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Impact of Air Pollution and Outdoor Temperature on the Rate of Chronic Obstructive Pulmonary Disease Exacerbations

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Background: Environmental pollution can be one of the main risk factors for acute exacerbations of chronic obstructive pulmonary disease (COPD).

Aim: To study the relationship between air pollution, outdoor temperature and exacerbations of COPD.

Materials and methods: COPD patients (n=1432) were followed up for one year. The levels of particulate matter up to 10 µm (PM₁₀), nitrogen dioxide (NO₂), sulfur dioxide (SO₂) and outside temperatures were collected from the Environmental Agency database.

Results: A total of 309 acute COPD exacerbations (AECOPD) were recorded in the analysis. The daily mean concentrations of PM₁₀ were found to correlate significantly with the daily mean concentrations of NO₂ and SO₂ (ρ 0.34 and ρ 0.49, respectively; p=0.0001). The negative correlations between the daily mean temperature and the daily mean levels of PM₁₀, NO₂ and SO₂ were also significant (ρ -0.44, ρ -0.11, and ρ -0.37, respectively; p=0.0001). The daily number of AECOPD correlated with the mean levels of PM₁₀ in the previous six days (ρ 0.14; p=0.02) and the lower outdoor temperature (ρ -0.2; p=0.001). The negative correlation between the daily number of AECOPD and the mean daily temperature was stronger in days with levels of PM₁₀ above 50 µg/m³ (ρ -0.3 p=0.02 vs. ρ -0.18 p=0.01).

Conclusion: Lower daily mean temperatures were associated with the levels of air pollutants. The level of PM₁₀ correlated with the levels of the other air pollutants. The daily number of AECOPD was found to correlate weakly, but significantly with the mean level of PM₁₀ in the previous six days.

BACKGROUND

There is increasing evidence of the significant effect of air pollutants on the respiratory system. According to the data of the World Health Organization (WHO) from 2014, there were more than 7 million premature deaths because of air pollution in 2012.¹ Especially sensitive are people with chronic respiratory diseases including chronic obstructive pulmonary disease (COPD).

COPD is a common, socially significant disease with an increasing effect on morbidity, disability and mortality. Environmental pollution can be one of the main risk factors for acute exacerbations of COPD, emergency department admissions, hospi-

talizations, and even death.²

Air pollution in Bulgaria continues to be a problem of significant magnitude. The country comprises approximately 1% of the European Union population but produces 2.5% from all particulate matter (PM) emissions.³ The weight of PM in one cubic meter of air (measured in µg/m³) is one of the main indicators for air pollution. The most studied effects on human health are for PM with size 10 µm (PM₁₀) and 2.5 µm (PM_{2.5}). According to the National Environmental Agency approximately 51% of Bulgarian population lives in higher than recommended levels of PM₁₀.³ The impact of air pollution on acute COPD exacerbations in Bulgaria

is still little studied.

The aim of this study was to explore the relationship between air pollution, outdoor temperature and COPD exacerbations.

MATERIALS AND METHODS

A group of consecutive COPD patients (n=1432) signed informed consent and were followed up prospectively for one year. The study was approved by the Research Ethics Committee of the Medical University, Pleven.

COPD was diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease 2017 (GOLD) criteria.⁴ The inclusion criterion was post bronchodilator obstruction defined as FEV₁/FVC<0.70. Patients without acute exacerbations of COPD during the follow-up period and the ones living outside the town of Pleven were excluded.

The data about patients' age, sex, post bronchodilator FEV₁, smoking status and AECOPD was collected from medical records and a specially designed study chart. Exacerbation was defined as acute worsening of the patient's respiratory symptoms from the stable state that necessitates treatment with antibiotic and/or systemic glucocorticosteroid (moderate) or hospitalization (severe).⁴ Severe exacerbations were the ones that required hospitalization while moderate exacerbations were treated in the ambulatory settings with antibiotics and/or corticosteroids.

The levels of particulate matter up to 10 µm (PM₁₀), nitrogen dioxide (NO₂), sulfur dioxide (SO₂) and outside temperatures (measured hourly from an automatic station placed in the middle of the town) were collected from the Environmental Agency database. Statistical analysis was performed with

Table 1. Detailed data about age, sex, post bronchodilator FEV₁, smoking status and AECOPD, GOLD stage, comorbidities and inhaler therapy

