The Effects of Short-term Pm 2.5 Exposure on Pulmonary Function Among Children With Asthma —A Panel Study in Shanghai, China

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Abstract

Background

Fine particulate matter with aerodynamic diameter ≤ 2.5 μm (PM_{2.5}) has been reported to be an important risk factor for asthma. Our study was designed to evaluate the relationship between air PM_{2.5} and lung function among children with asthma in Shanghai, China.

Methods

From 2016 to 2019, a total of 70 Chinese children aged 4 to 14 in Pudong, Shanghai were recruited for this panel study. Upon entry to the group, questionnaire was used to collect basic information, and the lung function covering forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1) and peak expiratory flow (PEF) were carried out for each child more than two times during follow-up. Meanwhile, the simultaneous daily air atmospheric pollutants and meteorological data were collected. The linear mixed effect (LME) model was used to assess the relationship between air pollutants and lung function adjusting other covariates like sex, age, season and so on.

Results

A significantly negative association was found between PM_{2.5} level and lung function in children with asthma. In the single-pollutant model, the largest effect of PM_{2.5} on lung function were found on lag 0-2, FVC and FEV1 decreased by 0.91% [95% confidence interval (CI): -1.75, -0.07] and 1.05% (95% CI: -2.09, 0.00) for every 10 mg/m³ increase of PM_{2.5}. In the multi-pollution model (adjusted PM_{2.5}+SO₂+O₃), the maximum effect of PM_{2.5} on FVC and FEV1 also appeared on lag 0-2, FVC and FEV1 decreased by 1.57% (95% CI: -2.69, -0.44) and 1.67% (95% CI: -3.05, -0.26) for every 10 mg/m³ increase of PM_{2.5}, respectively. In the subgroup analysis, boys, children and hot season more were sensitive.

Conclusion

The short-term exposure of ambient PM_{2.5} is a risk factor for the lung function of children with asthma, particularly in boys, preschoolers (<6 years old) and in the hot season.

1. Introduction

Asthma is one of the most common diseases in children [1], as a chronic disorder of the airways characterized by reversible airflow obstruction and airway inflammation, persistent airway hyper-reactivity, and airway remodeling [2]. About 14% of children worldwide are affected by asthma, and the prevalence rate is rising [3]. The number of asthma patients worldwide reached 339.44 million in 2016 [4], and low-income and middle-income countries contributing 96% of global asthma-related deaths and 84% of global disability-adjusted life-year [5]. In China, the average prevalence of asthma in children under 14 years of age increased by 32.7% during 2000 to 2010 [6]. Asthma affects 8.3% of children in the United

States [7]. Evidences have been collected that many factors were related to the asthma, such as air pollution, occupational exposures, genetics, stressful life events and tobacco exposures [8]. Among these factors, air pollutants from both outdoor and indoor were the major ones affecting asthma among children[9–11]. The strategies of controlling air pollution were reported to reduce the burden of disease from asthma[12]. Several air pollutants, including nitrogen dioxide (NO₂), sulfur dioxide (SO₂), ozone (O₃), fine particulate matter with aerodynamic diameter $\leq 2.5 \mu\text{m}$ (PM_{2.5}) and particulate matter with aerodynamic diameter $\leq 10 \mu\text{m}$ (PM₁₀) were reported to be associated with the increased risk of asthma[13–17]. The most health-harmful pollutants are fine PM_{2.5} particles which could penetrate deep into lung passageways[18].

A multi-center cohort study of the correlation between air pollutants and childhood asthma in China also reported that PM_{2.5} was significantly associated with asthma[6] and there are seasonal and lagging effects between PM_{2.5} and children with asthma[19, 20]. However, some studies suggested no evidence of a positive association between particulate matter and asthma prevalence [21, 22]. At present, most of the studies were big data analysis and animal experiments, but there were few panel studies based on cohort study data and these results may not be representative. Furthermore, China is the largest developing country with unprecedented socio-economic and urbanization changes, these changes are associated with a rapidly increasing prevalence of asthma and a significant burden on the health care system[23, 24]. Therefore, the effect of PM_{2.5} on asthma needs further study.

