Effect of Deep Breathing Test on Female Patients of Iron Deficiency Anemia

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Research Article

Abstract: The present study was conducted to find out whether the deep breathing test and thus the autonomic nervous system are affected in female patients of iron deficiency anemia. **Material and Method**: In this study the change in heart rate was recorded with the help of ECG machine during inspiration and expiration phases of deep breathing maneuver. The change in heart rate was compared between 60 women with iron deficiency anemia and 60 age and socioeconomically matched women. **Result**: it was found that the change in heart rate was significantly altered in women with iron deficiency anemia (P<0.0001) when compared to controls. **Conclusion**: altered deep breathing test suggestive of altered autonomic function in iron deficiency anemia.

Introduction

Iron deficiency has been recognized since medieval times. Chlorosis, a term derived from Greek word meaning green, was applied by Varandaeus to a disorder that was first described in 1954 by Johannes Lange as "de morbovirgineo". The disease became well known as "green sickness" occurring almost exclusively in teenage girls. It was depicted very well in paintings by Dutch masters and was alluded to by Shakespeare and other literary figures of the period.[1] One third of the world population is suffering from iron deficiency anemia, of which 60% to 70% is in India. The prevalence of iron deficiency anemia is higher among the people living in chronic poverty. Also it tends to run in families, possibly because of economic factors. The iron deficiency anemia is defined by cut off haemoglobin value of 12 gm/dl in women and 13 gm/dl in men. [2] The autonomic nervous system in our body provides a rapidly responding mechanism to control wide range of functions such as cardiovascular, respiratory, gastrointestinal, renal, endocrine and other systems. All the above systems are regulated by parasympathetic or sympathetic autonomic nervous systems or both. In iron deficiency anemia, the affection of autonomic nervous system has to be elucidated as it plays a vital role in body homeostasis and is also a life saving mechanism in stressful situations. The testing of autonomic nervous system can be done by using the battery of autonomic function tests, deep breathing test is one of them, which is simple, non invasive and reproducible.

Aims and Objectives

Aim:

The aim of present study was to find out whether the deep breathing test and thus the autonomic functions are affected in female patients of iron deficiency anemia.

Objectives:

- To study and compare deep breathing test in female patients with severe iron deficiency anemia and normal age-matched controls.

Materials and Methods

Study Population

The study was conducted in Topiwala National medical college and Nair hospital with prior permission of ethical committee. The study was conducted over a period of 2 years (2010-2011).

Inclusion Criteria:

Cases

60 female patients of iron deficiency anemia belonging to the age-group of 20 to 40 years, attending hematology clinic in hospital were selected for study. Patients included were those with:

1) Iron deficiency anemia with[3]
   All the three condition when full filled by the case then only it was selected for study
   a. Hb level <12 gm%
   b. Serum iron <30 microgram/dl
   c. Total iron binding capacity > 400 micrograms/dl
2) Age group of 20 to 40 yrs.
3) Symptoms of anemia like weakness, early fatigue etc.

Controls

For comparison 60 healthy female subjects belonging to age group that is 20 to 40years, same socio-economic

conditions were selected from the general population as controls. Having

1) Hb level >12gm% [2]
2) Age group of 20 to 40 yrs.

Exclusion Criteria:

1) Subjects of age <20 yrs and>40 yrs.
2) Subjects with other type of anemia like sickle cell disease, thalassemia, vitamin B12 deficiency were excluded.
3) Diseases causing autonomic disturbances like diabetes mellitus, Parkinson's disease, multiple sclerosis, asthma, rheumatoid arthritis, hypertension etc. were excluded. [4]
4) Subjects who were taking medication for iron deficiency anemia like ferrous sulphate etc.

Method

For this study subjects were divided into two groups, that is iron deficiency anemia patients and healthy controls. Written consent was taken. Hb level was measured with the help of electronic counter Sysmex k-100. Serum iron and serum total iron binding capacity of the both the groups was measured manually by Ferrozine method.

