

Slow Breathing Exercise Improves Cardiac Autonomic Dysfunction in Male Patients with Transfusion Dependent Thalassemia: A Power Spectral Analysis of Heart Rate Variability

Kamol Chandra Das^{1,*}, Sultana Ferdousi²

ABSTRACT

Background and Aim: Iron overload induced cardiac autonomic dysfunction is a major contributor to fatal arrhythmia and cardiac morbidity and mortality in transfusion-dependent thalassemia (TDT) patients. Slow breathing exercise (SBE) increases cardiac parasympathetic activity in health and disease. This study aimed to assess the effect of slow breathing exercise (SBE) on frequency domain measures of heart rate variability in TDT patients. **Methods:** This prospective interventional study was done on 60 diagnosed male TDT patients aged 15-30 years. They were subdivided into 30 patients with conventional treatment only and 30 patients performed SBE for consecutive 3 months along with the conventional treatment. Age and gender matched healthy control were also studied without SBE. HRV parameters were recorded by Power Lab 8/35. For statistical analysis paired *t* test and independent sample *t* test were done as applicable. **Results:** Total power (TP), High frequency power (HF), HFnu and Low frequency power (LF) were found significantly lower but LFnu and LF/HF were found significantly higher in TDT patients compared to healthy control at baseline. After 3 months of SBE, significant increment of TP, HF and HFnu and significant decrement of LF, LFnu and LF/HF occurred with trend of improvement in cardiac autonomic nerve function in TDT patients. No significant change in these parameters was found in patients without SBE after 3 months of follow-up. **Conclusion:** SBE can improve cardiac autonomic dysfunction by restoring cardiac vagal activity and reducing sympathetic activity with shifting of autonomic balance to parasympathetic predominance in TDT patients.

Key words: Transfusion Dependent Thalassemia, Autonomic dysfunction, Heart rate variability, Slow breathing exercise, Sympathovagal balance.

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INTRODUCTION

Thalassemia is the most common inherited blood disorder in the world.^[1] Worldwide it is an increasing public health problem.^[2] Globally, approximately 60000-70000 born children present with severe form of anemia. In Bangladesh, approximately six thousands children are born with this disease.^[3,4] As a result of ineffective erythropoiesis and extra medullary hemolysis, anemia manifest as predominant clinical feature.^[5] Transfusion dependent thalassemia (TDT) patients requires regular blood transfusion to sustain their life.^[6] Though regular and repeated blood transfusion is mandatory in this group of patient for their life, but it causes the most serious complication iron overload.^[7] The fatal consequence of iron deposition in heart causing oxidative induced cardiac tissue damage, cardio toxicity and cardiomyopathy which are the most frequent causes of death among these patients.^[8-10] Decrement in heart rate variability (HRV) is related with a higher risk of arrhythmias after myocardial infarction and heart failure.^[11] Evaluation of cardiac autonomic nerve function (CANF) in thalassemic

patients showed depressed HRV in them by a group of researchers.^[12]

HRV is a sensitive non-invasive procedure for evaluation of cardiac autonomic nerve function. It detects the beat to beat change in heart rate or RR interval.^[13,14] HRV analysis has been popularly used as an investigation for autonomic nervous system in diabetes, other cardiovascular disease.^[13-16]

Akserold *et al.* was the pioneer scientist in demonstrating the frequency specific signal of heart rate by modulation of dynamic cardiovascular central system.^[17] Later by the observation of many scientist, different frequency bands are obtained from tachogram which is obtained by plotting RR intervals in each beat by time series. In frequency domain method, power spectral density (PSD) calculates the information of total power (variance) which distributes as a function of frequency. Very low frequency (VLF, frequency range 0.0-0.04 Hz), low frequency (LF, frequency range 0.04-0.15) and high frequency (HF, frequency range 0.15-0.4 Hz) are the

