Short-Term Exposure to Fine Particulate Matter and Risk of Ischemic Stroke

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Background and Purpose—There is a strong association between ambient concentrations of particulate matter (PM) and cardiovascular disease. However, it remains unclear whether acute exposure to fine PM ($PM_{2.5}$) triggers ischemic stroke events and whether the timing of exposure is associated with stroke risk. We, therefore, examined the association between ambient $PM_{2.5}$ and occurrence of ischemic stroke.

Methods—We analyzed data for 6885 ischemic stroke patients from a multicenter hospital-based stroke registry in Japan who were previously independent and hospitalized within 24 hours of stroke onset. Time of symptom onset was confirmed, and the association between PM (suspended PM and $PM_{2.5}$) and occurrence of ischemic stroke was analyzed by time-stratified case-crossover analysis.

Results—Ambient $PM_{2.5}$ and suspended PM at lag days 0 to 1 were associated with subsequent occurrence of ischemic stroke (ambient temperature–adjusted odds ratio [95% confidence interval] per 10 μg/m^3: suspended PM, 1.02 [1.00–1.05]; $PM_{2.5}$, 1.03 [1.00–1.06]). In contrast, ambient suspended PM and $PM_{2.5}$ at lag days 2 to 3 or 4 to 6 showed no significant association with stroke occurrence. The association between $PM_{2.5}$ at lag days 0 to 1 and ischemic stroke was maintained after adjusting for other air pollutants (nitrogen dioxide, photochemical oxidants, or sulfur dioxide) or influenza epidemics and was evident in the cold season.

Conclusions—These findings suggest that short-term exposure to $PM_{2.5}$ within 1 day before onset is associated with the subsequent occurrence of ischemic stroke. (***Stroke*. 2016;47:3032-3034. DOI: 10.1161/STROKEAHA.116.015303.**)

Key Words: case-crossover ■ particulate matter ■ ischemic stroke ■ risk ■ stroke

The association between ambient concentrations of particulate matter (PM) and cardiovascular disease, particularly coronary heart disease, is well documented and accepted.[1,2] Long-term exposure to PM increases the risk of cardiovascular outcomes, including stroke.[3] Furthermore, short-term exposure to PM may be related to increased risk of stroke mortality and stroke hospitalization.[4] However, whether acute exposure to PM plays a direct causative role in stroke occurrence remains controversial. Moreover, the effects of PM size and timing of exposure on the occurrence of stroke events are unclear.

Fine PM (diameter <2.5 μm [$PM_{2.5}$]) was recently reported to produce significant health problems because of its higher toxicity compared with larger sized PM.[2] However, few studies have investigated the effects of short-term $PM_{2.5}$ exposure on stroke risk, and findings have varied from no[5,6] or nonsignificant associations[7] to positive associations.[4,8,9] Recently published meta-analyses have also reported various associations between $PM_{2.5}$ and ischemic stroke.[10–13] We, therefore, aimed to determine whether short-term exposure to $PM_{2.5}$ was associated with an increased risk of ischemic stroke using the large-scale stroke database of a multicenter registry in Fukuoka Prefecture, Japan.

Methods

Patient and Environmental Data

We analyzed data of 6885 patients (Figure I in the online-only Data Supplement) registered in the Fukuoka Stroke Registry (UMIN Clinical Trial Registry 000000800).[14] Detailed methods are provided in the online-only Data Supplement. We obtained hourly data on air pollutants, including $PM_{2.5}$, suspended particulate matter (SPM), nitrogen dioxide, photochemical oxidants, and sulfur dioxide from the atmospheric environment database of the National Institute for

Received August 31, 2016; final revision received August 31, 2016; accepted September 27, 2016.

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The online-only Data Supplement is available with this article at http://stroke.ahajournals.org/lookup/suppl/doi:10.1161/STROKEAHA.116.015303/-/DC1.

