



# Impact of air pollution on benign paroxysmal positional vertigo incidence: a retrospective study of the citizens of Seoul, South Korea

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## Abstract

Benign paroxysmal positional vertigo (BPPV) is among the most common inner ear diseases. Although BPPV is one of the most common causes of dizziness, its pathogenesis remains unknown. Air pollutants might reach the middle ear through the eustachian tube and be absorbed into the inner ear through the round window membrane, increasing the risk of BPPV. We investigated the relationship between air pollution and BPPV risk. Data were extracted from the Korean Health Insurance Review and Assessment Service database, which contains health claims information of the entire South Korean population. Variables of interest included the number of patients diagnosed with BPPV in Seoul, South Korea, patients' clinical and demographic characteristics, and osteopenia status. Seoul's daily air pollution indicators, including SO<sub>2</sub>, CO, O<sub>3</sub>, NO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>, were obtained from the Korea Environment Corporation website. Overdispersed Poisson regression analysis was performed. In the multivariable analysis, NO<sub>2</sub> air concentration (ppb) was associated with increased incidence of BPPV. In analysis stratified by gender, levels of NO<sub>2</sub> were associated with increased incidence of BPPV in both men and women. In the analysis stratified by age, NO<sub>2</sub> air concentration was associated with increased incidence of BPPV among all adults over the age of 19 years. In the analysis stratified by osteopenia status, NO<sub>2</sub> was associated with increased incidence of BPPV in patients with and without osteopenia. Air levels of NO<sub>2</sub> were associated with increased incidence of BPPV in the present study. This finding contributes toward a better understanding of BPPV pathogenesis and improved prevention and management of this condition.

**Keywords** Benign paroxysmal positional vertigo · Air pollution · Nitrogen dioxide · Inner ear · Seoul · South Korea

## Introduction

Benign paroxysmal positional vertigo (BPPV) is among the most common causes of dizziness (Strupp and Brandt 2013). In the USA alone, 1–2.4 million patients present annually at a hospital due to BPPV (Hanley et al. 2001; Katsarkas 1999; Schappert 1992). In addition, the lifetime prevalence of BPPV

has been reported as 2.4% (von Brevern et al. 2007). Although BPPV is not associated with any serious central nervous system disorder (Baloh et al. 1987), the dizziness experienced by patients during the course of the disease can cause emotional distress and quality of life deterioration (Park et al. 2019; Roberts et al. 2009). BPPV increases the risk of falls and causes major inconveniences in everyday life (Lopez-Escamez et al. 2005).

BPPV occurs when the otoconia detach from the otolith organ, which is part of the inner ear (Hoseinabadi et al. 2016; Singh and Apeksha 2016). The detachment of the otoconia may be caused by various inner ear diseases or head trauma. It is commonly reported in women, older adults, and patients with osteopenia (Chan et al. 2017; Mizukoshi et al. 1988). However, in most cases, the cause of otoconia detachment from the otolith organ remains unknown. Understanding the risk factors associated with BPPV might help elucidate the mechanisms of its pathogenesis.

The air that enters the nose passes through the nasopharynx before going down the lower airway. The nasopharynx is

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connected to the middle ear through the eustachian tube located behind the nasopharynx; this direct connection means that the inhaled air can affect the middle ear. In fact, several previous studies have revealed an association between air pollution and the risk of otitis media (Bowatte et al. 2018; Girguis et al. 2018; Leach et al. 2020; MacIntyre et al. 2011; Park et al. 2018; Zemek et al. 2010). Going a step further, one notices that the middle ear is connected to the inner ear through a round window membrane, which allows gas exchange to take place between the two structures (Ars 2008). The way the ear is built and thus allows air pollutants to enter the middle and inner ear through the round window membrane and reach the inner ear organs such as the otolith organ, creating a plausible pathway for the development of BPPV.

To the best of our knowledge, no previous studies have examined the association between air pollution and BPPV risk. Elucidating this association might contribute toward the better understanding of BPPV pathogenesis and improved prevention and management of this condition.

## Methods

This study was approved by the institutional review board of Chung-Ang University Hospital (1911-019-16290). The written informed consent requirement was waived for this study, as anonymized data were used. All research was performed in accordance with the tenets of the Declaration of Helsinki.

