

Occupational Asthma in Korea

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Occupational asthma (OA) is the leading occupational respiratory disease. Cases compensated as OA by the Korea Workers' Compensation and Welfare Service (COMWEL) (218 cases), cases reported by a surveillance system (286 cases), case reports by related scientific journals and cases confirmed by the Occupational Safety and Health Research Institute (OSHRI) over 15 yr from 1992 to 2006 were analyzed. Annual mean incidence rate was 1.6 by compensation and 3.5 by surveillance system, respectively. The trend appeared to increase according to the surveillance system. Incidence was very low compared with other countries. The most frequently reported causative agent was isocyanate followed by reactive dye in dyeing factories. Other chemicals, metals and dust were also found as causative agents. OA was underreported according to compensation and surveillance system data. In conclusion, a more effective surveillance system is needed to evaluate OA causes and distribution, and to effectively prevent newly developing OA.

Key Words: Occupational Asthma; Incidence; Causative Agent; Korea; Isocyanates; Surveillance System

INTRODUCTION

Asthma is a disease presenting with reversible and repeated symptoms, such as wheezing, dyspnea, chest tightness and cough due to increased bronchial responsiveness from chronic inflammation in the respiratory tract (1). Occupational asthma (OA) is a type of asthma originating from the working environment, and is the most common occupational respiratory disease (2). OA is especially important because it can lead to respiratory disturbance and restrict economic activity by developing in a young and healthy population. More than 300 causative agents of OA have been documented (3), and the number is increasing due to the introduction of new chemicals. The detection of occupational causative agents and reduction or elimination of exposure to such agents can prevent OA.

Although estimates vary, occupation-related adult-onset asthma in a normal population was reported to be 2% in the United States (4) and 15% in Japan (5), and a recent study in 13 European countries reported an OA prevalence of 10-25% (6). A recent systematic analysis of all reports in the world indicated that 15-20% of adult-onset asthma was caused by occupational exposure (7). In Korea, new cases of OA are being reported every year since the first OA case due to inhaled polyurethane was reported in 1978, and a study at a university hospital reported 3.9% of adult-onset asthma cases were OA (8).

The aim of this study was to examine the incidence and the trend of OA in Korea for 15 yr (1992-2006) through compensation data from the Industrial Accident Compensation Insurance

(IACI) Act and regional and national OA surveillance system data; and to understand the causative agents and prevalence of OA in Korea through literature and deliberations of occupational cases by the Occupational Safety and Health Research Institute (OSHRI).

MATERIALS AND METHODS

Annual incidence and trend of OA

In order to understand the incidence and trend of OA in Korea, workers' compensation data between 1992 and 2006 and 1999-2006 data from regional and national OA surveillance systems were analyzed (surveillance system was initiated in 1999).

OA data by industrial accident compensation insurance (1992-2006)

Workers in workplaces with less than 5 employees were not covered by the IACI Act before 2000, but from 1 July 2000 all workplaces with one or more employees have been covered. Any workplaces is covered by IACI regardless of employment type or work type, e.g. contract workers, temporary workers, day laborers, part-timers, trainees, student apprentices, workers on overseas business trips, migrant workers (including illegal residents) and labor union full-timers.

The article No. 34 of the IACI Act specifies the diagnostic criteria of occupational diseases. More specifically, it stipulates in the attached document of the Enforcement Decree that occupational asthma conforms to 'poisoning from chemicals or symptoms originating therefrom', particularly 'poisoning from diiso-

cyanates or symptoms originating therefrom': when asthma symptoms develop during work, and a specific antigen for the causative agent is detected, a peak expiratory flow rate (PEFR) changes by work and the methacholine challenge test is positive, or the challenge test with a causative agent is positive, the bronchial asthma is compensated by IACI. Cases asking for compensation are submitted to and judged by the Regional Headquarters and Branches of the Korea Workers' Compensation and Welfare Service (COMWEL) with the help of advisory doctors. OSHRI and university institutions are entrusted with epidemiological investigation when needed.