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Table 1. Association Between Particulate Matter and Risk of Ischemic Stroke

	Lag 0–1	Lag 0–2	Lag 0–3	Lag 0–4	Lag 0–5	Lag 0–6
SPM	1.02 (1.00–1.04)	1.01 (0.99–1.04)	1.01 (0.98–1.03)	1.01 (0.98–1.03)	0.99 (0.97–1.02)	0.99 (0.96–1.02)
PM$_{2.5}$	1.02 (0.99–1.05)	1.01 (0.98–1.05)	1.01 (0.97–1.04)	1.00 (0.96–1.04)	0.99 (0.95–1.02)	0.99 (0.95–1.03)

PM indicates particulate matter; and SPM, suspended particulate matter.

Environmental Studies. Meteorologic data on ambient temperatures were obtained from the Japan Meteorological Agency. We also collected data on the weekly influenza incidence from the Japan National Institute of Infectious Diseases.

Statistical Analyses

We performed a case-crossover analysis to evaluate the effects of short-term exposure to PM on ischemic stroke events. We selected control periods using a time-stratified method; that is, 3 or 4 control periods from the same day of the week, month, and year as the case period. We calculated odds ratios (ORs) with 95% confidence intervals of a 10 μg/m^3 increase in PM using a conditional logistic regression model. The multivariate model included concentrations of SPM or PM$_{2.5}$ at all lag periods and ambient temperature. Other copollutants (nitrogen dioxide, photochemical oxidants, or sulfur dioxide) at all lag periods (days 0–1, 2–3, and 4–6) were additionally adjusted for in the 2-pollutant model.[15] P values <0.05 were considered significant.

Results

Patient Characteristics and Environmental Data

The mean±standard deviation age of 6885 subjects was 72.2±11.9 years, 39.4% were women, and 20.5% had a history of ischemic stroke (Table I in the online-only Data Supplement). The mean±SD daily concentrations of ambient SPM and PM$_{2.5}$ were 29.3±16.4 and 20.5±11.2 μg/m^3, respectively (Table II in the online-only Data Supplement).

Association Between PM and Ischemic Stroke

The estimated OR of ischemic stroke was high for SPM or PM$_{2.5}$ at lag 0 to 1 but decreased with longer durations of exposure (Table 1). When PM at lags 0 to 1, 2 to 3, and 4 to 6 were simultaneously included in the multivariate model along with ambient temperature, the ORs of ischemic stroke increased significantly with SPM or PM$_{2.5}$ at lag 0 to 1 but not at lags 2 to 3 or 4 to 6 (Table 2). These associations were unchanged after adjusting for other air pollutants (nitrogen dioxide, photochemical oxidants, or sulfur dioxide).

Sensitivity Analyses

Sensitivity analyses were performed to confirm the robustness of our findings (Table 3). The association was evident during the cold season (November to April) when PM$_{2.5}$ concentration is affected by transboundary air pollution rather than local air pollution emitted at each site. The estimated ORs were strengthened by restricting study subjects to patients admitted to hospitals in Fukuoka city. The trends were essentially unchanged after excluding patients admitted on a national holiday or after additionally adjusting for influenza epidemics.

Discussion

The present study showed that increased ambient PM$_{2.5}$ concentrations within 1 day before stroke onset were associated with the occurrence of ischemic stroke. Fine, rather than coarse, PM may be a particularly important trigger for ischemic stroke (Table IV in the online-only Data Supplement). However, the association between short-term exposure to PM$_{2.5}$ and ischemic stroke remains controversial, and apparent discrepancies may partly be caused by ambiguities in the timing of stroke onset, given that most studies analyzed administrative data that contained information on hospital visit, admission, or mortality, but not time of stroke onset. Variations in PM$_{2.5}$ concentrations, sources or components of PM$_{2.5}$, and measurements of lag time may also contribute to apparent differences.

