ASSESSING THE EFFICACY OF ORAL VITAMIN B 12 TO PARENTERAL VITAMIN B12 IN TREATING CHILD SUBJECTS WITH NUTRITIONAL MACROCYTIC ANEMIA

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ABSTRACT

Background: Information on the effectiveness of several delivery methods for vitamin B12 in children with macrocytic-megaloblastic anaemia and vitamin B12 deficiency is limited in the literature.

Aim: The purpose of this study was to evaluate the relative effectiveness of parenteral vs oral vitamin B12 in the treatment of nutritional macrocytic anaemia in paediatric patients.

Methods: A total of 160 kid patients, ranging in age from 3 months to 18 years, were evaluated for the study. Laboratory and clinical results pointed to megaloblastic macrocytic anaemia. One parenteral dosage of 1000µg of vitamin B12 was administered to each individual. The participants were then split into two groups at random: Group I received 1500 µg of vitamin B12 orally every day for three months (500 µg if the subjects were younger than two years old), and Group II received 1000 µg of B12 intramuscularly every three days for ten years or older, respectively, followed by two doses of 1000 µg. For both groups, iron and folic acid were administered. After three months, serum vitamin B12 and haemoglobin levels were compared.

Results: Group II showed a substantial improvement in their vitamin B12 levels (p=0.01). Haemoglobin levels in Group II also showed a substantial improvement (p=0.001). **Conclusion**: The research findings indicate that parenteral vitamin B12 administration, as opposed to oral vitamin B12, significantly improves haemoglobin and blood vitamin B12 levels in children with macrocytic anaemia.

Keywords: methylcobalamin, macrocytic anaemia, megaloblastic anaemia, and knuckle pigmentation.

INTRODUCTION

Anaemia is a very common illness everywhere, including in India. Anaemia has an impact on individuals of all ages, although it particularly affects subjects who are children. Almost one-third of the occurrences of anaemia in Indian subjects are thought to be caused by a folate/vitamin B12 deficiency. In adolescents and young children aged 5 to 9, iron deficiency anaemia is the leading cause of anaemia, followed by vitamin B12 or folate inadequacy.1

There are several treatment options for vitamin B12 deficiency that may be used for both adults and children. Oral and parenteral vitamin B12 therapy have both been shown to be beneficial, with data indicating a noticeable improvement with oral therapy.2.

On the other hand, there is a dearth of information in the literature about the hematologic manifestations of these treatments in kid subjects, especially in Indian subjects, and there are also no clear indications or guidelines for their usage.3

Needlestick fear is common in paediatric patients, and receiving injections can be uncomfortable due to the needle's expense and the requirement for specialised professionals. When treating macrocytic anaemia in adult patients, oral vitamin B12 has demonstrated comparable effectiveness to parenteral vitamin B12.

However, because of its mode of absorption, oral vitamin B12 is rarely given.4 The purpose of this study was to compare the effectiveness of parenteral vs oral vitamin B12 in treating children with nutritional megaloblastic macrocytic anaemia and enhancing their vitamin B12 status after three months of treatment.

MATRIALS AND METHODS

After three months of therapy, the current clinical trial sought to compare the effectiveness of parenteral vs oral vitamin B12 in increasing the vitamin B12 status and treating paediatric patients with nutritional megaloblastic macrocytic anaemia. The research was conducted between.. and.., with approval from the relevant institutional ethical committee.

The participants in the study were members of the institute's Department of Pedodontics. Written and verbal informed permission was obtained from the parents of the research participants. 160 participants were included in the study after 280 people between the ages of 3 months and 18 years were screened in accordance with the inclusion and exclusion criteria. Children between the ages of three months and eighteen years, with at least one laboratory parameter from the following list—vitamin B12 level <150pg/mL, mean corpuscular volume (MCV) >110 fL, and all three in a peripheral blood smear, including thrombocytopenia, hyper segmented neutrophils, and macrocytic red blood cells—were eligible to participate in the study.

The study's exclusion criteria included participants with neurological disorders, nutritional anaemia, those who had taken vitamin B12 treatment within the previous month, those who had received a blood transfusion within the previous month, and those for whose informed permission was not obtained.
In the study, 160 juvenile participants of both sexes, ranging in age from 3 months to 18 years, were evaluated for clinical and laboratory characteristics that might indicate megaloblastic macrocytic anaemia. Following final inclusion, comprehensive demographic information was documented for each subject, in addition to their medical history, test results related to anaemia, anthropometry, nutritional evaluation, and baseline clinical presentation.

