

Asthma Mortality in Male Workers of the Dye Industry in Korea

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Abstract: Asthma Mortality in Male Workers of the Dye Industry in Korea: Dong-Hee KOH, et al. Occupational Safety and Health Research Institute, Korea Occupational Safety and Health Agency, Korea—Workers in the dye industry are exposed to various chemicals, of which reactive dye is a well-known occupational asthmagen. This study examined the relationship between asthma mortality and occupational exposure in the dye industry. The cohort comprised 66,089 male workers, including 904 workers in the dye industry, who underwent medical examinations from 1995 to 2003 at a medical service institute located in Incheon, Korea. Deaths were also observed during the 1995 to 2003 period. The mortality was analyzed using the standardized mortality ratio (SMR) compared to the Korean general population, and the mortalities from asthma in dye manufacturing workers and other workers were compared using the standardized rate ratio (SRR). The all-cause mortality in dye industry workers was significantly lower than in the general population (SMR=0.40, 95% CI 0.24–0.63), while the asthma mortality (SMR=9.03, 95% CI 1.86–26.39) was significantly higher. Deaths from non-malignant respiratory diseases were higher in dye industry workers, but were not statistically significant (SMR=2.0, 95% CI 0.41–5.86). In the internal comparison, the all-cause mortality was the same in both groups, while the mortalities from non-malignant respiratory diseases (SRR=6.04, 95% CI 4.00–9.44) and asthma (SRR=23.29, 95% CI 11.05–58.83) were higher in dye industry workers than in workers in other industries. Because asthma is a life-threatening disease, special consideration and preventive

measures must be taken for workers in the dye industry. (*J Occup Health 2008; 50: 130–135*)

Key words: Asthma, Occupational, Dye, Reactive dye, Mortality

Workers in the dye industry are exposed to many hazardous chemicals, such as the carcinogens β -naphthylamine and benzidine. Some dyes are well-known occupational astmagens, such as reactive dye, and in Korea, dye industry workers have been compensated for occupational asthma since 1988. Moreover, reactive dye was one of the most frequent causes of compensated occupational asthma in Korea until the 1990s.

Reactive dye, a potent asthmagen, has been used worldwide since 1956 for dyeing cotton and wool¹). In Korea, the production of reactive dye began in the 1970s. In European countries, the production of β -naphthylamine was banned between the 1930s and 1950s, while that of benzidine was banned between the 1950s and 1970s; both are known urological carcinogens. In Japan, the production and use of benzidine, β -naphthylamine, 4-aminophenyl, and 4-nitrobiphenyl are banned and the Japanese government shut down dye manufacturing in 1972²). Since then, the Korean dye manufacturing industry has expanded markedly through the transfer of these technologies from Japan³). Nevertheless, in Korea, benzidine chloride and the manufacture of benzidine-based dyes have been prohibited since 2000.

Occupational asthma, now mainly due to isocyanates, has become an emerging issue in Korea, and many new industrial materials causing asthma are being reported⁴).

Asthma is a chronic inflammatory disorder of the airways characterized by variable airflow obstruction and airway hyperresponsiveness⁵). Asthma can be life-threatening, but few studies have examined the

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occupational mortality of the disease. Some studies, however, have elucidated the relationship by occupation, and others by industry, such as in pulp and paper workers, sulfite mill workers, and ferroalloy plants⁶⁻⁹.

We investigated the excess risk of death due to asthma in dye workers. This study examined 66,089 workers, including 904 workers in the dye industry, who underwent medical examinations between 1995 and 2003 in a medical service institute located in Incheon, Korea, and compared asthma mortality in dye workers to that of the general population and workers in other industries.

Methods

The study subjects consisted of 66,089 male workers who were employed by various companies in and around Incheon, and who underwent at least one medical examination during the period from 1995 to 2003. Female workers were excluded because none were reported to have died because of asthma. In Korea, manufacturing workers must undergo an annual health examination, which consists of a screening and confirmatory examination for those exposed to specific hazardous agents, such as benzene, silica dust, and noise. The general health examination includes screening and confirmatory examinations for hypertension, hypercholesterolemia, diabetes mellitus, liver disease, renal disease, and anemia, among other conditions¹⁰.

The periodic medical examinations are conducted by an occupational service institute located in Incheon, Korea. We constructed a retrospective health examinee cohort consisting of 66,089 workers, including 904 workers from nine dye manufacturing companies, by collecting computerized health examination data from 1995 to 2003. The data included each worker's resident registration number (unique personal identification number for Koreans), department, and company information.

Using the Korean Standard Industrial Classification (KSIC), the companies were divided into two categories: the dye industry and other industries. The KSIC has been revised based on the International Standard Industrial Classification (ISIC), and we distinguished industry groups using major sector categories. Each worker was assigned using this industrial classification according to the company employing the worker when he underwent his first health examination between 1995 and 2003. Employers can choose health service institutes and workers can change jobs, so the exposure circumstances can differ from the time of entry into the cohort. We, however, did not consider such changes.

