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Original Article

Evaluation of cardiac autonomic function using heart rate variability in children with acute carbon monoxide poisoning

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Abstract *Introduction:* Carbon monoxide poisoning may cause myocardial toxicity and cardiac autonomic dysfunction, which may contribute to the development of life-threatening arrhythmias. We investigated the potential association between acute carbon monoxide exposure and cardiac autonomic function measured by heart rate variability. *Method:* The present study included 40 children aged 1–17 years who were admitted to the Pediatric Intensive Care Unit with acute carbon monoxide poisoning and 40 healthy age- and sex-matched controls. Carboxyhaemoglobin and cardiac enzymes were measured at admission. Electrocardiography was performed on admission and discharge, and 24-hour Holter electrocardiography was digitally recorded. Heart rate variability was analysed at both time points – 24-hour recordings – and frequency domains – from the first 5 minutes of intensive care unit admission. *Results:* Time domain and frequency indices such as high-frequency spectral power and low-frequency spectral power were similar between patient and control groups ($p > 0.05$). The ratio of low-frequency spectral power to high-frequency spectral power was significantly lower in the carbon monoxide poisoning group ($p < 0.001$) and was negatively correlated with carboxyhaemoglobin levels ($r = -0.351$, $p < 0.05$). The mean heart rate, QT dispersion, corrected QT dispersion, and P dispersion values were higher in the carbon monoxide poisoning group ($p < 0.05$) on admission. The QT dispersion and corrected QT dispersion remained longer in the carbon monoxide poisoning group compared with controls on discharge ($p < 0.05$). *Conclusion:* The frequency domain indices, especially the ratio of low-frequency spectral power to high-frequency spectral power, are useful for the evaluation of the cardiac autonomic function. The decreased low-frequency spectral power-to-high-frequency spectral power ratio reflects a balance of the autonomic nervous system, which shifted to parasympathetic components.

Keywords: Carbon monoxide poisoning; children; heart rate variability

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Carbon monoxide is a colourless, odourless, non-irritating gas that is produced primarily as a result of the incomplete combustion of any carbonaceous fossil fuel, such as gas, domestic or bottled, charcoal, coke, oil, and wood. Potential sources include gas stoves, fires, boilers, gas-powered water heaters, car exhaust fumes, charcoal barbeques, paraffin heaters, solid fuel-powered stoves, and room heaters that are faulty or inadequately ventilated.[1] Carbon monoxide is the leading cause of mortality due to poisons and may be responsible for more than half of all fatal poisonings worldwide.[2] Carbon monoxide poisoning accounts for an estimated 40,000 annual emergency department visits in the United States of America.[3–4] Carbon monoxide inhalation is a common method of suicide in some countries, but mortality related to carbon monoxide

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poisoning in Turkey primarily results from accidents. Leaks from coal heaters cause poisoning, especially during winter.[5] The frequency of carbon monoxide poisoning in overall childhood poisoning cases in our Paediatric Intensive Care Unit was previously reported as 6.4–13.2%.[6–8] Infants and children may have an increased susceptibility to carbon monoxide toxicity because of their higher basal metabolic rate and consequent higher tissue oxygen demand. Initial symptoms after carbon monoxide exposure include headache, nausea, and dizziness. Patients develop more pronounced and severe symptoms as exposure increases, and oxygen-dependent organs, especially the brain and the heart, exhibit the earliest signs of injury.[4] Cardiac involvement in carbon monoxide poisoning manifests primarily as an ischaemic insult with elevated enzyme levels and electrocardiogram changes that range from ST segment depression to transmural infarction.[9] Cardiovascular manifestations of acute carbon monoxide poisoning include myocardial dysfunction, ischaemia, infarction, lethal arrhythmias, and cardiac arrest. Carbon monoxide may also affect autonomic cardiac regulation.[10–13]