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components of different frequency band of total power (frequency range 0.0-0.4 Hz) in a spectrum of 2-5 min recording. Taskforce recommended 5 min recording for spectral analysis and 24 hr recording for time domain method.^[13,18]

Measurements of two major LF and HF power components (μs^2), also expressed in normalized units (n.u.) which represent the relative value of each autonomic component contributing to the variability as neural contributor. The vagal activity is a major contributor to the HF component. The LF component is an indicator of sympathetic modulation, but few researchers also propose it is contributed by both sympathetic and vagal influences. LF-HF ratio is considered as a mirror of sympathovagal balance.^[13-14,18-19]

SBE is one kind of yoga is voluntary regulation of breathing through alternate nostrils in order to regulate rhythmical respiration and to keep the mind calm. SBE has role on autonomic balance by increasing parasympathetic activity and decreasing sympathetic activity.^[20] This exercise improve CANF by increasing parasympathetic activity or decreasing sympathetic activity in some diseases and also in normal healthy person.^[21-22]

Although few studies published effect of SBE on HRV in migraine, diabetes mellitus but effect of SBE on HRV in transfusion dependent patient is not known. Therefore this study has been designed to investigate the effect of SBE on frequency domain measures of HRV in TDT patients so that SBE can be recommended in addition to conventional treatment and improve CANF as well as reduce the cardiovascular complications.

This study aimed to compare the power spectral parameters of HRV between TDT patients with SBE and without SBE to observe the effect of SBE on cardiac autonomic function in TDT. We hypothesized that slow breathing exercise will reverse the autonomic dysfunction in TDT patients.

MATERIALS AND METHODS

Study Design and Setting

This prospective quasi experimental study with parallel design was carried out in 2018 in Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka to observe the effect of SBE on CANF in male TDT patients by assessing frequency domain measures of HRV. The protocol was approved by the Institutional Review Board of BSMMU, Dhaka. After explaining the aim and benefit and procedure of the study, informed written consent was taken from each subject.

Sampling and Sample Size

Sample size was calculated by a statistical equation based on effect size published in a similar study^[23] Consecutive sampling was followed for preliminary selection of the TDT patients from the outpatient department of Blood transfusion and Hematology.

Study Participants

A total of 60 male TDT patients, diagnosed by hematologists, aged 15-30 years were enrolled for this study. For comparison of CANF, 30 apparently healthy male subjects with similar age range were taken as control to detect autonomic dysfunction in TDT patients. The patients were selected from the outpatient department of Transfusion Medicine and Hematology, BSMMU and the healthy controls were selected from the attendants of patients, hospital staff and students of BSMMU. All the subjects were free from respiratory disease, renal disease, diabetes mellitus, thyroid disorder and other hematological diseases. All these enrolled patients were subdivided equally into two groups. In experimental group, 30 patients were assigned with slow breathing

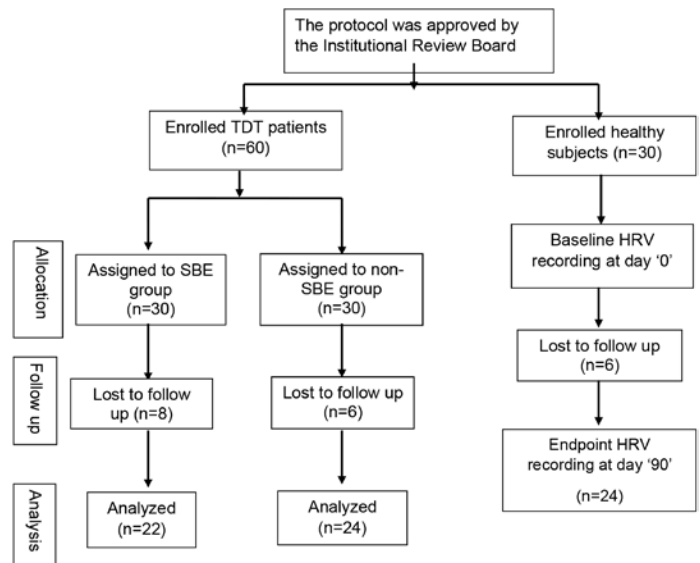


Figure 1: Outline of progression of participants during study period.

exercise and in control group, 30 patients were without slow breathing exercise. All patients received conventional treatment throughout the study period. Data of both the groups were collected at baseline before intervention with SBE or without intervention with SBE and also after 3 months of intervention or follow-up. Similarly healthy subjects were studied at baseline and after 3 months. The flow chart of recruitment of participants and the work flow is given in Figure 1.

