

The Association of Short- and Long-term Exposures to Particulate Matters with Expression of High-sensitivity C-reactive Protein in People on Health Examination

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Abstract

Introduction and Objectives: High-sensitivity c-reactive protein (hs-CRP), used to stratify the risk of cardiovascular disease on health examination, was also reported to be predictive for progression of chronic kidney disease. However, the impact of ambient exposure to particulate matters (PMs) on health examination was not clear. Thus, the association of short- and long-term exposures to PMs with hs-CRP level was surveyed among people on health examination.

Methods: People who visited the health management center for health examination were retrospectively reviewed. The clinical data, including age, gender, hs-CRP level, residential district and concentrations of PMs were collected and analyzed.

Results: During the study interval, 455 individuals on health examination were enrolled and divided into 4 groups due to the level of hs-CRP. Trend analysis revealed that long-term exposure to PMs was associated with high hs-CRP expression. Regression analysis further revealed that exposure to PM₁₀ was seemingly associated with those who had the hs-CRP level more than 5 mg/L (OR: 1.07, 95% CI: 0.99-1.14, P=0.052), though there was no statistical significance.

Conclusion: Long-term exposure to PMs seemed to affect the level of hs-CRP to a certain extent in the population on health examination. Hence, the history of PM exposure should be taken into consideration for individuals who had a high hs-CRP level on health examination.

Keywords: Chronic kidney disease; Health examination; High-sensitivity c-reactive protein; Particulate matter 2.5; Particulate matter 10

Introduction

Chronic Kidney Disease (CKD) has been recognized as one of the risk factors developing Cardiovascular Diseases (CVD) [1]. It has been indicated that CVD is the leading cause of mortality in the CKD population [2]. Previous studies further revealed that both decreased Glomerular Filtration Rate (GFR) and significant proteinuria increased the risk of CVD. Besides, CKD patients were prone to present with atypical symptoms, which could lead

to delayed diagnosis and adverse outcomes [3,4]. On the contrary, it was reported that CKD was associated with poor prognosis in patients with co-existing CVD. Hence, a strategy ought to be established to screen and monitor the progression in healthy population and those with earlier stages of CKD. High-sensitivity C-reactive protein (hs-CRP), a biomarker commonly used to evaluate the risk of cardiovascular events and mortality in clinical, appeared to be an important tool for identifying people at risk [5,6]. Though the cut-off value of hs-CRP for risk stratification could vary in different countries, ethnics or cultures, it was generally considered that hs-CRP of 1 mg/L was associated with remarkably high risk developing CVD-related morbidity and mortality [6,7].

Recently, it was reported that hs-CRP could be predictive for progression of CKD [8]. Nevertheless, a variety of factors may interfere with the risk stratification by hs-CRP, including diabetes [9], body fat composition [10], air pollution [11], and so on. Among these, the impact of exposure time of Particulate Matter (PM) air pollution on hs-CRP could also differ. Hence, we aimed to investigate the association of short- and long-term exposures to PM_{2.5} and PM₁₀ with hs-CRP level among people on health examination.

Methods

From January 1st, 2015 to December 31st, 2016, people who visited health management center in Far Eastern Memorial Hospital for health examination were retrospectively reviewed. The clinical data, including age, gender, hs-CRP level, were collected. Four groups were divided based on the level of hs-CRP (group 1: hs-CRP < 1 mg/L; group 2: 1 mg/L ≤ hs-CRP < 3 mg/L; group 3: 3 mg/L ≤ hs-CRP < 5 mg/L; and group 4: hs-CRP > 5 mg/L). The residential district in individuals was also acquired. For data collection and analysis of PMs, the report of air quality status in Taiwan from July 1st, 2014 to December 31st, 2016 was referred to the Taiwan Air Quality Monitoring Network (TAQMN). The data of air quality were recorded by a network of 21 monitoring stations spreading in Northern part of Taiwan (Taipei city, New Taipei city, Taoyuan city and Keelung city). The parameters of air quality, PM_{2.5} and PM₁₀, recorded by the nearest monitoring station to the residential district of individuals were collected. The 24-hour mean concentrations of PM_{2.5} and PM₁₀ before the visiting day (lag 1 day; 1-day exposure), the lag 1 to lag 3 days (3-day exposure), the lag 1 to lag 90 days (3-month exposure), and the lag 1 to lag 180 days (6-month exposure) were calculated respectively for each individual. Statistical analyses were performed using the SPSS (version 19.0; SPSS Inc., Chicago, USA) statistical software for data analysis. The descriptive data were expressed as the mean ± standard deviation. Trend analysis using one-way Analysis of Variance (ANOVA) and multivariate binary logistic regression

