

The Exposure Status and Biomarkers of Polycyclic Aromatic Hydrocarbons in Shipyard Workers

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Abstract

Because shipyard workers are involved with various manufacturing process in shipyard industry, and they are exposed to many kinds of hazardous materials. Especially, painting workers were exposed polycyclic aromatic hydrocarbons (PAH). This study was conducted to assess the exposure status of PAH based on job-exposure matrix. We investigated the effect of genetic polymorphism of xenobiotic metabolism enzymes involved in PAH metabolism on levels of urinary metabolite. A total of 93 shipbuilding workers were recruited in this study. Questionnaire variables were age, sex, use of personal protective equipment, smoking, drinking, and work duration. The urinary metabolite was collected in the afternoon and corrected by urinary creatinine concentration. The genotypes of CYP1A1, CYP2E1, GSTM1, GSTT1 and UGT1A6 were investigated by using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) methods with DNA extracted from venous blood. Urinary 1-OHP levels were significantly higher in direct exposed group (spray and touch-up) than indirect exposed group. Urinary 1-OHP, concentration of the high exposure with wild type of UGT1A6 was significantly higher than that of the high exposure with other UGT1A6 genotype. In multiple regression analysis of urinary 1-OHP, the regression coefficient of job grade was statistically significant ($p < 0.05$) and

UGT1A6 was not significant but a trend ($p < 0.1$). The grade of exposure affected urinary PAH concentration was statistically significant. But genetic polymorphism of xenobiotics metabolism enzymes was not statistically significant. Further investigation of genetic polymorphism with large sample size is needed.

Keywords: Polycyclic aromatic hydrocarbons, Genetic polymorphism, 1-hydroxypyrene

Polycyclic aromatic hydrocarbons (PAHs) are organic compounds containing two or more fused aromatic rings. They are distributed widely in the environment. Major contaminators are very diverse such as thermo-electric power plants, home and industrial heating systems, tar paint, burning, and smoking. PAHs produced in such manners have been reported to be exposed to humans via working places, food, drugs, and other factors. The International Agency for Research on Cancer (IARC) has reported that 11 types of PAHs including benzo(a)pyrene is carcinogenic in animals, and in epidemiological studies, a significantly increased incidence of cancer in workers exposed to PAHs has been reported¹. In addition, as they have been recognized as an endocrine disruptor, it needs a special care for environmental controls.

In shipbuilding industry, painting is an essential process, and painting workers can be heavily exposed to various harmful substances contained in paints during blasting process, primer-painting process, and painting process of a ship². The paint materials used in shipbuilding industry paints, thinners, hardeners contain aromatic hydrocarbon, aliphatic hydrocarbon, ketone, and alcohol primarily, and in addition, ester, glycol ether, and other organic chemicals are contained. Particularly, among them, about 40 different types of paint containing coal tar are used in shipyards in Korea and they account for 13% of all shipyard paints³. However, the evaluation of the exposure and health of workers exposed to PAHs has not been performed yet.

This study was conducted to assess the exposure status of PAH based on job-exposure matrix. We investigated the effect of genetic polymorphism of xenobiotic metabolism enzymes involved in PAH metabolism on levels of urinary metabolite.

Table 1. General characteristics of study subjects. (Unit: number (%))

| Characteristics | Direct exposed | | In-direct exposed | p value |
|-----------------------|----------------|-----------|-------------------|---------|
| | Spray | Touch up | Mix+Assist | |
| Age (years) | | | | |
| < 40 | 3 (11.1) | 3 (10.0) | 12 (33.3) | .04 |
| 40-49 | 22 (81.5) | 20 (66.7) | 20 (55.6) | |
| ≥ 50 | 2 (7.4) | 7 (23.3) | 4 (11.1) | |
| Work duration (years) | | | | |
| < 10 | 2 (7.4) | 2 (6.7) | 6 (16.7) | .34 |
| 10-14 | 9 (33.3) | 10 (33.3) | 16 (44.4) | |
| ≥ 15 | 16 (59.3) | 18 (60.0) | 14 (38.9) | |
| Smoking | | | | |
| Yes | 11 (40.7) | 13 (43.3) | 7 (19.4) | .08 |
| No | 16 (59.3) | 17 (56.7) | 29 (80.6) | |
| Alcohol | | | | |
| Yes | 10 (37.0) | 17 (56.7) | 17 (47.2) | .45 |
| No | 17 (63.0) | 13 (43.3) | 19 (52.8) | |

The General Characteristic of the Study Population

Both the direct exposure group and the indirect exposure group were all males, and the age of direct exposure groups was significantly higher than the indirect exposure group ($p < 0.001$). Regarding their working period, the working period according to their job was not significant ($p > 0.05$) (Table 1).

