ASSESSMENT OF AUTONOMIC FUNCTIONS IN INDIVIDUALS WITH CEREBRAL PALSY

Sowmya Panju[1], B. L.Preethi[2], G. Jaisri[3],

Assistant Professor[1], Associate Professor[2], Professor[3], Department of Physiology, M.S Ramaiah Medical College, Bangalore 560054, India

Abstracts: Background and objective: Cerebral palsy(CP) is the major physical disability affecting the functional development of children. Very few studies have been done to assess the Autonomic nervous system in children with CP. The objective of our study was to assess and compare the functions of autonomic nervous system between the CP and normal children using Heart rate variability (HRV). **Methodology:** Fourteen age and sex matched cerebral palsy and normal children were recruited for the study. Autonomic function was assessed using Heart rate variability. HRV in supine position was recorded in Lead II for 3 minutes [11]under quiet, calm conditions. Time domain parameters and frequency domain parameters were analyzed. **Results**: There was no statistically significant difference in any of the HRV parameters. Whereas a trend toward reduction was seen in normalized LF and LF/HR ratio in cases though not statistically significant. Mann-Whitney U test was employed to compare the HRV values. **Conclusion**: There was no significant difference in HRV parameters in children with CP and healthy children indicating a normal sympatho-vagal balance. The presence of normal sympatho vagal balance in CP predicts that patients with CP have the same predilection as the general population to abnormalities associated with sympatho-vagal balance.

Key Words: HRV, Cerebral Palsy, sympathovagal balance, Autonomic nervous sytem.

Author for correspondence: Dr. Sowmya Panju, Department of Physiology, M.S Ramaiah Medical College, Bangalore 560054, India. e- mail: sowmya.panju@gmail.com

Introduction:

"Cerebral" refers to the brain, and "Palsy" refers to muscle weakness/poor control. It is defined as an "umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of its development".[1] The problem with moving his or her muscles is not because there is something wrong with the muscles or nerves but because of problems in the brain. The problem could be a manifestation of an injury to the brain, or improper development of the brain. Cerebral palsy can result from brain injury occurring before, during or after birth.[2,3] It is frequently a combination of both motor and sensory involvement.

Many studies prove that CP occurs due to brain damage. However, very few studies have been done to assess the Autonomic nervous system in CP. various procedures like heart rate variability, valsalvamaneuver, deep breathing, isometric handgrip test, cold pressor test, mental arithmetic, orthostatic test, head up tilt test, and baroreceptor sensitivity testing have been described to monitor autonomic dysfunction. Some of them are mostly used for research purposes. Based on the need of the study, complexities involved in various recording, we have selected Heart rate variability for assessment of the autonomic nervous system.

HRV is a non - invasive test to assess autonomic functions. The physiological background of HRV has been attributed to the sympathovagal system. Cardiac automaticity is intrinsic to various pacemaker tissues; heart rate and rhythm are largely under the control of the autonomic nervous system. The parasympathetic influence on heart rate is mediated by the vagus nerve.[5] Variations in heart period are largely dependent on vagal modulation.[6] The vagal and sympathetic activity constantly interact.[4] HRV is used to demonstrate the development of tonic vagal influence on the heart.[7] Even at rest the RR interval changes continuously around its mean value. Neural mechanisms account for part of this variability. Conventionally the interplay between sympathetic and vagal modulation of sinus node pacemaker activity is believed to be reciprocal-with increased activity in one system being accompanied by decreased activity in the other.[8]

HRV is the temporal variation in consecutive heart beats measured from a standard electrocardiogram (ECG). R wave is the peak of QRS complex; the duration between two consecutive R wave peaks is termed the RR interval. It is also

called NN intervals when the heart is beating at sinus rhythm. The assessment of this difference is performed in time domain and frequency domain. These parameters were used to assess cardiac autonomic balance or the balance between sympathetic and parasympathetic mediators of heart.[4] The RR interval variations present during resting conditions represent a fine tuning of the beat-to-beat control mechanisms.[9,10]

OBJECTIVES OF THE STUDY

1. To assess and determine any disturbances in autonomic nervous system in children with cerebral palsy using HRV.
2. To compare autonomic functions in childrenwith cerebral palsy and normal children.

Methodology

Materials and methods:

Source of collection of data

Fourteen known cerebral palsy cases of age group 6-14 years were recruited from schools for individuals with special needs. Fourteen age and sex matched controls were recruited from the neighborhood for the study.

Testing procedure and protocol was explained to study group, control group and their parents/guardian. An informed written consent was obtained from parents/guardian of the case and control group to participate in the study.

Ethical clearance was obtained from Rajiv Gandhi University and M.S Ramaiah Medical College Institutional scientific and ethical committee.

INCLUSION CRITERIA

1. Study group includes both males and females with cerebral palsy in age group 6-14 years.
2. Control group includes age and sex matched normal individuals.

