EFFECTS OF NITROGEN DIOXIDE AND METEOROLOGICAL CONDITIONS ON THE NUMBER OF PATIENTS PRESENTING TO EMERGENCY DEPARTMENT

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SUMMARY – In recent years, there is ever more awareness about the impact of polluted air on the incidence of acute and chronic cardiac disease. The aim of this study was to evaluate the correlation of certain meteorological factors, NO_2 concentration in the air and number of patients presenting to Emergency Department of Internal Medicine, Sestre milosrdnice University Hospital Center (ED), during a two-year period, with special reference to the incidence of patients with a cardiac referral diagnosis according to the International Classification of Diseases (ICD-10). The total number of patients was 44,245, of which 12,946 with a cardiac referral diagnosis. Meteorological parameters (temperature and air pressure) during the warm and cool periods of the year and NO_2 concentrations during the study period were recorded. Study results showed the total number of patients presenting to ED to be greatest in summer, while the number of cardiac patients was highest in winter. There was positive correlation between the number of ED patients with cardiac referral diagnosis and increasing NO_2 concentrations in the air. Despite the fact that the highest concentrations of NO_2 were recorded in the cool period of the year when there were more traffic jams, the influence of the air NO_2 concentration on the number of patients with cardiac diagnoses was statistically most significant in the warm period of the year when the slightest increase in the concentration of NO_2 in the air significantly increased the number of cardiac patients presenting to ED. These results indicate the need for further research of the importance of photochemical processes and their impact on cardiovascular patients.

Key words: *Nitrogen dioxide concentration; Cardiac patients; Air pollution; Weather conditions; Emergency department*

Introduction

Recent reviews indicate that environmental pollution has important short- and long-term effects on human health. The exposure to air pollutants ($PM_{10,}$ $PM_{25,}$ $NO_{2,}$ SO_2, CO, O_3) is directly related to higher morbidity and mortality of cardiovascular patients and to a higher number of patients examined at Emergency Department (ED)[1-3].

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The exact pathophysiological mechanisms responsible for the acute and chronic effects of air pollutants have not yet been clarified, but inflammation, changes in the function of autonomic nervous system and vascular dysfunction are thought to be some of the possible mechanisms[4].

Nitrogen dioxide (NO_2) is adverse aerosol widespread all over the world because of the high number of natural and artificial origins. NO_2 precipitates in the lower layers of the atmosphere due to the mass higher than air mass, which makes it an easily accessible inhalant toxin[5-7].

The correlation between the concentration of NO_2 in the air and the higher number of patients with stroke and asthma has already been established and reported, but the correlation between NO_2 and the exacerbation of symptoms in cardiovascular patients has not yet been described[8].

The aim of this study was to evaluate the correlation of particular meteorological parameters, i.e. temperature (°C), air pressure (hPa), relative air humidity (%) and NO_2 concentration ($\mu g/m^3$) in the air with the number of patients presenting to ED during a 2-year period, with special reference to the incidence of patients with a cardiac referral diagnosis according to the International Classification of Diseases (ICD-10).

Patients and Methods

During a 2-year period, from June 30, 2008 until July 1, 2010, a total of 44,245 patients, of which 12,946 patients with a cardiac referral diagnosis according to the ICD-10 (100-199) presented to Emergency Department of Internal Medicine, Sestre milosrdnice University Hospital Center. Due to the summer migration in July and August, the number of patients was increased by 20%.

The total number of patients and the number of patients with a cardiac referral diagnosis were compared with meteorological conditions and NO_2 concentration in the air throughout the study period and across all seasons. The seasons were observed by weather conditions, not calendar division (spring = March to May; summer = June to August; autumn = September to November; winter = December to February).

The concentration of NO_2 was measured daily by the method of chemical luminescence at the height of 3 meters and data were taken from the National Monitoring Stations Zagreb-1 (Environmental Protection Agency). The concentrations of other air pollutants, i.e. sulfur dioxide (SO_2), particles of dimensions ~10 micrometers or less (PM_{10}) and ozone (O_3) were also measured by the National Monitoring Stations Zagreb-1. SO_2, PM_{10} and O_3 were statistically analyzed to exclude synergistic effect on the number of patients at ED.

The average air temperature (°C), the relative air humidity (%) and the average values of air pressure (hPa) were based on the data obtained from the Meteorological and Hydrological Service of Croatia.