Parameters Studied

After enrollment, the subjects were advised to follow some instructions in the previous night of HRV test day as part of preparation for HRV data collection. They were advised to finish their meal by 9:00 pm on previous night, to remain free from any type of stress, not to take sedative hypnotic medication. They were requested to take light breakfast without tea and coffee and to attend the autonomic nerve function test laboratory in the department of Physiology, BSMMU between 8:00 am to 10:00 am on the test day. A thorough physical examination including heart rate (HR), blood pressure (BP), height, weight, waist circumference, hip circumference was measured and BMI was calculated.

The subject was advised to take rest for 15-20 min in a controlled laboratory environment. During this period he was not allowed to talk, eat or drink, to perform physical or mental activity, even sleep. ECG was recorded on lead II for 5 min by data acquisition device Power Lab 8/35 (AD instrument, Australia). Power spectral analysis of HRV signals based on FFT was generated by Lab chart software. All data were recorded in a prefixed data schedule.

Intervention

For intervention with SBE, alternate nostril breathing procedure was chosen in order to observe the improvement in the level of compliance and to reduce the dropout rate of study population. This form of yoga is easy to perform than other relaxation technique of yoga.^[20] For ensuring the adequate performance of the procedure the principal investigator organized a training session for the participants. The procedure was demonstrated by an expert and participants in a small group practiced the steps of alternate nostril breathing till the trainer was satisfied with their performance.

The patients were advised to exercise slow breathing in a sitting position daily in the morning before breakfast and at evening for half an hour for

consecutive three months at home. For recording the event of exercise, a diary with time schedules including the pictures and steps of SBE in native language were provided to each patient in experimental group. For compliance of intervention, performance of patients was monitored by frequent home visits whenever possible, during their appointment in the hospital for blood transfusion and also was communicated 3-5 times per week via telephone calls. Monthly contact with those patients without intervention was maintained by the research team.

All study patients with or without intervention was advised to report for follow up data collection after 3 months in the Autonomic Nerve Function Lab of the Department of Physiology of BSMMU.

Study Outcomes

The primary target of the study was to observe the effect of SBE on CANF in TDT patients after 3 months of intervention. Spectral measures of HRV in TDT patients after 3 months of intervention were studied. This can be achieved by observing the changes in the power spectral measures of HRV (TP, LF, HF, LFnu, HFnu, LF/HF) by comparing its values at baseline to endpoint after 3 months intervention with SBE. Furthermore, it can be supported by comparing these values in TDT patients without SBE. Again the effect of SBE on CANF can be confirmed by comparing the data collected after 3 months between both groups. In addition, comparison of the baseline data between healthy control and all TDT patients confirmed the existence of autonomic dysfunction in TDT patients before intervention and follow-up.

Statistical Analysis of Data

Data were expressed as Mean and standard error of mean and percentage. Statistical analysis was done using SPSS version 16 and Microsoft Excel 2007. One way ANOVA followed by post hoc analysis, paired sample *t* test and independent sample *t* test were done as applicable. P value of < 0.05 was considered as statistically significant.

