Original Article

Evaluation of the sensitivity and specificity of MCH and MCV for screening of Beta thalassemia minor

Kaveh Tari¹,²*, Shayan Alikhani³, Mahnoosh Abbasszadehribavar², Fatemeh Kianinodeh¹, Farshid Karami⁴, Amir Atashi⁵

ARTICLE INFO

Article History:
Received 12 February 2018
Revised 27 August 2018
Accepted 20 September 2018

Keywords:
Beta thalassemia
Hypochromic microcytic
Anemia
Mean corpuscular volume
Mean corpuscular hemoglobin

INTRODUCTION

Beta thalassemia minor (BTM) is a hypochromic and microcytic anemia that is determined by reduced mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH). The important screening methods for this disease are lack of patient recovery after 2 months of iron therapy and increased Hemoglobin A2 (HbA₂). In this study, we evaluated the sensitivity and specificity of MCH and MCV for diagnosis of BTM.

METHODS:

This cross-sectional study was performed among patients with BTM. CBC samples were taken and hematological parameters were measured. Two months of iron therapy and measurement of HbA₂ were carried out for definitive diagnosis of beta-thalassemia. After definitive diagnosis, the specificity, sensitivity, positive predictive value (PPV) and negative predictive value (NPV) for MCV and MCH were calculated. To investigate the relationship between HbA₂ and hematological parameters (MCV and MCH), the linear regression test was performed using the SPSS18 software.

RESULTS:

From 300 patients, 154 (51.3%) were men and 146 (48.7%) women. According to the results, the highest sensitivity was associated with MCH with 90% sensitivity and specificity, respectively. Linear regression analysis showed the negative correlation -0.53 and -0.51 between HbA₂ and MCV, and MCH, respectively.

CONCLUSION:

According to the results, using parameters like MCH are more appropriate than time consuming and expensive HbA₂ measurements for diagnosis of BTM. However, none of the aforementioned parameters showed 100% specificity and sensitivity.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
globins are often examined by cellulose acetate electrophoresis and DE-52 microchromatography or HPLC. Molecular diagnosis of beta thalassemia often includes PCR-based techniques. Important methods used for these purpose are Reverse Dot Blotting method and Primer-Specific-Amplification (PSA). If the examination does not determine the type of mutation, beta gene sequencing could be used to detect mutations (6-8). Prenatal diagnostic methods are amniocentesis which is usually done around 15-18 weeks of pregnancy, or examination of chorionic villus in week 11. Fetal cells and fetal DNA analysis could be useful for diagnosis (9). Prevalence of BTM was reported about 4% in Iran which is higher than the prevalence of BTM-related gene (1.5%). The prevalence of BTM in the province of Mazandaran, Sistan and Baluchestan, Hormozgan and Kerman was high, and the lowest rate was in four provinces of Tehran, Khorasan, Hamedan and Yazd (10).

MCV and MCH are the blood parameters representing the average size of RBCs and hemoglobin in RBCs, that are both reduced in BTM and cause microcytic hypochromic anemia. HbA₂ is one of the human hemoglobin types that is normally 1.5 to 3.5 percent, and consists of two β and δ chains. In patients with defects in the construction of the beta chain, the amount of this hemoglobin increases. The current study was done to assess the specificity and sensitivity of MCH and MCV for diagnosis of BTM, and also evaluate the association of HbA₂ with MCV and MCH.

Methods

Patients

In this cross-sectional study, 300 BTM patients referring to Sina laboratory in Sanandaj were included. According to the previous studies, the BTM criteria included hypochromic-microcytic anemia with MCV<80 and MCH<26.5 (11, 12). Definitive diagnosis was based on the lack of response to iron therapy for two months and increased HbA₂.