Statistics

The mean values of individual variables were tested by nonparametric Mann-Whitney test which included two samples and a non-parametric analysis of Kruskal-Wallis ANOVA for multiple samples. The relation between the number of patients and each of the meteorological variables and air pollution was tested by non-parametric Spearman's rank correlation. The influence of the group of variables on the number of patients examined at ED was tested by multiple regression. The level of statistical significance was set at $P<0.05$. Statistical analysis was made with Statistica 6.0.

Results

During the period from June 30, 2008 until July 1, 2010, a total of 44,245 patients, of which 12,946 (29.3%) with a cardiac diagnosis, were admitted to ED. The largest number of admitted patients were recorded in summer (n=11,689; 26.4%), while the largest number of cardiac patients were admitted in winter (n=3345; 25.8%). The average number of patients admitted to ED was 60 (range, 29-96), while the average number of cardiac patients was 18 (range, 4-35) *per* day. The total number of patients examined in ED was highest in spring (mean 63.5, range 39-83), while the highest number of patients

Table 1. Number of patients examined at Emergency Department from June 30, 2008 until July 1, 2010 according to seasons (the number of patients examined in summer was corrected by 20%)

	Total number of patients	Number of cardiac patients
Total	44 245 (100.0%)	12 946 (100.0%)
Spring	11 561 (26.1%)	3320 (25.7%)
Summer	11 689 (26.4%)	3055 (23.6%)
Autumn	10 503 (23.8%)	3226 (24.9%)
Winter	10 492 (23.7%)	3345 (25.8%)

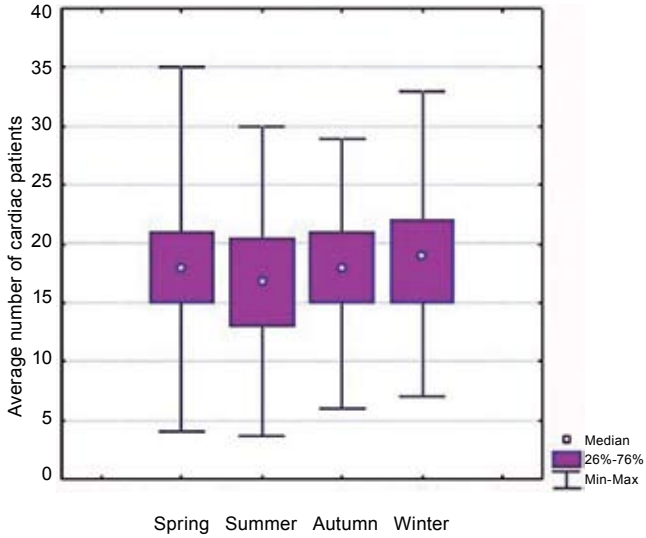

Fig. 1. Number of patients with cardiac symptomatology at Emergency Department according to seasons.

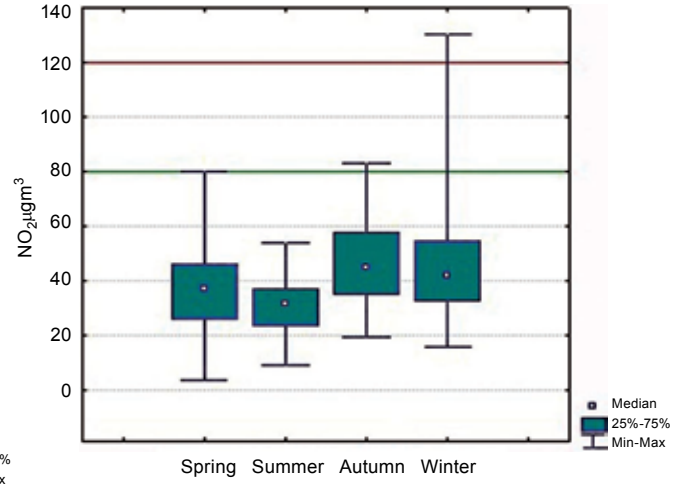

Fig. 2. Average NO_2 concentrations according to seasons.

with a cardiac diagnosis was recorded in winter (mean 19, range 7-33) *per* day (Table 1, Fig. 1).

The highest concentrations of NO_2 were observed in winter (130.4 μg/m^3), whereas the lowest concentrations of NO_2 were recorded in spring (3.6 μg/m^3) (Fig. 2). The mean daily concentrations of NO_2 were highest in fall (44.7 μg/m^3) and lowest in summer (31.5 μg/m^3, *P*=0.0000).