RESULTS

At the beginning of study, total 90 subjects were enrolled. Among them, 60 were patients and 30 were control subjects. During the period of study 14 (8+6) patients were dropped due to their inability to come to the laboratory. Data of about 13 of these patients were missed as they live outside Dhaka. One patient was undergone surgery. Six healthy subjects were outside Dhaka, so they could not come to Dhaka for follow up data recording. Therefore finally data of 46 patients and 24 healthy controls were used in data analysis. Values of data were normally distributed. Among 46 patients 3 patients were β thalassemia and 43 patients were Hb E- β thalassemia.

In this study, no significant difference was found in age and waist-hip ratio between TDT patients and healthy control. In addition there was no significant difference between SBE and non SBE patients in all these parameters (Table 1).

At baseline TP, LF, HF and HF nu were significantly decreased ($P<0.001$), but HR, LF nu and LF/HF ratio were significantly ($P<0.001$) higher in both SBE and non SBE groups compared to control. Again no significant

Table 1: Age and waist-hip ratio of participants.

Parameters	Control (n=24)	Non-SBE (n= 22)	SBE (n=24)
Age (years)	18.75 \pm 0.84	19.4 \pm 0.88	18.75 \pm 0.81
Waist-hip ratio	0.86 \pm 0.02	0.86 \pm 0.02	0.86 \pm 0.01

Data were expressed as mean \pm SE. Statistical analysis was done by independent sample *t* test. SBE: Slow breathing exercise.

Table 2: Baseline values of HR, BP and frequency domain measures of HRV in different groups.

Parameter	Control (n=24)	Non-SBE (n= 22)	SBE (n=24)
HR (beats/min)	70.00 \pm 1.69	90.09 \pm 2.17***	87.9 \pm 2.31***
SBP(mm of Hg)	116.75 \pm 1.06	101.55 \pm 1.74***	100.58 \pm 1.9***
DBP(mm of Hg)	74.58 \pm 1.15	63.45 \pm 1.08***	62.92 \pm 1.84***
TP	2999.84 \pm 413.04	564.51 \pm 98.13 ***	655.38 \pm 107.04 ***
LF power	815.23 \pm 131.54	179.18 \pm 34.23***	232.55 \pm 39.38 ***
HF power	1256.49 \pm 232.54	140.84 \pm 35.6 ***	155.24 \pm 36.61***
LF nu	42.33 \pm 2.5	61.81 \pm 3.72***	62.64 \pm 3.36***
HF nu	56.51 \pm 2.41	36.63 \pm 3.48***	35.39 \pm 3.03***
LF/HF	0.83 \pm 0.08	2.56 \pm 0.48**	2.46 \pm 0.4***

Data were expressed as mean \pm SE. Statistical analysis was done by independent sample *t* test. SBE: Slow breathing exercise; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TP: Total Power; LF power: Low frequency power; HF power: High frequency power; LFnu: LF power in normalized unit; HFnu: High frequency power in normalized unit; LF/HF: Low frequency and high frequency power ratio.

*** $P<0.001$

* symbol indicates comparison with control group.

differences were observed between SBE and non SBE patients in all these above parameters (Table 2).

After 3 months follow up, TDT patients without SBE had similar pattern of these parameters when compared to their baseline values, whereas after three months of SBE, mean value of HR, LF power, LF nu and LF/HF significantly ($P<0.01$, $P<0.05$, $P<0.001$ and $P<0.001$ respectively) decreased but TP, HF power and HFnu significantly ($P<0.01$, $P<0.01$ and $P<0.001$ respectively) increased in patients (Table 3).

Again post intervention values of all these parameters except LF power showed different trends in SBE group compared to their non-SBE counterparts and it was statistically significant. Though HR, TP, LF power and HF power in SBE group were significantly different from control, LFnu, HFnu and LF/HF reached close to control value (Table 4).

DISCUSSION

The present study assessed cardiac autonomic nerve function in diagnosed TDT patients before and after slow breathing exercise with conventional treatment for 3 months by power spectral analysis of frequency domain parameters of HRV and compared these results with control.