Mortality data were matched to death statistics from the National Statistical Office (NSO) from 1995 to 2003 using resident registration numbers. The classification of the cause of death followed the tenth revision of the International Classification of Diseases (ICD-10). Death

from asthma was defined by codes J45 (asthma) and J46 (status asthmaticus), and mortality from overall non-malignant respiratory disease (NMRD) was defined by all J codes.

Statistical analysis

The observation period was 9 yr from Jan. 1, 1995 to Dec. 31, 2003. The entry point into the cohort was the date of the first medical examination during the 1995 to 2003 period. If the worker survived until the termination point of the study, then person-years was calculated from the date of the first medical examination to Dec 31, 2003. If the worker died during the observation period, his person-years were calculated from the date of the first medical examination to the date of death.

The expected numbers were calculated from age-specific mortality rates for 5-yr age groups and 3-yr calendar periods, 1995 to 1997, 1998 to 2000, and 2001 to 2003.

The indirectly standardized mortality ratios (SMRs) for all deaths, all non-malignant respiratory disease (NMRD), including asthma, and asthma were estimated by comparing the observed number of deaths with the expected number at the midpoint of each calendar period, that is, 1996, 1999, and 2002, for the Korean male population¹¹⁻¹³.

Internal analyses were used to investigate the excess risk of death from all causes, all NMRD, and asthma between workers in the dye industry and other industries. Directly standardized rate ratios (SRRs) were calculated for 5-yr age groups and 3-yr calendar periods to compare the dye industry with other industries¹⁴.

The program PAMCOMP (Person-years and Mortality Computation Program) was used to calculate person-years, SMRs, and exact Poisson confidence intervals (CIs)¹⁵. SRRs and exact Poisson CIs were computed using LogXact 8 with tabulated data by PAMCOMP¹⁶.

Results

Subjects aged 30 to 39 yr constituted 36.14% of the cohort, the largest subgroup. The subject's age is the age at the time of the first medical examination (Table 1). The health service institute computerized the data on the health examinees and their companies beginning in 1995; therefore, 36.3% of the subjects were first included in this cohort in 1995. From then, new workers who underwent an initial medical examination at this health service institute entered into the cohort every year until 2003. For the dye industry, 60.29% of the workers were enrolled in 1995, which was much larger than the 35.97% for workers in other industries.

Twelve deaths from asthma were reported among 66,089 workers during the follow-up period. Eleven of these deaths occurred in the manufacturing industry sector (Table 2). Three deaths occurred in the dye industry, and

Table 1. General characteristics of the study subjects

	Dye industry		Other industries		All	
	No.	%	No.	%	No.	%
Age*						
20–29	280	30.97	19,495	29.91	19,775	29.92
30–39	307	33.96	23,580	36.17	23,887	36.14
40–49	197	21.79	13,894	21.31	14,091	21.32
50–59	109	12.06	6,843	10.50	6,952	10.52
60–69	11	1.22	1,373	2.11	1,384	2.09
Year*						
1995	545	60.29	23,444	35.97	23,989	36.30
1996	92	10.18	7,781	11.94	7,873	11.91
1997	57	6.31	7,019	10.77	7,076	10.71
1998	39	4.31	4,356	6.68	4,395	6.65
1999	25	2.77	5,106	7.83	5,131	7.76
2000	40	4.42	6,589	10.11	6,629	10.03
2001	58	6.42	4,497	6.90	4,555	6.89
2002	17	1.88	2,492	3.82	2,509	3.80
2003	31	3.43	3,901	5.98	3,932	5.95
Total	904	100.01	65,185	100	66,089	100

* At the time of the first medical examination in the health service institute.

Table 2. Mortality cases due to asthma by sector

The Korean Standard Industrial Classification	Mortality due to asthma	No. of health examinees	%
Recreational, cultural, and sporting activities	0	26	0.04
Mining and quarrying	0	50	0.08
Private households with employed persons	0	57	0.09
Post and telecommunications	0	111	0.17
Public administration and defense	0	112	0.17
Transport	0	240	0.36
Wholesale and retail trade	0	295	0.45
Financial institutions and insurance companies	0	319	0.48
Real estate and renting and leasing	0	360	0.54
Electricity, gas, and water supply	0	669	1.01
Education	0	1,027	1.55
Business activities	0	1,196	1.81
Health and social work	0	2,436	3.69
Other community, repair, and personal service activities	1	2,642	4.00
Construction	0	2,732	4.13
Manufacturing	11	53,817	81.43
Total	12	66,089	100

nine deaths in other industries.

