FOLIA MEDICA CRACOVIENSIA
Vol. LVIII, 1, 2018: 69–79
PL ISSN 0015-5616

Air pollution is associated with incidence of viral croup among children living in Kraków area, Poland

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Abstract: Background: Air pollution is a severe problem in Poland, with Kraków area being among the regions with the worse air quality. Viral croup or pseudocroup is a common childhood disease that may manifest with severe upper respiratory tract obstruction. Our aim was to evaluate the associations between incidence and severity of viral croup symptoms among children living in Kraków area, Poland, and air pollution.
Methods: The retrospective cross-sectional study included Kraków area residents <18 years of age admitted to the Emergency Department of St. Louis Children Hospital in Kraków, Poland over 2-year period. Daily mean concentrations of air pollutants: particulate matter (PM_{10} and $PM_{2.5}$), nitric oxides (NO_x), carbon oxide (CO), sulfur dioxide, ozone, and benzene were retrieved from public database of measurements performed at three local stations. Numbers of cases of viral croup per week were correlated with weekly mean concentrations of air pollutants. Mean air temperature was treated as a cofactor.
Results: During the studied period, mean concentrations of PM_{10}, $PM_{2.5}$, and NO_x exceeded the allowable levels (yearly means) specified by Polish law regulations. Significant positive correlations of moderate strength were observed between weekly mean concentrations of most air pollutants, especially PM_{10}, $PM_{2.5}$, CO and benzene, and numbers of cases of viral croup recorded per week, confirmed in the analysis restricted to non-holiday period and to winter months only. The correlations between NO_x, CO, benzene and croup prevalence were independent of temperature in non-holiday period.
Conclusions: Our results support adverse impact of air pollution on children's respiratory health.

Key words: air pollution, pseudocroup, PM_{10}, $PM_{2.5}$, pediatric laryngitis, viral croup.

Introduction

Air pollution and its consequences to the public health have been the subject of public debate in Poland for several years. The problem is real: in 2016 European Environmental Agency report, Poland occupies second position among European countries regarding annual mean concentrations of both particulate matter (PM) of diameters ≤10 μm (PM_{10}) and PM of diameters ≤2.5 μm ($PM_{2.5}$). It is also estimated that in Poland $PM_{2.5}$ contributes to 48,270 premature deaths annually [1].

Viral croup (otherwise: pseudocroup) is a common childhood disease manifesting as mild to severe upper respiratory tract obstruction. Acute laryngitis and acute laryngotracheitis are often used as synonyms of viral croup in clinical practice. Parainfluenza virus as well as rhinovirus are the most common etiological agents of pseudocroup, but other respiratory viruses can also cause the disease. In most cases, the manifestation of the disease is mild but in some cases the patient might require admission to the Intensive Care Unit [2]. Recent literature data suggest that both smoking and air pollution exposure may exacerbate viral croup symptoms [3].

The aim of this study was to evaluate whether there is an association between incidence and severity of viral croup symptoms among children living in Kraków area, Poland and the level of air pollution.

Material and methods

Subjects

The study was conducted as a retrospective cross-sectional study with the use of databases. Patients admitted to the Emergency Department (ED) of St. Louis Children Hospital in Kraków, Poland between January 1, 2014 and December 31, 2015 were included in the study. All participants were the residents of the City of Kraków and Kraków County (Fig. 1).

Study protocol

Patients' records in hospital database were searched in the terms of diagnosis. The following ICD-10 diagnoses were considered to be likely covering patients with viral croup: J04.4 acute laryngitis, J04.2 acute laryngotracheitis, J05.0 acute obstructive laryngitis (croup). The following information from the patients' records were obtained: age, district of residence, date of admission to the ED, Westley scale [4] score, O_2 saturation, admission to hospital ward (yes/no), the length of hospitalization, ED nebulized adrenaline administration, ED systemic steroid administration. The data were correlated with daily mean concentrations of air pollutants: PM_{10}, $PM_{2.5}$, nitric oxides (NO_x), carbon oxide (CO), sulfur dioxide (SO_2), ozone (O_3), and

