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EMERGENCY CASES OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN ADULTS AND AIR POLLUTION IN ZAGREB *

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The aim of this study was to assess a possible relationship between the concentration of total suspended particles (TSP) and aggravation of symptoms in patients with chronic obstructive pulmonary disease (COPD) with regard to the trend, seasonality and weather conditions. Data on the number of COPD patients reporting aggravated symptoms, mean TSP concentrations, temperature, air pressure, and relative humidity were collected daily for years 1994 and 1995 in Zagreb, Croatia.

The authors found a statistically significant correlation between the number of aggravated COPD cases and the TSP concentrations on the previous day. There was a significant autocorrelation in residuals with a lag of 8 days. The estimated value of the regression coefficient for the concentration of TSP on the previous day was 0.001692 (s.e.=0.000797, p=0.0345). The estimated relative risk, corresponding to a change of 10 μg/m³ in the mean daily concentration of suspended particles, was 1.184 (95% confidence interval: 1.013–1.385).

Key words:
chronic obstructive pulmonary disease, COPD, time series, total suspended particles, TSP

It is a rather challenging task to establish recommended and limit values for the concentrations of various pollutants in the air. In addition to scientific estimates, a whole range of circumstances specific for each particular country should be taken into account. The scientist's task is to evaluate the effect of the environmental pollution on health, as accurately as possible. In order to carry out this task as efficiently as possible, a scientist should have access not only to data obtained from the daily monitoring of environmental pollution, but also to relevant epidemiological and meteorological data. The data should be as complete and accurate as possible. When

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performing the analysis, one should bear in mind that it is impossible to encompass all factors and causal agents which may affect human health. The analysis of epidemiological, meteorological, and time series obtained by monitoring environmental pollution should attempt to include various factors which influence the man and the environment. It is necessary to take all possible steps to exclude the occurrence of spurious correlations. It should also be taken into account that data in the time series are autocorrelated, that is, that data on consecutive days are mutually more similar than data taken on days selected randomly, even if within the same season. Hence, it is important to apply relevant statistical procedures during data analysis, in order to control estimation bias as much as possible.

Many recently published retrospective epidemiological studies analyse the correlation between morbidity and/or mortality and air pollution, and especially the correlation between the number of urgent hospital admissions of patients with chronic obstructive pulmonary disease (COPD) and the concentration of suspended particles (1–3). Although most such studies have consistent estimates of relative risk, other studies find no statistically significant correlation between the analysed events, while some authors oppose the above approach (4). The most important objections refer to the difficulties in controlling the interaction of different factors, the very poor association between the analysed factors (low value of R^2 and relative risk), and the lack of experimental results which would confirm cause-effect relationship and which would offer a physiological explanation. On the other hand, the *in vivo* and *in vitro* experiments of *Li et al.* (5) confirmed that particulate matter of less than 10 μm in diameter (PM_{10}) causes oxidative stress and induction of free radicals at the cellular level as well as inflammation and alteration of the respiratory epithelium. These results corroborate the results of epidemiological studies.

The aim of this study was to assess the relation between the concentration of suspended particles (TSP) and the number of urgent hospital admissions due to aggravated health status in patients with COPD in Zagreb during 1994 and 1995. Furthermore, the intention was to compare the estimate of relative risk with those obtained in other locations. The fact that the composition of suspended particles depends on several local factors (from the structure of industry and type of heating to climatic conditions) additionally baffles the comparison of the results of the analyses carried out in different locations as the same TSP concentrations do not necessarily contain the same amount of active substances which have a detrimental effect on the health of patients with COPD. It is important that such analyses are performed in different countries as the relative risks obtained at different locations must be used judiciously.

SUBJECTS, MATERIALS AND METHODS

The number of urgent cases of COPD, mean concentration of suspended particles, and meteorological data in Zagreb were collected for years 1994 and 1995. The recorded counts of urgent COPD cases were taken from three hospitals in Zagreb which account for approx. 80% of COPD cases in the Zagreb region. The study was limited to patients aged over 18 with the following diagnoses on admittance: 490–492, 494, and 496 (ICD-9, International Classification of Disease and Cause of Death).

The concentration of suspended particles was measured in the town centre by the Department for Environmental Hygiene of the Institute for Medical Research and Occupational Health in Zagreb. Samples were collected by gravimetric method using a filter paper (diameter: 102 mm; pores size: 0.3 μm; air flow: 250 m^3/day) (6). The meteorological data included mean daily temperature, mean daily air pressure, and relative humidity and were provided through the courtesy of the National Hydrometeorological Institute of the Republic of Croatia. The counts of emergency room visits and meteorological data were complete containing a total of 730 observations, while data in the time series for suspended particles were incomplete and contained only 382 measurements. The data referring to weekends (Friday, Saturday and Sunday) were consistently lacking.