Since Shanghai is the biggest city and has the highest prevalence of childhood asthma in China [25, 26], it is necessary to design a panel study to explore the effect of PM_{2.5} on asthma. Therefore, this study will explore the relationship between PM_{2.5} and lung function in children with asthma with a panel study design in Shanghai, and analyze the effect of season in subgroup analysis, so as to provide a scientific basis for the prevention and control of asthma.

2. Materials And Methods

2.1 Design and population

From January 2016 to December 2019, we recruited 117 asthmatic children in Pudong of Shanghai, China. These participants were included based on the following criteria: 1) no history of chest surgery; 2) asthma cases were extracted from the hospital information systems according to the International Classification of Disease codes, Revision 10 (ICD-10, J45 and J46) or diagnosed by a professional doctor; 3) ages 4–14 years and parent-reported asthma or a history of symptoms including wheezing, cough, or dyspnea. Finally, we included a total of 70 children (39 boys and 31 girls, aged 4-14 years) with asthma for statistical analysis (Fig. 1.). All participants in this study took questionnaires, lung function measurement and received written informed consent and were approved by the Ethics Committee of Shanghai Children's Medical Center (SCMCIRB-K2016037).

2.2 Lung function test and questionnaire

In this study, the spirometry was performed by experienced operators (medical doctors specialized in pediatric pulmonology) and the specific recommendations for spirometry in the pre-school age were considered [27]: 1) children were instructed how to do the manoeuvres, repeating them at least three times; 2) a training period was considered to familiarise them with the equipment and technician; 3) the operator observed the child closely to ensure there was no leak, and that the manoeuvre was performed optimally; 4) To examine volume-time curves and flow-volume curves in real time with eye [28]. The adolescents were all in sat position and no nasal clips were used in any of the operations.

With standard questionnaires, the trained interviewers collected the data on basic demographic information, parents' allergy history, allergy history, cigarette exposure and so on. In this study, the frequency of smoking in places where children often move or rest was classified into the following groups: 0 unit/day, <1 unit/day, 1~5 unit/day, >5 unit/day. The frequency of contact between smokers and children was classified into the following groups: 0 h, <1 h/day, 1~4 h/day, 4~8 h/day and >8 h/day. Body mass index (BMI) was calculated as weight (kg) divided by the square of the height (m²).

2.3 Exposure

Daily concentrations of air pollutants, including PM₁₀, PM_{2.5}, NO₂, SO₂, carbon monoxide (CO) and O₃, were collected from Pudong monitor stations (31.23°N, 121.52°E) [29]. Daily concentrations were calculated by 24-hour average of air pollutant concentrations except for O₃, which was calculated as daily maximum 8-h values. The meteorological parameters, including ambient temperature, high temperature, low temperature and relative humidity were monitored at Pudong Supersites, respectively.

2.4 Statistical analysis

We set up the questionnaire information database through EpiData (Version 3.0) and used double input for quality control. In the descriptive analysis for baseline characteristics of the asthmatic children and exposure data for environmental factors, categorical variables were described as frequency and percentage, and continuous variables were given as means and standard deviations.

Because there were repeated measures for all participants, the linear mixed effect (LME) model was used to estimate the effects of PM_{2.5} on lung function [30]. This model allows each subject to act as self-control of time and to explain the correlation between repeated measurements collected by each person by including the random effects of the subjects [31]. Due to the abnormal distribution of lung function, the measured values of lung function were transformed logarithmically. We controlled three-day moving average temperature (lag 0-3) and three-day moving average relative humidity (lag 0-3) for potential lagged meteorological confounders. In addition, the time of lung function tests, holidays and day of the week effects were adjusted in the model. The respiratory health indicators were regressed on moving average concentrations of exposure variables from 1 day to 7 days before the measurements to estimate the potential cumulative effects of the exposures. The mixed-effects model is as follows:

$$\text{Log}(Y_{ij}) = u + b_i + \beta_1 X_1 + \beta_2 X_2 \dots \beta_n X_n + \xi_{ij}$$