### HIRA database

South Korea launched a nationwide health insurance system in 1977 and achieved universal coverage of the entire population in 1989. Nearly all of the data collected by the health system are stored in large centralized databases. The Korean Health Insurance Review and Assessment Service (HIRA) database includes information on diagnoses, prescribed procedures and drugs, and personal data (de-identified beneficiary ID, age, sex, and type of insurance, among others) (Kim et al. 2017). The HIRA uses codes from the Korean Classification of Diseases (KCD), which are based on the tenth edition of the International Classification of Diseases and used in diagnostic practice. The database is comprehensive and does not include duplicates as all South Korean residents receive a unique identification number at birth. For the purpose of this study, we obtained claims data recorded from January 1, 2014, to December 31, 2015, for patients diagnosed with BPPV in Seoul, South Korea.

### Study population

Throughout the year 2015, we counted the daily number of patients newly diagnosed with BPPV in Seoul, South Korea.

A positive BPPV diagnosis was defined as follows: a first-time primary diagnosis under KCD code H811 recorded between January 2015 and December 2015. To control for cases of recurrent BPPV, patients were excluded if they had received a diagnosis of BPPV (KCD code H811) between January 2014 and December 2014. Data on the date of diagnosis and patient characteristics at diagnosis (including age, gender, and osteopenia or osteoporosis status) were extracted from the HIRA. Patients were considered to have osteopenia (including osteoporosis) if they had received a diagnosis corresponding to KCD code M80-82 during 1 year prior to their BPPV diagnosis. Seoul 2015 population data, including information on gender and age distribution, were extracted from the Seoul statistical service available online (<https://data.seoul.go.kr/dataService/boardList.do#submenu7>).

### Air pollution indicators

We extracted Seoul's daily air pollution indicators for the period from January 2015 to December 2015, including levels of sulfur dioxide (SO<sub>2</sub>), carbon monoxide (CO), trioxxygen (O<sub>3</sub>), nitrogen dioxide (NO<sub>2</sub>), particulate matter ≤ 10 μm in aerodynamic diameter (PM<sub>10</sub>), and particulate matter ≤ 2.5 μm in aerodynamic diameter (PM<sub>2.5</sub>), from the Korea Environment Corporation website ([https://www.airkorea.or.kr/web/last\\_amb\\_hour\\_data?pMENU\\_NO=123](https://www.airkorea.or.kr/web/last_amb_hour_data?pMENU_NO=123)). These parameters were measured hourly by the National Institute of Environmental Research at 39 monitoring stations across Seoul. The daily average value of each monitoring station represented an arithmetic average of the hourly values. The average daily value for Seoul was calculated by arithmetically averaging daily values obtained from all stations. As the levels of SO<sub>2</sub>, CO, O<sub>3</sub>, and NO<sub>2</sub> were lower than 1 ppm, a unit of ppb was used to facilitate the determination of the effect of changes in SO<sub>2</sub>, CO, O<sub>3</sub>, and NO<sub>2</sub> on the number of BPPV patients. These values were used for analysis.

### Statistical analysis

Overdispersed Poisson regression analysis was performed. First, univariable analysis was performed to identify air pollution indicators associated ( $p < 0.05$ ) with the daily number of new BPPV patients. Then, multivariable analysis was performed with factors that were statistically significant in the univariable analysis. This analysis was performed for the entire sample; subsequently, we performed the same type of analysis on data stratified by gender, age, and osteopenia status. The values of  $\text{Exp}(\beta)$  means incidence rate ratio (IRR). For example, the IRR value of NO<sub>2</sub> is 1.05. This means that the daily number of new BPPV patients will be 1.05 times greater for each 1 ppb of NO<sub>2</sub>. A  $p$  value  $< 0.05$  was considered indicative of statistical significance. Statistical analyses

were performed using the IBM SPSS software version 21.0 (IBM, Armonk, NY, USA).

## Results

In 2015, the total population of Seoul was 10,369,067. Of these, 49,770 people (0.480%) developed BPPV; 1-year gender-specific incidence rate for men was 0.288% ( $n = 14,707$ ), and the corresponding value for women was 0.666% ( $n = 35,063$ ). One-year age-specific incidence rate was the highest among people in their 70s at 1.228% ( $n = 576,397$ ), followed by that among people in their 80s and 60s (Table 1). The monthly distribution of air pollution indicators and the number of newly diagnosed BPPV patients are presented in Fig. 1. The average monthly number of new BPPV diagnoses was 136.3, while the average  $\text{NO}_2$  level was 38.4 ppb (0.0384 ppm). BPPV incidence was the highest in March, which was also the month when  $\text{NO}_2$  levels were the highest (Fig. 1).