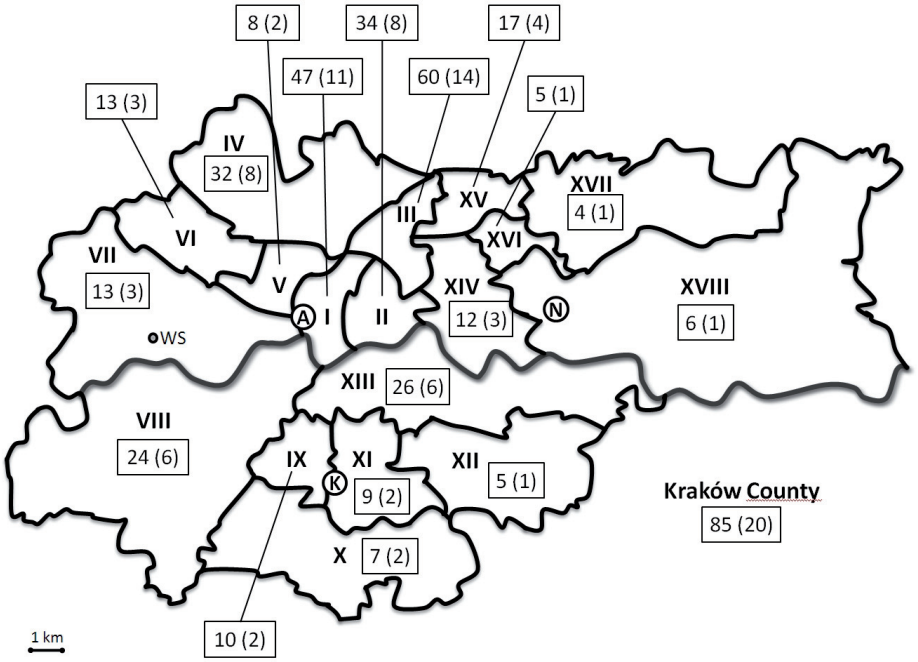

Fig. 1. The plan of Kraków City showing the places of residence of studied children with viral croup and the localization of measurement stations used to monitor air pollution as well as weather station that recorded air temperature. The roman numbers denote the districts within Kraków City; the numbers in boxes denote number (percentage) of cases from each district of Kraków City and from Kraków County. The letters in circles show approximate localization of measurement stations: A — Aleje Krasińskiego, K — Kraków-Kurdwanów (Bujaka street) and N — Nowa Huta (Bulwarowa street). The circle described WS shows the localization of weather station.

benzene (C_6H_6), based on automatic and manual measurements performed at three stations localized in Kraków: Aleje Krasińskiego, Kraków-Kurdwanów (Bujaka street) and Nowa Huta (Bulwarowa street) (Fig. 1). The data on air pollution were retrieved from a database published by a district inspectorate for environmental protection, Wojewódzki Inspektorat Ochrony Środowiska in Kraków, Poland [5]. Air temperature was considered as the cofactor. Mean daily temperatures recorded at weather station Kraków-Obserwatorium (Fig. 1) were retrieved from the database of Institute of Meteorology and Water Management — National Research Institute in Warsaw, Poland [6, 7].

Ethics

The study protocol was approved by the Jagiellonian University Bioethical Committee (no. of approval 122.6120.39.2016). The study complies with Declaration of Helsinki.

Statistical analysis

Quantitative data are shown as median (lower; upper quartile), and range where indicated. Number of cases (percentage of the group) are reported for categories. Mann-Whitney's test was used to assess differences between groups.