Significantly decreased TP, HF power, HFnu and LF power along with significantly increased LFnu and LF/HF in both TDT groups compared to healthy counterpart before intervention is suggestive of impaired autonomic harmony characterized by lower cardiac vagal activity and higher sympathetic activity and autonomic balance shifted to sympathetic predominance in these groups of TDT patients. This result is in concordant with previous research findings in thalassemic patients compared to healthy subjects.^[11] These change in HRV noted in thalassemic patients predicts their greater vulnerability to the risk of adverse cardiac incidence.

Transfusion-mediated iron overload due to repeatedly blood transfusion is the major problem in TDT patient. Excess iron generates excessive amount of free radicals in different tissues that impair many cellular activity and organ or system function which leads to autonomic imbalance.^[12] Moreover, after three months performance of SBE, there was significant increment of these parameters in these patients, which point towards improvement of autonomic harmony that has been

Table 3: Pre and post intervention comparison of HR, BP and frequency domain measures of HRV in different groups.

Parameters	Non-SBE (n=24)		SBE (n=22)	
	Pre	Post	Pre	Post
HR (beats/min)	90.09±2.17	90.82±2.2	87.9±2.31	82.42±2.1**
SBP(mm of Hg)	101.55±1.74	102.82±1.21	100.58±1.9	101.25±1.91
DBP(mm of Hg)	63.45±1.08	64.36±0.91	62.92±1.84	63.08±1.79
TP	564.51±98.13	504.66±97.09	655.38±107.04	874.73±97.24**
LF power	179.18±34.23	179.18±33.68	232.55±39.38	170.76±19.35*
HF power	140.84±35.6	124.72±28.54	155.24±36.61	345.27±58.77**
LF nu	61.81±3.72	64.94±2.96	62.64±3.36	37.61±3.2***
HF nu	36.63±3.48	33.29±2.87	35.39±3.03	57.75±3.51***
LF/HF	2.56±0.48	2.55±0.36	2.46±0.4	0.92±0.25***

Data were expressed as mean ± SE. Statistical analysis was done by paired sample *t* test. SBE: Slow breathing exercise; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TP: Total Power; LF power: Low frequency power; HF power: High frequency power; LFnu: LF power in normalized unit; HFnu: High frequency power in normalized unit; LF/HF: Low frequency and High frequency power ratio.

***P<0.001, **P<0.01, *P<0.05

* symbol indicates comparison of Post SBE with Pre SBE.

Table 4: Post follow-up values (after 3 months) of HR, BP and power spectral parameters in different groups.

Parameters	Control (n=24)	Non-SBE (n= 22)	SBE (n=24)
HR (beats/min)	69.83±1.8	90.82±2.2	82.42±2.1***
SBP (mmHg)	117.33±0.75	102.82±1.21	101.25±1.91***
DBP (mmHg)	74.00±1.00	64.36±0.91	63.08±1.79***
TP	2966.37±417.45	504.66±97.09	874.73±97.24****
LF power	878.97±125.06	179.18±33.68	170.76±19.35***
HF power	1248.64±219.5	124.72±28.54	345.27±58.77****
LF nu	43.64±2.58	64.94±2.96	37.61±3.2***
HF nu	54.34±2.53	33.29±2.87	57.75±3.51***
LF/HF	0.9±0.1	2.55±0.36	0.92±0.25***

Data were expressed as mean ± SE. Statistical analysis was done by independent sample *t* test. SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TP: Total Power; LF power: Low frequency power; HF power: High frequency power; LFnu: LF power in normalized unit; HFnu: High frequency power in normalized unit; LF/HF: Low frequency and high frequency power ratio.

P<0.001, **P<0.01, *P<0.001

* symbol indicates comparison with non-SBE;

symbol indicates comparison with control group.

achieved by SBE. On the other hand, no significant change was observed in these parameters in the patients those who did not perform SBE which imply continued autonomic disharmony in absence of intervention. Though the value of TP, LH power and HF power in SBE group of TDT patients after 3 months did not reach close to control but LF nu, HF nu and LF/HF ratio were near to control and there were no significant difference in these parameters of sympathovagal balance between SBE group and control. This finding strongly suggested that SBE may help regain the sympathovagal balance close to healthy control.