EXCLUSION CRITERIA

1. Neonatal orthopedic pathologies.
2. Recent surgeries (1 year).
3. Use of botulinum toxin within the six-month period prior to the study.
4. Congenital heart diseases.
5. Other cardiopulmonary diseases.
6. Drugs influencing autonomic nervous system
7. Epilepsy and anti - epileptics[12]

Study design

A detailed medical and family history was taken. History of any medication affecting the ANS was noted. A thorough physical examination was done. A complete medical examination including cardiovascular and respiratory system were done.

Autonomic function was assessed using HRV. The subjects scheduled for HRV recording were instructed to avoid consumption of stimulants and beverages like coffee or tea. All recordings were done in the morning from 10 am to 12 pm in a quiet room to avoid the effect of circadian influence. Precautions were taken to obtain an artefact free recording, repeated recordings were done in CP patients in order to avoid artefacts. Subjects were rested comfortably in supine position for 5 minutes and then ECG of the subjects were recorded in Lead II for 3 minutes[11] using three electrodes placed in right infraclavicular region, left infraclavicular region and left iliac region. HRV parameters, time and frequency domain both were measured according to the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology. The artifact free recording was analyzed using RMS Vagus HRV software (RMS, India)

The following parameters were analyzed:

TIME DOMAIN: The following parameters were assessed:-

SDNN- Standard deviation of Normal to Normal RR interval, SDNN reflects all the cyclical components responsible for variability in the period of recording.

RMSSD- It is square root of the mean squared difference of successive Normal to Normal RR interval.

NN50 - Number of interval differences of successive Normal to Normal RR intervals greater than 50 milliseconds.

pNN50 - The proportion of successive Normal to Normal RR interval greater than 50 milliseconds.

FREQUENCY DOMAIN

Power spectral analysis was used to determine the frequency domain parameters.

Power Spectral Density analysis (PSD) extrapolates the heart rate signal into its frequency components and then it is quantified in term of their relative intensity, which is termed as power.

Low Frequency (LF)- Normal range is (0.04-0.15 Hz) is influenced by both parasympathetic and sympathetic activity.

High Frequency (HF) - Normal range is (0.15-0.4 Hz) influenced by parasympathetic activity.

LF/HF ratio - indicates sympatho-vagal balance.

VLF (0-0.04 Hz) - is influenced by non-neuronal components affecting the heart like Renin-Angiotensin system, local factors, and thermoregulation.

Power Spectral Density analysis are plotted in ms^2/Hz against preset frequency. Power of spectral bands is calculated in ms^2 (millisecond^2), absolute power and in normalized units.

STATISTICAL ANALYSIS

The following statistical methods have been used in this study. The coefficient of variation was assessed for all the parameters. The data following normal distribution was expressed as (mean $\pm$ standard deviation) and data with skewed values were expressed as median. The data is presented in Tables and Figures.

1. Mann-Whitney U test

Mann-Whitney testwas used to compare the difference in HRV values in cases and controls.

2. Independent sample t test

Independent sample t testwas used to determine the quantitative variables like age, height, weight, BMI, head circumference, mid arm circumference, waist and hip circumference of cases and controls.

The level of significance was fixed at $p < 0.05$

Data analysis was carried out using Statistical Package for Social Science (SPSS Software, Version 20).

Results:

The data from fourteen cerebral palsy cases along with fourteenage and sex matched controls satisfying the inclusion and exclusion criterion were analyzed. The time domain parameters SDNN, RMSSD, NN50 and pNN50 were measured. Mann-Whitney U test was employed to compare the values. They are expressed as median and range. The differences for SDNN, RMSSD, NN50 and PNN50 components of HRV between children of CP and normal children were not statistically significant. However a trend towards reduction is seen in all the time domain parameters in controls (Table no 1).

The frequency domain parameters absolute LF, absolute HF, normalized LF, normalized HF and LF/HR ratio were measured. Mann-Whitney U test was employed to compare the values. All these measures are expressed as median and range. On statistical analysis no significant differences were observed. A trend towards reduction is seen in absolute LF, absolute HF, normalized HF in controls (Table no 2), whereas a trend toward reduction in cases was seen in normalized LF and LF/HR ratio (Table no 2).

Table 1: Comparison of Time domain parameters between CP and normal children.

Group		Median (Range)	p value
SDNN (ms)	Case	46.11 (17-88)	0.435
	Control	40.41 (22-73)	
RMSSD	Case	36.81 (10.9-60.6)	0.646
	Control	31.79 (17.5-61.3)	
NN50 (ms)	Case	38 (0-96)	0.909
	Control	30 (1.0-120)	
pNN50	Case	19.85(0-50.3)	0.462
	Control	14.15 (0.40-49.1)	

Mann Whitney U testwas employed with the level of significance fixed at $p < 0.05$

Table:2 : Comparison of Frequency domain parameters between CP and normal children.