Heart rate variability is an oscillation of the intervals between consecutive heart beats (RR intervals), which are related to the influence of the autonomic nervous system on sinus node.[14] Heart rate variability is a widely used non-invasive method to investigate cardiovascular autonomic control. Reduced spontaneous heart rate variability is associated with increased mortality in patients who have suffered from a myocardial infarction and may be a risk factor for a life-threatening arrhythmia, ischaemic events, and progressive heart failure. Heart rate variability plays an important role in describing fatal or near-fatal arrhythmias, because increases in sympathetic activity may cause severe arrhythmias and sudden death. Heart rate variability analyses have been carried out in children afflicted with several different illnesses including β-thalassaemia,[15] obstructive sleep apnoea,[16] obesity,[17] dilated cardiomyopathy,[18] Hashimoto's thyroiditis,[19] attention-deficit hyperactivity disorder,[20] Asperger syndrome,[21] atopic asthma,[22] Duchenne muscular dystrophy,[23] and diabetes mellitus.[24] We recently evaluated heart rate variability in children with tricyclic antidepressant intoxication, and our study results showed the value of heart rate variability analysis in determining the risk of arrhythmia and convulsion in patients poisoned with tricyclic antidepressants.[25]

Recent studies suggest associations between ambient particle levels, carbon monoxide, nitric oxide, and sulphur dioxide, and reduced heart rate variability, but heart rate changes in children after acute carbon monoxide poisoning have not been investigated.[10–13,26,27] This study investigated the potential association between acute carbon monoxide exposure and changes in cardiac autonomic function using heart rate variability and the potential association between acute carbon monoxide exposure and cardiac arrhythmias using electrocardiography in children admitted to the Pediatric Intensive Care Unit with acute carbon monoxide poisoning.

Materials and methods

Study group

We evaluated 40 children (18 boys and 22 girls) aged 1–17 years who were consecutively admitted to the Pediatric Intensive Care Unit of Eskisehir Osmangazi University Hospital with accidental acute carbon monoxide poisoning between November, 2010 and April, 2012. The control group included 40 age- and sex-matched healthy children. Healthy children visiting clinics for routine examinations and for follow-up of previously treated mild-to-moderate upper respiratory tract infections were included as controls. Children with obesity (body mass index over >95%), obstructive sleep apnoea, chronic cardiac, or pulmonary conditions, and children receiving daily drugs for any conditions, were excluded because of their influence on heart rate variability. The Local Ethics Committee of the Osmangazi University Faculty of Medicine approved the study protocol, and parental consent was obtained before enrolment.

Carboxyhaemoglobin concentrations were measured from venous blood gases at admission. A significant level of carboxyhaemoglobin for carbon monoxide poisoning was accepted above 2% because all patients were non-smokers. We provided normobaric oxygen therapy to all patients at a rate of 10 L/minute through a face mask that prevented re-breathing at ambient pressure until their carboxyhaemoglobin levels decreased below 2% or their symptoms resolved.

The following levels of poisoning were described: mild carbon monoxide poisoning, carboxyhaemoglobin levels ˂10% without clinical signs or symptoms of carbon monoxide poisoning; moderate carbon monoxide poisoning, carboxyhaemoglobin levels over 10%, but under 25%, with minor clinical signs and symptoms of poisoning, such as headache, lethargy, or fatigue; and severe carbon monoxide poisoning, carboxyhaemoglobin levels above 25%, with loss of consciousness and confusion or signs of cardiac ischaemia, or both.[1] Blood samples were collected from patients on admission, and troponin-I, myoglobin, lactate dehydrogenase, and creatine kinase-MB levels were measured.

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Holter recording

Within the first half hour of hospitalisation, 24-hour Holter electrocardiography was initiated. Heart rate variability was analysed in time and frequency domains. Time and frequency domain measures of heart rate variability described by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology were calculated using a digital Holter recorder (Rozinn Electronics Inc., New York, United States of America) in the Pediatric Cardiology Department. Holter records were edited using visual checks and manual corrections of individual RR intervals and QRS complex classifications. Records with >20% artefacts were excluded. An experienced paediatric cardiologist also evaluated Holter records for any arrhythmias.