Data on concentrations of air pollutants were retrieved from the database [5] as mean concentrations per day as reported for each measurement station. As the concentrations of particular air pollutants measured at various stations were well correlated, we aggregated the data by calculating mean daily and weekly concentrations of each pollutant, including available measurements from all the studied stations. We calculated Spearman's rank correlations between such weekly mean concentrations and the sum of cases of viral croup recorded per week as well as the measures of severity (mean Westley scale score per patient, and sum of hospitalized children per week). We used multiple linear regression to test whether the correlations were independent of air temperature. Weekly mean temperature calculated as an arithmetic mean of mean daily temperature retrieved from the database [6, 7] was included as a covariate. We report standardized regression coefficients (beta) ± standard errors (SE). Except for analyses covering the whole studied period, we also performed analyses restricted to non-holiday period (with exclusion of July and August as holiday months in Poland) and restricted to winter months only (December, January, Fabruary), in an attempt to diminish the impact of non-controlled cofactors on the results.

The statistical tests were two-tailed, and the results were considered significant at $p < 0.05$. Statistica 12 (StatSoft, Tulsa, USA) was used for computations.

Results

During the studied period, 417 cases of viral croup were admitted to the ED of St. Louis Children Hospital in Kraków, Poland (Table 1). The majority of children (277 cases, 66% of the group) were in the age of up to 3 years. Most cases were not associated with severe decrease in O_2 saturation; one-fifth of patients required nebulized adrenalin and nearly 40% were administered systemic steroids (Table 1).

In general, higher numbers of cases were observed in the autumn and winter months (Fig. 2). As expected, lowest numbers of cases were recorded in July and August, i.e. the holiday months. However, we have not observed any clear trends regarding severity of viral croup, as reflected by Westley scale scores. The concentrations of most air pollutants (except of ozone) followed the same pattern, with lowest concentrations during the warmer part of the year, from May to September (Fig. 2). Conversely, the concentrations of ozone were parallel to air temperature, being the highest in July and August.

Table 1. Characteristics of studied patients.

Characteristic	Values among 417 children with viral croup
Age, months	27 (13; 42); range 0–189
Westley scale, points	1 (1; 2); range 0–10
O_2 saturation, %	98 (96; 99); range 87–100
Hospitalization, N (%)	128 (31)
Length of hospitalization, days	3 (2; 4); range 1–12
Nebulized adrenalin administration, N (%)	83 (20)
Systemic steroid administration, N (%)	156 (37)