Log (Y_{ij}) represents the logarithmic value of the lung function index for study subject i on measurement j ; u represents the fixed intercept; b_i is individual-specific random intercept; β_1 through to β_n represent the fixed effect variable coefficients for variables X_1 through X_n ; and ξ_{ij} represents the error for participant i on measurement j . We reported the results as the estimated percentage change in FVC, FEV1 and PEF with 95% confidence interval (CI) with each $10 \mu\text{g}/\text{m}^3$ increase in air pollutants. The estimated percent changes were calculated as $[10^{(\beta \times 10)} - 1] \times 100$, with $\{95\% \text{CI} [10^{10 \times (\beta \pm 1.96 \times \text{SE})} - 1] \times 100\}$, where β and SE are the effect estimate and its standard error [32].

We used the single-pollutant model and multi-pollutant model to test the consistency of exposure effects. Pollutants that were highly related to $\text{PM}_{2.5}$ ($r > 0.7$) were excluded in order to reduce the collinearity among pollutants, so SO_2 and O_3 were included in the multi-pollutant model (Fig. S1.). To control for intra-participant variability, the subject was included in the LME as random variables and adjusted for questionnaire information (atopic dermatitis, allergic rhinitis, food or drug allergies, mother's or father's history of allergies, frequency of smoking in places where children often move or rest and frequency of contact between smokers and children), age, sex and BMI.

We conducted a subgroup analysis by sex (boy vs. girl), age (child was defined as aged less than 6 years old vs. teenager was defined as aged older than or equal to 6 years old) and season (cold season was defined the period of Nov to Mar, and the hot season was defined as the period of May to Sept [20]) to control for potential modifying effects.

The Mixed Linear Effect Model were performed with the "lme4" package and "Matrix" package in R software (R Development Core Team; <http://R-project.org>) [33]. Other statistical analysis was achieved in SPSS 22.0 (IBM SPSS, Chicago, IL, USA), and $P < 0.05$ (two-tailed) was considered statistically significant.

3. Results

3.1 Descriptive analysis

Table 1 shows the basic demographic information of the study population. After the filtration of population information, we included 39 boys and 31 girls in this study and their BMI was 16.55 ± 2.82 . Of the 70 children, 87.14% of children with asthma had allergic rhinitis, 62.86% had atopic dermatitis and 87.14% of parents chose not to smoke in places where their children often had activities or rest. Table 2 shows the descriptive results of the meteorological variables, air pollutants and lung function indicators. The daily average temperature and relative humidity were 19.17°C and 74.86%, respectively. The daily average concentrations of $\text{PM}_{2.5}$, PM_{10} , O_3 , SO_2 , NO_2 and CO were $34.15 \mu\text{g}/\text{m}^3$, $50.69 \mu\text{g}/\text{m}^3$, $107.34 \mu\text{g}/\text{m}^3$, $9.92 \mu\text{g}/\text{m}^3$, $40.38 \mu\text{g}/\text{m}^3$ and $663.23 \mu\text{g}/\text{m}^3$, respectively. The average of FVC, FEV1 and PEF were 1.63 L, 1.36 L and 3.03 L/s, respectively.

3.2 Regression analysis.

Figure 2. shows the changes in lung function of asthmatic children with each $10 \mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ in a single-pollution or multi-pollution model. The changes of lung function in the single-pollution or multi-pollution model were similar, indicating that the model was stable. Delayed effects of $\text{PM}_{2.5}$ were significantly associated with FVC and FEV1 on lag 0, lag 0-1 and lag 0-2 both in single-pollution or multi-pollution model, with the largest effect observed on lag 0-2. Per $10 \mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ on lag 0-2 corresponded with a 1.57% (95% CI: -2.69, -0.44) decreased FVC and 1.67% (95% CI: -3.05, -0.26) decreased FEV1 in the multi-pollution model (adjusted $\text{PM}_{2.5}+\text{SO}_2+\text{O}_3$). However, in the double-pollution model (adjusted $\text{PM}_{2.5}+\text{O}_3$) and the single-pollution model, the delayed effect of $\text{PM}_{2.5}$ was significantly related to the effect of PEF on lag 0, with the largest effect of PEF on lag 0-3 in the single-pollution model. For each $10 \mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ on lag 0-3, the PEF decreased 2.12% (95% CI: -4.18, -0.02).