- *Time domain variables*: For heart rate variability analysis, the term normal-to-normal is used in place of RR to emphasise the fact that the processed beats are "normal" beats. The measured time domain variables were the standard deviations of all normal-to-normal intervals, the standard deviations of the means of normal-to-normal intervals in all 5-minute segments of the entire recording, the square root of the mean of the sum of the squares of differences between adjacent normal-to-normal intervals, the mean of the standard deviations of all normal-to-normal intervals for all 5-minute segments of the entire recording, the number of pairs of adjacent normal-to-normal intervals differing by >50 ms in the entire recording, and the NN50 count divided by the total number of all normal-to-normal intervals. We analysed these time domain indices during the 24-hour recordings in patient and control groups.[14,28,29]
- *Frequency domain variables*: The measured frequency domain variables were high-frequency spectral power, low-frequency spectral power, and the ratio of low-frequency spectral power to high-frequency spectral power. We analysed these frequency domain indices during the first 5 minutes of the 24-hour recordings in patient and control groups, and the frequency domain indices were calculated in normalised units.

Electrocardiogram

All 12-lead electrocardiographies were performed at a paper speed of 25 mm/second using standard lead positions (Nihon Kohden Europa GmbH, Rosbach, Germany). Electrocardiography findings of all hospitalised children with carbon monoxide poisoning were noted at first admission to our unit and also at discharge from hospital. During the hospitalisation period, children were monitored on the basis of electrocardiography findings. Patients underwent multiple electrocardiographies; however, for the study protocol, we used only two records – electrocardiographies at admission and discharge. For the control group, electrocardiography findings were recorded once. Maximum and minimum QT intervals were measured. QT dispersion was defined as the difference between the longest and shortest QT intervals. The QT intervals for each lead were measured and corrected for heart rate using Bazett's formula ($QT/\sqrt{RR}$). The corrected QT dispersion was calculated as the difference between corrected QT intervals of the leads with the longest and shortest corrected QT intervals. The mean heart rate, P wave, P dispersion, that is, the difference between P wave durations of the leads and the longest and shortest P waves, QT, corrected QT, QT dispersion, and corrected QT dispersion intervals were measured from the electrocardiographies performed at admission and discharge.

Statistical analyses

All statistical analyses were performed using the SPSS 16.0 packet programme (SPSS Inc., Chicago, Illinois, United States of America). We performed the Mann–Whitney U test to compare the two independent groups when the variables were not normally distributed; the results are shown as medians and 25 and 75% values. Values that were normally distributed were analysed using independent Student's t-test, and the results are shown as means and standard error of the mean. Wilcoxon's signed-rank test was used for the dependent variables, according to the results of the normality tests. The Pearson's test was used for normally distributed parameters to investigate the relationship between the variables, and Spearman's correlation test was used for parameters without normal distribution. A p-value <0.05 was considered statistically significant.

Results

We evaluated 40 children (18 boys and 22 girls) aged 1–17 years who were consecutively admitted to our Pediatric Intensive Care Unit with a diagnosis of accidental acute carbon monoxide poisoning between November, 2010 and April, 2012. Table 1 presents the demographic and clinic characteristics of all patients. Among all, three patients in our study group were diagnosed with mild carbon monoxide poisoning, 14 patients were diagnosed with moderate carbon monoxide poisoning, and 23 patients were diagnosed with severe carbon monoxide poisoning.

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Heart rate variability analysis

No significant differences were detected between the study and control groups for the following time domain indices: the standard deviation of all normal-to-normal intervals, the standard deviation of the averages of normal-to-normal intervals in all 5-minute segments of the entire recording, the square root of the mean of the sum of squares of differences between adjacent normal-to-normal intervals, the mean of the standard deviations of all normal-to-normal intervals for all 5-minute segments of the entire recording, and the number of pairs of adjacent normal-to-normal intervals differing by >50 ms in the entire recording ($p > 0.05$) (Table 2). High-frequency spectral power and low-frequency spectral power levels were similar between patient and control groups ($p > 0.05$), but the ratio of low-frequency spectral power to high-frequency spectral power was significantly lower in study group ($p < 0.05$) (Table 2).