Temperature median was 22.5 °C (13.3 to 28.5) in summer and 2.6 °C (-7.9 to 14.5) in winter, while in spring and fall the medians of air temperature were almost equal, i.e. 13.4 °C (-1.2 to 26.5) in spring and 13.8 °C (1.0 to 25.4) in autumn (*P*=0.0000). Relative air humidity was highest in winter (mean 78.9%, range 43.6% to 94.0%) and lowest in spring (mean 60.7%, range 37.7% to 91.4%; *P*=0.0000) (Table 2).

The correlation of the number of patients admitted to ED (N=44,245) with meteorological conditions and air pollution parameters showed that the total number of patients admitted to ED was proportionally higher with higher temperature (*P*=0.0000, R=0.1638) and NO_2 concentration (*P*=0.0000, R=0.2195), and inversely proportional with the average daily humidity (*P*=0.0017, R=-0.1160) and average daily air pressure (*P*=0.0091, R=-0.0965). Considering the time of the year, during summer months more patients were admitted to ED, especially on the days when the NO_2 value was high (*P*=0.000, R=0.5699 (Fig. 3) as well as when there were high air temperatures (*P*=0.0081, R=0.1947). It is interesting that spring weather conditions were not statistically significant factors associated with the frequency of patients presenting to ED (temperature *P*=0.4377; humidity *P*=0.1133; pressure *P*=0.2682), whereas the high concentration of NO_2 was found to be a signifi-

Table 2. Medians of meteorological characteristics according to seasons

	Number of days	Temperature Median (range)	Relative humidity Median (range)	Pressure Median (range)
Total	730	13.4 (-7.9-28.5)	68.9 (37.7-95.3)	996 (966-1020)
Spring	184	13.8 (-1.2-26.5)	60.7 (37.7-91.4)	997 (966-1009)
Summer	184	22.5 (13.3-28.5)	61.5 (41.0-89.5)	996 (984-1004)
Autumn	182	13.4 (1.0-25.4)	73.5 (44.4-95.3)	998 (979-1013)
Winter	180	2.6 (-7.9-14.5)	78.9 (43.6-94.0)	994 (971-1020)
Kruskal-Wallis ANOVA		*P*=0.0000	*P*=0.0000	*P*=0.0000

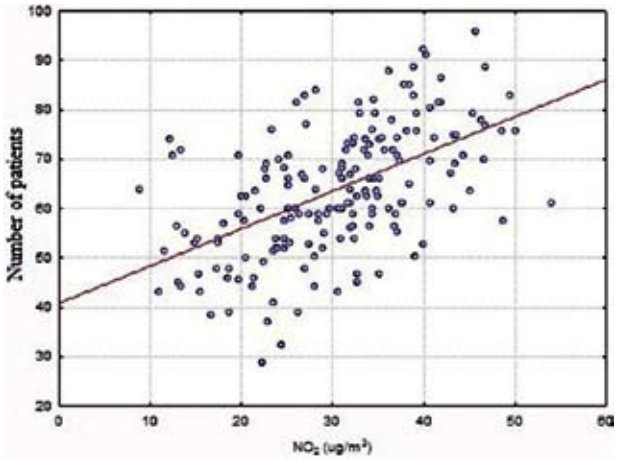

Fig. 3. Correlation of the number of patients at Emergency Department and NO_2 concentration in summer (Spearman's rank correlation: R=0.5699; P=*0.0000).*

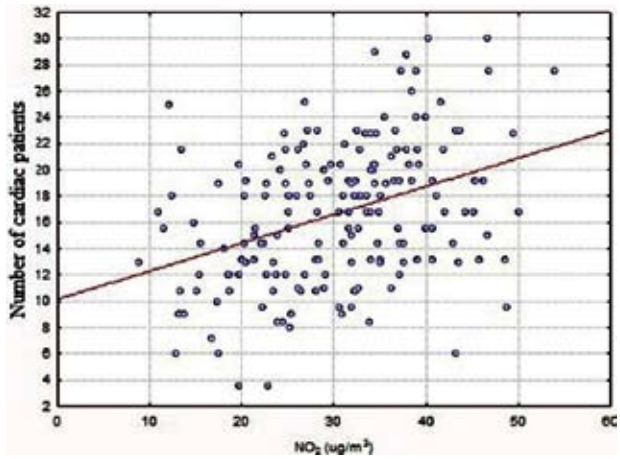

Fig. 4. Correlation of the number of patients with cardiac symptomatology at Emergency Department and NO_2 concentration in summer (Spearman's rank correlation: R=0.3763; P=0.0000).

