Volume 1 Issue 3
www.escientificlibrary.com

ES Journal of Clinical Medicine

The Influence of Low Serum Ferittin on Cardiac Autonomic Regulation in Libyan Patients

Short Communication

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Received: Apr 30, 2020; **Accepted:** June 09 2020; **Published:** June 11, 2020

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Abstract

Autonomic nervous system activity is impaired in anemic patients with various etiology such as vitamin B12 deficiency, thalasemia major and sickle cell trait however there are insufficient data about autonomic function in patient with iron deficiency anemia in general population study

Aim

In present study we aimed to investigate the relationship between serum ferritin level and heart rate variability (HRV).

Patients and methods

This is case control study of 20 patients with iron deficiency anemia (case subject) and 20 healthy subject.

ECG record was used for studying HRV; we used serum level of iron, ferritin, iron binding capacity, C reactive protein, vitamin B12 and folate to exclude other causes of anemia.

Result

Age, gender, vitamin B12, folate and serum electrolyte were not different between the groups, HRV value were lower in patients with iron deficiency anemia compared to control group.

Heart rate of study group (116±19) was significantly greater than control group (78±19, P< 0.05), Hb, HCT, MCV and ferritin value were significantly lower in study group than in control group (8.5±2.3 vs 13.2±0.4, P<0.05 30.1±1.1 vs 41.2±1.1, P<0.05, 67.3±2.1 vs 84.5±2.4, P<0.05, 5.1±0.4 vs 97±6.5, P<0.05 respectively).

SDNN, SDANN and RMSSD were significantly lower in study group than in control group (116±38 vs 139±41, P<0.05 96±32 vs 122±38, P<0.05 23±12 vs 29±11, P=0.26 respectively)

Conclusion

Lower serum ferritin is associated with lower HRV putting anemic patient at high cardiac risk.

Keywords

Heart rate variability; Autonomic function; Iron deficiency anemia; Electrocardiographic

Introduction

Heart rate variability (HRV) asses the difference of the period between consecutive heart beats, which vary under autonomic control. Decreased HRV has been recognized as strong indicator of risk related to adverse events in healthy individual as well as diseased patient, reflecting the vital role of the autonomic nervous system in maintain health [1-3].

HRV can be measured by the time domain [2].

Cardiac autonomic function have been demonstrated to be impaired in various disorder including diabetes mellitus [3], hypertension [4], ischemic heart disease [5,6], the degree of fluctuation of the beat to beat difference in cardiac rhythm is an indirect method for cardiac autonomic function determination it has extensively used for that purpose as reliable and noninvasive.

Method

This is case control study of 40 patients, 20 patients with iron deficiency anemia (case subject) and 20 healthy subject (control subject), data were collected through interview cases and controls, physical examination done by the study physician. Patients were included if they were between 20 and 40 year.

Subjects with past medical history suggestive of smoking, diabetes, hypertension, heart diseases, vitamin B12 or folate deficiency, sickle cell disease, thalasemia were excluded from the study.

The diagnosis of anemia was made according to complete blood count, serum ferritin, vitamin B12 and folate level.

Apart from lower serum ferritin level < 100µg/L[7], whole hemoglobin value below 11.7 g/ dl for female and 13g/dl for males were recorded as satisfactory criteria for the diagnosis of iron deficiency anemia. We used serum iron, serum iron binding capacity C reactive protein for excluding the patient with other cause of anemia.

Heart rate variability

ECG recorder was used for studying HRV. Patients were advised to lie down (in supine position) and breath comfortably ensuring clean ECG signals, the ECG recording was initiated. Heart rhythm scanner, manually finish the trial session once it is time expire (5 minutes). Any medication was stopped at least one week prior to ECG examination.

Time domain indices for HRV from ECG were calculated by cardiologist.

The time domain HRV parameters that measured in our study, were the standard deviation of all normal sinus R-R interval (SDNN), the standard deviation of all averaged normal sinus R-R interval for each 5-minutes segment (SDANN), the root mean square of successive difference between normal sinus R-R interval (RMSSD) can be calculated [2].

Statistical analysis

Was performed by using SPSS software (version 12), difference among groups was analyzed by (t- test) and P value 0.05 was considerable significant.