Group		Median (Range)	p value
LF (ms^2)	Case	144 (33.00-505)	0.890
	Control	140.5 (65-445)	
LF (nu)	Case	69 (53.40-79.10)	0.765
	Control	69.1(57.50-76.60)	
HF (ms^2)	Case	86.5 (17-305)	0.927
	Control	84 (38-225)	
HF (nu)	Case	32.1(20.90-46.60)	0.646
	Control	30.95(22.90-42.50)	
LF/HF	Case	2.15 (1.15-3.79)	0.679
	Control	2.23 (1.35-3.27)	

Mann Whitney U test was employed with the level of significance fixed at $p < 0.05$

Discussion:

Cerebral palsy is one of the debilitating disabilities which affects person suffering from it physically, mentally and psychologically. In many of these patients the quality of life is poor despite a relatively normal intelligence. In present study we compared various heart rate variability parameters between children with and without cerebral palsy. Most studies involving patients of CP have concentrated on motor disabilities and role of central nervous system. However, very few studies have taken into account the role of autonomic nervous system in CP. Hence this study is one of the first of its kind to be ever undertaken in the Indian population to study the role of ANS.Cross-sectional comparative study is the commonest type in the field of CP. This method has been usedfor comparing the sympatho-vagal balance in individuals suffering from CP (Yang et al 2002; Zamuner et al 2011). Great care has to be taken in prevention of occurrence of various artifacts as the individual has to stay still during HRV and this is very difficult in children with CP. This precludes repeated HRV measurements. So, a prospective study design was not considered. However, with adequate caution and instructions, this procedure was carried out in the present study. Based on previous literature survey a sample size of 14 cases with 14 age and gender matched controls was chosen. A similar sample size has been used in earlier studies. Zamuner et al (2011) recruited 12 cases of CP for their study of HRV,EunSook Park et al (2001) recruited twelve children with spastic CP and twelve normal childrenand Kerpers et al (2009) included 18 patients of CP in their sample.

The presentation of data in our study as well as the other studies has been done in terms of median rather than mean. This was done because of the high range of standard deviation obtained. Thus in such cases the presentation of measures in median is found to be statistically more accurate.

In our study the HRV was recorded in their normal environment without subjecting them to any special test (Orthostatic tilt test). Our study group included mild to moderate patients with CP and HRV was recorded in the supine position. The results of this study show that there were no statistically significant differences between casesand controls across all the parameters of HRV in both time and frequency domain parameters studied.

Most of the studies so far have produced contradictory findings regarding the HRV related data in CP patients. In a study carried out on children with cerebral palsy and a normal control group, Park et al. found no significant differences in the autonomic heart response.

Yang et al. found no significant difference in sympathetic response between children with CP and a normal control group. The authors also report that heart rate variability was greater in the group with athetoid CP than the group with spastic CP when the determination employed 10-s intervals (the time domain used was 1 min 20 s). The above studies did not show major differences in the sympatho-vagal balance.

A trend towards reduction was seen in normalized LF and LF/HR ratio in cases. The findings in our study tend to show that there was no increase in sympathetic activity and that the parasympathetic was normal in our subjects.

In Kerpers et al (2009) study, significant differences were not seen between individuals classified with spastic and athetoid CP. Greater SNS activity was seen in relation to PNS activity in cases (increased absolute LF values).

Zamenur et al (2011) found that in supine position, the experimental group presented greater sympathetic autonomic predominance in heart rate than the control group which was based on their findings of significantly low LF values and high HF values in experimental group individuals (CP patients) in comparison to the normal group individuals.

In the study by Yang et al (2002) both supine and head-up positions were used for test subjects. There was no significant difference in the LF , HF or LF/HF ratio between the study and control groups. The analysis of LF, HF and LF/HF ratio in controls showed a normal sympathovagal balance in head-up position. A similar phenomenon was not observed for the study group. Thus the observed difference was seen only in the head-up position rather than in resting position.

In present study, we only conducted the HRV recording in the resting supine position. In supine position there was no significant difference for the

low frequency component of heart rate variability, high frequency component of heart rate variability, or the low frequency/high frequency ratio between the study and control groups. There was also no significant difference in the time domain parameters between the cases and controls. Since the recordings were conducted only in resting supine position the effect of posture has not been evident in autonomic functions in CP patients observed in our study.

This study provides a unique and value added addition about the autonomic status of subjects suffering from CP and their comparison with normal control subjects. Thus our study is an important addition showing that HRV could be actually similar in CP patients and normal individuals.

Conclusion:

Ours is a cross sectional comparative study consisting of 14 mild to moderate patients with CP with age and sex matched controls. HRV was recorded in resting supine position under quiet environmental conditions without subjecting them to any special test (Orthostatic tilt test). The results show that there were no statistically significant differences among the cases and controls across all the parameters of HRV studied. A trend towards reduction was seen in normalized LF and LF/HR ratio in cases. This shows that there was no increase in sympathetic activity and that the parasympathetic tone was normal in our subjects.

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Disclosure: No conflicts of interest, financial, or otherwise are declared by authors