3.3 Subgroup analysis

Figure 3. shows the gender difference in the relationship between lung function and $\text{PM}_{2.5}$ in the multi-pollution model (adjusted $\text{PM}_{2.5}+\text{SO}_2+\text{O}_3$). Generally, the change of lung function in boys was more obvious than that in girls. For boys, the maximum effect of $\text{PM}_{2.5}$ on both FVC and FEV1 occurred in on lag 0-2, FVC and FEV1 decreased by 3.65% (95% CI: -5.28, -1.98) and 3.12% (95% CI: -5.25, -0.95) respectively for each $10 \mu\text{g}/\text{m}^3$ increase of $\text{PM}_{2.5}$. In the girl group, the maximum effect of $\text{PM}_{2.5}$ on FEV1 occurred on lag 0-4, FEV1 decreased 2.33% (95% CI: -4.38, -0.24) for each $10 \mu\text{g}/\text{m}^3$ increase of $\text{PM}_{2.5}$. These results were similar in other models (adjusted $\text{PM}_{2.5}$, $\text{PM}_{2.5}+\text{O}_3$, $\text{PM}_{2.5}+\text{SO}_2$ in Fig. S2. to S4.).

Figure 4. shows the age difference in the relationship between lung function and $\text{PM}_{2.5}$ in the multi-pollution model (adjusted $\text{PM}_{2.5}+\text{SO}_2+\text{O}_3$). For each $10 \mu\text{g}/\text{m}^3$ increase of $\text{PM}_{2.5}$ on lag 0-3 was associated with decreased FVC and FEV1 by 3.77% (95% CI: -5.72, -1.77) and 4.25% (95% CI: -6.62, -1.81) in children. As for PEF, each $10 \mu\text{g}/\text{m}^3$ increase of $\text{PM}_{2.5}$ on lag 0-6 was associated with a maximum effect decreased of 6.89% (95% CI: -10.55, -3.09). But for teenager, none of them were statistically significant. The results were similar in other models (adjusted $\text{PM}_{2.5}$, $\text{PM}_{2.5}+\text{O}_3$, $\text{PM}_{2.5}+\text{SO}_2$ in Fig. S2. to S4.).

Figure 5. shows the season difference in the relationship between lung function and $\text{PM}_{2.5}$ in the multi-pollution model (adjusted $\text{PM}_{2.5}+\text{SO}_2+\text{O}_3$). No statistically significant relationship between lung function and $\text{PM}_{2.5}$ was located in the cold season (November to March). During the hot season (May to September), both FVC and FEV1 had the largest decline when exposed to $\text{PM}_{2.5}$ on lag 0-2. For each $10 \mu\text{g}/\text{m}^3$ increase of $\text{PM}_{2.5}$, FVC decreased by 2.56% (95% CI: -4.74, -0.33) and FEV1 decreased by 3.28% (95% CI: -5.78, -0.72). In the seasonal subgroup analysis, the results were not quite the same for different pollutant models (adjusted $\text{PM}_{2.5}$, $\text{PM}_{2.5}+\text{O}_3$, $\text{PM}_{2.5}+\text{SO}_2$ in Fig. S2. to S4.). Among them, the results in the two-pollutants model controlling $\text{PM}_{2.5}$ and SO_2 (Fig. S4.) were similar to the multi-pollution model (adjusted $\text{PM}_{2.5}+\text{SO}_2+\text{O}_3$).

4. Discussion

In the present study, we found $PM_{2.5}$ had a negative effect on lung function in children with asthma after adjusted for other confounding factors with significant cumulative effect, particularly in hot seasons. In the subgroup analysis, the change of lung function in boys was more obvious than that in girls, children were more vulnerable to the effects of $PM_{2.5}$ than teenagers.

Consistent with many previous studies [34–37], we also found that the influence of air pollution on asthma were obvious. A study in Brazil and the International Study of Asthma and Allergies in Childhood (ISAAC) have both suggested that the environmental factors may be the major risk factors for childhood asthma [22, 38], especially $PM_{2.5}$, which is a well-recognized risk factor for worsening asthma [16]. The significant effect of $PM_{2.5}$ on the asthma of children may be due to the greater toxicity of $PM_{2.5}$ and smaller diameter, which lead to a larger surface area and greater allergen uptake [39].