cant parameter (*P*=0.0001, R=0.2932). The increased number of patients examined at ED correlated inversely with air pressure (*P*=0.0493, R=-0.1460) and proportionally with NO_2 (*P*=0.0256, R=0.1893) in autumn. Likewise, in winter air pressure correlated inversely (*P*=0.0192, R=-0.1745) and NO_2 concentration proportionally (*P*=0.0000, R=0.3253) with the increased number of ED patients.

The number of examined patients with a pronounced cardiac symptomatology correlated proportionally with the concentration of NO_2 (*P*=0.0000, R=0.2714) and inversely with air temperature (*P*=0.0001, R=-0.1464), while humidity and air pressure were not statistically significant variables for the number of cardiac patients admitted to ED. The same results were observed in spring and autumn, whereas in summer and winter the number of patients with a referral cardiac diagnosis proportionally depended on air temperature (*P*=0.0000, R=0.3763) and concentration of NO_2 (*P*=0.0000, R=0.3763) in summer (Fig. 4) and winter (*P*=0.05494, R=0.0449 and *P*=0.0057, R=0.2095, respectively).

Considering all the variables investigated, the results recorded throughout the study period and across all four seasons indicated the increased air concentration of NO_2 to be directly associated with an increased number of cardiac patients admitted to ED. Although the highest concentrations of NO_2 were recorded in the cooler part of the year when there were more traffic jams, the influence of the air concentration of NO_2 on the number of patients with cardiac diagnoses was statistically most important in the warmer period of the year when the slightest increase in the air concentration of NO_2 significantly increased the number of cardiac patients admitted to ED.

Discussion

In this study, we tried to provide answers to the question if there any relations between the air pollution by NO_2 in different weather conditions and the number of patients presenting to ED, with special reference to cardiovascular patients (ICD-10: 100-199).

Air pollutants are a heterogeneous, complex mixture of gases, liquids and particulate matter, which according to the epidemiological studies, are connected with an increased risk of cardiovascular events. Inhalation of air pollutants interferes with cardiac activity and causes heart rate variability, an increased tendency to thrombosis, influences blood pressure and accelerates atherosclerotic process[5,7,9-11]. Numerous studies conducted in large European and American cities have shown negative impact of air pollutants (PM_{10}, PM_{25}, NO_2, SO_2, CO, O_3)[8,11] and meteorological conditions on cardiac function and autonomic nervous system function[11-13]. The effect of NO_2 on cardiovascular patients and the connec-

tion between air concentrations of NO_2 and the incidence of ED patients have not been so thoroughly investigated.

There are very few studies demonstrating correlation between air pollution and the incidence of cardiovascular patients in ED. The results of study conducted in 31 hospitals in Atlanta, Georgia, including 4,407,535 patients during a 7-year period (1993-2000) showed a statistically significant correlation between air pollution and the number of people with cardiovascular symptomatology examined at ED[8], and these results are consistent with those obtained in the present study.

Our results showed the number of patients with cardiovascular symptomatology examined at ED to be directly dependent on the air concentrations of NO_2 throughout the study period.

Due to the possible interference of NO_2 with the autonomic nervous system, a high number of patients had palpitations and the feeling of increased heart rate. The higher incidence of heart attacks and angina pectoris exacerbations is explained by the possible prothrombotic and proatherosclerotic effects of NO_2. These results confirmed the results of a study conducted in five European cities, Augsburg, Barcelona, Helsinki, Rome and Stockholm, which demonstrated strong influence of air pollutants on the morbidity and mortality of cardiovascular patients (higher incidence of heart attacks, angina pectoris, arrhythmias, heart failure and strokes)[11,14].

A study from eastern Massachusetts revealed repeated implantable cardioverter defibrillator interventions two days after extreme air concentrations of NO_2[15]. There is a high possibility that NO_2 directly affects the cardiac conduction system and thus increases the risk of arrhythmias. On the other hand, NO_2 might affect the action potential and the excitability of morphologically altered heart muscle that might be the sources of malignant arrhythmias.

