ASTHMA ALLERGY IMMUNOLOGY
ASTIM ALLERJİ İMMÜNOLOJİ

doi: 10.21911/aai.414
Asthma Allergy Immunol 2019;17:78-82

RESEARCH ARTICLE/ARAŞTIRMA

Received: 04/03/2018 • Accepted: 23/11/2018
Online Published: 28/07/2019

Is There An Effect of Inhaled Steroid Treatment on Heart Rate?

Mehmet Yaşar ÖZKARS[1], Mustafa ARGUN[2]

[1] **Department of Pediatric Immunology and Allergy, Kahramanmaraş Sütçü İmam University, School of Medicine, Kahramanmaraş, Turkey**
[2] **Department of Pediatric Cardiyology, Kahramanmaraş City Hospital, Kahramanmaras, Turkey**

Corresponding Author: Mehmet Yaşar ÖZKARS ✉ myozkars@hotmail.com

ABSTRACT

Objective: To evaluate the effect of inhaled steroids on the heart rate variability in pediatric patients with asthma.

Materials and Methods: The study included 17 pediatric patients with asthma using inhaled steroids and a control group of 17 healthy, age- and gender-matched children. A 24-hour Holter monitor was applied and the time domain and frequency domain parameters of heart rate variability were examined. The values were obtained for night, day, and a 24 hour cycle.

Results: No statistically significant difference was found between asthmatic children treated with inhaled steroids and the control group in regards to night, day, and whole day values of the time and frequency domain parameters of heart rate variability.

Conclusion: There was no change in the variability of heart rate of pediatric asthma patients with symptoms under control by inhaled steroids.

Keywords: Asthma, inhaled steroid, heart rate variability

INTRODUCTION

Asthma is a chronic inflammatory disease and, like all chronic diseases, affects patient quality of life. As one of the most frequently observed chronic diseases, the prevalence of asthma is approximately 5.0%, and it is estimated that more than 300 million people are affected worldwide. Moreover, a continuous increase has been observed in the frequency and severity of asthma in the last six decades (1, 2).

Correct diagnosis and appropriate treatment decrease the side-effects related to the unnecessary use of drugs, and complications related to the disease are reduced upon optimal treatment. In this context, the accumulated knowledge of the pathogenesis obtained from studies are important.

Inflammation with remodeling and bronchial hyperreactivity are the basic components of asthma (3). With excessive bronchoconstriction response of the airway together with inflammation against aeroallergens in asthma patients, the underlying pathophysiological cause has not yet been fully been understood. It is possible that this hyper-reactivity occurs together with abnormal autonomic nerve system control, especially when the parasympathetic system is involved. In respect to the cardiac autonomous nerve system of asthma patients, there are many studies that have shown increased cardiac vagal activity in parallel with abnormal autonomous control in the airway. However, in other studies, bronchial parasympathetic regulation has been reported to be related to airway irritation. The respiratory and cardiac systems have been examined independently at this point and it has been reported that there is no increased vagal cardiac activity (4, 5).

ORCID Mehmet Yaşar ÖZKARS / 0000-0003-1290-8318, Mustafa ARGUN / 0000-0003-2357-7980

The aim of this study was to evaluate fluctuations in the cardiac autonomous nerve system and heart rate variability parameters using a 24-hour Holter monitor in pediatric asthma patients on inhaled steroid therapy.

MATERIALS and METHODS

The study was conducted at Kahramanmaraş University Medical Faculty Hospital between September and November 2017. Approval of the study protocol was granted by the Ethics Committee of Kahramanmaraş University Medical Faculty. Informed consent was obtained from the parents or legal guardian of each study participant.

The study included 17 pediatric asthmatic patients using inhaled steroids (fluticasone proprionate 2 x125 μgr/day) and a control group of 17 healthy, age- and gender-matched children. The asthma group included 10 males and 7 females with a mean age of 115.29±28.52 months. The control group included 9 males and 8 females with a mean age of 120.94±35.83 months.

Each of the patients and the control group underwent physical examination, electrocardiography, and 24-hour Holter examination. Any subject in either group with a concomitant disease or findings of infection was excluded from the study.