The all-cause mortality rate was significantly lower than in the general population (SMR=0.40, 95% CI 0.24–0.63), while the asthma mortality was significantly higher than in the general population (SMR=9.03, 95% CI 1.86–

26.39) in dye industry workers (Table 3). In comparison to other industries, deaths from non-malignant respiratory diseases were higher in dye industry workers, but the difference was not statistically significant (SMR=2.0, 95% CI 0.41–5.86).

Table 3. SMRs of death due to all causes, NMRD, and asthma

Cause of death	Dye industry No.=904 PY=6,284				Other industries No.=65,185 PY=380,544				All No.=66,089 PY=386,829			
	Obs	Exp	SMR*	95% CI	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
All causes	19	47.1	0.40	0.24–0.63	968	2714.6	0.36	0.33–0.38	987	2761.7	0.36	0.34–0.38
NMRD [†]	3	1.5	2.00	0.41–5.86	30	90.8	0.33	0.22–0.47	33	92.3	0.36	0.25–0.50
Asthma	3	0.3	9.03	1.86–26.39	9	20.8	0.43	0.20–0.82	12	21.1	0.57	0.29–0.99

*standardized mortality ratio. [†]non-malignant respiratory disease.

Table 4. SRRs of death from all causes, NMRD, and asthma

Cause of death	SRR*	95% CI
All causes	1.09	0.00–1.19
NMRD [†]	6.04	4.00–9.44
Asthma	23.29	11.05–58.83

*standardized rate ratio. [†]non-malignant respiratory disease.

Table 5. Characteristics of deaths due to asthma in the study subjects

Case	Age at death	Year of employment	Year of entry*	Year of death	The Korean Standard Industrial Classification
1	57	1990	1995	2001	Manufacture of synthetic coloring matter, tanning materials, and other coloring agents
2	59	1988	1996	2000	
3	41	1991	1996	1998	
4	54	1976	1995	2002	Manufacture of general paints and similar products
5	57	1991	1995	2001	Manufacture of other furniture
6	55	1979	1995	2003	
7	70	1996	1997	2003	Manufacture of wooden packing boxes, cable drums, and similar items
8	59	–	1995	1998	Other casting of nonferrous metals
9	56	1987	1995	2003	Manufacture of all other fabricated metal products
10	56	1994	1996	1999	Metal product plating services
11	71	1987	1997	2003	Manufacture of printed circuit boards
12	51	1994	1999	2003	Non-hazardous waste disposal

*At the time of the first medical examination in the health service institute.

To perform an internal comparison with workers in other industries, we calculated the age-standardized SRRs for all-cause mortality, non-malignant respiratory disease mortality, and asthma mortality (Table 4). The all-cause mortality was nearly the same in both groups, while the mortality from non-malignant respiratory diseases and asthma was higher than for workers in other industries: SRR=6.04 (95% CI 4.00–9.44) and SRR=23.29 (95% CI 11.05–58.83), respectively.

Ten deaths from asthma occurred among active workers, and two presumably retired workers in their 70s died (Table 5). Three deaths were reported in the dye industry, three in the furniture and wood industries, one in paint manufacturing, two in metal production, and one in the plating industry. Two deaths (cases 7 and 12) involved office workers, and the other ten deaths were manufacturing workers.

Discussion

Several studies have examined the occupational burden of asthma, and it was reported that the prevalence of physician-diagnosed asthma was higher for certain industries in the United States¹⁷. In Caucasians, the prevalence and age- and sex-adjusted odds ratios (OR) were significantly elevated for the printing, publishing and allied industries (OR=2.4, 95% CI 1.2–5.0) and health care (OR=1.3, 95% CI 1.0–1.7). In African-Americans, the ORs were elevated for the furniture, lumber, and wood (OR=1.3, 95% CI 1.4–25.4), and entertainment and recreation (OR=4.1, 95% CI 1.1–15.9) industries. A cohort study investigated the mortality attributable to asthma among Swedish workers between 1981 and 1992 by linking official mortality statistics with occupational information in the 1980 national census⁶. It found that the smoking-adjusted SMRs were elevated in male farmers (8/3.1, SMR=146, 95% CI 105–187), male professional drivers (43/29.9, SMR=144, 95% CI 101–209), and female hairdressers (8/2.4, SMR=332, 95% CI 102–561).