After this the Resting Heart Rate and Blood Pressure was measured. The heart rate of subject and controls was calculated from ECG tracing and blood pressure was measured in the right upper extremity by sphygmomanometer. The recording was taken only when two consecutive heart rate and blood pressure readings taken 5 minutes apart were identical. This meant that in all probability they had reached their basal values. [5]

After recording the resting heart rate and blood pressure the deep breathing test was performed on subjects and patients and alteration in the heart rate was recorded. Procedure was as follows

Procedure: In the supine position the subject was asked to breathe slowly and deeply at the rate 6 breaths per minute, with each phase of respiration that is inspiration and expiration lasting for 5 seconds each. A continuous ECG tracing was recorded after making the individual practice twice. The heart rate variations are maximum when the test is performed in this manner. [6]

Calculation: The maximum and minimum R-R intervals during each breathing cycle are measured with ruler. The result is then expressed as the mean of difference between maximum and minimum heart rates for six measured cycles in beats per minute. [5]

Heart rate variation = maximum heart rate during inspiration – minimum heart rates during expiration.

Interpretation of results

Heart rate variation (Maximum ─ Minimum heart rate)	
Normal	≥ 15 beats /min difference in heart rate
Borderline	11-14 beats/ min difference in heart rate
Abnormal	≤ 10 beats /min difference in heart rate.

Mechanism: The rhythmic variation in heart rate associated with the breathing is called as 'respiratory sinus arrhythmia'. Typically the cardiac rate accelerates during inspiration and decelerates during expiration. The basic mechanism underlying sinus arrhythmia can be explained as follows:

a) Central effect of respiration on heart rate.

Traube, in 1865 postulated that respiratory cardiac arrhythmia is due to an influence of brain stem respiratory centre on cardiac autonomic centres. Thus vasomotor tone varies periodically at frequency of respiration and results in rhythmic fluctuation in blood pressure. This in turn alters the heart rate through baroreceptor stimulation or inhibition.

b) Mechanical effect of respiration on ventricular outflow

With inspiration there is a decrease in intra thoracic pressure which results in an increase in right atrial inflow whereas the left atrial inflow is transiently reduced consequent to increase in pulmonary vascularity. A transient increase in heart rate, mediated by "Bainbridge effect" may occur due to an increase in right atrial pressure which occurs predominantly in early inspiration and is over by mid inspiration. When the increase in systemic venous return eventually reaches the left atrium the increase in left ventricular output results in an increase in systemic pressure, returning the blood pressure to its level. This effect normally occurs in mid or end-expiration. This increase in arterial pressure frequently results in reflex cardiac slowing.

c) Stretch receptors located in lungs are also capable of affecting the heart rate. With moderate degree of pulmonary inflation cardio acceleration may be evoked reflexly. [7]

The finding of reduction in sinus arrhythmia is associated with depressed baroreflex sensitivity. This abnormality could be due to impaired afferent, central or vagal efferent mechanisms. [8, 5]

Statistical Analysis

Statistical analysis was done by using Graph Pad In Stat^R software version 3.10, created on July 10, 2009. Descriptive statistics i.e. mean and standard deviation was used for numerical data. Comparison of numerical variables among groups was done by using unpaired t-test. P – value < 0.05 was considered as statistically significant.

Observations and Results

Table 1: Comparison of age in cases and controls

	Group wise comparison of age			Unpaired t- test applied		
	Group	Mean	SD	t-value	p-value	Significance
Age(Yrs)	Cases	25.45	3.92	0.7524	0.4533	Not significant
	Controls	25.85	1.23			

In above table, the age of iron deficiency anemia patients (mean 25.45 ± 3.92) is compared with the age of controls (mean 25 ± 1.23) with the help of unpaired t test. From the above results we can conclude that there is no significant difference in the age of both the groups.

