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Effects of Asian dust on daily cough occurrence in patients with chronic cough: A panel study

Tomomi Higashi [a,*], Yasuhiro Kambayashi [b], Noriyuki Ohkura [c], Masaki Fujimura [c,i], Satoshi Nakai [d], Yasushi Honda [e], Kiyofumi Saijoh [a], Kazuichi Hayakawa [f], Fumihisa Kobayashi [g], Yoshimasa Michigami [h], Anyenda Enoch Olando [b], Yoshiaki Hitomi [b], Hiroyuki Nakamura [b]

[a] Department of Hygiene, Graduate School of Medical Sciences, Kanazawa University, Takaramachi 13-1, Kanazawa, Ishikawa 920-8640, Japan
[b] Department of Environmental and Preventive Medicine, Graduate School of Medical Sciences, Kanazawa University, Japan
[c] Department of Respiratory Medicine, Cellular Transplantation Biology, Graduate School of Medical Sciences, Kanazawa University, Japan
[d] Graduate School of Environment and Information Sciences, Yokohama National University, Japan
[e] Faculty of Health and Sport Sciences, University of Tsukuba, Japan
[f] Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Japan
[g] College of Science and Engineering, Kanazawa University, Japan
[h] Environment Preservation Center, Kanazawa University, Japan
[i] Respiratory Medicine, National Hospital Organization Nanao Hospital, Japan

HIGHLIGHTS

- *Kosa* is an environmental factor which induces cough in patient with chronic cough.
- A dose–response association was observed between *kosa* and daily cough occurrence.
- The association was stronger among the patients without asthma.
- *Kosa* effect on cough was independent of spherical particles or $PM_{2.5}$.
- The potential time lag effect of *kosa* was observed for up to three days.

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ABSTRACT

Asian dust, known as *kosa* in Japanese, is a major public health concern. In this panel study, we evaluated the effects of exposure to *kosa* on daily cough occurrence. The study subjects were 86 patients being treated for asthma, cough variant asthma, or atopic cough in Kanazawa University Hospital from January 2011 to June 2011. Daily mean concentrations of *kosa* and spherical particles were obtained from light detection and ranging (LIDAR) measurements, and were categorized from Grade 1 (0 μg/m^3) to 5 (over 100 μg/m^3). The association between *kosa* and cough was analyzed by logistic regression with a generalized estimating equation. *Kosa* effects on cough were seen for all Grades with potential time lag effect. Particularly at Lag 0 (the day of exposure), a dose–response relationship was observed: the odds ratios for Grades 2, 3, 4, and 5 above the referent (Grade 1) were 1.111 (95% confidence interval (CI): 0.995–1.239), 1.171 (95% CI: 1.006–1.363), 1.357 (95% CI: 1.029–1.788), and 1.414 (95% CI: 0.983–2.036), respectively. Among the patients without asthma, the association was higher: the odds ratios for Grades 2, 3, 4 and 5 were 1.223 (95% CI: 0.999–1.497), 1.309 (95% CI: 0.987–1.737), 1.738 (95% CI: 1.029–2.935) and 2.403 (95% CI: 1.158–4.985), respectively. These associations remained after adjusting for the concentration of spherical particles or particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$). Our findings demonstrate that *kosa* is an environmental factor which induces cough in a dose–response relationship.

Abbreviations: TSP, Total suspended particulate; PM, Particulate matter; $PM_{2.5}$, particulate matter with an aerodynamic diameter of less than 2.5 μm; LIDAR, Light detection and ranging.

* Corresponding author.
E-mail address: tomotomo@med.kanazawa-u.ac.jp (T. Higashi).

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1. Introduction

The desert dust storms are major contributors to the atmospheric particulate matter (PM) with an aerodynamic diameter of less than 10 μm (PM_{10}). The adverse health effects of desert dust are demonstrated in many reports; The desert dust have relation with cardiac and respiratory mortality (Barnett et al., 2012; Jimenez et al., 2010; Mallone et al., 2011; Perez et al., 2012) and daily hospitalization (Alessandrini et al., 2013). Asian dust, known as *kosa* in Japanese, originates from the Taklamakan and Gobi deserts and the Loess plateau of interior China. The dust is then blown eastwards by the westerly winds to countries such as Korea, Taiwan and Japan (Iwasaka et al., 2003; Minoura et al., 1998). Epidemiological studies show that *kosa* decreases peak expiratory flow values in patients with asthma (Park et al., 2005), and increases the number of hospitalizations and emergency visits through exacerbation of asthma (Kanatani et al., 2010; Yang et al., 2005). These findings are supported by experimental studies in which *kosa* inhalation enhanced allergen-induced airway inflammation in mouse models (Hiyoshi et al., 2005; Ichinose et al., 2008; Lei et al., 2004).

Asthma is a chronic inflammatory airway condition characterized by repetitive coughing, wheezing, dyspnea, reversible airway narrowing, and airway hyperresponsiveness (Ohta et al., 2011). The prevalence of asthma amongst Japanese adults has increased over the past decade (Fukutomi et al., 2010), and the number of patient suffering from chronic cough without wheezing or dyspnea has also increased in recent years. In Japan, most patients in the latter group are diagnosed with either cough variant asthma or atopic cough (Fujimura et al., 2005). Cough variant asthma is a precursor of asthma (Corrao et al., 1979; Irwin et al., 1997), whereas atopic cough is defined as a non-asthmatic bronchodilator-resistant chronic cough associated with atopy (Fujimura et al., 1992).

