Original Article

Assessment of cardiac autonomic nerve function status in female with iron deficiency anemia

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Abstract

Iron deficiency anemia is considered as one of the major public health problem in Bangladesh. Cardiac autonomic nerve dysfunction may present in iron deficiency anemia which increases the risk and further complications of this disease. Assessment of heart rate variability (HRV) is a non-invasive technique to evaluate cardiac autonomic nerve function status. To assess the cardiac autonomic nerve function status by heart rate variability analysis, 100 female subjects with iron deficiency anemia aged 20-45 years were included in the study group. For comparison, age and sex matched 100 apparently healthy female were selected as control. The HRV parameters were recorded by a 4 active channels, Polyrite-D. Mean resting pulse rate, LF power, LF norm and LF/HF were significantly (p <0.0001) higher and total power, HF power, HF norm were significantly (p <0.0001) lower in subjects with iron deficiency anemia in comparison to those of control group. This study concludes that cardiac parasympathetic activity was reduced in female with iron deficiency anemia.

Key words: Heart rate variability, iron deficiency anemia.

Introduction

Anemia may be defined as decreased concentration of hemoglobin level in the blood below the lower limit of the normal range in respect of age and sex of the individual.[1]It is the most common disorder of the blood. Here the number of red blood cell is decreased and consequently their oxygen-carrying capacity is insufficiento meet the body's physiological needs. Anemia is a global public health problem affecting both developing and developed countries with major consequences for human health, social and economic development. Globally anemia affects 1.62 billion people which correspond to 24.8% of the population.[2] The prevalence of anemia among adult non pregnant females in Bangladesh is 45%. The causes of anemia in a population are multiple. Iron deficiency is the most important cause of nutritional anemia worldwide.[3]

There are more than 400 types of anemia, which are divided into three groups. Anemia caused by blood loss such as gastric ulcers, CA-rectum, hook worm infestation, menorrhagia etc. Anemia caused by decreased or faulty red blood cell production such as iron deficiency, vitamin B12 deficiency, sickle cell anemia, bone marrow and stem cell disorder, leukemia etc. Anemia caused by destruction of red blood cells such as thalassemia, sickle cell anemia, other hemolytic anemia.[4] Causes of iron deficiency anemia in female of 20-45 years include- lack of iron in diet, blood loss due to any etiology, inability to iron absorb and pregnancy.[5] Anemia is an independent risk factor for adverse cardiovascular outcomes in the general population.[6] It was previously reported that heart rate variability was decreased in anemic patients.[7,8,9] And the low heart rate variability can potentially increase the cardiac risk.[8]

Autonomic nervous system (ANS) plays an important role in the regulation of the physiological processes of the human during normal and pathological conditions. Among the techniques used in its evaluation, the heart rate variability (HRV) has been a simple and non-invasive measure of the autonomic impulses. It represents one of the most promising quantitative markers of the autonomic balance. The HRV describes the oscillations in the interval between consecutive heart beats (RR interval), as well as the oscillations between consecutive instantaneous heart rates. It is a measure that can be used to assess the ANS modulation under physiological conditions, such as wakefulness and sleep conditions, different body positions and physical training. HRV also assess the ANS changes during any pathological conditions. Changes in the HRV patterns provide a sensible and advanced indicator of health involvements.[10]

Heart rate is influenced by sympathetic and

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nervous systems, reflexes and respiration. HRV enables clinicians and researchers to examine the influences of autonomic activity on heart rate.[11] HRV reflects autonomic nervous control. Normally heart rate variation is related to the balance between sympathetic & parasympathetic nervous system which provides early better qualitative and quantitative interpretation of sympathovagal modulation and can detect autonomic impairment.High HRV reflects good adaptability and well-functioning autonomic control. On the other hand, reduced heart rate variability acts as a strong predictor of risk for adverse events in patients with wide range of diseases.[12] HRV assesses the difference of the periods between consecutive heart beats. These differences of the periods vary under autonomic control. Decreased HRV has been recognized as a strong indicator of risk in healthy as well as diseased individuals.

The relationship between anemia and heart rate variability have been searched in several types of anemia like thalassaemia[13] Vitamin B12 deficiency and megaloblastic anemia,[14] sickle cell trait.[15] However, there are insufficient data about autonomic functions in patients with iron deficiency anemia, the leading cause for anemia in the general population.[16] Yokusoglu et al[17] reported impairment in HRV indices due to increased sympathetic or decreased parasympathetic activity in iron deficiency anemia. It is reported that supplementation of iron is effective in improving the dysregulation of autonomic nervous system reflexes.[18]

It was reported that HRV parameters were decreased in patients with vitamin B12 deficiency. But the decrease in sympathetic HRV parameters was greater than those measured in parasympathetic HRV parameters.14 On contrary some investigators observed there was no significant difference between the healthy group and iron deficient anemic patients in regard to HRV parameters.[16,19]

The exact relationship between HRV parameters and anemia remains elusive. So far it is known that the changes in HRV parameters as a result of iron deficiency anemia by both microcomputer based time and frequency domain method or conventional method has not yet been done in our country. Again, we need to know the value of HRV parameters in female subjects with iron deficiency anemia of Bangladesh for our own standard baseline as well as for reference value. Therefore, this study has been designed to assess the cardiac autonomic nerve function by analyzing the HRV parameters in adult female subjects with iron deficiency anemia.

