The Assessment of Air Pollution Exposure and Paracetamol Use Related to Children Allergic Disease: A Population-Based Cohort Study in Taiwan

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In Taiwan, there are nearly 70 % people living in the urban areas which have more serious air pollution year by year. It causes that the prevalence of children allergic disease increases every year. Recently, there are many studies showing that air pollution is a significant risk factor to cause allergic disease. In Taiwan, paracetamol is the most common drug to decrease pain, because paracetamol causes less stomach irritation than aspirin. But there are some studies showing that paracetamol is a risk factor of allergic disease. The objective of this study is to assess air pollutants exposure and paracetamol use related to children allergic disease. There were two databases used in this study: 1) Longitudinal Health Insurance Database 2005 (LHID2005) and 2) Environmental Protection Agency (EPA) air monitoring database. Geographic Information Systems (GIS) was used in estimating air pollution exposure. Paracetamol use and children allergic disease records were collected by LHID2005. Furthermore, we used cox proportion regression models to estimate the relationship between air pollution, paracetamol use and children allergic disease. The results showed that air pollution and paracetamol use individually increased the risk of children allergic disease. Furthermore, patients who were using paracetamol and exposed to air pollution had more serious effects on children allergic disease. It is necessary to protect children from the adverse effects of air pollution, especially considering the potential interaction with paracetamol use.

Keywords: Children allergic disease; Paracetamol; Air pollution; Longitudinal Health Insurance Database 2005(LHID2005)

Introduction

Asthma is an important issue in public health. In allergic diseases, asthma, allergic rhinitis and eczema are related with air pollution exposure in early life. In Taiwan, air pollution is very serious and the incidence of allergic diseases increases year by year. It causes huge burden of medical expenses. Therefore, how to verify the epidemiological risk factors for asthma may be especially important. The air pollution exposure will increase the amount of inflammatory substances in the human respiratory tract and increase the risk of asthma and respiratory diseases. Recent studies indicated that paracetamol drug usage will also cause respiratory tract inflammation, and induce asthma and respiratory diseases.

Objective

The objective of this study was to investigate the effect of air pollution exposure and paracetamol drug usage in early life (before one year old) on asthma incidence during childhood.

Methods

This study was a retrospective cohort study. Children who were born form 2000 to 2004 and exposed to air pollution and postnatal paracetamol drug usage before one year old was followed up to ages 7-11. This study collected the children's asthma data and assessed their residence code thought primary health care outpatient visit location by Longitudinal Health Insurance Database 2005 (LHID2005). We estimated air pollutants concentration by Geographic Information Systems (GIS) with air quality monitoring stations in Taipei. Furthermore we used the nearest 12 monitoring stations to calculate every district's air pollutants concentration in Taipei by Inverse Distance Weighting (IDW). At last, we recorded children's paracetamol usage in exposure period by LHID 2005.

To estimate the risk of asthma related to air pollution and paracetamol drug usage,

we used Cox Proportional Hazard Regression Models and adjusted gender, antibiotic, household income, temperature and relative humidity.

Result

Table 1 showed the demographic variables in this study. There were 10.87% children developing asthma. More than 60% children had paracetamol exposure in our study in Taipei. Table 2 showed the Spearman's rank correlation coefficient between air pollutants. There was high positive correlation coefficient between PM_{10} and $PM_{2.5}$. In addition, there was negative correlation between O_3 and other air pollutants. The effect of air pollutants and paracetamol use on developing asthma showed in table 3 The significant interaction effect was found between PM_{10} and paracetamol, and $PM_{2.5}$ and paracetamol. There was higher risk of children having both paracetamol use and air pollution exposure. Two pollutants model showed that $PM_{2.5}$ was significantly related to asthma only among children with paracetamol use after adjusting O_3 and CO (Table 5).

Discussion and Conclusion

In our finding, air pollution and paracetamol use were both related to children asthma in Taipei. Furthermore, PM_{10} and $PM_{2.5}$ have more consistent results. Paracetamol use also has significant interaction effect with PM_{10} and $PM_{2.5}$ on developing asthma. The strengths of this study are having complete and comprehensive drug usage record through LHID 2005. Our subjects are more than 10,000 children. LHID2005 is based on the all population in Taiwan. It may reduce the possibility of selection bias. However our limitation includes no other environmental factors like dust, pollen and second hand cigarette exposure in children early life. Because there aren’t collected in LHID and no national survey data.

In conclusion, children early life exposed to air pollutants and paracetamol will have significant impacts on the occurrence of asthma. Paracetamol is popular used.

Avoiding exposure to air pollution during paracetamol use can be important. Wearing masks in order to reduce air pollution damage to the respiratory tract of children and taking public transportation to reduce air pollutant from traffic are suggested.

Table 1. Characteristic of study population with asthma in Taipei.

Characteristics	Total		Female		Male		High urbanization level		Mild urbanization level	
	N	(%)	N	(%)	N	(%)	N	(%)	N	(%)
	11,447	(100.00)	5,440	(47.52)	6,007	(52.48)	9,233	(80.57)	2,224	(19.43)
Asthma										
With	1,244	(10.87)	523	(9.61)	721	(12.00)	1,016	(11.02)	228	(10.25)
Without	10,203	(89.13)	4,917	(90.39)	5,286	(88.00)	8,207	(88.98)	1,996	(89.75)
Paracetamol										
Yes	7,311	(63.87)	3,282	(60.33)	4,029	(67.07)	5,889	(63.85)	1,422	(63.94)
No	4,136	(36.13)	2,158	(39.67)	1,928	(32.93)	3,334	(36.15)	802	(36.06)
Antibiotic										
Yes	4,071	(35.57)	1,771	(32.56)	2,300	(38.30)	3,202	(34.72)	869	(39.09)
No	7,375	(64.43)	3,669	(67.44)	3,706	(61.70)	6,021	(65.28)	1,354	(60.91)
Birth year										
2000’s	2,917	(25.48)	1,418	(26.07)	1,499	(24.95)	2,337	(25.34)	580	(26.08)
2001’s	2,356	(20.58)	1,150	(21.14)	1,206	(20.08)	1,886	(20.45)	470	(21.13)
2002’s	2,147	(18.76)	1,008	(18.53)	1,139	(18.96)	1,742	(18.89)	405	(18.21)
2003’s	2,096	(18.31)	971	(17.85)	1,125	(18.73)	1,698	(18.41)	398	(17.90)
2004’s	1,931	(16.87)	893	(16.42)	1,038	(17.28)	1,560	(16.91)	371	(16.68)