The estimated OR per 10 μg/m^3 increase in PM$_{2.5}$ in our study (1.03) was in accord with recent meta-analyses of positive results.[10,12] Given that the number of people at risk is large, we cannot discount the health effect of PM$_{2.5}$, despite the relatively small increased risk. We found no evidence for a subtype-specific effect of ambient PM$_{2.5}$ (Results and Table V in the online-only Data Supplement) or any effect modification by patient characteristics (Results and Figures II and III in the online-only Data Supplement). Subjects with any risk factor

Table 2. Association Between Particulate Matter and Risk of Ischemic Stroke

	Lag 0–1	Lag 2–3	Lag 4–6
SPM	1.02 (1.00–1.05)	0.98 (0.96–1.01)	1.00 (0.98–1.02)
Adjusted for NO$_2$	1.03 (1.00–1.05)	0.99 (0.96–1.01)	0.99 (0.97–1.02)
Adjusted for Ox	1.03 (1.00–1.05)	0.99 (0.97–1.02)	1.00 (0.98–1.03)
Adjusted for SO$_2$	1.02 (1.00–1.05)	0.99 (0.96–1.02)	0.99 (0.96–1.02)
PM$_{2.5}$	1.03 (1.00–1.06)	0.98 (0.94–1.01)	1.00 (0.97–1.03)
Adjusted for NO$_2$	1.04 (1.00–1.07)	0.98 (0.94–1.01)	0.98 (0.94–1.02)
Adjusted for Ox	1.04 (1.00–1.07)	0.99 (0.95–1.02)	1.01 (0.97–1.05)
Adjusted for SO$_2$	1.03 (0.99–1.07)	0.97 (0.93–1.02)	0.98 (0.93–1.02)

NO$_2$ indicates nitrogen dioxide; Ox, photochemical oxidants; PM, particulate matter; SO$_2$, sulfur dioxide; and SPM, suspended particulate matter.

Table 3. Sensitivity Analyses for Association Between Particulate Matter and Risk of Ischemic Stroke

	Lag 0–1	Lag 2–3	Lag 4–6
Cold season (n=3529)			
SPM	1.05 (1.02–1.08)	0.98 (0.95–1.01)	1.01 (0.98–1.04)
$PM_{2.5}$	1.07 (1.02–1.12)	0.96 (0.92–1.01)	1.03 (0.98–1.08)
Fukuoka city (n=2543)			
SPM	1.05 (1.01–1.08)	0.95 (0.91–0.98)	1.02 (0.98–1.05)
$PM_{2.5}$	1.07 (1.02–1.12)	0.92 (0.87–0.97)	1.02 (0.97–1.08)
Workday (n=6589)			
SPM	1.02 (1.00–1.05)	0.98 (0.96–1.00)	1.00 (0.98–1.03)
$PM_{2.5}$	1.03 (1.00–1.06)	0.97 (0.94–1.01)	1.00 (0.97–1.04)
Adjusted for influenza epidemics (n=6703)			
SPM	1.02 (1.00–1.05)	0.99 (0.96–1.01)	1.00 (0.97–1.02)
$PM_{2.5}$	1.03 (1.00–1.06)	0.98 (0.95–1.01)	0.99 (0.96–1.03)

PM indicates particulate matter; and SPM, suspended particulate matter.

should, thus, take care during exposure to high $PM_{2.5}$ concentrations, particularly in winter. However, it remains unclear whether avoiding exposure to ambient $PM_{2.5}$ or paying particular attention to health after exposure is actually beneficial.

Our study had several potential limitations. We did not consider the physical activity levels of the patients, and the measured PM concentrations may have been inadequate indices of actual exposure. Furthermore, this study was performed in a limited area of western Japan that is susceptible to transboundary air pollution, and further studies are needed to investigate the generalizability of our findings.

Acknowledgments

We thank all investigators for participating in this study and the clinical research coordinators at the Hisayama Research Institute for Lifestyle Diseases for help in obtaining informed consents and collecting clinical data. We also thank Dr Akinori Takami (National Institute for Environmental Studies) for critical input to this study.

Sources of Funding

This study was supported by Japan Society for the Promotion of Science KAKENHI Grant Nos 24310024, 26293158, and 15K08849 from the Japanese Ministry of Education, Culture, Sports, Science and Technology.

Disclosures

None.

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