The univariable analysis of data from the entire sample revealed an association ( $p < 0.05$ ) between the daily number of new BPPV patients and the levels of CO,  $\text{O}_3$ ,  $\text{NO}_2$ , and  $\text{PM}_{10}$ . In the multivariable analysis, CO ( $p = 0.013$ ; IRR = 0.999; 95% confidence interval [CI]: 0.999, 1.000),  $\text{O}_3$  ( $p = 0.010$ ; IRR = 0.991; 95% CI: 0.984, 0.998),  $\text{NO}_2$  ( $p < 0.001$ ; IRR = 1.013; 95% CI: 1.006, 1.021), and  $\text{PM}_{10}$  ( $p = 0.040$ ; IRR = 1.001; 95% CI: 1.000, 1.003) levels remained independently associated with the number of new BPPV patients. Moreover,  $\text{NO}_2$  and  $\text{PM}_{10}$  levels were associated with the increased incidence of BPPV. In contrast, CO and  $\text{O}_3$  levels were associated with the reduced incidence of BPPV (Table 2).

In the analysis stratified by gender,  $\text{NO}_2$  levels (for men and women, respectively:  $p = 0.005$ ; IRR = 1.007; 95% CI 1.002, 1.011;  $p < 0.001$ ; IRR = 1.013; 95% CI 1.006, 1.021)

were associated with the increased incidence of BPPV among both men and women. Meanwhile, the levels of  $\text{PM}_{10}$  ( $p = 0.043$ ; IRR = 1.001; 95% CI: 1.000, 1.003) were associated with the increased incidence of BPPV among women. Finally, the levels of CO ( $p = 0.027$ ; IRR = 0.999; 95% CI: 0.999, 1.000) and  $\text{O}_3$  ( $p = 0.005$ ; IRR = 0.990; 95% CI: 0.982, 0.997) were associated with the reduced incidence of BPPV among women (Table 3).

In the analysis stratified by age, the levels of  $\text{NO}_2$  were associated with the increased incidence of BPPV among all adults over the age of 19 years ( $p < 0.05$ ). Concurrently, the levels of  $\text{PM}_{10}$  were associated with the increased incidence of BPPV among people in their 50s and 70s ( $p < 0.05$ ). In contrast, the levels of CO were associated with the reduced incidence of BPPV among people in their 30s, 50s, and 70s ( $p < 0.05$ ). Finally, the levels of  $\text{O}_3$  were associated with the reduced incidence of BPPV among children under the age of 10 years and among people in their 30s, 50s, 60s, and 70s ( $p < 0.05$ , Table 3).

In the analysis stratified by osteopenia status, the levels of  $\text{NO}_2$  were associated with the increased incidence of BPPV in patients with and without osteopenia ( $p < 0.001$ ). In contrast, the levels of CO and  $\text{O}_3$  were associated with the reduced incidence of BPPV in patients with and without osteopenia ( $p < 0.05$ , Table 3).