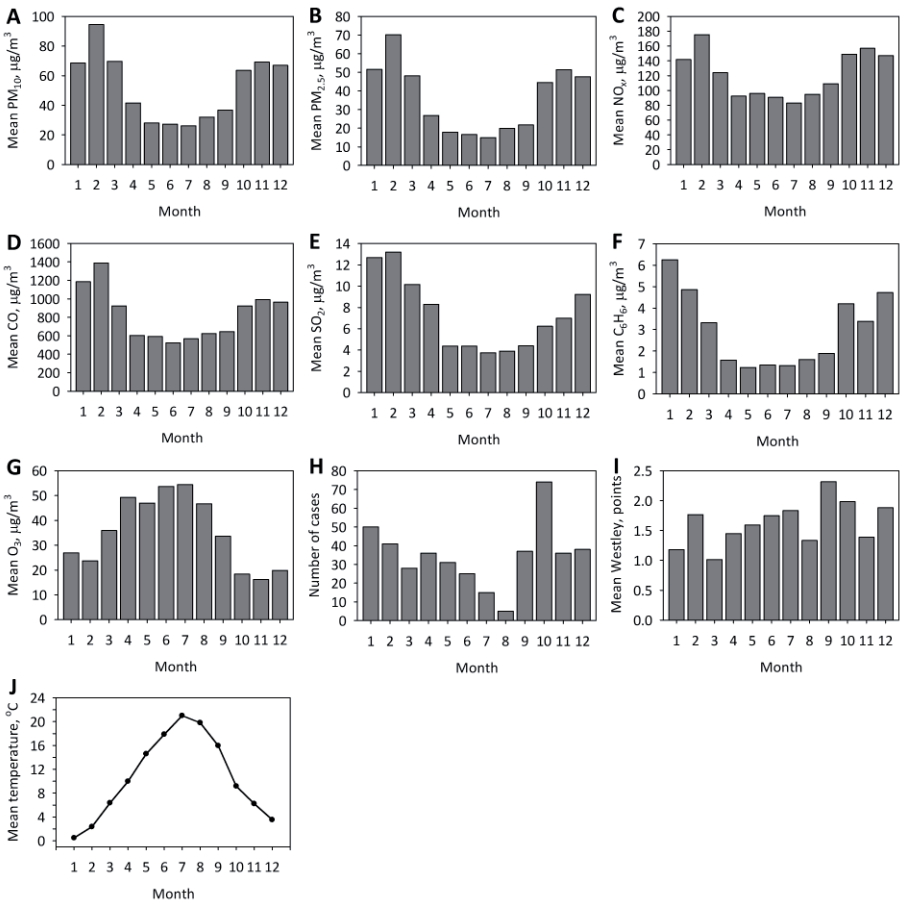

Fig. 2. Mean concentrations of air pollutants (A–G), number of recorded cases of viral croup (H) and mean Westley score per patient (I) during the subsequent months of the year. Mean temperature is shown for comparison (J).

During the studied period, mean concentrations of PM_{10}, $PM_{2.5}$, and NO_x exceeded the allowable levels (yearly means) specified by Polish law regulations [8] (Table 2). According to the Index of Air Quality [9] used in Kraków area, the concentrations of PM_{10} >140 μg/m³ and $PM_{2.5}$ >84 μg/m³ are reported as "bad" to "very bad" air quality. The "bad" or "very bad" daily mean concentrations of PM_{10} or $PM_{2.5}$ occurred during 33 out of 105 analyzed weeks (31%). The numbers of cases of viral croup recorded during such weeks [median 5 (3; 7)] were significantly higher than during the weeks with better air quality [median 3 (1; 4); p = 0.003].

Table 2. Yearly mean concentrations of selected air pollutants during the studied period in comparison with allowable yearly means as specified by Polish law regulations [8].

Substance, unit	Allowable yearly mean level	Yearly mean level in 2014	Yearly mean level in 2015
PM_{10}, μg/m³	40	52.0	52.0
$PM_{2.5}$, μg/m³	25*	36.0	36.0
NO_x, μg/m³	30	123.0	119.0
CO, μg/m³	not specified	890.0	768.0
SO_2, μg/m³	20	7.2	7.3
C_6H_6, μg/m³	5	3.4	2.6

* The allowable level to be achieved in 2015.

Significant positive correlations were observed between weekly mean concentrations of most air pollutants, except for ozone, and numbers of cases of viral croup recorded per week (Table 3). The correlations (with exception of SO_2) were confirmed when the holiday months (July and August) were excluded from the analysis, and when only the winter months (December, January, February) were included (Table 3).

Table 3. Correlations between number of cases of viral croup registered per week and weekly mean concentrations of studied substances. Correlations between number of cases of viral croup registered per week and weekly mean temperature are shown for comparison.

Substance	Whole year		Without holiday period		Winter months only	
	R	p	R	p	R	p
PM_{10}	0.44	<0.0001	0.32	0.0020	0.52	0.005
$PM_{2.5}$	0.46	<0.0001	0.31	0.0030	0.47	0.014
NO_x	0.39	<0.0001	0.24	0.0190	0.38	0.048
CO	0.45	<0.0001	0.35	0.0009	0.40	0.037
SO_2	0.37	0.0001	0.13	NS	0.29	NS
C_6H_6	0.49	<0.0001	0.40	0.0002	0.46	0.021
Temperature	−0.44	<0.0001	−0.18	NS	−0.08	NS

The strongest correlations were observed in case of PM_{10}, $PM_{2.5}$, CO and benzene. To the contrary, weekly mean air temperature was significantly negatively correlated with number of cases per week in unrestricted analysis, but not in the analysis restricted to non-holiday or winter period (Table 3). Moreover, we observed positive correlations between weekly mean concentrations of PM_{10} (R = 0.34; p = 0.0004), $PM_{2.5}$ (R = 0.36; p = 0.0002), NO_x (R = 0.30; p = 0.002), CO (R = 0.35; p = 0.0003), SO_2 (R = 0.32; p = 0.0009), and C_6H_6 (R = 0.38; p = 0.0002) and numbers of cases of viral croup that occurred in children up to 3 years of age (≤36 months).