The Working Place and the Status of Using Protective Equipment of the Study Population

Examining the distribution of the working place of the study population, for spray painters, outdoor block work was 11 persons and inter block work was 16 persons, and among touch up painters, outdoor block work was 11 persons and inter block work was 19 persons, and among painter assistant workers, outer block work was 19 persons and inter block work was 17 persons. The status of using protective equipment dependent on job was that among spray painters, not wearing was 4 persons, occasional wearing was 16 persons, and always wearing was 7 persons. Among touch up painters, not wearing was 5 persons, occasional wearing was 20 persons, and always wearing was 5 persons. Among the painter assistant group, always wearing was none, not wearing was 14 persons, and occasional wearing was 22 persons. In other words, not wearing protective equipment was most prevalent in the painter assistant group, and continuously wearing protective equipment was most frequent in spray painter group, and the difference was statistically significant (Table 2).

Table 2. Distribution of work place and personal protective equipment by job characteristics. (Unit: number (%))

| Characteristics | Direct exposed | | In-direct exposed | p value |
|--------------------------|----------------|-----------|-------------------|---------|
| | Spray | Touch up | Mix+Assist | |
| Work place | | | | |
| Outer block | 11 (40.7) | 11 (36.7) | 19 (52.8) | 0.39 |
| Inter block | 16 (59.3) | 19 (63.3) | 17 (47.2) | |
| Use of protect equipment | | | | |
| No | 4 (14.8) | 5 (16.7) | 14 (38.9) | 0.01 |
| Intermittent | 16 (59.3) | 20 (66.7) | 22 (61.1) | |
| Continuous | 7 (25.9) | 5 (16.7) | — | |

Table 3. The mean concentration of PAH in air by job characteristics. (Unit: $\mu\text{g}/\text{m}^3$)

| Job title | A.M. | S.D. | G.M. | G.S.D. | p value |
|------------|-------|------|-------|--------|---------|
| Spray | 12.79 | 6.58 | 11.13 | 1.80 | 0.004 |
| Touch up | 3.71 | 3.25 | 2.32 | 3.35 | |
| Mix+Assist | 1.60 | 1.33 | 1.12 | 2.66 | |

A.M.: arithmetic mean, S.D.: standard deviation, G.M.: geometric mean, G.S.D.: geometric standard deviation

The Level of the Exposure to PAH According to the Job of Workers

Comparing the concentration of the exposure to PAH according to the job, it was found that spray painters was highest with the mathematical mean $12.79 \mu\text{g}/\text{m}^3$, geometrical mean was $11.13 \mu\text{g}/\text{m}^3$, and regarding touch up painters, mathematical mean was $3.71 \mu\text{g}/\text{m}^3$, and geometrical mean was $2.32 \mu\text{g}/\text{m}^3$. In the indirect exposure group painter assistant group showed the lowest exposure with the mathematical mean $1.60 \mu\text{g}/\text{m}^3$, and the geometrical mean $1.12 \mu\text{g}/\text{m}^3$ (Table 3).

Urinary 1-OHP of Painters

The 1-OHP concentration according to the job title of the study population showed a statistically significant difference. In touch up painters, it was $4.41 \pm 4.96 \mu\text{mole}/\text{mole}$ creatinine that was highest, in spray painters, it was $4.02 \pm 4.86 \mu\text{mole}/\text{mole}$ creatinine, and in the indirect exposure group, it was 0.96 ± 1.16 that was lowest. The 1-OHP concentration according to working place was that in comparison with the outer block $2.24 \pm 3.57 \mu\text{mole}/\text{mole}$ creatinine, inter block was higher, $3.51 \pm 4.53 \mu\text{mole}/\text{mole}$ creatinine, but a significant difference was not detected. The 1-OHP concentration according to the status of wearing protective equipment was in the order of not wearing group was $3.45 \pm 4.54 \mu\text{mole}/\text{mole}$ creatinine that was highest, occasional wearing group was