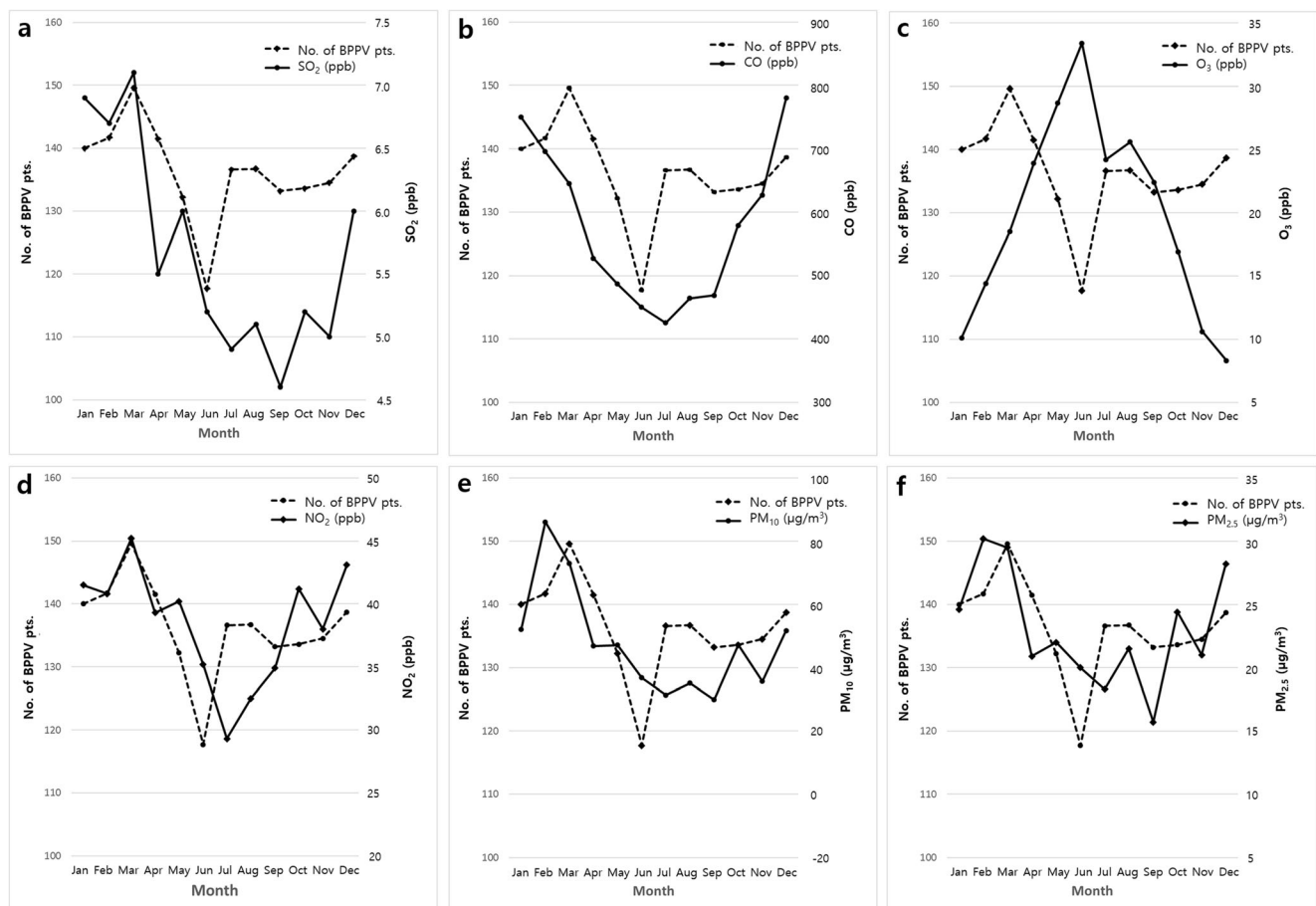
## Discussion

The inner ear is located within the temporal bone and includes a cochlea that processes signals related to sound and semicircular canals and otolith organs that process signals related to balance. While the middle ear is filled with air, the inner ear is filled with fluid including perilymph and endolymph. The

**Table 1** Population distribution and the number of patients diagnosed with BPPV in Seoul

		No. of the population in Seoul	No. of the BPPV pts. in Seoul	Incidence (%; 95% CI)
Gender	Male	5,106,034	14,707	0.288 (0.283, 0.293)
	Female	5,263,033	35,063	0.666 (0.659, 0.673)
Age	0–9	800,462	129	0.016 (0.013, 0.019)
	10–19	1,036,922	1418	0.137 (0.130, 0.144)
	20–29	1,519,585	3978	0.262 (0.254, 0.270)
	30–39	1,757,677	6140	0.349 (0.341, 0.358)
	40–49	1,779,431	8130	0.457 (0.447, 0.467)
	50–59	1,661,155	10,976	0.661 (0.648, 0.673)
	60–69	1,020,389	9958	0.976 (0.957, 0.995)
	70–79	576,397	7078	1.228 (1.200, 1.256)
	80–89	183,204	1819	0.993 (0.947, 1.038)
	≥ 90	33,845	117	0.346 (0.283, 0.408)
Total	10,369,067	49,770	0.480 (0.476, 0.484)	

BPPV benign paroxysmal positional vertigo, pts patients, CI confidence interval



**Fig. 1** Air pollution indicators and the number of new BPPV patients by month. **a** SO<sub>2</sub>. **b** CO. **c** O<sub>3</sub>. **d** NO<sub>2</sub>. **e** PM<sub>10</sub>. **f** PM<sub>2.5</sub>. No, number; BPPV, benign paroxysmal positional vertigo; pts, patients; SO<sub>2</sub>, sulfur dioxide;