Following their participation, a single 1000µg intravenous or intramuscular B12 dosage was administered to each of the 160 research participants. Following that, the participants were split

into two groups at random: Group I received oral vitamin B12, whereas Group II received parenteral vitamin B12. Mankind Pharma Ltd.'s Nurokind OD, a 1500 µg oral form of methylcobalamin, was administered to Group I (oral). For 12 weeks, it was administered as half a tablet to participants under 2 years old and as one tablet to those between the ages of 2 and 18. In Group II (parenteral), patients with a platelet count of <50×109/L received three intravenous and five intramuscular doses of vitamin B12, respectively, for subjects aged <10 and 10–18 years. At the conclusion of the first and second follow-up months, two more doses of the same strength were administered.

All of the participants in both groups received age-appropriate dietary and nutritional guidance in addition to a 5-mg folic acid tablet supplement. For the first four weeks, all the participants were remembered once a week. After that, they were assessed once a month until the conclusion of the third month. Following a three-month period, all laboratory assessments were re-examined and clinical parameters such as adverse medication responses, mood swings, overall health and well-being, tingling feeling, knuckle pigmentation, and pallor were examined.

Using Mann Whitney U and the student t-test, SPSS software version 21.0 was used to evaluate and statistically analyse the collected data. A significance threshold of $p<0.05$ was maintained.
Outcomes
After three months of therapy, the current clinical trial sought to compare the effectiveness of parenteral vs oral vitamin B12 in increasing the vitamin B12 status and treating paediatric patients with nutritional megaloblastic macrocytic anaemia. In the study, 160 juvenile participants of both sexes, ranging in age from 3 months to 18 years, were evaluated for clinical and laboratory characteristics that might indicate megaloblastic macrocytic anaemia. Table 1 contains a list of the research individuals' demographic information. Group I and II's research subjects were 13.2±2.4 and 11.4±1.8 years old, respectively, on average. Group I had 52.5% (n = 42) and Group II had 75% (n = 60) of the research patients.

In Group I, 75% (n = 60) and Group II, 62.5% (n = 50) of the trial participants received iron treatment, respectively. While 20% (n=16), 15% (n=12), and 65% (n=52) of research respondents in Group II followed a nursing, mixed, and vegetarian diet, respectively, 17.5% (n=14), 12.5% (n=10), and 70% (n=56) of study subjects reported following these diets in Group I. 15% (n=12) of Group I patients had overweight, 27.5% (n=22) had undernutrition, and 57.5% (n=46) of Group II subjects had normal nutrition, compared to 7.5% (n=6), 40% (n=32), and 52.5% (n=42) of Group I subjects, respectively.

After evaluating the clinical characteristics of the two research subject groups, it was found that 17.5% (n=14), 95% (n=76), 7.5% (n=6), 2.5% (n=2), 15% (n=12), and 65% (n=52) of the study patients had jaundice, knuckle pigmentation, tremors, apathy, irritation, and pallor. As indicated by Table 1, jaundice, knuckle pigmentation, tremors, apathy, irritability, and pallor were seen in 15% (n = 12), 92.5% (n = 74), 22.5% (n = 18), 5% (n = 4), 17.5% (n = 14), and 60% (n = 48) of the research patients in Group II, where parenteral vitamin B12 treatment was administered. Regarding the alteration in the laboratory parameters in the two research subject groups, the oral

and parenteral group saw a drop in platelet counts of -8000 (-92000, 70300) and -30000 (-87000, 136000), respectively. This difference was not statistically significant (p=0.49).

Between the oral and parenteral groups, the change in lymphocytes, neutrophils, decline in mean corpuscular volume, and WBCs was statistically not significant (p-values of 0.87, 0.86, 0.55, and 0.67, respectively). Haemoglobin levels improved by 0.3 g/dL in the oral group and 2.5 g/dL in the parenteral group, respectively. Parenteral vitamin B12 treatment significantly improved haemoglobin levels (p=0.001). Table 2 shows that there was a statistically significant improvement in vitamin B12 levels (p=0.01), with improvements of 397 pg/mL in the oral group and 600 pg/mL in the parenteral group.

The iron levels of the 160 research subjects were not tracked. However, depending on the clinical characteristics of research subjects or the dimorphic anaemia recorded in 45% (n=72) of study subjects, extra administration of iron treatment was administered to 27.5% (n=22) and 62.5% (n=50) of study subjects from the oral and parenteral groups, respectively.

The clinical study under review evaluated 160 children, aged between 3 months and 18 years, of both genders. The study's laboratory and clinical findings suggested the presence of megaloblastic macrocytic anaemia.The study individuals in Group I and II had mean ages of 13.2±2.4 and 11.4±1.8 years, respectively.Group I had 52.5% (n = 42) and Group II had 75% (n = 60) of the research patients. In Group I, 75% (n = 60) and Group II, 62.5% (n = 50) of the study participants had iron treatment, respectively.