analysis were performed. The data were presented with Odds Ratio (OR) with 95% Confidence Interval (CI). The P value less than 0.05 was considered statistically significant.

Results

During the study interval, a total of 455 individuals on health check-up were enrolled. Eleven was excluded due to incompleteness of clinical data. Among these, the mean age was 45.3±12.9 years, 207 were female and 175 had a hs-CRP level of 1 mg/L and more. Of those who had high hs-CRP level, 121 had the hs-CRP level of 1 mg/L and more but not more than 3 mg/L; 23 had the hs-CRP level of 3 mg/L and more but not more than 5 mg/L; and 31 had the hs-CRP level of 5 mg/L and more. As shown in Table 1, the association of short- and long-term exposures to PM_{2.5} and PM₁₀ with hs-CRP expression was analyzed in people on health examination. It revealed that 6-month exposure to PM_{2.5} seemed to be related to high hs-CRP level (P trend=0.067). Both 3- and 6-month exposures to PM₁₀ were significantly associated with high hs-CRP level (P trend=0.047 and 0.020, respectively). Besides, there was no association of short-term PM exposure to hs-CRP level in individuals receiving health check-up. Since long-term exposure to PM₁₀ were significantly associated with high hs-CRP level in people on health examination, we further survey performed binary univariate analysis to figure out whether 6-month exposure to PM₁₀ was confounding factor or not. Hence, two regression models were performed for the hs-CRP level ≥1 mg/L and ≥5 mg/L, respectively. The age, gender and 6-month exposure to PM₁₀ were also adjusted as confounding factors. As shown in Table 2, there was no effect of long-term PM₁₀ exposure on those who had the hs-CRP level more than 1 mg/L (OR: 1.02, 95% CI: 0.99-1.05, P=0.271). Furthermore, long-term exposure to PM₁₀ was seemingly associated with those who had the hs-CRP level more than 5 mg/L (OR: 1.07, 95% CI: 0.99-1.14, P=0.052), though there was no statistical significance. Taken together, these results suggested that long-term exposure to PMs could affect the level of hs-CRP to a certain extent in people on health check-up.

Variables	Group 1 (hs-CRP < 1 mg/L) (n=280)	Group 2 (1 mg/L ≤ hs-CRP < 3 mg/L) (n=121)	Group 3 (3 mg/L ≤ hs-CRP < 5 mg/L) (n=23)	Group 4 (hs-CRP > 5 mg/L) (n=31)	P trend
Exposure to PM _{2.5} concentration (µg/m ³)					
1-day exposure	17.78±10.89	17.97±11.07	16.06±9.07	17.23±13.25	0.665
3-day exposure	17.72±9.72	17.38±9.15	17.53±8.92	17.62±10.99	0.857
3-month exposure	17.75±4.55	18.17±4.65	18.92±4.74	18.37±5.41	0.217
6-month exposure	17.86±3.57	18.37±3.97	19.24±4.07	18.58±3.80	0.067
Exposure to PM ₁₀ concentration (µg/m ³)					
1-day exposure	37.43±18.12	37.11±19.21	35.48±13.72	38.44±18.04	0.987
3-day exposure	36.57±14.44	35.94±13.92	37.36±10.83	38.57±16.45	0.595
3-month exposure	36.54±6.50	36.64±6.25	39.13±5.93	38.49±8.12	0.047
6-month exposure	36.42±5.46	36.26±5.93	38.94±4.84	38.55±6.14	0.020

Data were presented with mean ± standard deviation.