Improvement of sympathovagal balance by SBE has been proved in many other investigations mostly in healthy subjects and also in diseased condition. They proposed that improvement has been linked to the fact that SBE improves peripheral oxygen consumption, neuronal oxygen uses and thus improved autonomic balance. This method causes increased tidal volume in lungs that trigger the inhibitory reflex by the stretch

receptor located in the wall of this organ and increases parasympathetic activity. SBE also improves sympathovagal balance by enhancing central inhibitory rhythm.^[20,24-25]

CONCLUSION

Based on the results of this study it can be concluded that slow breathing exercise may improve impaired autonomic function in TDT patients by increasing parasympathetic while decreasing sympathetic activity with the autonomic balance more parasympathetic dominance in the TDT patients.

So, SBE is an effective measure to minimize the risk of cardiovascular disease in TDT patients. Therefore, SBE can be recommended for thalassemic patients as a part of complementary medicine to protect these patients from cardiovascular morbidity.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

TDT: Transfusion-Dependent Thalassemia; **SBE:** Slow Breathing Exercise; **HRV:** Heart Rate Variability; **CANF:** Cardiac Autonomic Nerve Function; **SBP:** Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure; **TP:** Total Power; **LF power:** Low Frequency Power; **HF power:** High Frequency Power; **LFnu:** LF Power In Normalized Unit; **HFnu:** High Frequency Power in Normalized Unit; **LF/HF:** Low Frequency And High Frequency Power Ratio.

REFERENCES

- Rachmilewitz EA, Giardina PJ. How I treat thalassemia. *Blood J.* 2011;118:3479-88.
- Vichinsky EP. Changing patterns of thalassemia worldwide. *Ann NY Acad Sci.* 2005;1054:18-24. doi: 10.1196/annals.1345.003, PMID 16339647.
- Amin SK. Prevention of thalassemia by genetic counseling. *Anwer Khan Mod Med Coll J.* 2011;2:26-8.
- Tahura S. Thalassemia and other hemoglobinopathies in Bangladeshi children. *IJR.* 2016;3:180-4.