Chronic cough can result from hypersensitivity to environmental factors such as chemicals, cold air, and smoke (Matsumoto et al., 2012; Ternesten-Hasseus et al., 2011). Our preliminary data indicate that there are significantly more cough-positive patients during *kosa* period than non-*kosa* period among the adult patients with asthma, cough variant asthma, or atopic cough (Higashi et al., in press). In the present study, we assessed the relationship between exposure to *kosa* and cough occurrence among the same subjects by a panel study.

2. Methods

2.1. Subjects

We enrolled adult patients with physician-diagnosed at least one of asthma, cough variant asthma, or atopic cough between January 2011 and June 2011 at the Kanazawa University Hospital, Ishikawa Prefecture, Japan. This study was approved by the Medical Ethics Committee of Kanazawa University. All patients gave informed consent before participating in the study.

Asthma was diagnosed on the basis of the Japan Asthma Prevention and Management Guidelines 2011 (Ohta et al., 2011). Cough variant asthma was diagnosed using the criteria of the Japanese Cough Research Society (Kohno et al., 2006). Atopic cough was diagnosed according to previously reported criteria (Fujimura et al., 1992), which are based on bronchodilator-resistant cough and the resolution of the cough with the use of histamine H1 antagonists and/or inhaled corticosteroids (ICS).

Patients continued to take their usual medications, according to the standard medical treatment of each disease during the study period. Patients with asthma and cough variant asthma took medications such as bronchodilator and/or ICS, and patients with atopic cough took medications such as histamine H1 antagonists and/or ICS. No patient experienced symptoms suggestive of chronic obstructive pulmonary diseases or other potentially confounding cardiorespiratory disorders.

2.2. Surveys

At the first consultation day during the study period, each patient was required to record his/her symptoms in a cough diary every day. The time period of study for each patient was from his/her first consultation day to the end of the study, June 30 for all. To prevent patients dropout based on lack of recording, we asked the patients to show their diary to the doctor when they visited the hospital during the study period. We used the data regarding the presence or absence of cough for analyzing the effects of *kosa* on coughing.

2.3. Measurements

The daily mean concentrations of *kosa* and spherical particles were estimated as described previously (Onishi et al., 2012). Briefly, we used the dust extinction coefficient and the sphere extinction coefficient derived from light detection and ranging (LIDAR) system with a polarization analyzer which distinguishes mineral dust particles that are non-spherical, including *kosa*, from spherical particles by identifying the differences in the shape of the particles (Iwasaka et al., 2004; Shimizu et al., 2004; Sugimoto et al., 2011). We used the data at the Toyama monitoring station (Imizu City, Toyama Prefecture, Japan) which is the nearest, approximately 40 km east, from Kanazawa City. To obtain the daily near-surface extinction coefficients, the 6 h median values in 120–1000 m height areas were averaged over 24 h. The concentrations of *kosa* and spherical particles were calculated by conversion factors from the dust extinction coefficient and the sphere extinction coefficient, respectively (Shimizu et al., 2011; Sugimoto et al., 2013).

The concentrations of particulate matter with an aerodynamic diameter of less than 2.5 μm ($PM_{2.5}$) were monitored at a Mattou monitoring station (Hakusan City, Ishikawa Prefecture, Japan) which is the nearest, approximately 15.5 km west, from Kanazawa City. The temperature and rainfall were measured continuously at a Kodatsuno monitoring station in Kanazawa City.

2.4. Data analysis

To evaluate the effects of *kosa* on cough, we used logistic regression with a generalized estimating equation which is suitable for correlated data in individuals (Janes et al., 2008; Jennrich and Schluchter, 1986; Liang and Zeger, 1986), according to previous reports (Cesaroni et al., 2008; Gehring et al., 2010; Ma et al., 2008). Briefly, in the model of,

$$\text{logit } P(Y_{it} = 1/X_{it}) = \beta_0 + \beta^M X_{it},$$

Y_{it} represent the binary outcome, population average occurrence of cough, for subject *i* at time *t*, and X_{it} represent *kosa* level at time *t*. In a marginal model, $P(Y_{it} = 1/X_{it})$ represent the occurrence of cough as a function of the *kosa* level (Janes et al., 2008; Leisenring et al., 1997; Martus et al., 2004). The marginal parameter, β^M, was estimated using generalized estimating equation with independent working correlation and robust standard errors. We categorized the *kosa* concentration into five grades as follows: Grade 1, equated to 0 μg/m^3; Grade 2, 0–10 μg/m^3; Grade 3, 10–30 μg/m^3; Grade 4, 30–100 μg/m^3; and Grade 5, over 100 μg/m^3. It was reported that the standard threshold of the dust concentration for an Asian dust day was 100 μg/m^3 (Sugimoto et al., 2003). Besides these days, the