Our results showed NO_2 to be a statistically significant variable that appeared in all four seasons and affected the number of admitted patients (total and cardiac). Even the smallest increase in the air concentration of NO_2 caused a rise in the number of patients admitted to ED, including cardiac patients.

The highest concentrations of NO_2 were measured during autumn and winter, probably due to the increased use of motor vehicles and their exhaust gases. The number of patients with cardiovascular symptomatology was highest during that period. Due to the lowest concentrations of NO_2 in summer, the number of cardiac patients was lowest in this season. The results obtained are confirmed by a few studies showing that the number of hospitalized cardiovascular patients increased in the autumn and winter months when the levels of air pollutants were higher[11,16-20].

The influence of NO_2 concentration on the symptomatology of cardiovascular patients was significantly more pronounced in summer than in winter due to the higher values of air temperature. Despite the average low values of NO_2 concentration in summer, especially on the days when they were slightly higher, the number of cardiac patients in ED was significantly higher. The previously mentioned synergistic effect of the increased air temperature and NO_2 on the coagulation system might be the reason for this phenomenon. Due to the increased respiration rate and sweating, people are more prone to dehydration because of fluid loss. Fluid loss increases blood viscosity and heart rate and decreases cardiac input. The combination of dehydration and the procoagulant effect of NO_2 could be the cause of exacerbations of heart diseases.

The limitations of our study were related to the impact of NO_2 concentrations on patients with certain cardiac diagnoses within overall cardiac diagnoses (e.g., acute coronary syndrome, arrhythmia, heart failure). We believe that such a study could provide answers about particular risk groups that are vulnerable to elevated concentrations of NO_2. Also, further investigations of the importance of photochemical processes and of other air pollutants such as ozone (O_3), and their impact on cardiovascular patients should be performed.

References

1. ISSEVER H, DISCI R, HAPCIOGLU B, VATANSEVER S, AKIF KARAN H, AKKAYA V, ERK O. The effect of air pollution and meteorological parameters in Istanbul on hospital admissions for acute coronary syndrome. Indoor Built Environ 2005;14:157-64.
2. HASSING C, TWICKLER M, BRUNEKREEF B, CASSEE F, DOEVENDANS P, KASTELEIN J, CRAMER HJ. Particulate air pollution, coronary heart disease and individual risk assessment. Eur J Cardiovasc Prev Rehabil 2009;16:10-5.