Table 2. Correlation coefficients of ambient air pollutants average concentration during exposure period.

	PM_{10}	$PM_{2.5}$	NO	NO_2	NO_X	O_3	CO	SO_2	RH	Temp
PM_{10}	1	0.87	0.49	0.72	0.62	-0.61	0.20	0.66	-0.20	-0.01
$PM_{2.5}$		1	0.24	0.59	0.41	-0.14	0.11	0.65	-0.32	0.07
NO			1	0.78	0.93	-0.63	0.36	0.18	0.45	0.13
NO_2				1	0.92	-0.64	0.36	0.49	0.17	0.26
NO_X					1	-0.69	0.41	0.34	0.33	0.19
O_3						1	-0.27	-0.16	-0.53	-0.29
CO							1	-0.04	0.10	0.32
SO_2								1	-0.21	0.15
RH									1	-0.14
Temp										1

Temp：temperature ; RH：relative humidity ; All P-value < 0.001

Table 3. The hazard ratios and interaction term between air pollution and drug use for asthma children in Taipei.

Pollutant	Model 1 (Main Effect)						Model 2
	Air pollutants	*β*	*p*-value	Paracetamol	*β*	*p*-value	*p*-value for Interaction term
PM_{10}	1.02 (1.00-1.03)	0.015	0.05	1.23 (1.09-1.39)	0.209	<0.001	0.03
$PM_{2.5}$	1.01 (0.98-1.04)	0.008	0.64	1.24 (1.09-1.40)	0.211	<0.001	0.02
NO	1.01 (1.00-1.02)	0.010	0.03	1.23 (1.09-1.40)	0.211	<0.001	0.41
NO_2	1.02 (0.99-1.05)	0.018	0.20	1.24 (1.10-1.40)	0.213	<0.001	0.10
NOx	1.01 (1.00-1.02)	0.008	0.04	1.24 (1.09-1.40)	0.211	<0.001	0.26
O_3	1.04 (1.01-1.08)	0.040	0.02	1.23 (1.09-1.39)	0.206	0.001	0.29
CO	1.10 (0.98-1.23)	0.091	0.12	1.23 (1.09-1.39)	0.209	<0.001	0.99
SO_2	1.12 (1.01-1.24)	0.113	0.03	1.23 (1.09-1.39)	0.206	0.001	0.15

Model 1: Without interaction term and adjusted sex, temperature, relative humidity, antibiotic and birth year.

Model 2: With interaction term

Table 4. Adjusted association between air pollution (per unit in exposure period) and drug use for asthma children: single-pollutant models in Taipei.

Pollutant	Drug exposure (Adjusted HR, 95% CI)		
	All cases	With Paracetamol	Without Paracetamol
PM_{10}	1.02 (1.00-1.03)	1.02 (1.01-1.04)	1.00 (0.97-1.03)
$PM_{2.5}$	1.01 (0.99-1.04)	1.03 (0.99-1.07)	0.96 (0.91-1.02)
NO	1.01 (1.00-1.02)	1.01 (1.00-1.02)	1.01 (0.99-1.03)
NO_2	1.02 (0.995-1.05)	1.03 (0.998-1.06)	1.00 (0.96-1.05)
NOx	1.01 (1.00-1.02)	1.01 (1.00-1.02)	1.01 (0.99-1.02)
O_3	1.04 (1.01-1.08)	1.03 (0.99-1.07)	1.06 (0.997-1.13)
CO	1.11 (0.99-1.24)	1.13 (0.99-1.28)	1.04 (0.82-1.31)
SO_2	1.12 (1.02-1.24)	1.13 (1.00-1.28)	1.07 (0.89-1.29)

All models adjusted sex, temperature, relative humidity, antibiotic and birth year.

Table 5. Adjusted association between air pollution (per unit in exposure period) and drug use for asthma children: two-pollutant models for $PM_{2.5}$ in Taipei.

Pollutant	Drug exposure (Adjusted HR, 95% CI)		
	All cases	With Paracetamol	Without Paracetamol
$PM_{2.5}$ With NO	0.996 (0.97-1.02)	1.02 (0.98-1.05)	0.95 (0.91-1.00)
$PM_{2.5}$ With NO_2	0.99 (0.95-1.03)	1.01 (0.97-1.06)	0.94 (0.87-1.00)
$PM_{2.5}$ With NOx	0.99 (0.96-1.02)	1.01 (0.98-1.05)	0.94 (0.89-0.997)
$PM_{2.5}$ With O_3	1.03 (0.99-1.06)	1.05 (1.01-1.09)	0.98 (0.92-1.04)
$PM_{2.5}$ With CO	1.01 (0.98-1.04)	1.03 (1.00-1.06)	0.96 (0.92-1.01)
$PM_{2.5}$ With SO_2	0.99 (0.96-1.02)	1.01 (0.97-1.06)	0.94 (0.89-1.00)

All models adjusted sex, temperature, relative humidity, antibiotic and birth year.