There was no relationship between carboxyhaemoglobin levels and high-frequency spectral power or low-frequency spectral power levels in the study group ($p > 0.05$); however, carboxyhaemoglobin levels had a weak, negative correlation with the ratio of low-frequency spectral power to high-frequency spectral power ($r = -0.351$, $p < 0.05$). Carboxyhaemoglobin levels did not correlate with any of the time domain measures of heart rate variability in the study group. The median and interquartile range (25th–75th percentile) of serum creatine kinase-MB level were 1.05 ng/ml and 0.54–1.78, troponin-I 0.02 ng/ml and 0.002–0.04, myoglobin 27 ng/ml,[21–37] and lactate dehydrogenase 452 IU/L and 401–586, and all values were in the normal limits. There were no relationships between the levels of cardiac enzymes – creatine kinase-MB, troponin-I, myoglobin, lactate dehydrogenase – and the time and frequency domain measures of heart rate variability in the study group ($p > 0.05$). During 24-hour Holter monitoring, no arrhythmias were detected in the patient and control groups.

Table 1. Demographic data of the study groups and clinical findings at admission in the carbon monoxide (CO) poisoning group.

	CO poisoning group (n = 40)	Control group (n = 40)
Age (year)*	9.7 ± 4.4**	9.6 ± 4.2
Sex (boys/girls)*	18/22	17/23
Symptoms at admission		
Headache	13 (33%)	–
Nausea/vomiting	13 (33%)	–
Minor neurological symptoms	19 (48%)	–
Syncope, loss of consciousness	7 (18%)	–
Seizures	6 (15%)	–
Cardiac symptoms of healthy children	0 (0%)	–

*There were no statistically significant difference between the two groups regarding age and sex
**Data are expressed as mean ± SD

Electrocardiography findings

The mean QT dispersion, corrected QT max, corrected QT dispersion, maximum P wave, P dispersion values, and mean heart rate were significantly higher in the patient group on admission when compared with the control group. Minimum QT values of patients on admission were lower compared with the control group, but no significant differences were

Table 2. Time domain measures of heart rate variability of the carbon monoxide (CO) poisoning group and the control group during 24-hour Holter monitoring and frequency domain measures of heart rate variability of the CO poisoning group and the control group during first 5 minutes of Holter monitoring.

	CO poisoning group (n = 40)	Control group (n = 40)	p
Time domain measures (24 hours)			
SDNN (ms)	140 (121–167)	150 (110–175)	0.79
SDANN (ms)	47 (35–63)	43.0 (28.5–53.5)	0.17
RMSSD (ms)	11 (86–144)	106 (72–122)	0.07
SDNN index (ms)	92 (73–114)	94 (66–111)	0.43
NN50	28,559 (18,808–39,151)	31,676 (17,020–40,520)	0.90
pNN50 (%)	23.8 (14.3–33.3)	27.9 (14.1–34.7)	0.93
Frequency domain measures (first 5 minutes of monitoring)			
LF (n.u.)	35.4 (26.1–56.7)	42.1 (23.1–65.6)	0.63
HF (n.u.)	34.4 (19.5–56.7)	37.5 (9.92–52.4)	0.24
LF/HF	0.97 (0.77–1.96)	1.91 (0.83–3.72)	**0.038**

HF = high frequency; HRV = heart rate variability; LF = low frequency; NN = normal-to-normal; n.u. = normalised unit, pNN50 = percentage of successive normal sinus RR intervals >50 ms; RMSSD = root-mean-square of the successive normal sinus RR interval difference; SDANN, standard deviation of the averaged normal sinus RR intervals for all 5-minute segments; SDNN, standard deviation of all normal sinus RR intervals over 24 hours; SDNN index, mean of the standard deviations of all normal sinus RR intervals for all 5-minute segments
Values are given as median (25–75%)

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Table 3. Electrocardiographic findings of the carbon monoxide (CO) poisoning group on admission and the control group.