The unrestricted analysis adjusted for air temperature did not confirm most correlations between weekly mean concentrations of air pollutants and number of cases of viral croup per week. In this analysis, only natrium oxides concentrations were significantly associated with the number of recorded cases (Table 4). However, weekly mean concentrations of air pollutants were strongly negatively correlated with temperature (R = –0.73 for PM_{10}; R = –0.79 for $PM_{2.5}$; R = –0.48 for NO_x; R = –0.68 for CO; R = –0.83 for SO_2; R = –0.77 for C_6H_6; each p <0.0001). Thus, the regression models were affected by strong collinearity of both predictors. Nonetheless, in the analysis restricted to non-holiday period, the concentrations of NO_x, CO and benzene were significantly positively associated with viral croup incidence independently of temperature, while in the analysis restricted to winter months the association was significant for PM_{10}, $PM_{2.5}$, NO_x, CO, and benzene (Table 4).

Table 4. The associations between weekly mean concentrations of air pollutants and the numbers of cases of viral croup recorded per week after adjustment for weekly mean temperature. The standardized coefficients are reported calculated in multiple linear regression to predict number of cases per week.

Substance	Whole year		Without holiday period		Winter months only	
	beta ± SE	p	beta ± SE	p	beta ± SE	p
PM_{10}	0.15 ± 0.12	NS	0.20 ± 0.13	NS	0.51 ± 0.18	0.008
$PM_{2.5}$	0.14 ± 0.13	NS	0.21 ± 0.14	NS	0.50 ± 0.18	0.009
NO_x	0.22 ± 0.10	0.031	0.22 ± 0.11	0.050	0.57 ± 0.19	0.007
CO	0.19 ± 0.11	NS	0.26 ± 0.13	0.043	0.46 ± 0.18	0.019
SO_2	0.13 ± 0.15	NS	0.08 ± 0.16	NS	0.25 ± 0.21	NS
C_6H_6	0.19 ± 0.12	NS	0.27 ± 0.13	0.044	0.44 ± 0.18	0.024

We did not observe significant correlations between mean Westley score per patient and the concentrations of air pollutants. Weekly means of CO and benzene positively correlated with numbers of hospitalized children per week (R = 0.20; p = 0.045 and R = 0.32; p = 0.001, respectively), however, the correlations were not confirmed when analysis was restricted to non-holiday or winter period, neither after adjustment for temperature.

Discussion

Annual incidence rate for pseudocroup is estimated to 2–6 cases/100 children [10, 11]. The disease predominantly occurs between 6 months and 6 years of age, more often among males with proportion 3 : 2 [2, 12]. A seasonal morbidity is observed, as more cases of pseudocroup are observed in autumn and winter. Our results are consistent with these observations. The high incidence of viral croup observed in autumn months (in particular October) may be explained by several factors: the changes in weather conditions[1–3], the increase in time spend in heated home, school and work spaces, and simply the increase in the numbers of city residents (returning from holiday, including over 200,000 high-grade students in September and October).

The same factors may cause the increase in concentrations of most air pollutants, associated with combustion of fossil fuels, including seasonal coal heating (PM_{10}, $PM_{2.5}$) and produced by increased road traffic (nitric dioxide, benzene) [13]. Conversely, ozone is generated by photochemical reactions from NOx and volatile organic compounds and is further consumed in reactions with other air pollutants, resulting in lower ozone concentrations in autumn-winter season [13].