The statistical analysis was performed on a PC-486 using SAS® 6.12 (7). The statistical methods included descriptive analysis and local regression analysis (LOESS) (8). Spectral analysis of time series and autoregressive linear regression were performed using SAS procedures SPECTRA and AUTOREG (9). The analysed model assumed the autocorrelated error of up to eight lags. It was necessary to include autocorrelation in residuals as we could not assume that all time-varying predictors were accounted for, and standard linear regression assumes independent error. The autoregressive model used the maximum likelihood parameter estimates. Only lagged error terms significantly different from 0 were retained.

RESULTS

The results of the descriptive analysis are presented in Table 1. The distribution of the number of urgent cases approximated the Poisson's distribution and showed overdispersion. The distribution of TSP concentrations was also positively skewed. The observed concentrations were within the recommended values.

Table 1 *Descriptive statistics for the count of urgent COPD cases, meteorological data and TSP in Zagreb for years 1994 and 1995*

Variable	Mean	Var	Min	25%	50%	75%	Max
Cases	3.82	8.33	0	2	3	5	19
TSP (μg/m^3)	78.2	1454.4	1	53	73	99	256
Temperature (°C)	11.7	63.4	–6.6	5.6	11.6	18.5	26.6
Rel. humidity (%)	74.1	140.9	35	66	75	83	98
Air pressure (hPa)	1001.9	49.3	979	998	1002	1006	1023

Annual TSP concentrations
recommended C_{avg}=75, C_{max}=120
limit C_{50}=150, C_{98}=350

As the counts approximated the Poisson's distribution, we have used logarithmic transformation after increasing the observed counts by one in order to avoid taking

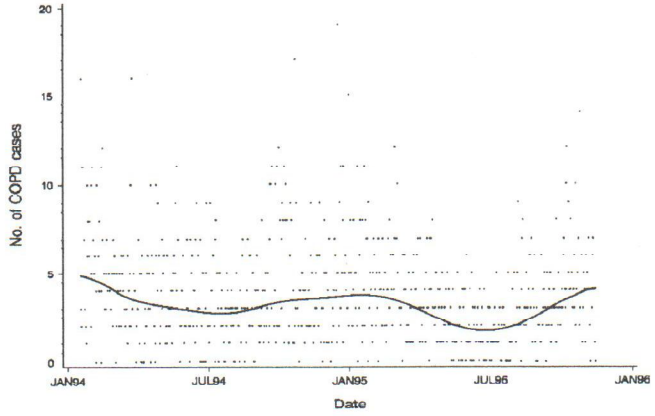

Figure 1 *Count of emergency COPD cases in Zagreb in 1994 and 1995 with fitted LOESS curve superimposed*

a logarithm of zero. The counts and the TSP concentrations showed periodic behaviour within a period of one year. Spectral analyses of the time series of the counts and meteorological data showed that, in addition to the basic period of 365 days, a period of 121 days (ca 4 months) and 7 days (one week) were marked. Due to the missing data for suspended particles, it was impossible to carry out the spectral analysis. For both time series, the periodicity was modelled using the local regressive method (LOESS) with a bandwidth of 91 days (approx. 3 months) and normal weight function, which explained the systematic variations in time. Predictions from the locally weighed regression represent the expected number of urgent cases and the expected concentration of suspended particles for a particular day in the year. Deviations in the number of events and TSP concentrations from the expected values may show spu-

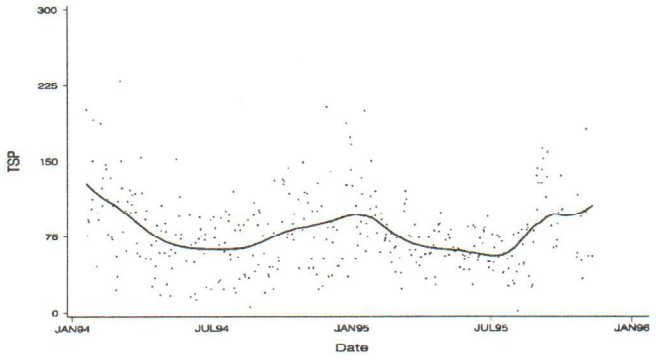

Figure 2 *Average daily concentration of total suspended particles in Zagreb in 1994 and 1995 with fitted LOESS curve superimposed*

rious correlation due to weather conditions. Figures 1 and 2 present the count of urgent COPD and the concentration of suspended particles with fitted LOESS curves in the original units. Deviations in the count of urgent COPD cases and TSP from the expected values did not correlate with the mean temperature, mean air pressure and relative humidity.