CO, carbon monoxide; O<sub>3</sub>, trioxxygen; NO<sub>2</sub>, nitrogen dioxide; PM<sub>10</sub>, particulate matter ≤ 10 µm in aerodynamic diameter; PM<sub>2.5</sub>, particulate matter ≤ 2.5 µm in aerodynamic diameter

inner ear is separated from the middle ear by a round window membrane, which permits the exchange of substances between the inner ear and its environment (Goycoolea and Lundman 1997). In otolaryngology, the round window membrane is used as a channel for administering drugs into the inner ear. For example, in cases of sudden sensorial hearing loss, when cochlear function is suddenly reduced,

corticosteroids are administered into the middle ear. Subsequently, they are absorbed into the inner ear through the round window membrane and restore cochlear function (Mirian and Ovesen 2020). Given this phenomenon, we suspected that air pollutants reaching the middle ear may be absorbed into the inner ear through the round window membrane and induce inner ear disease such as BPPV, which

**Table 2** Association between air pollutants and BPPV incidence: overdispersed Poisson regression analysis

	Univariable analysis			Multivariable analysis		
	<i>p</i> Value	Exp (β)	95% CI	<i>p</i> Value	Exp (β)	95% CI
SO <sub>2</sub> (ppb)	0.053	1.038	1.000, 1.078			
CO (ppb)	0.009	1.000	1.000, 1.001	0.013	0.999	0.999, 1.000
O <sub>3</sub> (ppb)	0.004	0.992	0.987, 0.997	0.010	0.991	0.984, 0.998
NO <sub>2</sub> (ppb)	< 0.001	1.009	1.004, 1.013	< 0.001	1.013	1.006, 1.021
PM <sub>10</sub> (µg/m <sup>3</sup> )	0.018	1.001	1.000, 1.002	0.040	1.001	1.000, 1.003
PM <sub>2.5</sub> (µg/m <sup>3</sup> )	0.071	1.004	1.000, 1.008			

BPPV benign paroxysmal positional vertigo, CI confidence interval SO<sub>2</sub> sulfur dioxide, CO carbon monoxide, O<sub>3</sub> trioxxygen, NO<sub>2</sub> nitrogen dioxide, PM<sub>10</sub> particulate matter ≤ 10 µm in aerodynamic diameter, PM<sub>2.5</sub> particulate matter ≤ 2.5 µm in aerodynamic diameter

**Table 3** Association between air pollutants and BPPV incidence, stratified by gender, age, and osteopenia status: overdispersed Poisson regression analysis

