

Iron Profile in Cobalamin Deficiency: a prospective single centre based study

MD. ABDUL AZIZ

Associate Professor, Department of Haematology
Bangabandhu Sheikh Mujib Medical University, Dhaka

SHAFIQUL ISLAM

Medical Officer, Department of Haematology
Bangabandhu Sheikh Mujib Medical University, Dhaka

FARZANA RAHMAN

Assistant Professor, Department of Haematology
Bangabandhu Sheikh Mujib Medical University, Dhaka

AMIN LUTFUL KABIR

Associate Professor, Department of Haematology
Bangabandhu Sheikh Mujib Medical University, Dhaka

MESBHA UDDIN AHMED¹

MS in Microbiology, Bangladesh University of Health Sciences

MASUDA BEGUM

Chairman, Department of Haematology
Bangabandhu Sheikh Mujib Medical University, Dhaka

Abstract:

Haematinics are agents that increase haemoglobin level and number of RBCs in blood. Among all the haematinics, cobalamin is one of the key factors for DNA synthesis. Its deficiency hampers DNA maturation followed by ineffective erythropoiesis. Cobalamin deficiency in absence of other deficiency causes development of Megaloblastic anaemia; whereas concomitant iron deficiency may cause Dimorphic anaemia. We have studied total 16 patients diagnosed as cobalamin deficiency on basis of complete blood count,

¹ Corresponding author: mesba.lab@gmail.com

peripheral blood film, serum vitamin B12 with normal iron profile. Serum iron profile was measured at presentation and after completion of therapy. We found a significant decrease in body iron store after cobalamin deficiency correction. Possibly the cause was increased demand of iron while correcting anaemia due to cobalamin deficiency.

Key words: Iron Profile, Cobalamin Deficiency

INTRODUCTION

Nutritional anaemia is common in Bangladesh. Among these, Iron, cobalamin and folic acid deficiencies are the commonest. There may be combined deficiency of those factors. Iron act as a raw material for Hb synthesis, whereas cobalamin and folic acid act as key factors for DNA synthesis. Iron deficiency causes microcytic hypochromic anaemia with low MCV, MCH and MCHC. Folate and cobalamin deficiencies cause megaloblastic anaemia with high red cell indices. Dimorphic population with normal MCV may be seen in combined deficiency anaemia. These deficiencies are usually caused by decreased intake or malabsorption.

METHODS

Samples

This is a prospective single centre study. Patient attended to Haematology department of BSMMU form Jan 2014 to December 2014 with cobalamin deficiency was enrolled for this study and followed up for 6 months irrespective of the aetiology of cobalamin deficiency. Patients who had hypothyroidism or liver disease were excluded.

Measurements

Complete blood counts, serum iron, total iron binding capacity (TIBC), ferritin and vitamin B12 levels were determined at diagnosis and after cobalamin therapy. Iron indices were re-assessed when vitamin B12 deficiency findings disappeared (generally 1-3 months after initiating cyanocobalamin therapy). Serum vitamin B12 concentrations were measured using an electrochemiluminescence-immunoassay technique intended for use with the Elecsys reagent kit supplied by Roche Diagnostics GmbH (Mannheim, Germany), and run on Cobas e 601 immunoassay analyser (Roche Diagnostics).

Serum iron and TIBC were measured by the ferrozine method (Roche Diagnostics), and serum ferritin was measured by an immunoturbidimetric method (Roche Diagnostics) and run on a Cobas e 601 immunoassay analyser. Complete blood counts of all patients were analysed with a Sysmex XT 2000i haematological analyser.

Definition

Cobalamin deficiency was defined as serum cobalamin level <150 pg/ml with macrocytosis, and iron deficiency was defined as a serum ferritin level <15 ng/mL and/or transferrin saturation <16% according to the World Health Organization criteria.

Treatment

Cyanocobalamin was used to treat cobalamin deficiency in all patients. Patients received 1,000 µg vitamin B12 intramuscularly three times a week for 2 weeks, then 1,000 µg three monthly for maintenance therapy.

Statistical Analysis

Patient characteristics were examined using descriptive statistics. Continuous variables are presented as mean ±

standard deviation (SD), and categorical variables are defined as percentages. The Chi square and t-tests were used to compare proportions and means for categorical and continuous variables, respectively. Variables with significant p values were <0.05 . SPSS 17.0 for Windows statistical software (SPSS Inc., Chicago, IL, USA) was used for all statistical calculations.

RESULT

This study included total 16 patients, where 10 patients were male and 6 were female. Mean age of all patients was 47.87 ± 7.57 years (male 49.4 ± 7.47 and female 45.3 ± 7.03 years). The result of iron profile before and after cobalamin treatment is shown in Table-1.

There is a significant reduction of iron store after correction of cobalamin deficiency with cyanocobalamin. Comparison of pre- and post-treatment values were statistically significant (p value $<.001$) for Ferritin, iron, haemoglobin and MCV.

Table 1: Red cell indices and biochemical profile of the patients before and after treatment with for cobalamin deficiency

Parameter	Before treatment	After treatment	p value
Haemoglobin	9.76 \pm 1.07	12.7 \pm 0.847	$<.001$
MCV	117 \pm 6.9	92.4 \pm 9.2	$<.001$
S. Vit B12	84 \pm 55.23	301 \pm 70	$<.001$
S. Iron	105 \pm 43.7	61 \pm 34.3	$<.001$
S. Ferritin	147 \pm 73.5	54 \pm 30.1	$<.001$

DISCUSSION

Iron, cobalamin and folate are important factors for proper erythropoiesis. Iron is needed by erythroblast for haemoglobin synthesis. Cobalamin and folate helps in maturation and proliferation. In deficiency states of these two vitamins DNA synthesis is impaired and intramedullary haemolysis results in

ineffective erythropoiesis while iron stores seem to be adequate. We assumed correction of cobalamin deficiency improves DNA synthesis and increased haemoglobin synthesis so iron utilization was also increased. This increased 'effective' erythropoiesis caused iron store depletion.

Atrah and Davidson reported that iron deficiency is a common complication in patients with long-standing pernicious anaemia and that its diagnosis and treatment are commonly neglected. Demiroglu and Du'ndar found that iron deficiency commonly accompanies patients with pernicious anaemia and that is more pronounced in elderly patients. Our study also agrees to these observations that even iron status fall down significantly from critical level or significant reduction within normal limit.

Similarly, Gafter-Gvili et al showed in their study that in pernicious anaemia vitamin B₁₂ therapy can rapidly reverse abnormalities in iron metabolism associated with megaloblastic anaemia.

Hillman et al. also reported that patients with pernicious anaemia prior to vitamin B₁₂ therapy show very poor Fe utilization, and that Fe utilization increases after vitamin B₁₂ therapy which stands our assumption of low utilization of iron in cabalamin deficiency.

STUDY LIMITATIONS

This study has some limitations. Sample size should be more to limit the error. Bone marrow examination with iron stain is gold standard for assessment of iron store but couldn't be done due to logistic problem and also because it is an invasive procedure. Same dietary source or supplement for all patient cannot be maintained, differences in dietary content of haematinics are supposed to be a confounding factor.

CONCLUSION

We recommend each patient diagnosed with cobalamin deficiency to screen for iron deficit state before and especially after cobalamin treatment as our study shows post-treatment iron deficiency is common in cobalamin deficiency. As there are limited data or study on this condition we also encourage to further larger study.

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