While 20% (n=16), 15% (n=12), and 65% (n=52) of research respondents in Group II followed a nursing, mixed, and vegetarian diet, respectively, 17.5% (n=14), 12.5% (n=10), and 70% (n=56) of study subjects reported following these diets in Group I. 15% (n=12) of Group I patients had overweight, 27.5% (n=22) had undernutrition, and 57.5% (n=46) of Group II subjects had normal nutrition, compared to 7.5% (n=6), 40% (n=32), and 52.5% (n=42) of Group I subjects, respectively. These results were consistent with research conducted by Oh RC5 in 2003 and Vidal Alball J et al6 in 2005, when the authors evaluated participants based on demographic traits that were different from those of the current study.

Jaundice, knuckle pigmentation, tremors, apathy, irritability, and pallor were observed in 17.5% (n=14), 95% (n=76), 7.5% (n=6), 2.5% (n=2), 15% (n=12), and 65% (n=52) of the study subjects, respectively, according to the assessment of clinical characteristics in the two groups of research participants. Jaundice, knuckle pigmentation, tremors, apathy, irritability, and pallor were seen in 15% (n=12), 92.5% (n=74), 22.5% (n=18), 5% (n=4), 17.5% (n=14), and 60% (n=48) of the trial participants in Group II, where parenteral vitamin B12 treatment was administered. The findings aligned with the research conducted by Kolber MR et al7 in 2014 and Sezer RG et al8 in 2018, as stated by the authors. Comparable clinical characteristics to those in the current investigation in individuals with vitamin B12 insufficiency

When the laboratory parameters of the two study subject groups were evaluated, it was found that the oral and parenteral group's platelet counts had fallen by -8000 (-92000, 70300) and by -30000 (-87000, 136000), respectively. These changes were not statistically significant (p=0.49).

Between the oral and parenteral groups, the change in lymphocytes, neutrophils, decline in mean corpuscular volume, and WBCs was statistically not significant (p-values of 0.87, 0.86, 0.55, and 0.67, respectively). Haemoglobin levels improved by 0.3 g/dL in the oral group and 2.5 g/dL in the parenteral group, respectively. Parenteral vitamin B12 treatment significantly improved haemoglobin levels (p=0.001).

Vitamin B12 levels showed a comparable and statistically significant increase, increasing by 397 pg/mL in the oral group and 600 pg/mL in the parenteral group (p=0.01). These results were consistent with research by Bahadir A et al. (2014) and Verma D et al. (2017), whose authors proposed that parenteral vitamin B 12 therapy might lead to a notable improvement similar to what was shown in this study.

All 160 research participants' iron levels were not monitored in the current investigation. However, depending on the clinical characteristics of the study subjects or the dimorphic anaemia recorded in 45% (n=72) of the study subjects, extra administration of iron treatment was administered to 27.5% (n=22) and 62.5% (n=50) of study subjects from the oral and parenteral groups, respectively. 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.

REFERENCES

1. Butler CC, Vidal-Alaball J, Cannings-John R, et al. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency: A systematic review of randomized controlled trials. Family Pract. 2006;23:279-85.
2. Sinclair L. Recognizing, treating, and understanding pernicious anemia. JRSM Open 2008;101:262-4.
3. Nutritional Anemias in Infancy and Childhood. *In*: Parthasarathy A. IAP Textbook of Pediatrics, 5th Edition Jaypee Brothers Medical Publishers. 2013.p. 653-54.
4. Sarna A, Porwal A, Ramesh S, et al. Characterization of the types of anemia prevalent among children and adolescents aged 1-19 years in India: a population-based study. Lancet Child Adolesc Health. 2020;4:515-25.
5. Oh RC, Brown DL. Vitamin B12 deficiency. Am Fam Physician. 2003;67:979-86.
6. Vidal Alaball J, Butler C, Cannings John R, et al. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. Cochrane Database Syst Rev. 2005;3:CD004655.
7. Kolber MR, Houle SK. Oral vitamin B12: A cost-effective alternative. Can Fam Physician. 2014;60:111-2.

8. Sezer RG, Akoðlu HA, Bozaykut A, et al. Comparison of the efficacy of parenteral and oral treatment for nutritional vitamin B12 deficiency in children. Hematology. 2018;23:653-7.
9. Bahadir A, Reis PG, Erduran E. Oral vitamin B 12 treatment is effective for children with nutritional vitamin B 12 deficiency. J Paediatr Child Health. 2014;50:721-5.
10. Verma D, Chandra J, Kumar P, et al. Efficacy of oral methylcobalamin in treatment of vitamin B12 deficiency anemia in children. Pediatr Blood Cancer. 2017;64:e26698.
11. Nyholm E, Turpin P, Swain D, et al. Oral vitamin B12 can change our practice. Postgrad Med J. 2003;79:218-9.
12. Bolaman Z, Kadikoylu G, Yukselen V, et al. Oral versus intramuscular cobalamin treatment in megaloblastic anemia: A single-center, prospective, randomized, open-label study. Clin Ther. 2003;25:3124-34.

TABLES

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**				
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 ($X10^3$/µL)**	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