin B12 therapy was given, jaundice, knuckle pigmentation, tremors, apathetic, irritability, and pallor were recorded respectively in 15% (n=12), 92.5% (n=74), 22.5% (n=18), 5% (n=4), 17.5% (n=14), and 60% (n=48) study subjects as shown in Table 1.

Concerning the change in the laboratory parameters in two groups of study subjects, platelet counts were decreased by -8000 (-92000, 70300) and by -30000 (-87000, 136000) in the oral and parenteral group which was non-significant with p=0.49. The change in lymphocytes, neutrophils, fall in MCV (mean corpuscular volume), and WBCs was statistically non-significant between oral and parenteral groups with respective p-values of 0.87, 0.86, 0.55, and 0.67 respectively. An improvement in hemoglobin was seen by 0.3 g/dL in the oral group and by 2.5 g/dL in the oral and parenteral groups respectively which was significantly better with parenteral vitamin B12 therapy (p=0.001). A similar significant improvement was seen in vitamin B12 levels where it was improved by 397 pg/mL in the oral group and by 600 pg/mL in the parenteral group which was statistically significant with p=0.01 as depicted in Table 2.

The status of iron levels was not followed for all 160 study subjects. However, additional administration of iron therapy was followed in 27.5% (n=22) and 62.5% (n=50) study subjects from oral and parenteral groups respectively depending on dimorphic anemia reported in 45% (n=72) study subjects or the clinical parameters of the study subjects.

DISCUSSION

The present clinical study assessed 160 child subjects from both genders in the age range of 3 months to 18 years with clinical and laboratory parameters suggestive of megaloblastic macrocytic anemia. The mean age of the study subjects in Group I and II was 13.2±2.4 and 11.4±1.8 years. There were 52.5% (n=42) and 75% (n=60) of study subjects in Group I and II respectively. Iron therapy was done in 75% (n=60) and 62.5% (n=50) study subjects respectively in Group I and II. In Group I, breastfeeding, mixed, and vegetarian diet were reported in 17.5% (n=14), 12.5% (n=10), and 70% (n=56) study subjects respectively, whereas, in Group II, breastfeeding, mixed, and vegetarian diet was taken by 20% (n=16), 15% (n=12), and 65% (n=52) study subjects respectively. The nutritional state was overweight in 15% (n=12), undernutrition in 27.5% (n=22), and normal in 57.5% (n=46) subjects in Group I and 7.5% (n=6), 40% (n=32), and 52.5% (n=42) subjects from Group II respectively. These data were in line with the studies of Oh RC[5] in 2003 and Vidal Alball J et al[6] in 2005 where authors assessed subjects with demographic characteristics compared to the present study.

Concerning the assessment of clinical features in the two groups of study subjects, jaundice, knuckle pigmentation, tremors, apathetic, irritability, and pallor were seen in 17.5% (n=14), 95% (n=76), 7.5% (n=6), 2.5% (n=2), 15% (n=12), and 65% (n=52) study subjects respectively. In Group II where parenteral vitamin B12 therapy was given, jaundice, knuckle pigmentation, tremors, apathetic, irritability, and pallor were recorded respectively in 15% (n=12), 92.5% (n=74), 22.5% (n=18), 5% (n=4), 17.5% (n=14), and 60% (n=48) study subjects. These results were consistent with the studies of Kolber MR et al[7] in 2014 and Sezer RG et al[8] in 2018 where authors reported similar clinical features in subjects with vitamin B12 deficiency as in the present study.

On assessing the changes in the laboratory parameters in two groups of study subjects, platelet counts were decreased by -8000 (-92000, 70300) and by -30000 (-87000, 136000) in the oral and parenteral group which was non-significant with p=0.49. The change in lymphocytes, neutrophils, fall in MCV (mean corpuscular volume), and WBCs was statistically non-significant between oral and parenteral groups with respective p-values of 0.87, 0.86, 0.55, and 0.67 respectively. An improvement in hemoglobin was seen by 0.3 g/dL in the oral group and by 2.5 g/dL in the oral and parenteral groups respectively which was significantly better with parenteral vitamin B12 therapy (p=0.001). A similar significant improvement was seen in vitamin B12 levels where it was improved by 397 pg/mL in the oral group and by 600 pg/mL in the parenteral group which was statistically

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significant with p=0.01. These findings were in agreement with the studies of Bahadir A et al[9] in 2014 and Verma D et al[10] in 2017 where authors suggested significant improvement with parenteral vitamin B 12 as in the present study.

In the present study, iron levels were not followed for all 160 study subjects. However, additional administration of iron therapy was followed in 27.5% (n=22) and 62.5% (n=50) study subjects from oral and parenteral groups respectively depending on dimorphic anemia reported in 45% (n=72) study subjects or the clinical parameters of the study subjects. These findings were similar to the studies of Nyholm E et al[11] in 2003 and Bolaman Z et al[12] in 2003 where authors reported similar changes in iron levels as in the present study.

CONCLUSION

Considering its limitations, the present study concludes that a significant improvement in hemoglobin and serum vitamin B12 levels is seen in child subjects with macrocytic anemia with parenteral vitamin B12 compared to oral Vitamin B12.

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S. No	Characteristics	Oral Group (I)		Parenteral group (II)	
		Number (n)	Percentage (%)	Number (n)	Percentage (%)
1.	**Mean age (years)**	13.2±2.4		11.4±1.8	
2.	**Gender**				
a)	Females	42	52.5	60	75
b)	Males	38	47.5	20	25
3.	**Iron therapy**	60	75	50	62.5
4.	**Diet**				
a)	Breastfeeding	14	17.5	16	20
b)	Mixed	10	12.5	12	15
c)	Vegetarian	56	70	52	65
5.	**Nutritional state**				

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a)	Overweight	12	15	6	7.5
b)	Undernutrition	22	27.5	32	40
c)	Normal	46	57.5	42	52.5
6.	**Features**				
a)	Jaundice	14	17.5	12	15
b)	Knuckle pigmentation	76	95	74	92.5
c)	Tremors	6	7.5	18	22.5
d)	Apathetic	2	2.5	4	5
e)	Irritable	12	15	14	17.5
f)	Pallor	52	65	48	60

Table 1: Demographic and disease characteristics in study subjects

S. No	Laboratory parameters	Oral group	Parenteral group	p-value
1.	**Increase in platelet counts**	-8000 (-92000, 70300)	-30000 (-87000, 136000)	0.49
2.	**Lymphocyte change (%)**	8 (-5, 24)	6 (-7, 22)	0.87
3.	**Neutrophil change (%)**	-2 (-13, 19)	-4 (-15, 14)	0.86
4.	**MCV fall (fl)**	6.3 (2.2, 13.7)	8.5 (1.3, 18.6)	0.55
5.	**WBC change ($X10^3/\mu L$)**	0 (-1452, 1352)	402 (-2500, 2300)	0.67
6.	**Hemoglobin change (g/dL)**	0.3 (-0.1, 1.4)	2.5 (0.4, 4.4)	**0.001**
7.	**Vitamin B12 change (pg/mL)**	397 (311, 604)	600 (387, 773)	**0.01**

Table 2: Changes in pre and post-vitamin B12 therapy after 3 months in two groups of study subjects