		Univariable analysis			Multivariable analysis		
		<i>p</i> Value	Exp ( $\beta$ )	95% CI	<i>p</i> Value	Exp ( $\beta$ )	95% CI
<b>Gender</b>							
Men ( <i>n</i> = 14,707, 29.5%)	SO <sub>2</sub> (ppb)	0.224	1.025	0.985, 1.066			
	CO (ppb)	0.100	1.000	1.000, 1.001			
	O <sub>3</sub> (ppb)	0.136	0.996	0.991, 1.001			
	NO <sub>2</sub> (ppb)	0.001	1.007	1.003, 1.012	0.005	1.007	1.002, 1.011
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.034	1.001	1.000, 1.002	0.243	1.001	0.999, 1.002
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.142	1.003	0.999, 1.008			
Women ( <i>n</i> = 35,063, 70.5%)	SO <sub>2</sub> (ppb)	0.028	1.043	1.005, 1.084	0.936	0.998	0.942, 1.056
	CO (ppb)	0.003	1.000	1.000, 1.001	0.027	0.999	0.999, 1.000
	O <sub>3</sub> (ppb)	0.001	0.991	0.985, 0.996	0.005	0.990	0.982, 0.997
	NO <sub>2</sub> (ppb)	< 0.001	1.009	1.005, 1.014	< 0.001	1.013	1.006, 1.021
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.016	1.001	1.000, 1.002	0.043	1.001	1.000, 1.003
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.056	1.004	1.000, 1.009			
<b>Age</b>							
0–9 ( <i>n</i> = 129, 0.3%)	SO <sub>2</sub> (ppb)	0.334	1.065	0.937, 1.211			
	CO (ppb)	0.142	1.001	1.000, 1.002			
	O <sub>3</sub> (ppb)	0.014	0.977	0.958, 0.995	0.014	0.977	0.958, 0.995
	NO <sub>2</sub> (ppb)	0.072	1.014	0.999, 1.029			
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.675	0.999	0.993, 1.004			
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.717	0.997	0.982, 1.013			
10–19 ( <i>n</i> = 1418, 2.8%)	SO <sub>2</sub> (ppb)	0.635	1.014	0.958, 1.073			
	CO (ppb)	0.936	1.000	1.000, 1.000			
	O <sub>3</sub> (ppb)	0.391	1.003	0.996, 1.011			
	NO <sub>2</sub> (ppb)	0.059	1.006	1.000, 1.013			
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.510	0.999	0.997, 1.001			
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.964	1.000	0.993, 1.006			
20–29 ( <i>n</i> = 3978, 8.0%)	SO <sub>2</sub> (ppb)	0.802	1.006	0.960, 1.054			
	CO (ppb)	0.277	1.000	1.000, 1.000			
	O <sub>3</sub> (ppb)	0.189	0.996	0.990, 1.002			
	NO <sub>2</sub> (ppb)	0.003	1.008	1.003, 1.013	0.003	1.008	1.003, 1.013
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.169	1.001	1.000, 1.002			
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.521	1.002	0.997, 1.007			
30–39 ( <i>n</i> = 6140, 12.3%)	SO <sub>2</sub> (ppb)	0.080	1.038	0.995, 1.083			
	CO (ppb)	0.004	1.000	1.000, 1.001	0.037	0.999	0.999, 1.000
	O <sub>3</sub> (ppb)	0.003	0.991	0.985, 0.997	0.023	0.991	0.984, 0.999
	NO <sub>2</sub> (ppb)	< 0.001	1.010	1.006, 1.015	< 0.001	1.015	1.007, 1.024
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.061	1.001	1.000, 1.002			
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.095	1.004	0.999, 1.009			
40–49 ( <i>n</i> = 8130, 16.3%)	SO <sub>2</sub> (ppb)	0.010	1.054	1.013, 1.096	0.945	1.002	0.943, 1.064
	CO (ppb)	0.002	1.000	1.000, 1.001	0.362	1.000	0.999, 1.000
	O <sub>3</sub> (ppb)	0.004	0.992	0.986, 0.997	0.183	0.994	0.985, 1.003
	NO <sub>2</sub> (ppb)	< 0.001	1.010	1.006, 1.015	0.001	1.013	1.005, 1.021
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.014	1.001	1.000, 1.003	0.081	1.002	1.000, 1.003
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.031	1.005	1.000, 1.010	0.531	0.997	0.986, 1.007
50–59 ( <i>n</i> = 10,976, 22.1%)	SO <sub>2</sub> (ppb)	0.055	1.039	0.999, 1.080			
	CO (ppb)	0.017	1.000	1.000, 1.001	0.037	0.999	0.999, 1.000