	Inpatient	Outpatient	All
Number	138	111	249
Age (years)	68.53±9.46	68.49±10.73	68.51±10.02
Male sex %	71.01%	71.17%	71.08%
FEV ₁ % pred., (SD)	42 (30-57)	49 (36-66)	44 (31-62)
Smokers %	71.74%	71.17%	71.49
Pack years (SD)	40 (30-50)	38 (29-48)	40 (30-50)
Mean AECOPD, n	1.16	1.34	1.24
Group classification according to GOLD 2011 criteria at inclusion			
A	-	20.72%	9.24%
B	-	35.14%	15.66%
C	30.44%	17.11%	24.50%
D	69.56%	27.03%	50.60%
Comorbidity			
Arterial hypertension	76.09%	66.67%	71.89%
Congestive heart failure	58.7%	38.74%	49.80%
Diabetes mellitus	16.67%	20.72%	18.47%
Gastrointestinal disease	25.36%	11.71%	19.28%
Bronchiectasis	8.70%	5.41%	7.23%
Therapy at inclusion			
ICS+LABA+LAMA	51.45%	47.76%	49.8%
ICS+ LABA	24.64%	31.53%	27.71%
LABA+ LAMA	2.17%	1.8%	2.01%
LAMA	6.52%	6.31%	6.26%
LABA	2.17%	2.7%	2.41%
Others	13.05	9.9%	11.81%

Statgraphics plus v.2.1. Continuous variables were presented as mean $\pm$ standard deviation. Pearson correlation was used to test the linear dependence between the variables.

RESULTS

A total of 309 AECOPD (160 severe and 149 moderate) generated by 249 patients were recorded in the analysis. Mean age was 68.5 ± 10 years and 71.1% were male. Detailed data about age, sex, post

bronchodilator FEV₁, smoking status, comorbidity, GOLD stages and AECOPD is shown in **Table 1**.

The annual mean level of PM₁₀ was $45.48 \mu\text{g}/\text{m}^3$. There were 106 days with daily mean level of PM₁₀ above $50 \mu\text{g}/\text{m}^3$ (the recommended level is less than 35 days). The daily mean concentrations of PM₁₀ were found to correlate significantly with the daily mean concentrations of NO₂ and SO₂ (ρ 0.34 and ρ 0.49, respectively; $p=0.0001$) (**Fig. 1**).

The negative correlations between the daily

Figure 1. Relations between levels of PM₁₀ and levels of NO₂ and SO₂ ($p=0.0001$).

Figure 2. Relationship between daily mean outdoor temperature and daily mean level of PM₁₀.

mean temperature and the daily mean levels of PM_{10} , NO_2 and SO_2 were also significant (ρ -0.44, -0.11, and -0.37, respectively; $p=0.0001$) (**Fig. 2**).

The number of AECOPD per day correlated with the mean levels of PM_{10} in the preceding six days (ρ 0.14; $p=0.02$) and the lower outdoor temperature (ρ -0.2; $p=0.001$) (**Fig. 3**).

The negative correlation between the number of AECOPD per day and the mean daily temperature was stronger in the days with levels of PM_{10} above $50 \mu g/m^3$ (ρ -0.3 $p=0.02$ vs. ρ -0.18 $p=0.01$) (**Fig 4**).

DISCUSSION

LEVELS OF PM_{10}

Particulate matter is constantly found in the environmental air. It can be emitted either by natural sources (wild fires, dust storms, etc.) or by artificial ones (biomass, coal and wood burning, traffic, including dusty roads, industry, etc.).²

The measured levels of PM_{10} in Pleven in 2012 showed mean yearly level of $45.48 \mu g/m^3$ and 106 days with levels of PM_{10} above $50 \mu g/m^3$. It makes it one of most polluted cities in the Europe.⁵ Increased PM_{10} level has significant effect

Figure 3. Relation between mean levels of PM_{10} in previous six days and daily number of AECOPD.

Figure 4. Relationship between daily mean temperature and daily AECOPD.

on the worsening of symptoms in patients with COPD.⁶ It has an effect on medical visits because of COPD worsening too⁷, and even on mortality⁸. Furthermore, it has been proven that decreasing the annual level of PM₁₀ from 70 µg/m³ to 20 µg/m³ has a significant effect in terms of reduction of air pollution-related deaths by around 15%.⁹

Applying threshold levels is extremely difficult because of the difference between individual susceptibility. Furthermore, the correlation between the PM₁₀ level and PM₁₀ concentration is not constant and depends on the atmospheric conditions.¹⁰ The WHO recommends maintaining levels of PM₁₀ as low as possible and determines threshold of mean yearly level of 20 µg/m³ and mean daily level of 50 µg/m³.¹¹ An additional recommendation is to have less than 35 days in a year with levels of PM₁₀ above 50 µg/m³. The measured levels of PM₁₀ in the town of Pleven in 2012 significantly exceeded the WHO's recommended thresholds.