Parameters of Heart Rate Variability

Heart rate variability (HRV) was evaluated using analysis of the time and frequency domains obtained from the 24-hour Holter examination. The parameters related to the time domain of HRV that were used were mean heart rate (HR), the mean RR interval, the standard deviation of all normal sinus RR intervals over 24 h (SDNN), the mean of the SDNN (SDNN index), the mean of the standard deviation of all averaged normal sinus intervals for each 5-min segment in the 24-h recording (SDANN index), the root mean square of successive differences between normal sinus NN intervals (rMSSD), and the measure of the number of adjacent NN intervals that differ by more than 50 ms (pNN50).

The parameters related to the frequency domain of HRV that were used were the total spectral power: very low frequency (VLF; 0.0033-0.04 Hz), low frequency (LF; 0.04-0.15 Hz), high frequency (HF; 0.15-0.40 Hz), the VLF/HF ratio and the LF/HF ratio. In addition, the sympathetic activity (%), parasympathetic activity (%), and the sympathetic activity/parasympathetic activity ratio were examined.

Data obtained in the study were analyzed using SPSS v18 software. Differences between variables were evaluated using the Mann-Whitney U-test. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

The study group included 10 males and 7 females with a mean age of 115.29±28.52 months (range: 7-16 years). The control group included 9 males and 8 females with a mean age of 120.94±35.83 months (range: 7-16 years). No difference was determined between the groups in respect to age, gender, height, or weight ($p=0.615$).

No statistically significant difference was determined between the groups in respect to the night, day and whole day values of all the parameters of heart rate variability (Tables I-III).

DISCUSSION

The results of this study showed that there was no change in the HRV parameters evaluated using a 24-hour Holter monitor in asthmatic children on inhaled steroid therapy.

For the maintenance of airway calibration and because of the inspiratory reflex cholinergic activity at rest, the bronchi are a tonic construct. At the same time, the parasympathetic nerve system has a role in reflex bronchoconstriction. It is suggested that airway inflammation contributes to the development of disease in asthma patients by leading to cholinergic hyper-reactivity.

Glucocorticoids are currently the most effective drugs in asthma treatment. The anticholinergic drug, ipratropium bromide, and inhaled β2 agonists reduce the airway hyperresponsiveness and constriction in asthma patients and have been used for the treatment of asthma (6-8).

All these show an imbalance between the parasympathetic and the sympathetic system in the form of parasympathetic suppression in the respiratory system of asthma patients. Therefore, researchers have conducted many studies on HRV to both show this increased parasympathetic dysfunction on the respiratory system and to investigate the effects on the heart.

Table I. All day HRV parameters. No statistically significant difference was determined between the groups in respect to whole day values of all the parameters of heart rate variability.

All Day	Healthy Controls (n=17) (mean ± sd)	Asthma Patients (n=17) (mean ± sd)
Mean heart rate (BPM)	88.0±20.6	87.7±8.8
Mean RR interval (ms)	715.3±135.8	679.4±67.6
SDNN (ms)	151.0±57.0	130.8±28.0
SDNN index(ms)	70.9±25.7	70.2±18.1
SDANN index (ms)	126.0±42.0	113.5±25.4
rMSSD (ms)	46.4±19.7	49.5±18.8
pNN50 (ms)	21.4±13.9	21.5±11.7
Total spectral power (ms^2)	5404±3788	4740±2197
VLF (ms^2)	3686±3047	2912±1525
LF (ms^2)	1039±530	1046±454
HF (ms^2)	627±348	724±353
VLF/HF ratio	5.88±2.81	4.91±2.79
LF/HF ratio	1.86±0.64	1.76±0.90
Sempatic (%)	86.9±5.3	84.2±6.6
Parasempatic (%)	13.1±5.3	15.8±6.6
Sempatic/parasempatic ratio	7.8±3.2	6.6±3.6

Table II. Day time HRV parameters. No statistically significant difference was determined between the groups in respect to day values of all the parameters of heart rate variability.