Table 2: Group wise comparison of various parameters

	Group	Mean	SD	t value	p value	Significance
Heart Rate	Cases	96.5	9.63	8.93	<0.0001	Significant
	Control	82.08	7.94			
Basal Systolic blood pressure	Cases	111.50	10.10	4.42	<0.0001	Significant
	Control	118.30	6.30			
Basal diastolic blood pressure	Cases	73.30	8.01	4.28	<0.0001	Significant
	Control	78.56	5.14			
Deep breathing test(heart rate variation)	Cases	9.86	5.95	9.76	<0.0001	Significant
	Control	18.71	3.71			

The above table shows the values of meanand standard deviation of various parameters like heart rate, systolic blood pressure, diastolic blood pressure, and heart rate variation during deep breathing test. The mean heart rate of patients (96.5 ±9.63) was found to be significantly (<0.0001) higher than that of controls (82.08± 7.94). The mean systolic blood pressure of patients (111.50 ± 10.10) was found to be significantly (<0.0001) lower than that of controls (118.30 ± 6.30). The mean diastolic blood pressure of patients (73.30 ± 8.01)was significantly (<0.0001) lower than that of controls (78.56 ± 5.14). The mean heart rate variation during deep breathing test in patients was found to be 9.86 ± 5.95 and that of controls was 18.71 ± 3.71. It was found that the heart rate variation during deep breathing test was significantly (<0.0001) lower in cases than that of controls.

Discussion

The aim of the present study was to find out whether the deep breathing test affected in iron deficiency anemia patients or not. Both the study group (patients of iron deficiency anemia and controls) were matched for age. This is very important because there are previous studies which suggest that advancing age is known to diminish the vagal tone,[9] which affects the autonomic functions.

Resting heart rate: In present study, a comparison between the resting heart rate in iron deficiency anemia patients and controls was made. The basal heart rate in iron deficiency anemia patients was 96.5 ± 9.63 and in controls it was 82.08 ± 7.94. Thus there was increase in heart rate in iron deficiency anemia patients which was statistically significant(<0.0001) as compared to control subjects. Findings of this study correlate with those of NityaNand et al who also found higher basal heart rate in severely anemic patients (p <0.001) in their study of autonomic functions in chronic severe anemic patients.[10]Lakhotia et al in their study Clinical assessment of autonomic functions in anemics noted increase in heart rate of anemics. According to their study short circulatory time and peripheral vasodilatation occurred as a compensatory mechanism to increase the heart rate in anemics. [11] Glick et al in the year, 1964 also found increased heart rate in acutely induced anemia in unanesthetised dogs. He suggested that this increased heart rate could be due to 1) elevation of right atrial pressure, which, by increasing the tension of the atrial wall may increase the rhythmicity of the sinoatrial node, 2) local metabolic changes resulting from the changes in tissue partial pressure of oxygen produced by anemia and 3) noncatecholamine humoral substances released during anemia. [12] In humans, lack of oxygenation in tissue due to anemia results in local accumulation of metabolite like lactic acid due to anaerobic metabolism. This leads to vasodilatation and consequent increase in heart rate.[13]. In present study the decreased peripheral resistance may be the cause for increased heart rate in iron deficiency anemia patients.

Resting blood pressure: The mean systolic blood pressure in iron deficiency anemia patients was 111.50 ± 10.10 and in controls it was 118.30 ± 6.30. Thus the systolic blood pressure is significantly lower (<0.0001) in iron deficiency anemia patients. Also the mean diastolic blood pressure in iron deficiency anemia patients was 73.30 ± 8.01 and in controls it was 78.56 ± 5.84. This means diastolic blood pressure was also significantly