The deleterious effects of PM on human health were observed in even lower levels than those recommended by the WHO. The mean annual level of PM₁₀ of 70 µg/m³ is related to 15% increase in risk of long-term death than the recommended level of 20 µg/m³. Lowering this level from 70 µg/m³ to 50 µg/m³ decreases the risk of premature death by 6%.¹¹

THE CORRELATION BETWEEN THE LEVELS OF PM, NO₂, SO₂ AND OUTDOOR TEMPERATURE

We found a statistically significant correlation between the levels of air pollutants, as well as a negative correlation between them and outdoor temperatures. The latter relationship supports the hypothesis that domestic heating is the main source of PM₁₀ in Bulgaria.³

Finding stable correlations between the levels of air pollutants is difficult because they are in a continuous dynamic interaction. Contributing factors are the origin of pollutants, the time from beginning of their emission and the atmospheric conditions. A study from Gothenburg, Sweden, showed 24 hour instability of the correlation between the levels of NO₂ and PM₁₀.¹²

THE CORRELATION BETWEEN AECOPD, PM₁₀, NO₂, SO₂, AND THE OUTDOOR TEMPERATURE

We found a significant relationship between the level of PM₁₀ and the number of AECOPD per day. We could not find the same relationship with the levels of NO₂ and SO₂. The negative correlation of the AECOPD with the outdoor temperature was

also significant.

There is scanty data about the relationship between the AECOPD and the air pollution or outdoor temperature. A study from China showed that the air pollution in the workplace further increased the risk of AECOPD by 7% for every 10 µg/m³ increase of the level of PM₁₀. This study also found no relationship between the AECOPD and the levels of NO₂ or SO₂.¹³ The relationship between the AECOPD and the outdoor temperature was studied by Almagro et al. who found that the decrease of temperature by 1 degree resulted in 4.7% increase in the mean number of hospitalizations.¹⁴

It is worth noting that the negative correlation we found between the AECOPD and the outdoor temperature was stronger in days with PM₁₀ level above 50 µg/m³. The air temperature is known to modify the level and quality of PM. Higher level of PM could modulate the effect of low outdoor temperature on the local immunity reaction in the airways, as well, which can contribute to AECOPD.¹⁵

POTENTIAL LIMITATION OF THE STUDY AND DIRECTIONS FOR FURTHER INVESTIGATIONS

The number of studied patients with AECOPD during 2012 is relatively small. The frequency of mild exacerbations is unknown, although they have a significant effect on COPD progression.¹⁶ These factors could lead to underestimation of the real effect of PM₁₀ and outdoor temperatures on the frequency of AECOPD. Thus, it is appropriate to conduct a multicenter study in polluted cities in Bulgaria. Mild AECOPD can be detected by filling validated daily cards for patients with COPD.¹⁷

CONCLUSION

The level of PM₁₀ in the town of Pleven in 2012 exceeded the WHO recommended thresholds. Lower daily mean temperatures were associated with the levels of air pollutants. The level of PM₁₀ correlated with the levels of the other air pollutants. The number of AECOPD per day was found to correlate weakly, but significantly with the mean level of PM₁₀ in the preceding six days.

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Влияние загрязнения воздуха и температуры окружающей среды на частоту exacerbаций хронической обструктивной болезни лёгких

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Введение: Загрязнение окружающей среды может рассматриваться в качестве одного из главных факторов риска наступления острой exacerbации хронической обструктивной болезни лёгких (ХОБЛ).

Цель: Исследовать связь между загрязнением воздуха, температурой окружающей среды и exacerbацией ХОБЛ.

Методы: Развитие болезни у пациентов с ХОБЛ (n=1432) было прослежено в течение одного года. Уровни тонкодисперсных частиц пыли до 10 µm (PM₁₀), диоксида азота (NO₂), диоксида серы (SO₂) и температура окружающей среды были установлены на базе данных Агентства окружающей среды.

Результаты: В анализе было зарегистрировано 309 случаев острой exacerbации ХОБЛ. Установлено, что средние дневные концентрации PM₁₀ коррелируют в значительной степени с дневными средними корреляциями NO₂ и SO₂ (ρ 0,34 и ρ 0,49 соответственно; p=0,0001). Отрицательная корреляция между средней дневной температурой и средними дневными уровнями PM₁₀, NO₂ и SO₂ тоже оказалась значительной - ρ -0,44, ρ -0,11 и ρ -0,37 соответственно (p=0,0001). Число дневных случаев проявления острой exacerbации ХОБЛ коррелировало со средними уровнями PM₁₀ предшествующих шести дней (ρ 0,14; p=0,02) и низкой температурой окружающей среды (ρ -0,2; p=0,001). Отрицательная корреляция между дневными случаями проявления острой exacerbации ХОБЛ и средней дневной температурой оказалась более высокой в течение дней с PM₁₀, превышающим 50 µg/m³ (ρ -0,3 p=0,02 vs. ρ -0,18 p=0,01).

Заключение: Низкая средняя дневная температура оказалась связанной с уровнями загрязнителей воздуха. Уровень PM₁₀ коррелирует с уровнями других загрязнителей воздуха. Установлено, что число дневных случаев острой exacerbации ХОБЛ коррелировало слабо, но значительно со средним уровнем PM₁₀ предшествующих шести дней.