Data from the OA surveillance system (1999-2006)

OSHRI has started to support regional surveillance systems (Incheon, Gumi, Busan/Ulsan/Gyeongnam) since 1999, and a nationwide 'OA Surveillance System' since 2004. In the Surveillance System, OA was defined according to the criteria developed by the National Institute for Occupational Safety and Health (NIOSH) and used in the surveillance systems of 6 states in the US: when a case satisfies A and B, and meets one or more of any criteria of C described below, it is defined as OA.

- A. Healthcare professional's diagnosis is consistent with asthma.
- B. An association between symptoms and work is observed.
- C. Meets one or more of any of the following:
 - ① Positive response to non-specific challenge test (methacholine challenge test)
 - ② Work-related changes in serially measured forced expiratory volume in 1 second (FEV1) or peak expiratory flow rate (PEFR)
 - ③ Work-related changes in bronchial responsiveness as measured by serial nonspecific inhalation challenge testing
 - ④ Positive response to specific inhalation challenge testing with an agent to which the patient has been exposed at work

Allergologists and respiratory physicians were the core source of information in the OA Surveillance System, and data from occupational physicians who diagnose occupational diseases at outpatient clinics for occupational medicine in hospitals, regional surveillance centers, and compensated cases by COMWEL, were also used. Regional (1999-2003) and national (2004-2006) surveillance system data were analyzed.

Estimation of the incidence rate

Annual incidence was calculated by dividing (annual number of cases recognized for medical care for OA and number of cases reported by the surveillance system) with (total number of workers covered by the IACI), and presented as incidence per year per million workers. For the annual mean incidence of cas-

es compensated by IACI, the mean number of workers covered by IACI and the mean number of cases during 1992-2006 were used. Likewise, the mean during 1999-2006 was used for the annual mean incidence of cases reported by the surveillance system.

Causative agents and prevalence of OA in Korea

Causative agents for OA in Korea were examined through surveillance system data, cases reported in scientific journals, and cases definitely diagnosed as OA by OSHRI through epidemiological investigation.

OA cases reported by the surveillance system

OA reported by the surveillance system were classified into being definitely, probably, possibly, and questionably work-related, and all cases were analyzed in this study regardless of the extent of work-relatedness.

OA cases reported in scientific journals in Korea

When diagnosing OA in clinical practice, allergologists and respiratory physicians at hospitals report characteristic cases (such as an asthma from newly discovered asthma-causing agent) in the Korean Journal of Asthma, Allergy and Clinical Immunology, and sometimes in the Korean Journal of Occupational and Environmental Medicine, the Korean Journal of Preventive Medicine, and the Korean Journal of Internal Medicine.

OA cases deliberated by OSHRI

When entrusted with work-related disease deliberation by COMWEL, OSHRI appoints a physician responsible for epidemiological investigation, and decides on the direction of examination through meetings. Then OSHRI conducts literature searches, and through interviews with the worker or his/her guardian and related persons, identifies the past history, possible hazardous factors, presence or absence of similar cases and information on colleagues. In the case of an indefinite medical diagnosis, health status and asthma diagnosis of the worker are verified through the physical examination by OSHRI itself or blood test, pulmonary function test, skin prick test, non-specific (methacholine) bronchial challenge test by a university hospital specialized in the relevant area and entrusted under consultation with COMWEL. In addition, asthma induction by workplace hazards is identified by the specific bronchial challenge test, and work-relatedness is verified by measuring the PEFR at a workplace. The acceptance of OA is determined by the Committee on Occupational Disease Judgement after careful consideration of all results and data.

Prevalence of OA by hazard as reported in Korean publications

Studies on the prevalence of workers exposed to specified OA causative agents or working in specified job categories were ex-

amined in Korean literature.

RESULTS

Incidence rate and trend of OA over 15 yr

Total number of compensated OA cases as accepted by COMWEL during 1992-2006 was 216. Annual incidence rates were 0.5-2.6 per million workers, and the mean incidence rate over the 15 yr was 1.6. Number of annual cases was less than 20 before the year 2000, more than 20 from 2000-2004, and decreased again since 2004 (Fig. 1).

Total number of OA cases reported by the regional and national surveillance systems during 1999-2006 was 286. Mean number of cases over the 8 yr was 35.8, with the mean incidence rate of 3.5 per million workers. The annual incidence rates were 2.2-4.9 (Fig. 1).