For sensitive populations, previous studies have shown inconsistent results. A study in China showed the effects of $PM_{2.5}$ in 5–14 years old were higher than 0–4 years old and no significant difference in gender subgroup analysis[40]. But in a Brazilian study showed the highest asthma prevalence in the 0-4 years age group and boys [38]; some studies found that boys were more likely than girls to suffer from asthma during childhood [41, 42], these results are similar to our study. This is probably because that boys prefer and enjoy being outdoors activities, which caused more frequent exposure to atmospheric pollutants than girls, and the preschoolers are more susceptible to $PM_{2.5}$ due to their immature immune function. A study has confirmed the cytotoxic effect of $PM_{2.5}$ on airway epithelial cells [43], the soluble $PM_{2.5}$ extract induces oxidative stress by activating NF- κ B and MAPK signaling pathways, and promotes the expression of pro-inflammatory factors, which increases nasal mucus and decreases airway barrier function [18, 44]. Sex-related differences in asthma prevalence also could be due to the difference of sex hormones and the difference of airway relative to lung size [45, 46]. But unlike the study in Hefei [47], $PM_{2.5}$ has a stronger effect on school-age children (≥ 6 years old) than preschoolers (< 6 years old). This may be explained by the higher level of air pollutants like NO_2 , which may affect the lung function differently.

Consistent with the results found in a meta-analysis including 87 studies [19] and a study in Shanghai [39], $PM_{2.5}$ had a greater impact on lung function in children with asthma during the warm season. This result can be explained from two aspects. On one hand, there are higher levels of aerosol molecules compared with cold seasons, such as fungal spores and pollen, which may trigger more allergy attacks [48, 49]. On the other hand, children spend more time outdoors and get involved in more physical activities in the warmer season, which increases their per-minute ventilation and thus inhale more air pollutants. However, a study conducted in Shenzhen and a time-stratified case-crossover study in Philadelphia metropolitan region showed that the risk was significantly greater in the cold season than warm season [50, 51]. This is likely to be related to factors such as the chemical composition and levels

of ambient particulate matter, the exposure patterns of the local population, and local climatic conditions [52, 53].

This study has three important strengths. Firstly, compared to traditional time series study, our participants were all from a panel study. Each participant had at least two repeated measures of lung function, allowing a longitudinal study to be conducted. In order to control the effects of the participants themselves, we used the mixed linear effects model. Secondly, our study chose PM_{2.5} as the main pollutant in Pudong, Shanghai. We not only determined the effect of PM_{2.5} on childhood asthma using the panel study data but also conducted subgroup analysis to explore the effects in hot and cold seasons. We found that PM_{2.5} exhibited various effects on childhood asthma in different seasons. Finally, all health data (i.e., lung function, questionnaires) were completed by professional researchers, which can minimize investigator bias.

Although we found the close relationship between air pollutant and lung function among children with asthma, this study also has several limitations. Firstly, due to the lack of specific home addresses of participants, the data of air pollutants and meteorological factors from monitor station could not represent the specific exposure level for each participant. Secondly, this study only considered the effects of external atmospheric pollutants and meteorological factors, without regard to indoor pollution [10, 54, 9], which may lead to misclassification and bias. What's more, this study did not analyze PM_{2.5} components due to technical limits, which may result in an underestimate of the effect. The last but not least, the analysis of temperature in this study was in a subgroup analysis only, and the interaction between PM_{2.5} and temperature was not considered, which may cause an underestimation of the results.

5. Conclusions

This panel study indicates that the short-term exposure of ambient PM_{2.5} is a risk factor for the lung function of children with asthma, particularly in boys, preschoolers (<6 years old) and in the hot season. The results suggest that more attention should be paid on the effect of PM_{2.5} on lung health of asthma children.