5. Muncie HL, Campbell JS. Alpha and beta thalassemia. *Am Fam Physician*. 2009;80(4):339-44. PMID 19678601.
6. Viprakasit V, Origa R. Genetic basis, pathophysiology and diagnosis. In: Cappellini MD, Cohen A, Porter J, Taher A, Viprakasit V, editors. *Guidelines for the management of transfusion dependent thalassemia*. 3rd ed. Nicosia: Technopreneurship investment fund; 2014. p. 14-27.
7. Galanello R, Origa R. Beta thalassemia. *Orphanet J Rare Dis*. 2010;5:1-15.
8. Olivieri NF, Nathan DG, MacMillan JH, Wayne AS, Liu PP, McGee A, *et al*. Survival in medically treated patients with homozygous β -thalassemia. *N Engl J Med*. 1994;331(9):574-8. doi: 10.1056/NEJM199409013310903, PMID 8047081.
9. Borgna-Pignatti C, Rugolotto S, De Stefano P, Zhao H, Cappellini MD, Del Vecchio GC, *et al*. Survival and complications in patients with thalassemia major treated with transfusion and deferoxamine. *Haematologica*. 2004;89(10):1187-93. PMID 15477202.
10. Porter J, Viprakasit V. Iron overload and chelation. In: Cappellini MD, Cohen A, Porter J, Taher A, Viprakasit V, editors. *Guidelines for the management of transfusion dependent thalassemia*. 3rd ed. Nicosia: Technopreneurship investment fund; 2014. p. 14-27.
11. Rutjanaprom W, Kanlop N, Charoenkwan P, Sittiwangkul R, Srichairatanakool S, Tantiworawit A, *et al*. Heart rate variability in beta-thalassemia patients. *Eur J Haematol*. 2009;83(5):483-9. doi: 10.1111/j.1600-0609.2009.01314.x, PMID 19594617.
12. Silvilairat S, Charoenkwan P, Saekho S, Tantiworawit A, Phrommintikul A, Srichairatanakool S, *et al*. Heart Rate Variability for Early Detection of Cardiac Iron Deposition in Patients with Transfusion-dependent Thalassemia. *PLOS ONE*. 2016;11(10):e0164300. doi: 10.1371/journal.pone.0164300. PMID 27737009.
13. Heart rate variability: Standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation*. 1996;93(5):1043-65. doi: 10.1161/01.CIR.93.5.1043, PMID 8598068.
14. Rajendra Acharya U, Paul Joseph K, Kannathal N, Lim CM, Suri JS. Heart rate variability: A review. *Med Biol Eng Comput*. 2006;44(12):1031-51. doi: 10.1007/s11517-006-0119-0, PMID 17111118.
15. Zahorska-Markiewicz B, Kuagowska E, Kucio C, Klin M. Heart rate variability in obesity. *Int J Obes Relat Metab Disord*. 1993;17(1):21-3. PMID 8383637.
16. Billman GE. Heart rate variability – a historical perspective. *Front Physiol*. 2011;2:86. doi: 10.3389/fphys.2011.00086, PMID 22144961.
17. Akselrod S, Gordon D, Ubel FA, Shannon DC, Berger AC, Cohen RJ. Power spectrum analysis of heart rate fluctuation: A quantitative probe of beat-to-beat cardiovascular control. *Science*. 1981;213(4504):220-2. doi: 10.1126/science.6166045, PMID 6166045.
18. Ernst G. Hidden signals-the history and methods of heart rate variability. *Front Pub Heal*. 2017;5:265.
19. Pomeranz B, Macaulay RJB, Caudill MA, Kutz I, Adam D, Gordon D, *et al*. Assessment of autonomic function in humans by heart rate spectral analysis. *Am J Physiol*. 1985;248(1 Pt 2):H151-3. doi: 10.1152/ajpheart.1985.248.1.H151, PMID 3970172.
20. Pal GK, Velkumary S, Madanmohan. Effect of short-term practice of breathing exercises on autonomic functions in normal human volunteers. *Indian J Med Res*. 2004;120(2):115-21. PMID 15347862.
21. Li C, Chang Q, Zhang J, Chai W. Effects of slow breathing rate on heart rate variability and arterial baroreflex sensitivity in essential hypertension. *Medicine*. 2018;97(18):e0639. doi: 10.1097/MD.00000000000010639, PMID 29718876.
22. Yesmin J, Begum N, Ferdousi S. Effect on time domain parameters of HRV after slow breathing Exercise in type 2 diabetes mellitus. *J Bangladesh Soc Physiol*. 2017;12(1):15-20. doi: 10.3329/jbsp.v12i1.33923.
23. Kardelen F, Tezcan G, Akcurin G, Ertug H, Yesilipek A. Heart rate variability in patients with thalassemia major. *Pediatr Cardiol*. 2008;29(5):935-9. doi: 10.1007/s00246-008-9240-1, PMID 18551333.
24. Adhana R, Agarwal M, Gupta R, Divedi J. Effect of slow breathing training on heart rate, spontaneous respiratory rate and pattern of breathing. *Int J Res Med Sci*. 2016;4:1027-30. doi: 10.18203/2320-6012.ijrms20160724.
25. Joseph CN, Porta C, Casucci G, Casiraghi N, Maffei M, Rossi M, *et al*. Slow breathing improves arterial baroreflex sensitivity and decreases blood pressure in essential hypertension. *J Am Heart Assoc. Hypertension*. 2005;4(4):714-8. doi: 10.1161/01.HYP.00000179581.68566.7d, PMID 16129818.

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