A few asthma mortality studies have used an occupational cohort for a specific industry. Langseth and Kjaerheim observed 3,143 women from 1951 to 2000 who were first employed in the pulp and paper industry between 1920 and 1993⁷. Mortality due to non-malignant respiratory diseases (SMR=1.13, 95% CI 0.86–1.47) and the mortality due to chronic obstructive pulmonary disease (COPD) including asthma (SMR=1.21, 95% CI 0.77–1.57) were elevated slightly, but only 5 deaths from asthma were observed from 1960 to 2000 versus the 5.8 expected deaths. In a Norwegian cohort of 14,730 male workers employed for the first time in ferroalloy plants between 1933 and 1990 who had worked for at least 6 months in one of 12 plants, deaths were observed from 1962 to 1990⁹. The mortality from bronchitis, emphysema, and asthma was elevated for the employees in the ferrosilicon/silicon-metal plants (56/45.25, SMR=1.24, 95% CI 0.93–1.61), but not in ferromanganese/silicomanganese plants (32/33.17, SMR=0.96, 95% CI 0.66–1.36).

A case-control study of sulfite mill workers exposed mainly to sulfur dioxide, wood dust, and terpenes from the pulping process examined men who died between 1960 and 1989 and who were aged 40 to 75 yr at death (n=780); of these, 13 men died from asthma⁸. An increased mortality from asthma (OR=2.8, 90% CI 1.1–6.8) associated with irritant gas exposure was detected compared to the referent group. Another study of 1,112 workers compensated for occupational asthma or aggravation of asthma between 1980 and 1993 reported increased SMRs for asthma (2/0.1, SMR=18.2) and COPD (3/1.3, SMR=2.3)¹⁸.

Reactive dye is the most potent material that can elicit occupational asthma in the dye industry. It is inhaled in

powder form; it then binds covalently to the hydroxyl groups on proteins and acts as a hapten¹⁹. Occupational asthma caused by reactive dyes is prevalent in the dye industry, and the prevalence has been reported as 2.5%, 5.9%, and up to 14%^{20–22}. It has even been reported that six employees who worked in factories near reactive dye factories developed occupational asthma due to reactive dye exposure²⁰. We conducted the present study because asthma mortality in dye manufacturing workers had not been assessed.

Our study has certain limitations. We could not adjust for smoking status due to the lack of data. Our study is a record linkage study, and we did not have enough computerized information about potential confounding factors such as smoking status, air pollution, and socioeconomic status for the observation period. We analyzed the excess risk assuming that the smoking status of dye industry workers was equal to workers in other industries, because they were mostly manufacturing workers and lived in the same area. However, smoking is a crucial confounding factor for asthma, and lack of information on smoking is an important limitation of our study. We did not differentiate manufacturing workers from office workers because only two deaths were observed in office workers. Although the workers could have changed jobs and employers could have changed health service institutes during the study period, we did not consider this an issue because it was impossible to track the work histories of all workers. Since occupational asthma with a prolonged exposure to asthmagens can progress to chronic status even if the exposure has ceased, our findings may still reflect chronic asthma status. Death certificates can occasionally be misclassified because chronic obstructive lung disease (COPD) and asthma can become confused in the elderly. Therefore, we compared non-malignant respiratory diseases including both COPD and asthma in the dye industry with other industries and found a significant increase in the SRR of non-malignant respiratory diseases for dye industry workers. Loss of follow-up could occur in cases of emigration, but we consider it to be a very small portion of the whole. The possibility exists of a healthy worker effect because compensated occupational asthmatics exposed to isocyanates, the most frequent occupational asthmagens, could have left the cohort. In addition, because only three deaths from asthma were observed in dye industry workers, very wide confidence intervals due to the low statistical power constitute a final limitation of our study.

Reactive dyes have been increasingly used as coloring agents in the textile industry. In addition to manufacturing workers in the dye industry, a study has reported occupational asthma in a wool and cotton dyer handling reactive dyes²³. Considering the high risk of asthma death in the dye industry, more active preventive measures should be taken. Our study could be generalized to dye

manufacturing workers beyond Korean workers from a preventive point of view.

Two of three deaths involving the furniture and wood industries and the one death in paint manufacturing could possibly have been related to isocyanate exposure. In addition, the effect of chromium exposure cannot be ruled out for the two deaths in metal production and one death in the plating industry. We did not consider deaths from these asthmagens in this study, but special actions should also be taken regarding these occupational asthmagens to prevent deaths from occupational asthma.

Conclusions

Workers in the dye industry are exposed to various dyes, including reactive dye, a well-known occupational asthmagen. We studied 66,089 male workers, including 904 workers in the dye industry, who underwent medical examinations from 1995 to 2003 at a medical service institute located in Incheon, Korea, and compared the mortality from asthma in dye manufacturing workers with that of the general population and workers in other industries.

The asthma mortality was significantly higher than in the general population (SMR=9.03, 95% CI 1.86–26.39) in dye industry workers. In addition, the risk for asthma mortality was higher in dye industry workers than in workers in other industries (SRR=23.29, 95% CI 11.05–58.83). As occupational asthma is a life-threatening disease, special considerations and preventive measures must be taken for workers in the dye industry.

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