Abbreviations

PM_{2.5}: fine particulate matter with aerodynamic diameter ≤ 2.5 μ m; PM₁₀: particulate matter with aerodynamic diameter ≤ 10 μ m; NO₂: nitrogen dioxide; SO₂: sulfur dioxide; O₃: ozone; CO: carbon monoxide; FVC: forced vital capacity; FEV₁: forced expiratory volume in 1 second; PEF: peak expiratory flow; LME: the linear mixed effect model; SD: standard deviation; IQR: Interquartile range; BMI: body mass index.

Declarations

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Author's contributions

Ji Zhou: Conceptualization, Methodology, Funding acquisition. **Ruoyi Lei:** Writing - original draft, Software. **Jianming Xu:** Data curation, Resources. **Li Peng:** Data Curation, Resources. **Xiaofang Ye:** Project administration. **Dandan Yang:** Supervision, Investigation. **Sixu Yang:** Investigation. **Yong Yin:** Project administration, Writing – review & editing. **Renhe Zhang:** Project administration.

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Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to the need to protect the privacy of participants but are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

We have confirmed that all the methods and procedures were performed in accordance with the relative guidelines and regulations. This study was approved by the Ethics Committee of Shanghai Children's Medical Center (SCMCIRB-K2016037). Written informed consent was obtained before the investigation from the parents of the children for using the data for research.

Consent for publication

The authors consent on the publication of the manuscript.

Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Tables

Table 1 Description of basic demographic information (N=70).

	n	%
Sex		
boy	39	55.71
girl	31	44.29
Age		
<6	40	57.14
≥6	30	42.86
Body mass index (BMI) Mean ± SD	16.55 ± 2.82	
Atopic dermatitis		
Yes	44	62.86
No	26	37.14
Allergic rhinitis		
Yes	61	87.14
No	9	12.86
Food or drug allergies		
Yes	20	28.57
No	50	71.43
Mother's history of allergies		
Yes	52	74.29
No	18	25.71
Father's allergy history		
Yes	52	74.29
No	18	25.71
Frequency of smoking in places where their children often had activities or rest		
0 unit/day	61	87.14
<1 unit/day	2	2.86
1~5 unit/day	6	8.57
>5 unit/day	1	1.43
Frequency of contact between smokers and children		

0 h	43	61.43
<1 h/day	9	12.86
1~4 h/day	11	15.71
4~8 h/day	3	4.29
>8 h/day	4	5.71

Table 2 Description of basic meteorological pollutants and lung function indicators.

	Mean	SD	Min	Max	IQR
Daily temperature (°C)	19.17	9.03	-0.1	32.2	16.4
Relative humidity (%)	74.86	11.73	37	97.5	18.3
PM _{2.5} (mg/m ³)	34.15	25.13	9	173	28
PM ₁₀ (mg/m ³)	50.69	26.46	13	166	34
O ₃ (mg/m ³)	107.34	48.04	32	251	67
SO ₂ (mg/m ³)	9.92	4.3	5	40	5
NO ₂ (mg/m ³)	40.38	19.84	13	118	26
CO (mg/m ³)	663.23	236.13	400	1800	200
FVC (L)	1.63	0.52	0.57	3.85	0.62
FEV1 (L)	1.36	0.42	0.54	3.45	0.51
PEF (L/s)	3.03	1.605	1.05	21.80	1.43

SD, standard deviation; IQR, Interquartile range; PM_{2.5}, fine particulate matter with aerodynamic diameter ≤ 2.5 μ m; PM₁₀, particulate matter with aerodynamic diameter ≤ 10 μ m; O₃, ozone; SO₂, sulfur dioxide; NO₂, nitrogen dioxide; CO, carbon monoxide; FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second; PEF, peak expiratory flow.

Figures

Figure 1

The selection of the participants in this study.

Figure 2

Association between lung function and air pollutants in single- or multi-pollution models.

Figure 3

Association between lung function and PM_{2.5} in gender-stratified multi-pollution model (adjusted PM_{2.5}+SO₂+O₃).

Figure 4

Association between lung function and PM_{2.5} in age-stratified multi-pollution model (adjusted PM_{2.5}+SO₂+O₃).

Figure 5

Association between lung function and PM_{2.5} in a season-stratified multi-pollution model (adjusted PM_{2.5}+SO₂+O₃).

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