Table 1: The mean concentration of Particulate Matter (PM) exposures in groups with different high-sensitivity C-reactive protein (hs-CRP) levels.

Variables	OR (95% CI)	P value
hs-CRP ≥1 mg/L		
Age	1.01 (0.99-1.02)	0.494
Female gender	0.91 (0.62-1.33)	0.623
Six-month exposure to PM ₁₀	1.02 (0.99-1.05)	0.271
hs-CRP ≥5 mg/L		
Age	0.99 (0.97-1.02)	0.693
Female gender	1.16 (0.55-2.44)	0.697
Six-month exposure to PM ₁₀	1.07 (0.99-1.14)	0.052

Multivariate binary logistic regression analysis was performed by adjusting by age, female gender and 6-month exposure to PM₁₀ for those who had hs-CRP level ≥1 mg/L and ≥5 mg/L. hs-CRP, high-sensitivity c-reactive protein; PM, particulate matter; OR, odds ratio; CI, confidence interval.

Table 2: The association of hs-CRP level with 6-month exposure to PM₁₀.

Discussion

The present study revealed that people who had a long-term exposure to PMs were prone to have a higher hs-CRP level on health check-up. Although multivariate binary logistic regression analysis indicated that 6-month exposure to PM₁₀ was not significantly associated with hs-CRP expression, the

long-term exposure to PMs could affect the level of hs-CRP to a certain extent in the population on health examination. Thereby, the history of PM exposure should be taken into consideration for individuals who had a high hs-CRP level on health check-up. PMs were mainly composed of sulfate, nitrate, ammonium, organic and elemental carbons, trace metals, geological materials, and so on [12,13]. The significant impact of PMs on health has been

reported, affecting the occurrence and outcomes in a spectrum of diseases including respiratory and cardiovascular disorders, lung cancers, as well as non-respiratory diseases, such as liver cancers, Out-Of-Hospital Cardiac Arrest (OHCA), ischemic stroke, and so on [14-20]. The underlying mechanism has been investigated and proposed in the previous studies and it revealed that PMs could trigger inflammatory response, oxidative stress and mitochondrial dysfunction [21-23]. It also revealed that acute exposure to PM increased plasma expression of proinflammatory cytokines including interleukin (IL)-6 and Tumor Necrosis Factor (TNF)-alpha, and activated polymorphonuclear leukocytes systemically [24]. Besides, it was demonstrated that antioxidant treatment suppressed PM2.5-induced oxidative stress rather than the inflammatory response [25]. Although accumulating evidence suggested that environmental PMs elicited systemic inflammation and oxidative stress by multiple pathways, the detailed mechanism of PMs-induced inflammation on hs-CRP expression remains to be disclosed. Hence, the strategies concerning the hs-CRP testing and interpretation on health examination were warranted to be established in perspective of prevention medicine. Some major limitations existed in the present study. First, this is a retrospective study design in a single medical center. Additionally, it was unknown whether the individual on health check-up had any underlying disease or not. Furthermore, the measured PM levels could have been inadequate indices of actual exposure for people on health examination due to the unavailability of indoor air quality, leading to overestimated or underestimated correlation between hs-CRP level and environmental PMs.

Conclusions

In the present study, it revealed that individuals who had long-term exposure to PMs were prone to have a higher hs-CRP level on health examination. Although multivariate binary logistic regression analysis indicated that 6-month exposure to PM10 was not significantly associated with hs-CRP expression, the long-term exposure to PMs could partially affect the level of hs-CRP in the population on health examination. Hence, the history of PM exposure should be taken into consideration for individuals who had a high hs-CRP level on health examination.

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Conflicts of Interest: The authors declare no conflict of interest.

Author Contributions: Ching-Fang Hsu and Yu-Hui Tsai worked as co-first authors. Fu-Chien Hsieh contributed as the corresponding author. All authors read and approved the manuscript.

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