Methods

This cross sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2012 to June 2013. For this, 100 female subjects with iron deficiency anemia aged 20-45 years were included in the study group (Group B). The anemic subjects were selected from Outpatient Department of Haematology in Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. They were included in the study group on the basis of their pre-performed hemoglobin percentage, total count of RBC and serum ferritin level. Data were collected in pre-designed structured questionnaire by the researcher herself. For comparison, age and sex matched 100 apparently healthy female volunteers were selected as control (Group A) from the different areas of Dhaka city. All the subjects were free from hypertension, cardiovascular disease, any endocrine disorder, renal disease, psychic disorder and any hereditary disease. Subjects with pregnancy and habit of smoking were excluded. The subjects were thoroughly informed about detail procedure of the study and informed written consent was taken.

The subjects were advised to have their meal by 9:00 pm night before the examination and have to remain free from any physical or mental stress. They cannot take any sedatives or drugs affecting central nervous system. They were also asked to have light breakfast and avoid tea or coffee at breakfast. On the day of examination, the subjects were advised to attend the Autonomic NerveFunction Test Laboratory in the Department of Physiology of Bangabandhu Sheikh Mujib Medical University, Dhaka between 9 am to 1 pm on the day of examination. Whenever the subject appeared in the department, he/she was interviewed and detail history regarding personal history, drug history, past medical history were taken. Then thorough physical examinations and anthropometric measurement including height, weight and BMI were taken. Then the subject was prepared to perform Autonomic Nerve Function Test. She was kept in complete bed rest in supine position for 15-20 minutes in a cool and calm environment. During this period subject was advised not to talk, eat or drink and also not to perform any physical or mental activity, even sleep. Then all preparations for recording of the HRV parameters were made by connecting the channels of ECG. A five minutes recording of the time domain HRV parameters such as mean R-R interval, mean heart rate, SDNN (standard deviation of normal to normal R-R intervals), RMSSD (root mean square of successive heartbeat interval differences) were recorded by a 4 active channels, Polyrite-D. For statistical analyses, unpaired Student's t-test and Pearson's correlation coefficient test

were performed by using SPSS (version-19) as applicable.

Results

Both the groups were matched for age and BMI. Mean values of LF (low frequency) power, LF norm and LF/HF were significantly (p<0.05) higher and mean values of total power, HF (high frequency) power and HF norm were significantly (p<0.05) lower in group B than that of group A.(Table-I)

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Table-I: Spectral parameters of HRV in both groups

Parameters	Group A (n= 100)	Group B (n= 100)	P value Group A vs B
Total power(ms	2957.30± 961.33 (1143.65-4918)	1485.81± 452.81 (1005.34-3034.68)	0.0001
LF (ms^2)	622.84±138.85 (254.00-1094.50)	1182.37± 630.48 407.72-2882	0.0001
HF(ms^2)	842.08± 166.64 (422.62-1095.95)	379.93±162.40 (105.00-836.00)	0.0001
LF norm(n.u)	47.74±11.03 (20.4-71.9)	63.74±13.55 (29.4-84.4)	0.0001
HF norm(n.u)	52.15±11.21 (27.0-79.6)	36.64±13.69 (15.6-70.6)	0.0001
LF/HF	1.02±0.51 (0.25-2.56)	2.17±1.26 (0.42-5.4)	0.0001

Results are expressed as Mean ± SD. Figures in parenthesis indicate ranges. Unpaired Student's 't' test was performed to compare between groups. The test of significance was calculated and p values <0.05 was accepted as level of significance.
n=Number of subjects, Group A : Healthy subjects (control), Group B : Subjects with iron deficiency anemia
LF power = low frequency, HF power = High frequency, LF = Low frequency, HF = High frequency, LF/HF = Ratio of low frequency and high frequency

Discussion

In the present study, findings of HRV parameters in healthy control group were almost within normal range and also similar to those reported by the various investigators from different countries [9,14,17,20-22] and also from our country.[23-25] The total power, HF power and HF norm were significantly (p<0.0001) lower in subjects with iron deficiency anemia in comparison to that of control. Similar significant change of mean total power in anemic patients was also observed by various researchers.[20,22] Again Shetty et al[19] reported opposite finding but it was not statistically significant.

Significantly higher LF power, LF norm and LF/HF were observed in subjects with iron deficiency anemia when compared to healthy control. Opposite findings were observed by Shetty et al[19] in patients with iron deficiency anemia but it was not statistically significant.

There are some postulated mechanisms suggested by various researchers of different countries which may imply the possible mechanism regarding the involvement of autonomic nerve function activity in anemic patients. It has been suggested that parasympathetic activity decreases and sympathetic activity increases in patients with iron deficiency anemia. The imbalance between sympathetic and parasympathetic nerve activities can change the electrophysiologic activity of the heart.[17] In iron deficiency anemia, there is reduced oxygen carrying capacity of blood due to decreased hemoglobin concentration. Thus hypoxia occurs. This hypoxia is sensed through carotid bodies and increases sympathetic activity [26] The anemic hypoxia stimulates adrenergic nervous system.

Stimulated adrenergic nervous system is responsible for cardiovascular response i.e. tachycardia and increased

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