**Table 3** (continued)

		Univariable analysis			Multivariable analysis		
		<i>p</i> Value	Exp ( $\beta$ )	95% CI	<i>p</i> Value	Exp ( $\beta$ )	95% CI
60–69 ( <i>n</i> = 9958, 20.0%)	O <sub>3</sub> (ppb)	0.002	0.992	0.986, 0.997	0.005	0.990	0.983, 0.997
	NO <sub>2</sub> (ppb)	0.002	1.007	1.003, 1.012	0.008	1.010	1.003, 1.018
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.015	1.001	1.000, 1.003	0.024	1.001	1.000, 1.003
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.106	1.004	0.999, 1.008			
	SO <sub>2</sub> (ppb)	0.032	1.045	1.004, 1.087	0.824	1.007	0.948, 1.069
	CO (ppb)	0.007	1.000	1.000, 1.001	0.151	0.999	0.999, 1.000
	O <sub>3</sub> (ppb)	0.002	0.991	0.986, 0.997	0.027	0.990	0.981, 0.999
70–79 ( <i>n</i> = 7078, 14.2%)	NO <sub>2</sub> (ppb)	0.001	1.008	1.003, 1.013	0.010	1.010	1.002, 1.018
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.008	1.002	1.000, 1.003	0.113	1.001	1.000, 1.003
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.042	1.005	1.000, 1.009	0.955	1.000	0.990, 1.011
	SO <sub>2</sub> (ppb)	0.131	1.033	0.990, 1.077			
	CO (ppb)	0.032	1.000	1.000, 1.001	0.009	0.999	0.999, 1.000
	O <sub>3</sub> (ppb)	0.009	0.992	0.986, 0.998	0.010	0.990	0.982, 0.998
	NO <sub>2</sub> (ppb)	< 0.001	1.008	1.004, 1.013	0.001	1.014	1.006, 1.022
80–89 ( <i>n</i> = 1819, 3.7%)	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.018	1.001	1.000, 1.003	0.023	1.002	1.000, 1.003
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.073	1.004	1.000, 1.009			
	SO <sub>2</sub> (ppb)	0.419	1.022	0.970, 1.076			
	CO (ppb)	0.080	1.000	1.000, 1.001			
	O <sub>3</sub> (ppb)	0.071	0.993	0.986, 1.001			
	NO <sub>2</sub> (ppb)	< 0.001	1.012	1.007, 1.018	< 0.001	1.012	1.007, 1.018
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.306	1.001	0.999, 1.002			
$\geq 90$ ( <i>n</i> = 117, 0.2%)	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.453	1.002	0.996, 1.008			
	SO <sub>2</sub> (ppb)	0.199	1.092	0.955, 1.248			
	CO (ppb)	0.373	1.000	0.999, 1.001			
	O <sub>3</sub> (ppb)	0.636	1.005	0.985, 1.025			
	NO <sub>2</sub> (ppb)	0.026	1.018	1.002, 1.034	0.208	1.013	0.993, 1.033
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.051	1.003	1.000, 1.006			
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.044	1.015	1.000, 1.030	0.435	1.008	0.988, 1.028
Osteopenia Yes ( <i>n</i> = 6223, 12.5%)	SO <sub>2</sub> (ppb)	0.058	1.041	0.999, 1.085			
	CO (ppb)	0.017	1.000	1.000, 1.001	0.012	0.999	0.998, 1.000
	O <sub>3</sub> (ppb)	0.002	0.991	0.985, 0.997	0.004	0.987	0.977, 0.996
	NO <sub>2</sub> (ppb)	< 0.001	1.009	1.004, 1.014	< 0.001	1.015	1.007, 1.023
	PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )	0.006	1.002	1.000, 1.003	0.133	1.001	1.000, 1.003
	PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )	0.039	1.005	1.000, 1.010	0.569	1.003	0.992, 1.014
	No ( <i>n</i> = 43,547, 87.5%)	SO <sub>2</sub> (ppb)	0.056	1.037	0.999, 1.077		
CO (ppb)		0.009	1.000	1.000, 1.001	0.018	0.999	0.999, 1.000
O <sub>3</sub> (ppb)		0.005	0.992	0.987, 0.998	0.014	0.991	0.984, 0.998
NO <sub>2</sub> (ppb)		< 0.001	1.009	1.004, 1.013	< 0.001	1.013	1.006, 1.020
PM <sub>10</sub> ( $\mu\text{g}/\text{m}^3$ )		0.024	1.001	1.000, 1.002	0.056	1.001	1.000, 1.002
PM <sub>2.5</sub> ( $\mu\text{g}/\text{m}^3$ )		0.083	1.004	1.000, 1.008			

*BPPV* benign paroxysmal positional vertigo, *CI* confidence interval, *SO<sub>2</sub>* sulfur dioxide, *CO* carbon monoxide, *O<sub>3</sub>* trioxxygen, *NO<sub>2</sub>* nitrogen dioxide, *PM<sub>10</sub>* particulate matter  $\leq 10 \mu\text{m}$  in aerodynamic diameter, *PM<sub>2.5</sub>* particulate matter  $\leq 2.5 \mu\text{m}$  in aerodynamic diameter

might be associated with air pollution. BPPV is among the most common inner ear diseases; it presents with specific symptoms and follows clear diagnostic criteria, making it

relatively easy to identify and study. Consequently, these observations and considerations resulted in a hypothesis that air pollution might affect BPPV incidence.

For the consistency of the analysis of air pollution indicators, we restricted our study to one city, Seoul, which is the capital of South Korea with an area of 605.2 km<sup>2</sup> and a population of 10,369,067 people. We extracted daily BPPV incidence data from the HIRA database, which stores information on health insurance claims for the entire South Korean population, covered by universal health insurance. Based on this database, we were able to obtain correct BPPV incidence. Given the small number of countries worldwide with national insurance systems, this type of study is rare and only possible in select countries, making the present findings particularly valuable.

In the present study, the overall 1-year incidence of BPPV was 0.48%, which was comparable to that reported in a previous study, estimated at 0.6% (von Brevern et al. 2007). In addition, consistent with previous studies, in the present study, the incidence of BPPV was higher among women than among men and among older adults than among younger adults (Mizukoshi et al. 1988).