Day Time	Healthy Controls (n=17) (mean ± sd)	Asthma Patients (n=17) (mean ± sd)
SDNN (ms)	119.1±47.1	106.5±25.9
rMSSD(ms)	39.6±17.3	41.7±18.0
pNN50 (ms)	17.8±12.3	16.8±12.0
Total SpectralPower(ms^2)	5114±3890	4236±2303
VLF (ms^2)	3583±3147	2705±1608
LF (ms^2)	1019±565	957±462
HF (ms^2)	463±264	522±343
VLF/HF ratio	7.34±3.23	6.11±2.87
LF/HF ratio	2.34±0.61	2.21±0.97

Table III. Night time HRV parameters. No statistically significant difference was determined between the groups in respect to night values of all the parameters of heart rate variability.

Night Time	Healthy Controls (n=17) (mean ± sd)	Asthma Patients (n=17) (mean ± sd)
SDNN (ms)	111.2±35.1	111.2±34.4
rMSSD (ms)	61.0±24.4	65.8±26.3
pNN50(ms)	35.4±17.7	35.5±16.2
Total Spectral Power (ms^2)	5920±3754	5637±2468
VLF(ms^2)	3856±2938	3262±1645
LF(ms^2)	1072±565	1204±549
HF(ms^2)	935±559	1045±550
VLF/HF ratio	4.97±2.65	4.06±2.46
LF/HF ratio	1.53±0.90	1.44±0.79

In one of the early studies on this subject, Kallenbach et al. (9) showed a relationship between the degree of bronchial hyperreactivity and the amount of respiratory sinus arrhythmia, which shows parasympathetic system activity. It was stated that this result supported the view that increased parasympathetic activity could be an important factor in the pathogenesis of asthma.

Özkaya et al. (5) studied 77 atopic asthma pediatric patients separated into 3 groups of mild, moderate, and severe. They reported that an increase in RMSSD and PNN50 values and a decrease in LF/HF ratios showed parasympathetic nerve dysfunction. These changes were related to the severity of the disease. It was speculated that parasympathetic nerve system dysfunction could contribute to the severity of the disease in asthmatic children.

In a study by Fuji et al. (10), the change in autonomous nerve activity following exercise in asthmatic children was evaluated with HRV spectral analysis. The results of that study showed that airway obstruction following exercise occurred together with a vagal response in asthmatic children.

Several researchers have stated that asthma is related to increased bronchial sensitivity to cholinergic constriction and reduced sensitivity to B2 adrenergic stimulation. Studies of the respiratory system independent of the cardiovascular system have reported that impaired autonomic modulation only affects the respiratory system (11). This was considered to be a hypothesis that could explain the absence of HRV change in the asthma patients of the current study.

Chronic cardiopulmonary diseases are known to reduce HRV and this occurs due to an imbalance in the heart rate sympathetic and parasympathetic control. Garcia-Arauja et al. (12) reported that sympathetic activity was increased and consequently, HRV was decreased in young adults with chronic stable asthma. This could be considered a direct effect of hypoxia and the sustained exposure of adults to asthma affecting the pulmonary parenchyma, increasing the afterload on the right heart, and leading to right heart failure. In a study by Jartti et al. (13), 2 weeks of salbutamol treatment was reported to show an increase in sympathetic activity and a decrease in HRV in asthmatic children. As several studies have emphasized increased sympathetic activity as a factor of increased cardiovascular risk, its clinical importance is evident (10).

In the patients of the current study, the fact that there was no change in HRV may be explained by several possible mechanisms. The first is that the patients had asthma of a mild-moderate severity and used no medications other than inhaled steroids and the symptoms were under control. Second, the hypothesis that the autonomic modulation of the respiratory and the cardiovascular systems may be affected by local factors, and these work independent of each other. Finally, the short duration of exposure to asthma and protection of the pulmonary parenchyma may be a reason for the findings.

LIMITATIONS

Limitations of this study were the low number of patients and the lack of a longitudinal evaluation of the change over time.

CONCLUSION

In conclusion, HRV did not change in children with mild-moderate asthma under control with low dose inhaled steroid treatment.

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