	CO poisoning	Control	p
QT min (second)	0.28 (0.28–0.32)	0.32 (0.32–0.36)	**<0.001**
QT max (second)	0.36 (0.32–0.40)	0.36 (0.32–0.40)	0.71
QT dispersion (second)	0.08 (0.04–0.08)	0.04 (0.00–0.04)	**<0.001**
QTc min (second)	0.37 (0.35–0.40)	0.37 (0.35–0.39)	0.79
QTc max (second)	0.46 (0.44–0.49)	0.44 (0.42–0.46)	**<0.001**
QTc dispersion (second)	0.09 (0.07–0.12)	0.07 (0.04–0.10)	**<0.01**
P max (second)	0.08 (0.08–0.12)	0.08 (0.08–0.08)	**<0.01**
P min (second)	0.04 (0.04–0.04)	0.04 ± 0.003	0.32
P dispersion (second)	0.04 (0.04–0.08)	0.04 (0.04–0.04)	**0.001**
Rate (pulse/minute)	100 (88–125)	88 (72–100)	**<0.001**
PR interval (second)	0.16 (0.16–0.16)	0.16 (0.13–0.16)	0.49

P max = maximum P wave duration; P min = minimum P wave duration; QT max = maximum QT; QT min = minimum QT; QTc dispersion = corrected QT dispersion; QTc max = corrected QT maximum; QTc min = corrected QT minimum
*Values are given as median (25–75%)

Table 4. Electrocardiographic findings of the carbon monoxide (CO) poisoning group on discharge and the control group.

	CO poisoning	Control	p
QT min (second)	0.32 (0.32–0.32)	0.32 (0.32–0.36)	0.11
QT max (second)	0.38 (0.33–0.40)	0.36 (0.32–0.40)	0.07
QT dispersion (second)	0.04 (0.04–0.08)	0,04 (0.00–0.04)	**<0.001**
QTc min (second)	0.38 (0.35–0.40)	0.37 (0.35–0.39)	0.56
QTc max (second)	0.47 (0.43–0.49)	0.44 (0.42–0.46)	**<0.001**
QTc dispersion (second)	0.08 (0.06–0.11)	0.07 (0.04–0.10)	**0.018**
P max (second)	0.08 (0.08–0.10)	0.08 (0.08–0.08)	0.30
P min (second)	0.04 (0.04–0.04)	0.04 (0.04–0.04)	**0.041**
P dispersion (second)	0.04 (0.04–0.04)	0.04 (0.04–0.04)	0.94
Rate (pulse/minute)	88 (75–100)	88 (72–100)	0.79
PR interval (second)	0.16 (0.16–0.16)	0.16 (0.13–0.16)	0.25

P max = maximum P wave duration; P min = minimum P wave duration; QT max = maximum QT; QT min = minimum QT; QTc dispersion = corrected QT dispersion; QTc max = corrected QT maximum; QTc min = corrected QT minimum
*Values are given as median (25–75%)

detected in maximum QT, minimum corrected QT, minimum P wave durations, or PR interval (Table 3).

Electrocardiography recordings of patients at discharge revealed that the mean QT dispersion, maximum corrected QT, corrected QT dispersion, and minimum P wave durations were significantly higher compared with the control group. On the other hand, there was no significant difference in minimum QT, maximum QT, minimum corrected QT, maximum P wave, P dispersion durations, PR interval, or mean heart rate ($p > 0.05$) (Table 4).

Electrocardiograms on admission and discharge were compared (Table 5). The electrocardiography recordings of patients at discharge showed significantly higher mean minimum QT and maximum QT values compared with admission recordings, but showed lower mean maximum P wave duration, P dispersion, and mean heart rate. The maximum corrected QT, minimum corrected QT, QT dispersion, and corrected QT dispersion values, however, were not different from admission.

There were no relationships between carboxyhaemoglobin levels and cardiac enzymes such as creatine kinase-MB, troponin-I, myoglobin, and lactate dehydrogenase or electrocardiographic findings in the study group ($p > 0.05$).

Discussion

The results of this study show that the time domain and frequency indices such as low-frequency and high-frequency spectral power were similar between the carbon monoxide intoxication group and the control group. The ratio of low-frequency spectral power to high-frequency spectral power, however, was significantly lower in the carbon monoxide poisoning group, and carboxyhaemoglobin levels negatively correlated with the ratio of low-frequency spectral power to high-frequency spectral power.

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Table 5. Electrocardiographic (ECG) findings of carbon monoxide poisoning group on admission and on discharge.