Among air pollutants, NO<sub>2</sub> was most strongly associated with the increased incidence of BPPV in the overall sample as well as in the analysis stratified by gender, age, and osteopenia status. When the entire sample was analyzed, the IRR of NO<sub>2</sub> was 1.013. This means that with an increase of 1 ppb (0.001 ppm) of NO<sub>2</sub>, the daily number of new BPPV patients increases by 1.3%. The association between NO<sub>2</sub> and otitis media has been reported in several previous studies (Aguilera et al. 2013; Brauer et al. 2006; MacIntyre et al. 2014; Zemek et al. 2010), suggesting that air-borne NO<sub>2</sub> can reach the middle ear. Sasa et al. measured the perilymphatic oxygen tension after insufflation of oxygen to the round window membrane. They reported the increase of the oxygen tension in the inner ear, suggesting that gas in the middle ear can penetrate into the inner ear through the round window (Sasa et al. 1989). Given that gas exchange between the middle and inner ear occurs through the round window membrane that is easily permeable to molecules smaller than 45 Da (Ars 2008), which is approximately the molecular weight of hydrophilic NO<sub>2</sub> (46 Da), it is plausible that NO<sub>2</sub> permeates into the inner ear and dissolves in its fluid such as perilymph and endolymph. In the process, NO<sub>2</sub> becomes acidic, likely increasing perilymph and endolymph acidity. A previous study has shown that the degeneration of the otoconia is more likely to occur when the surrounding environment becomes acidic (Walther et al. 2014). The degeneration of the otoconia may weaken its attachment to the otolith organs, resulting in its detachment. Consequently, the elevated levels of NO<sub>2</sub> may facilitate otoconia detachment, triggering BPPV. Further research should test this hypothesis.

In the overall sample analysis, the levels of PM<sub>10</sub> were associated with increased BPPV incidence. Sub-group analysis revealed that this association was present among women rather than men and among people in their 50s and 70s rather than among other age groups. It was associated in women and older adults who are at an increased risk of BPPV. However, since

the IRR of PM<sub>10</sub> was low as 1.001 or 1.002, it is not thought to have a significant impact on the incidence of BPPV.

For all BPPV patients, CO and O<sub>3</sub> were associated with the reduced incidence of BPPV. Moreover, the levels of CO and O<sub>3</sub> were associated with the lower incidence of BPPV in women and some age groups. It is difficult to determine the exact mechanism by which CO and O<sub>3</sub> levels may reduce BPPV incidence. However, it is plausible that this association is indirect and mediated by the population's reduced activity when air pollution is particularly high.

This study has some limitations. First, there might be a discrepancy between BPPV diagnosis and occurrence date. However, the onset of BPPV is associated with symptoms so severe that patients tend to visit a hospital right away. As a major metropolitan area, Seoul has plenty of hospitals, which combined with universal health insurance facilitates access to healthcare and improves the quality of incidence estimates. Given the distinct features and straightforward diagnostics of BPPV, this condition can be confirmed quickly and easily in an outpatient setting and without complex or invasive tests. As a result, it is unlikely that any discrepancies exist between the data of BPPV onset and that of diagnosis in this dataset. Second, this study is based on epidemiological data. Therefore, the results of this study alone cannot fully elucidate the mechanism behind this phenomenon. Additional research, including animal experiments, is needed to compensate for this.

Several previous studies were conducted on the effects of air pollution on respiratory health and the risk of otitis media (Guan et al. 2016; Khilnani and Tiwari 2018; MacIntyre et al. 2014; Zemek et al. 2010). However, this is the first study to report on the effects of air pollution on the incidence of inner ear disease. This study is the first to show that air pollution may increase the incidence of BPPV. These findings contribute toward a better understanding of BPPV pathogenesis and improved prevention and management of this condition. In addition, these findings provide foundational evidence on the range of diseases triggered by air pollution, helping to expand this field of study.

**Authors' contributions** Seog-Kyun Mun: Writing, Investigation. Seung Ri Oh: Writing, Methodology. Bo Ram Yang: Writing, Methodology. Seung-Ha Oh: Writing—Review and Editing. Munyoung Chang: Project administration, Writing, Supervision. All authors have given approval to the final version of the manuscript.

**Data availability** The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval** The study was reviewed and approved by the Institutional Review Board of Chung-Ang University Hospital.

**Consent to participate** Not applicable.

**Consent to publish** Not applicable.

**Conflict of interest** The authors declare no competing interests.

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