Table 2 *Results of the autoregressive linear regression of the log counts of urgent COPD cases after accounting for the trend and periodicity*

				95% confidence limits		
Variable	**b**	**SE**	**RR**	**lower**	**upper**	**p ≈**
Constant	−0.022	0.029				0.452
AR(8)	−0.160	0.059				0.007
TSP(1) [10 μg/m³]	0.017	0.008	1.184	1.013	1.385	0.035

Table 2 shows the results of autoregressive linear regression. A statistically significant correlation was found between the count of urgent COPD cases and the TSP concentration on the previous day. The estimated relative risk associated with the change in TSP concentration of 10 $\mu g/m^3$ was 1.184, which corresponds to the increase of 18% in the number of urgent COPD.

DISCUSSION AND CONCLUSIONS

Using a meta-analysis of published results, *Pearce and Crowards* (10) estimated that 12,000 premature deaths in Great Britain every year may be attributable to the consequences of the usual concentration of PM_{10} in the environment. If one takes into account only the suspended particles resulting from human activity, the number drops to about 7,000. According to their estimation, the morbidity attributed to measured concentrations of PM_{10} costs the country 6.3 billion pounds annually, mainly through workdays lost to sick leaves due to chronic bronchitis. This example shows that an accurate evaluation of relative risk obtained in retrospective epidemiological studies is extremely important.

The only way to evaluate the results of retrospective studies, when it is impossible to carry out a controlled experiment, is through comparison with the results of other, similar studies. *Ponka and Virtanen* (1) analysed the number of urgent cases of COPD and the daily concentration of suspended particles in Helsinki for the period from 1987 to 1989. No significant correlation was found between the number of urgent cases of COPD and the concentration of suspended particles. However, *Schwartz* (2) found significant correlation between the number of urgent cases of COPD and the concentration of PM_{10} in Detroit for persons older than 65 years. The relative risk

connected with the change of 10 $\mu g/m^3$ was estimated at 1.020 (95% confidence interval 1.009–1.032). In a similar study carried out in the area of Minneapolis-St.Paul, also on persons over 65, the estimate of relative risk was 1.05 (95% confidence interval 1.02–1.07) (3). *Gamble and Lewis* (4) provided an extensive review of the results related to suspended particles.

Our values of relative risk were higher than those in the aforementioned studies and referred to workdays only. The fact that we found a significant autocorrelation of residuals indicated that other factors not included in the analysis most likely had an effect on patients with COPD. The use of other methods for the prediction of periodicity and trend, the inclusion of meteorological data for a greater number of previous days, and inclusion of other air pollutants in the analysis, are the options for alternative analyses of the same data.

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Sažetak

HITNI SLUČAJEVI ODRASLOG PUČANSTVA OBOLJELOG OD KRONIČNE OPSTRUKTIVNE BOLESTI PLUĆA (KOPB) I ONEČIŠĆENOST ZRAKA U ZAGREBU

Tijekom 1994. i 1995. godine zabilježeni su podaci o dnevnom prijmu oboljelih od kronične opstruktivne bolesti pluća (KOPB) u ambulantama hitnih službi pulmoloških ustanova u gradu Zagrebu. U istom razdoblju pribrani su podaci za srednju dnevnu koncentraciju lebdećih čestica. Skupljeni su podaci i o srednjoj dnevnoj temperaturi, tlaku i vlažnosti zraka tijekom 1994. i 1995. godine u gradu.
Svrha rada sastoji se od procjene moguće sprege između koncentracije lebdećih čestica u zraku grada Zagreba i pogoršanja simptoma oboljelih od KOPB uzimajući u obzir prirodni tijek značajki vremena.
Verificirana je statistički značajna povezanost broja slučajeva oboljelih od KOPB i koncentracije lebdećih čestica izmjerenih dan prije. Ustanovljena je i autokorelacija reziduala za pomak od 8 dana. Procijenjena vrijednost koeficijenta regresije uz koncentraciju lebdećih čestica iznosi 0,001692 (s.e.=0,000797; p=0,0345). Procjena relativnog rizika koji odgovara promjeni u srednjoj dnevnoj koncentraciji lebdećih čestica od 10 μg/m^3 jest 1,184 (95%-tni interval pouzdanosti: 1,013–1,385).

Ključne riječi:
lebdeće čestice, TSP, kronična opstruktivna bolest pluća, KOPB, vremenski nizovi

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