	ECG on admission	ECG on discharge	p
QT min (second)	0.28 (0.28–0.32)	0.32 (0.32–0.32)	**<0.001**
QT max (second)	0.36 (0.32–0.40)	0.38 (0.33–0.40)	**<0.001**
QT dispersion (second)	0.08 (0.04–0.08)	0.04 (0.04–0.08)	0.16
QTc min (second)	0.37 (0.35–0.40)	0.38 (0.35–0.40)	0.73
QTc max (second)	0.46 (0.44–0.49)	0.47 (0.43–0.49)	0.50
QTc dispersion (second)	0.09 (0.07–0.12)	0.08 (0.06–0.11)	0.42
P max (second)	0.08 (0.08–0.12)	0.08 (0.08–0.10)	**0.005**
P min (second)	0.04 (0.04–0.04)	0.04 (0.04–0.04)	0.08
P dispersion (second)	0.04 (0.04–0.08)	0.04 (0.04–0.04)	**0.002**
Rate (pulse/minute)	100 (88–125)	88 (75–100)	**<0.001**
PR interval	0.16 (0.16–0.16)	0.16 (0.16–0.16)	0.52

P max = maximum P wave duration; P min = minimum P wave duration; QT max = maximum QT; QT min = minimum QT; QTc dispersion = corrected QT dispersion; QTc max = corrected QT maximum; QTc min = corrected QT minimum
*Values are given as median (25–75%)

Associations between heart rate variability and chronic biological effects of particulate pollution or carbon monoxide were reported previously using longitudinal study designs.[10–13,27] To the best of our knowledge, however, there are no studies on the effects of acute carbon monoxide exposure to heart rate variability in children. Therefore, this study differs from previous studies that have focussed on the effects of daily increased ambient or indoor particulate air pollution levels or chronic effects of carbon monoxide poisoning in the elderly. Tarkiainen et al.[12] observed an association between short-term heart rate variability and acute carbon monoxide exposure in the elderly with stable coronary artery disease, and reported that carbon monoxide exposure over 2.7 ppm is associated with an increased square root of the mean of the sum of the squares of differences between adjacent normal-to-normal intervals, which suggests increased vagal control during carbon monoxide exposure. Dales et al.[10] reported a negative association between carbon monoxide levels and the standard deviation of all normal-to-normal intervals in a patient group with angina and a positive association in a group without angina. A positive association between standard deviation of all normal-to-normal intervals and carbon monoxide levels was observed in patients receiving statins. The authors concluded that urban exposure to carbon monoxide may exert a biological effect on the heart, which may be modified by medications.[10] Holguin et al.[13] reported reductions in high-frequency heart rate variability on days with higher ozone and particulates in 34 Mexican nursing home residents, but other pollutants such as nitric oxide, carbon monoxide, and sulphur dioxide were not related to heart rate variability. Min et al.[30] assessed the effect of carbon monoxide exposure on cardiac autonomic function by comparing changes in heart rate variability among patients with and without metabolic syndrome. The group with metabolic syndrome exhibited significant decreases in heart rate variability parameters, the standard deviation of all normal-to-normal intervals, and high-frequency spectral power, and these declines were significantly associated with carbon monoxide exposure for 24–48 hours preceding heart rate variability measurements. The associations of the standard deviation of all normal-to-normal intervals and high-frequency spectral power with carbon monoxide exposure were stronger in patients with high levels of fasting blood glucose and triglycerides.[30] The depression in standard deviations of all normal-to-normal intervals, which was observed in previous studies,[10,11,26,30] was not observed in our study. We also did not find any significant differences in the square root of the mean of the sum of the squares of differences between adjacent normal-to-normal intervals, unlike previous studies.[11–12] Cardiovascular findings are primarily related to myocardial hypoxia/ischaemia, but we did not find correlations between cardiac enzymes and the observed heart rate variability effects.