(<0.0001) lower in iron deficiency anemia patients. Nitya Nand et al in their study on chronic severe anemic patients found low systolic as well as diastolic blood pressure (P<0.001). [10] Justus et al in their study on chronic post hemorrhagic anemia in dogs, found that in response to infusion of blood at the rate of 1.0/ml/kg/min there was decrease in both cardiac output and arterial tension. [13] The blood pressure is lateral force exerted by the flowing blood against any unit area of vessel wall. [14] In iron deficiency anemia to fulfill the oxygen demand of tissue due to decrease oxygen content of blood, there occurs increase in cardiac output. Although the mechanism responsible for this increase in cardiac output has not been elucidated, a number of possibilities have been suggested. These include a decrease in peripheral resistance resulting from a fall in blood viscosity and arteriolar dilatation, an elevation of right heart filling pressures, stimulation of chemoreceptors sensitive to a decreased partial pressure of oxygen, the action of a non catecholamine humoral mediator, and the activity of the adrenergic nervous system. [13] The blood pressure is maintained by the cardiac output and the total peripheral resistance and these two show significant inverse relationship, that is, higher the cardiac output the lower is the vascular resistance. [15] The mechanism for decreased peripheral resistance in anemia is controversial. Justus et al in their study suggested that increased cardiac output and decreased peripheral resistance was due to humoral agents. However the exact nature and the mechanism of action of the agents are not specified. According to them several possible humoral agents which decrease peripheral vascular resistance include adrenal medullary hormones, V.E.M., serotonin and others. [13] Whereas Glick et al postulated a neural mechanism for decrease peripheral vascular resistance. According to this study, anemia profoundly reduces the tissue oxygen tension. Such a reduction in tissue oxygen tension lowers the total systemic resistance through local effects. [12] Local fall in oxygen tension initiates a program of vasodilatory gene expression secondary to production of Hypoxia inducible factor- 1α, thus causing arteriolar dilation resulting in secondary increase in cardiac output. [16] Thus the results of present study showed a significant fall in both systolic and diastolic blood pressure in anemics as compared to controls and this fall in blood pressure may be the result of decreased peripheral resistance due to anemia. [15]

Heart rate variation during deep breathing: The variation in heart rate in response to deep breathing exercise was 9.86 ± 6.95 in iron deficiency anemia patients and in the control group it was 18.71 ± 3.71. This variation in heart rate is significantly lower in iron deficiency anemia patients. The R-R interval variation during deep breathing is under vagal control (efferent).[7]During sinus arrhythmia, there is increase in heart rate in inspiration and decrease in heart rate during expiration. The heart rate response to cessation of vagal stimulation is very quick because the ACh released from vagus nerve is rapidly hydrolysed by cholinesterase, this short latency permits the heart rate to vary rhythmically at the respiratory frequency. Conversely the nor–epinephrine released periodically at sympathetic ending is removed very slowly. Therefore, the rhythmic variations in sympathetic activity that accompany inspiration do not induce appreciable changes in heart rate. Thus respiratory sinus arrhythmia is almost entirely brought about by changes in vagal activity. In fact respiratory arrhythmia increases with increased vagal tone.[18] In the present study deep breathing test show significantly lower values in iron deficiency anemia patients, thereby indicating a decrease in parasympathetic activity in these patients as compared to controls. Also S. Sangkatumvong et al had studied the cardiac autonomic response to transient episode of hypoxia in patients with sickle cell anemia. Results of the study indicated that post hypoxia autonomic functions showed a significant decrease in the parameters related to parasympathetic control and increase in parameters related to sympathetic activity.[19]Nitya Nand et al found that the patients with chronic severe anemia had significantly abnormal expiratory-inspiratory heart rate ratio during deep breathing test. He implicated that this is due to dysfunction of both sympathetic and parasympathetic reflex arc. [10] However Lakhotia et al found that there is no significant difference in deep breathing tests in anemics as compared to normal healthy individuals.[11]

In our study 60% of the severe iron deficiency anemia patients had evidence of lower heart rate variation to deep breathing exercise, thereby suggesting autonomic dysfunction in iron deficiency anemia patients. Thus, the overall interpretation of the results in the present study suggests that there occurs autonomic dysfunction in iron deficiency anemia patients. The cause of which may be the hypoxia and hypoxemia produced due to iron deficiency anemia which causes insensitivity or blunting of the carotid body and thus impairment of the autonomic reflex arc. The autonomic reflex arc can be tested deep breathing test, which is reliable, simple, non invasive. The autonomic nervous system controls wide range of functions such as cardiovascular, respiratory, gastrointestinal, renal, endocrine and other systems. Therefore it is necessary to further study autonomic dysfunctions occurring in iron deficiency anemia patients.

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