Sampling and measurement of hematological parameters

Blood samples were taken from patients and CBC was performed by cell counter device (Mindray, China). MCV and MCH parameters were extracted, and the data were entered into the software for analysis. Measurement of HbA₂ was done by electrophoresis for definitive diagnosis of BTM. Sensitivity, specificity, PPV, NPV and Youden’s index of MCV and MCH in the diagnosis of BTM was calculated.

\[
\text{Sensitivity} = \frac{\text{true positive}}{\text{true positive} + \text{false negative}} \times 100 \\
\text{Specivity} = \frac{\text{true negative}}{\text{true negative} + \text{false positive}} \times 100 \\
\text{PPV} = \frac{\text{true positive}}{\text{true positive} + \text{false positive}} \times 100 \\
\text{NPV} = \frac{\text{true negative}}{\text{true negative} + \text{false negative}} \times 100 \\
\text{Youden's index} = \left( \text{Sensitivity} + \text{specificity} \right) - 100
\]

Statistical analysis

Data were analysed by the SPSS 18 software using the t-test and regression test.

Results

From 300 patients, 154 (51.3%) were men and 146 (48.7%) women. Table 1 shows the results of hema-

| Table 1. Hematological findings of BTM patients |
|-----------------|------------------|------------------|------------------|
| MCV | HbA₂ | MCH | Age |
| Mean | 68.7 | 4.32 | 21.5 | 38.26 |
| Std. Error | 0.40 | 0.08 | 0.15 | 0.61 |
| Std. Deviation | 7.05 | 1.46 | 2.7 | 1.05 |
| Variance | 49.71 | 2.14 | 7.3 | 112.16 |

| Table 2. Sensitivity, specificity, PPV, NPV and Youden’s index of formulas |
|-----------------|------------------|------------------|------------------|------------------|
| Sensitivity | specificity | PPV | NPV | Youden’s index |
| MCV | 87.71 | 44.44 | 83.33 | 53.33 | 32.15 |
| MCH | 90.58 | 58.44 | 86.32 | 68.18 | 49.02 |

tological parameters of BTM patients. MCH had the highest sensitivity and specificity in the diagnosis of BTM. Evaluation of MCV and MCH sensitivity and specificity showed that MCV was more sensitive and specific than MCH, with 90% sensitivity and 58% specificity, versus 88% and 44% (Table 2).

Discussion

The best diagnostic method for BMT, which is a hypochromic-microcytic anemia, is measurement of HbA$_2$ and mutation in beta globin gene, but these tests are time consuming and expensive. Therefore, using other hematological parameters reported in CBC results, seems to be more effective and economic (13). Results of this study showed 90.58% and 87.71% sensitivity, and 58.44% and 44.44% specificity for MCH and MCV, respectively; in MCH=26.5 pg and MCV=80 fl cut-off point. Thus, unlike specificity, the sensitivity of MCH and MCV is low for Screening BTM. Many studies have been conducted in this regard. In our previous study, we evaluated the formulae based on RBC indices in differentiating between iron deficiency anemia and beta thalassemia minor, and suggested the King-Green formula (K and G)= MCV×RDW/Hb×100 for differentiating between them, because of its high sensitivity (14). In the present study, it was shown that the use of MCH and MCV can be helpful due to their high sensitivity in screening BMT, although, their sensitivity is not 100%. In a study by Karimi and colleagues (11), the highest sensitivity for MCH was reported similar to our study, but they reported 98.5% sensitivity for MCH in the diagnosis of BTM unlike our result which was 91%. This contrast may be due to differences in sample size and patients. In the study of Pranpanus and colleagues which was carried out on pregnant women, 95.6% sensitivity in the diagnosis of BTM was reported for MCH (12), that was consistent with our result. The advantage of our study was using proven cut off points for MCH and MCV based on previous studies, while in many studies it was calculated based on common values of sensitivity and specificity. Measurement of MCV and MCH could be helpful in the diagnosis of BTM without measuring HbA$_2$.

Conclusion

In conclusion, using MCH could be beneficial in the diagnosis of BTM because of its high sensitivity, low cost and easy measurement.

Ethical disclosure

All the data were extracted from the records.

Acknowledgment

The authors appreciate Mohammad Boshagh for all of his assistance.

Author contributions

All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Conflict of interest

The authors declare that they have no conflict of interest.

Funding/Support

None declared.

References