Since 2000 when IACI coverage was expanded from workplaces employing 5 or more workers to workplaces employing 1 or more workers, number of compensated cases rapidly increased. Compensated cases by COMWEL were 4 in 1997, increased to 25 in the early 2000s, trended downward again after that. In contrast, the surveillance system data showed as few as 20 cases in 2003, but this may have been due to the reduction of the regional surveillance system. Number of cases by the surveillance system increased again to 39 with the start of the national surveillance system in 2004, and to as many as 54 in 2005 (Fig. 1). The incidence rate by the surveillance system and by compensation data differed by more than two-fold.

OA causative agents in Korea

In surveillance system data, isocyanates accounted for 69 cases (52.3%). Other causative agents were: reactive dye (10 cases),

heavy metals (8 cases), wood dust (6 cases), chemicals (8 cases), organic solvents (paint in 5 cases and glue in 2 cases), and others (24 cases).

Isocyanates accounted for 50% (38 of 76 cases) of the OSHRI-deliberated cases followed by reactive dye (11 cases). Other causative agents included welding fumes, heavy metals (e.g. chromium and nickel), various chemicals, and dust (Table 1).

By industry category, isocyanate-related OA cases were most frequently reported in the furniture manufacturing industry,

Table 1. Causative agents of occupational asthma by OSHRI

Causative agents	Male	Female	No. of cases	%
Chemical	45	17	62	81.4
Isocyanate	21	17	38	50.0
Reactive dye	11	0	11	14.5
Latex	3	0	3	3.9
Azodicarbonamide	2	0	2	2.6
Formaldehyde	2	0	2	2.6
Phthalate	1	0	1	1.3
Dichlorofluoroethane	1	0	1	1.3
Cashew (paint)	1	0	1	1.3
Solvent	1	0	1	1.3
Exhaust	1	0	1	1.3
PASTE	1	0	1	1.3
Metal	7	0	7	9.2
Welding fumes	4	0	4	5.3
Nickel (fumes)	1	0	1	1.3
Cobalt	1	0	1	1.3
Aluminum	1	0	1	1.3
Wood dust	1	0	1	1.3
Cotton dust	0	1	1	1.3
Grain dust	1	0	1	1.3
Paper dust	0	1	1	1.3
Organic dust	1	0	1	1.3
Undetermined	2	0	2	2.6
Total	57 (75%)	19 (25%)	76	100.0

OSHRI, Occupational Safety & Health Research Institute.