Exposure to carbon monoxide may trigger changes in cardiac autonomic function. The decreased ratio of low-frequency spectral power to high-frequency spectral power in our study reflected that the balance of autonomic nervous system had shifted to parasympathetic components. These results suggest that exposure to carbon monoxide alters the balance of cardiac autonomic control, which may increase the susceptibility of high-risk patients to adverse cardiac events. Autonomic nervous system activation can result in significant changes of atrial electrophysiology and facilitate the induction of atrial flutter by both re-entry and triggered activity, probably through calcium-mediated mechanisms.[31]

The cardiovascular findings of acute carbon monoxide poisoning include myocardial dysfunction, ischaemia, infarction, lethal arrhythmias, and cardiac arrest. Cellular hypoxia due to impaired oxygen delivery is the primary cause of tissue injury, and decreased

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perfusion is a consequence of hypoxia-induced myocardial dysfunction.[32] Binding to myoglobin may reduce oxygen availability in the heart and lead to arrhythmias and cardiac dysfunction.[4] Carbon monoxide exposure is closely associated with hospital admissions for cardiovascular disease and cardiac mortality.[10,13,33] Carbon monoxide pollution increases heart failure risk factors, such as blood viscosity and arrhythmia, and decreases heart rate variability.[10,34]

Several electrocardiographic abnormalities or alterations are found in patients with carbon monoxide poisoning, including disturbances of repolarisation – for example, T-wave flattening and inversion – ischaemic changes – for example, ST segment depression or elevation – QT interval prolongation, P wave elevation, QRS widening, and R wave depression. Additional electrocardiography patterns may include supraventricular – for example, sinus tachycardia, atrial fibrillation, premature atrial complexes, and wandering pacemaker – or ventricular – premature ventricular complexes – arrhythmias.[35] Pro-arrhythmogenic effects of carbon monoxide exposure at the cellular level include elevated diastolic calcium, reduced sarcoplasmic reticulum calcium load, decreased systolic calcium release, a lengthening of calcium reuptake, and diminished calcium sensitivity of the myofilaments.[33] Many previous studies have reported that exposure to carbon monoxide causes electrocardiographic changes that may contribute to life-threatening arrhythmias.[35–39] Our study found that mean heart rate, QT dispersion, corrected QT dispersion, and P dispersion values were higher in the carbon monoxide poisoning group on admission compared with the control group, and QT dispersion and corrected QT dispersion remained longer in the carbon monoxide poisoning group on discharge compared with controls. In this study, we did not identify any ventricular or atrial arrhythmias after carbon monoxide exposure. The younger age of our patients and the absence of cardiac disease may have lowered the arrhythmogenic potential of carbon monoxide poisoning, despite increased QT dispersion. QT dispersion has been proposed as a non-invasive measure of the degree of homogeneity in myocardial re-polarisation, which may be a significant predictor of serious arrhythmias and cardiac mortality in humans.[36–44] Some studies reported an increased corrected QT dispersion in carbon monoxide-intoxicated patients.[36–40] P dispersion is used as a marker of variation in P wave duration between leads, and increased P maximum and P dispersion play a role in predicting paroxysmal or postoperative atrial fibrillation.[43] Increased Pd, P maximum, QT, QT dispersion, and corrected QT dispersion durations in acute carbon monoxide poisoning are observed, may be because of the effects of carbon monoxide on the myocardium, which likely cause inhomogeneous impulse formation/conduction in the atria and ventricles.[37,38]

A major limitation of this study was lack of information on personal exposures to other pollutants, especially particulate matter pollution, ozone, and sulphur dioxide, which also influence cardiac autonomical function. Holter electrocardiography with heart rate variability evaluation is widely used in routine paediatric cardiology practice: 24-hour recording for time domain measures are not practical, but 5-minute recordings for frequency domain measure may be used for evaluations in different situations. Further studies and new technologies for the practical use of heart rate variability in different clinical conditions are needed to incorporate these measures into routine practice.

To our knowledge, this is the first study to show changes in cardiac autonomic function using heart rate variability in children with acute carbon monoxide poisoning. We found that frequency domain indices recorded within the first 5 minutes on admission, especially the ratio of low frequency/high frequency, are useful for evaluating cardiac autonomic function. The decreased low frequency/high frequency ratio reflects that the balance of the autonomic nervous system has shifted to parasympathetic components.

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Conflicts of Interest

None.

Ethical Standards

The Local Ethics Committee of the Osmangazi University Faculty of Medicine approved the study protocol, and parental consent was obtained before enrolment. The present study was conducted according to the ethical guidelines and principles of the International Declaration of Helsinki.

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