3. TOULOUMI G, KATSOUYANNI K, ZMIROU D, SCHWARTZ J, SPIX C, *et al*. Short-term effects of ambient oxidant exposure on mortality: a combined analysis within the APHEA project Air Pollution and Health: a European Approach. Am J Epidemiol 1997;146:177-85.
4. CHAN CC, CHUANG KJ, SU TC, LIN LY. Association between nitrogen dioxide and heart rate variability in a susceptible population. Eur J Cardiovasc Prev Rehabil 2005;12:580-6.
5. TENIAS JM, BALLESTER F, RIVERA ML. Association between hospital emergency visits for asthma and air pollution in Valencia, Spain. Occup Environ Med 1998;55:541-7.
6. OKEN PJ, PIVER WT, YE F, ELIXHAUSER A, OLSEN LM, PORTIER CJ. Temperature, air pollution and hospitalization for cardiovascular diseases among elderly people in Denver. Environ Health Perspect 2003;111:1312-7.
7. RUIDAVETS JB, COURNOT M, CASSADOU S, GIROUX M, MEYBECK M, FERRIERES J. Ozone air pollution is associated with acute myocardial infarction. Circulation 2005;111:563-9.
8. SUNYER J, SPIX C, QUENEL P, *et al*. Urban air pollution and emergency admissions for asthma in four European cities: The APHEA project. Thorax 1997;52:760-3.
9. SUNYER J, BALLESTER F, LE TERTRE A, *et al*. The association of daily sulfur dioxide air pollution levels with hospital admissions for cardiovascular diseases in Europe (the APHEA-II study) Eur Heart J 2003;24:752-60.
10. KLEINMAN MT, DAVIDSON DM, VANDAGRIFF RB, CAIOZZO VJ, WHITTENBERGER JL. Effects of short-term exposure to carbon monoxide in subjects with coronary artery disease. Arch Environ Health 1989;44:361-9.
11. METZGER KB, TOLBERT PE, KLEIN M, PEEL J, FLANDERS W. Ambient air pollution and cardiovascular emergency department visits. Epidemiology 2004;15:46-56.
12. HESTERBERG TW, BUNN WB, McCLELLAN RO, HAMADE AK, LONG CH, VALBERG PA. Critical review of the human data on short-term nitrogen dioxide (NO2) exposure: evidence for NO2 no-effect levels. Crit Rev Toxicol 2009;39:743-81.
13. CLAYTON GD, CLAYTON FE, editors. Patty's industrial hygiene and toxicology. Toxicology. 3rd edition. New York, NY: John Wiley & Sons, 1994.
14. HOEK G, BRUNEKREEF B, FISCHER P. The association between air pollution and heart failure, arrhythmia, embolism, thrombosis, and other cardiovascular causes of death in a time series study. Epidemiology 2001;12:355-67.
15. PETTERS A, EMERSON L, VERRIER R, SCHWARTZ J, GOLD D, MITTLEMAN M, BALIFF J, ALLEN G, MONAHAN K, DOCKERY D. Air pollution and incidence of cardiac arrhythmia. Epidemiology 2000;11:11-7.
16. KWON HJ, CHO SH, NYBERG F. Effects of ambient air pollution on daily mortality in a cohort of patients with congestive heart failure. Epidemiology 2001;12:4.
17. ATKINSON RW, BREMNER SA, ROSSANDERSON H, STRACHAN DP, BLAND H, PONCE de LEON A. Short-term associations between emergency hospital admissions for respiratory and cardiovascular disease and outdoor air pollution in London. Arch Environ Health 1999;54:398-411.
18. WONG CM, ATKINSON RW, ANDERSON HR, HEDLEY AJ, MA S, CHAU PY, LAM TH. A tale of two cities: effects of air pollution on hospital admissions in Hong Kong and London compared. Environ Health Perspect 2002;110:67-77.
19. PÖNKÄ A, VIRTANEN M. Low-level air pollution and hospital admissions for cardiac and cerebrovascular diseases in Helsinki. Am J Public Health1996;86:1273-80.
20. LINN WS, SZLACHCIC Y, GONG HJ, KINNEY PL, BERHANE KT. Air pollution and daily hospital admissions in metropolitan Los Angeles. Environ Health Perspect 2000;108:427-34.

Sažetak

UČINAK DUŠIKOVA DIOKSIDA I VREMENSKIH UVJETA NA BROJ BOLESNIKA NA ODJELU HITNE MEDICINE

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Posljednjih godina sve je više spoznaja o utjecaju onečišćenog zraka na pojavnost akutnih i kroničnih kardioloških bolesti. Cilj ove studije bila je procjena ovisnosti nekih meteoroloških parametara, koncentracije dušikova dioksida (NO_2) u zraku i broja bolesnika koji su se javili u hitnu službu (HS) Interne klinike Kliničkoga bolničkog centra Sestre milosrdnice u razdoblju od dvije godine, uz poseban naglasak na incidenciju bolesnika s kardiološkom uputnom dijagnozom prema Međunarodnoj klasifikaciji bolesti (MKB-10). Ukupno je pregledano 44.245 bolesnika, od toga 12.946 s kardiološkom uputnom dijagnozom. U obzir su uzeti promatrani meteorološki parametri (temperatura i tlak zraka) tijekom toplijeg i hladnijeg dijela godine i koncentracije NO_2 tijekom razdoblja praćenja. Rezultati pokazuju kako je ukupan broj bolesnika koji se javljaju u HS najveći ljeti, dok je broj kardioloških bolesnika najveći zimi. Broj bolesnika s uputnom kardiološkom dijagnozom u HS bio je u korelaciji s povećanjem koncentracija NO_2 u zraku. Unatoč činjenici da su najveće koncentracije NO_2 zabilježene u hladnijem dijelu godine kada su najveće prometne gužve, utjecaj koncentracije NO_2 u zraku na broj bolesnika s kardiološkim dijagnozama bio je statistički značajniji u toplijem dijelu godine. Tada se već pri najmanjem povećanju koncentracija NO_2 u zraku značajno povećava broj kardioloških bolesnika u HS. Ovi rezultati ukazuju na potrebu dodatnog istraživanja važnosti fotokemijskih procesa i njihovog utjecaja na kardiovaskularne bolesnike.

Ključne riječi: *Dušikov dioksid, koncentracija; Srčani bolesnici; Onečišćenje zraka; Vremenski uvjeti; Odjel hitne medicine*