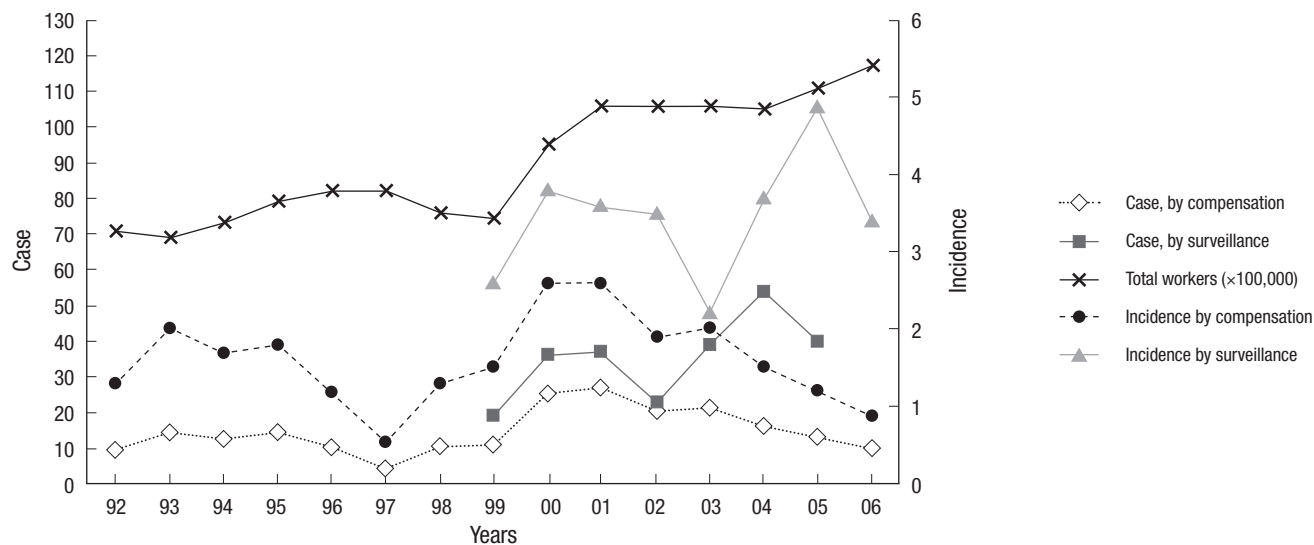


Fig. 1. Incidence and number of cases of occupational asthma as detected by compensation and surveillance system, 1992-2006. Incidence means cases per million workers.

Table 2. Industry category, job category and form of exposure in 38 isocyanates exposure cases

Industry category	Job category	Form of isocyanates exposure
Furniture manufacturing (14)	Factory managing (1)	Urethane paint (28)
Musical instrument manufacturing (4)	Glossing (1)	Glue (5)
Machinery manufacturing (1)	Machinery assembling (1)	Hardener (1)
Wood industry (2)	Painting (12)	Raw material (1)
Wood facility (1)	Wood processing (2)	Urethane resin (1)
Wooden products manufacturing (1)	Mixing (1)	MDI powder (1)
Sewing machine manufacturing (1)	Cleaning (1)	
Sprayer manufacturing (1)	Grinding (10)	
Textile products (1)	Linking width (1)	
Automobile parts (1)	Glueing (1)	
Artificial leather (2)	Assembling (1)	
Automobile industry (1)	Coating (2)	
Automobile mechanics (1)	Sheet metal making (1)	
Automobile manufacturing (2)	TPU manufacturing (1)	
Electronic machinery manufacturing (1)		
Sack manufacturing (1)		
Plastics (1)		
Chemical products manufacturing (2)		

and by job category, painting and grinding. The most common form of isocyanates exposure was urethane paint (Table 2).

OA cases from reactive dye occurred mostly in workers who directly handled reactive dye. A case of treating waste water from workplaces using reactive dye, and 2 cases of in workplaces near a dye manufacturing factory were also reported (Table 3).

Reports from OSHRI and related scientific journals found various new causative agents from 1992 to 2006. In 1992, heavy metals including nickel and chromium were newly reported as OA causative agents, and asthma due to an antibiotic in a pharmaceutical company was reported. Yearly reports include: in 1993, asthma due to ascidian, a macromolecular agent; in 1994, asthma due to licorice (an oriental medicine material) and aluminum; in 1996, Japanese cedar; in 1997, 7-Aminocephalosporanic acid (a cephalosporin antibiotic precursor); in 1998, tobacco, latex, exhaust gas, and dichlorofluoroethane; in 1999, macromolecular agents including *Ganoderma incidum karst* spore and *Metatetranychus citri*, and terephthaloyl chloride; in 2000, various agents including pig pancreas extract (used as a digestive), curry powder, oriental medicine material, cashew paint, and cotton dust; in 2001, organic, paper and dust; in 2002, cefteram pivoxil powder (a cephalosporin antibiotic) in a pharmaceutical company, cobalt, formaldehyde, PASTE (a material used in glass testing); in 2003, phthalic anhydride and aminocephalosporanic thiazine (an antibiotic precursor); in 2004, azodicarbonamide and wood dust; and in 2005, pronase powder and cyanoacrylate. No new causative agents were reported

Table 3. Industry category, job category and form of exposure in 11 reactive dye exposure cases

Industry category	Job category	Form of reactive dye exposure
Dye manufacturing (11)	Dyeing (8)	Dye (11)
	Treating the waste water of dye manufacturing factory (1)	
	Workers at workplace near dye manufacturing factory (2)	

in 2006 (Table 4).

As reported in literature, the prevalence of OA in workers exposed to pharmaceutical powder was 34.4%; in workers exposed to toluene diisocyanate (TDI), 0.58-21.6%; reactive dye, 5.9%; grain dust, 14%; phthalic anhydride, 6.7%; and bakery worker, 5% (Table 5).