Result

Table (1) There were no statistically significant difference between study group and control group in relation to age and gender. All subjects were detected to be in sinus rhythm without episode of sustained atrial or ventricle arrhythmia. Mean heart rate was significantly higher and mean hemoglobin, hematocrit and ferritin level were significantly lower in the study group in comparison with control group. Heart rate of study group (116±19) was significantly greater than control group (78±19), P< 0.05,

Table 1: Demographic and clinical characteristic of study and control group

P Value	Control group n(20)	Study group n(20)	characteristic
NS	8±30	6±32	Age(Year)
NS	6 (30%)	35%)) 7	Male
NS	14(70%)	13(65%)	Female
<0.05	78±19	116±19	Heart rate (bpm)
NS	116.6±13.6	118.6±10.4	Systolic blood pressure (mmHg)
NS	72.8±10.6	76.9±9.8	Diastolic blood pressure (mmHg)
NS	22.95±2.12	23±2.3	Body mass index (kg/m²)
NS	91.7±16.4	93.3±17.3	Random blood glucose
<0.05	13.2±0.4	8.5±2.3	Hb value (g/dl)
<0.05	41.2±1.1	30.1±1.1	HCT value (%)
<0.05	84.5±2.4	67.3±2.1	MCV (fl)
<0.05	97±6.5	5.1±0.4	Serum ferritin value (ng/ml)
NS	276±82	259±65	Vitamine B12 value (ng/L)
NS	7.3±1.2	6.5±1.3	Folate (ng/ml)

Hb, HCT, MCV and ferritin value were significantly lower in study group than in control group (8.5±2.3 vs 13.2±0.4, P<0.05 30.1±1.1 vs 41.2±1.1, P<0.05 67.3±2.1 vs 84.5±2.4, P<0.05 5.1±0.4 vs 97±6.5, P<0.05 respectively) and there was no difference between male and females with regard to clinical and laboratory parameter in both groups Table (2). All time domain indices of HRV except RMSSD showed statistically significant decrease in patient compared to control group. SDNN, SDANN were significantly lower in study group than in control group (116±38 vs 139±41, P<0.05 96±32 vs 122±38, P<0.05 23±12 vs 29±11, P=0.26 respectively).

Table 2: Statistical Comparison of HRV variables of study and control groups

P value	Control group	Study group	
<0.05	139±41	116±38	SDNN (m sec)
<0.05	122±38	96±32	SDANN (m sec)
=0.26	29±11	23±12	RMSSD (m sec)

SDNN: The standard deviation of all normal sinus; R-R: interval over 5 minutes; SDANN: The standard deviation of all averaged normal sinus; R-R: interval for each 5-minutes segment; RMSSD: The root mean square of successive difference between normal sinus R-R interval

Discussion

The main finding of this study was an alteration in HRV parameters of patients with iron deficiency anemia. The imbalance between sympathetic and parasympathetic nerve activities can disturb electrophysiological properties of the heart and may probably lead to increase mortality [8], demonstrated diminished sympathetic activity in anemic patient with thalesemia major are indicated by lower plasma nor epinephrine level compared with control group, similar decrease in time-domain parameter of HRV was also detected in non-anemic sickle cell trait carrier [9] and beta thalesemia [10], more over both sympathetic and parasympathetic components of HRV were significantly lower in anemic patients with vitamin B12 deficiency [11].

[12] detected impairment of global indices of HRV that might be caused by increased sympathetic activity and decreased parasympathetic activity in patient of iron deficiency anemia.

[5] proved that each 1 g/dl decrease in hemoglobin was associated with increase odds of having low HRV. This association was still strong enough after adjustment of other factors such as left ventricle mass and ejection fraction and diastolic dysfunction.

Low HRV may actually represent the early feature of cardiac disease in thalasemic patients with no evidence of ventricle dysfunction of routine evaluation [13]. Based on above account anemia is associated with low HRV which put anemic patients at higher risk of sudden death especially if concomitant heart disease exists [5].

[9] attributed these autonomic changes to altered hemorheogi cofactor such as blood viscosity and red blood cell deformability in sickle cell trait carriers. Red cell deformability in iron deficient stat is controversial issue, while [12,15] reported decreased erythrocyte deformability, some other author stating normal value [16]. Moreover iron deficiency has no effect on blood viscosity even in patients with cyanotic heart disease [17].

[12], proposed that low oxygen tension in tissue might be the cause of altered autonomic function in iron deficiency anemia, peripheral and central chemo reflexes are the dominant autonomic mechanism regulating ventilatory patterns in response to changes in partial pressure of oxygen and carbon dioxide in arterial blood, Both reflex pathway are capable of eliciting increase in sympathetic nerve impulse and consequently may explain altered autonomic activity in patients with anemic hypoxia [18].

Despite lacking adequate convincing evidence concerning exact mechanism of carotid body activation, it is assume as due either to hypoxia-related mitochondrial respiratory chain inhibition or potassium channel suppression which lead to intracellular calcium accumulation [19].

Conclusion

Lower serum ferritin is associated with lower HRV putting anemic patient at high cardiac risk.

Limitation

We have only been able to use the time domain parameters of HRV for technical reason. If frequency-domain parameters would have been included, the study may be more informative. However, we think that the study is still valuable because time-domain and frequency-domain parameters are related to each other. A change in one of them is generally suggestive of a change in the other [20].

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