We observed week to moderate positive associations between a group of most significant air pollutants, including particulate matter (PM_{10} and $PM_{2.5}$), nitric oxides, carbon dioxide and benzene, and the incidence of viral croup. The associations were confirmed in analysis excluding the holiday period (when children are on average less exposed to intense contact with each other at nursery schools and kindergartens), as well as in the analysis restricted to winter period, when air quality is the worse. The incidence of pseudocroup was associated with NO_x, CO and benzene concentrations independently of air temperature in non-holiday period, and the associations with PM_{10}, $PM_{2.5}$, NO_x, CO, and benzene were independent of temperature in winter months. We did not observe positive associations between concentrations of ozone and viral croup incidence. The associations between SO_2 and viral croup were very weak and may be explained by air temperature changes.

The associations between air pollution and childhood upper and lower respiratory tract infections have been observed previously. $PM_{2.5}$ was demonstrated to increase the risk of infant bronchiolitis [14], viral upper respiratory tract infections [15, 16], and rhinitis in the age of 1 and 2 years [17]. NO_2 exposure was demonstrated to increase the risk of dry cough or bronchitis [17], respiratory tract infections [18], and ear, nose and throat infections [16]. There is also evidence that air pollution increases infant mortality due to respiratory tract infections [19, 20]. The mechanisms in which air pollutants, especially particulate matters induce susceptibility to viral infections comprise immune system modulation [21] and mucous clearance impairment [22].

According to Polish recommendations for treatment of upper respiratory tract infections [23], mild pseudocroup can be treated with intramuscular injection of

steroids or inhaled steroids. The efficacy of both forms of steroid administration is equal. Severe form of pseudocroup is treated with inhaled adrenaline which should be administered before or at the time of steroid administration. Adrenaline inhalation can be repeated if no clinical improvement is observed, which indicates the need of hospital admission [24]. In our group, about 30% of children required hospital admission, however, the majority did not present significant decreases in hemoglobin saturation, and the average Westley scores were low. As we have observed, the increased air pollution may contribute to increased morbidity with viral croup but does not exacerbate the disease course, what stays in accordance with previous findings on other respiratory tract infections. To our best knowledge, there are not much studies addressing specifically the association between air pollution and viral croup. The results of recently published Polish study suggest that the exposure to air pollution exacerbates chronic laryngitis among adults [25]. On the other hand, German researchers did not observe correlation between childhood laryngitis and air pollution [26].

We analyzed individual air pollutants for the association with childhood viral croup occurrence what can be considered a strength of our study. However, our study has several limitations. Most importantly, considering the design of our study, we were not able to control for the epidemiologic situation regarding viruses responsible for viral croup. We attempted to adjust our analysis for air temperature, however, other environmental factors, such as air humidity, or cigarette smoking exposure may also influence the results. The study was conducted retrospectively, and children were examined by different physicians, which may be a source of bias, even though viral croup symptoms are difficult to be misdiagnosed. We have aggregated the data from measurement stations, however, this was justified by good correlations between measurements done at various stations; also, this allowed for better clarity of the report. Moreover, we included children admitted to a single center over two-year period; retrieving data from other hospitals in the area of interest and from longer period would allow for more robust analysis.

Concluding, our report shows moderate associations between the incidence of symptoms of viral croup in children and the concentrations of air pollutants, including PM_{10}, $PM_{2.5}$, NO_x, CO and benzene. The results support other observations on adverse impact of air pollution on children's respiratory health.

Acknowledgments, funding, and disclosures

The authors declare no conflict of interest.

The authors thank Ms Gabriela Klimek, M. Sc. Eng. from Databases and Expertise Office, Institute of Meteorology and Water Management — National Research Institute, Warsaw, Poland, for a kind help with retrieving data on daily air temperature.

Authors contribution: Katarzyna Anna Dyląg — data collection, manuscript drafting; Bartłomiej Wroński — data collection, Katarzyna Przybyszewska — data collection, Paulina Dumnicka — study design, data analysis and interpretation.

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