DISCUSSION

Since Ramazzini, the father of Occupational Medicine, observed and reported shortness of breath and urticaria in grain carriers exposed to organic dust in 1713, more than 300 OA causative agents have been determined (3). In Korean workplaces, all of these agents are widely used. In addition, new techniques and chemicals continuously introduced to workplaces will maintain the concern for OA.

Both the IACI and the surveillance system data demonstrated very low incidence rates of OA in this study. According to IACI data, the incidence was about 10 per million workers until the late 1990s, increased to approximately 20 in 2000s, and showed a downward trend again. This may be because exposure levels of hazardous substances have decreased recently, owing to improved working environment in spite of various kinds of hazardous substances. In addition, substitution for hazardous substances, e.g., substituting TDI, a major asthma causative agent, for less reactive methylene diphenyl diisocyanate (MDI) may be another reason for the downward trend. A review reported a clear downward trend of TDI-induced asthma worldwide (9). However, in Korea, it is hard to conclude that a decrease in cases according to IACI data reflects an actual decrease in OA, because the number of cases reported by the surveillance system during the same period was greater when compared to the IACI data, and the surveillance system data showed an upward trend.

IACI data showed low incidence of OA probably because only workers working at workplaces covered by ICAI could apply for compensation, leading to underestimation because workers not covered would be missed. However, this cannot fully explain the low incidence, considering that cases by the IACI decreased even after the expansion of its coverage in 2000. Therefore, there might be other more plausible reasons, including workers' ignorance of IACI and relevant procedures, fear of losing their

Table 4. Newly reported OA causative agents in Korea, 1992-2006

Year	Causative agents	Industry	Job	Source*
1992	Metals (supposed to be nickel, chromium)	Heavy machinery company	Metal arc welding	KJA 12 (2)
	Nickel, chromium	Plating factory	Plating	KJA 12 (2)
	Amoxicillin powder	Pharmaceutical company	Filling	KJA 12 (2)
1993	Ascidian	Farmed mussel processing factory	Executive	KJA 13 (4)
1994	Licorice	Oriental medicine warehouse	Oriental medicine material sorting	KJIM 47 (6)
	Aluminum	Kitchenware manufacturing	Casting assistant	OSHRI
1996	Japanese cedar	Private paperer	Papering	KJA 16 (2)
1997	7-Aminocephalosporanic acid (7-ACA)	Lab of graduate school	Cephalosporin synthesizing	KJA 17 (4)
1998	Tobacco	Tobacco factory	Raw material processing	KJAA 18 (2)
	Latex	Operating room of hospital	Operating room nurse	KJAA 18 (3)
	Diesel exhaust	Automobile mechanics	Mechanics	OSHRI
	Dichlorofluoroethane	Electric supply and control unit manufacturing	Grinding, cleaning	OSHRI
1999	<i>Ganoderma incidum karst</i> spore	Mushroom farm	Raising mushroom	KJAA 19 (5)
	<i>Metatetranychus citri</i>	Mandarin orange orchard	Mandarin orange farming	KJAA 19 (6)
	Terephthaloyl chloride	Synthetic fiber factory	Raw material manufacturing	KJAA 19 (2)
2000	Pig pancreas extract (PPE)	Internal medicine ward	Nurse	KJAA 20 (2)
	Curry powder (vegetable spice)	Food company	Vegetable spice mixing	KJAA 20 (4)
	Oriental medicine material	Medicine material seller	Oriental medicine material chopping	KJIM 59 (2)
	Cashew paint	Dyeing	Dye squeezing, modifying	OSHRI
	Cotton dust	Textile products manufacturing	Drawing	OSHRI
2001	Organic dust	Public office	Recycled goods sorting	OSHRI
	Paper dust	Toilet paper manufacturing	Toilet paper manufacturing assistant	OSHRI
	Grain dust	Polishing and milling	Raw material inputting, piling	OSHRI
2002	Ceferam pivoxil powder	Pharmaceutical company	Antibiotic powder pouring	KJAA 22 (3)
	Cobalt	Diamond cutter manufacturing	Cutter manufacturing	KJAA 22 (3)
	Formaldehyde	Musical instrument manufacturing	Glue mixing	OSHRI
	PASTE (lead compound, pine oil, terpineol)	Automobile glass manufacturing	Glass testing	OSHRI
2003	Phthalic anhydride (phthalate)	Polyester synthetic resin manufacturing	Raw material carrying, pouring	OSHRI
	Aminocephalosporanic thiazine (ACT)	Pharmaceutical company	ACT storage warehouse	KJAA 23 (3)
2004	Azodicarbonamide	Inorganic compound manufacturing	Sieving	OSHRI
	Wood dust	Sauna box manufacturing	Grinding, cutting	OSHRI
2005	Pronase powder	Hospital	Pharmacist	KJAA 25 (2)
	Cyanoacrylate	Shipbuilding	Glueing	KJAA 25 (3)
2006	No newly reported agents			

KJA, Korean Journal of Allergy; KJAA, Korean Journal of Asthma, Allergy and Clinical Immunology; KJIM, Korean Journal of Internal Medicine; OSHRI, Occupational Safety and Health Research Institute.

Table 5. Prevalence of occupational asthma according to agent or job, based on literatures

Agent or job	Prevalence (%)
Pharmaceutical dust	34.4
TDI	0.58-21.6
Grain dust	14.0
Phthalate	6.7
Reactive dye	5.9
Baker's asthma	5.0

TDI, toluene diisocyanate.

job, self-employed workers, or agreements with the employer (10). In addition, with varying asthma symptom severity, mild cases were likely to go unreported.

As shown above, though IACI data are useful, they have limitations due to various socioeconomic and medical factors, and low claiming rate. Therefore, some countries operate a surveillance system, which has proved to be very effective. In Korea, regional surveillance systems for OA have started since 1999, and the national OA Surveillance System, which is based on vol-

untary reporting, was initiated in 1998 (10). However, a voluntary surveillance system requires understanding of OA and active participation of clinicians. Korean surveillance system data greatly differ from data of other countries, indicating the need for vitalization of the surveillance system in Korea.

This study reveals that the most important OA causative agent in Korea was isocyanates. Although with different appearances in countries, isocyanates were reported as the major OA causative agent in most countries (11-13). This is attributable to the use of isocyanates in a variety of products, (e.g., car sheets, cushions, sofas, beds, insulating material, glue, and polyurethane paint) owing to their very high reactivity, which makes them important intermediates in producing polyurethane (14). However, in Korea there may be another reason: The diagnostic criteria of occupational diseases by the IACI Act specify 'asthma by isocyanates.' In other words, under present regulations, asthma occurring during work with isocyanates may be recognized right away without epidemiological investigation, whereas asthma from hazards other than isocyanates is examined by com-

plicated epidemiological investigation.

In Korea, reactive dye was the second most frequently reported agent, which differed from the results of other countries. This may be due to collective application for recognition of occupational diseases by some workplaces in some regions. However, reactive dye is also highly reactive, readily scattered, and frequently used in open-space worksites, and therefore may affect nearby neighborhoods. Asthma cases in workers who have worked near a reactive dye manufacturing factory were actually reported in Korea, indicating that careful exposure control is necessary (15).

While wheat flour and grain dust were major causes of OA in other countries, this was not the case with Korea. It may be because clinicians are reluctant to report upon relatively unknown hazardous factors without definite evidence, or workers may not apply for recognition of occupational diseases due to lack of information. However, recent surveillance system data report many cases of OA due to wheat flour dust and pharmaceutical dust. Therefore, it appears that understanding of asthma causative agents is gradually expanding.

In Korea, various chemicals, heavy metal dust and other dust, isocyanates and reactive dye have induced OA. At 34,797 manufacturing workplaces in Korea, 244,420 workers were exposed to dust or fumes (16). Accordingly, it has been estimated that various chemicals and heavy metal dust have induced a substantial number of OA cases. However, cases actually compensated as occupational diseases were very rare.

In prevalence studies of OA in Korea, prevalence and causative agents differed very much; for example, prevalence of TDI-induced OA varied greatly over 0.58-21.6%. This may be due to different reactivity of agents, different exposure levels and working environment for each asthma agent, as well as differing OA diagnosis criteria used.

In conclusion, more OA should be discovered through systematic and active surveillance systems, and workers exposed to actual hazards should be better protected by early detection and intervention, such as prompt avoidance of causative agents, and improvements in the working environment.

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