Table 4. The mean concentration of 1-OHP in urine by job characteristics. (unit: $\mu\text{mole/mole creatinine}$)

| Variables | No | A.M. | S.D. | G.M. | G.S.D. | p value |
|---------------------------------|----|------|------|------|--------|---------|
| Job | | | | | | |
| Spray | 27 | 4.02 | 4.86 | 2.60 | 2.66 | 0.01 |
| Touch up | 30 | 4.41 | 4.92 | 3.15 | 2.64 | |
| Mix+Assist | 36 | 0.96 | 1.16 | 0.94 | 2.36 | |
| Work place | | | | | | |
| Outer block | 41 | 2.24 | 3.57 | 1.46 | 3.14 | 0.14 |
| Inter block | 52 | 3.51 | 4.53 | 2.35 | 2.66 | |
| Use of protect equipment | | | | | | |
| No | 23 | 3.45 | 4.54 | 2.10 | 4.01 | 0.09 |
| Intermittent | 58 | 3.25 | 4.30 | 1.95 | 2.58 | |
| Continuous | 12 | 0.53 | 0.76 | 0.90 | 1.82 | |

A.M.: arithmetic mean, S.D.: standard deviation,
G.M.: geometric mean, G.S.D.: geometric standard deviation

Table 5. Distribution of Phase I enzyme genotype by job characteristics. (Unit: number (%))

| Genotype | Direct exposed | | In-direct exposed | Total |
|---------------|----------------|-----------|-------------------|-----------|
| | Spray | Touch up | Mix+Assist | |
| CYP1A1 | | | | |
| Ile/Ile | 16 (59.3) | 18 (62.1) | 20 (55.6) | 54 (58.7) |
| Ile/Val | 9 (33.3) | 10 (34.5) | 14 (38.9) | 33 (35.9) |
| Val/Val | 2 (7.4) | 1 (3.4) | 2 (5.6) | 5 (5.4) |
| CYP1A1 | | | | |
| Wild | 16 (59.3) | 18 (62.1) | 20 (55.6) | 54 (58.7) |
| Mutant | 11 (40.7) | 11 (37.9) | 16 (44.4) | 38 (41.3) |
| CYP2E1 | | | | |
| c1/c1 | 19 (70.4) | 22 (73.3) | 21 (58.3) | 62 (66.7) |
| c1/c2 | 8 (29.6) | 7 (23.3) | 14 (38.9) | 29 (31.2) |
| c2/c2 | – | 1 (3.3) | 1 (2.8) | 2 (2.2) |
| CYP2E1 | | | | |
| Wild | 19 (70.4) | 22 (73.3) | 21 (58.3) | 62 (66.7) |
| Mutant | 8 (29.6) | 8 (26.7) | 15 (41.7) | 31 (33.3) |

3.25 ± 4.30 , continuously wearing group was 0.53 ± 0.76 $\mu\text{mole/mole creatinine}$ (Table 4).

The Genetic Polymorphism of the Study Population

The distribution of the polymorphism of CYP1A1 gene and CYP2E1 gene among various jobs was not different substantially (Table 5). The GSTM1 gene of the study population was that negative was 60.2% and positive was 39.8%. Based on their job, in spray painters, negative was 44.4% and positive was 55.6%. In touch up painters, negative was 63.3% and positive was 36.76%. In the painter assistant group, negative was 69.4% and positive was 30.6% (Table 6). The GSTT1 gene of the study population was that

Table 6. Distribution of Phase II enzyme genotype by job characteristics. (Unit: number (%))

| Genotype | Direct exposed | | In-direct exposed | Total |
|---------------|----------------|-----------|-------------------|-----------|
| | Spray | Touch up | Mix+Assist | |
| GSTM1 | | | | |
| Negative | 12 (44.4) | 19 (63.3) | 25 (69.4) | 56 (60.2) |
| Positive | 15 (55.6) | 11 (36.7) | 11 (30.6) | 37 (39.8) |
| GSTT1 | | | | |
| Negative | 13 (48.1) | 17 (56.7) | 16 (44.4) | 46 (50.0) |
| Positive | 14 (51.9) | 12 (40.0) | 20 (55.6) | 46 (50.0) |
| UGT1A6 | | | | |
| Wild | 16 (59.3) | 18 (60.0) | 21 (58.3) | 55 (59.1) |
| P1 | 10 (37.0) | 8 (26.7) | 11 (30.6) | 29 (31.2) |
| P3 | – | 1 (3.3) | 1 (2.8) | 2 (2.2) |
| P4 | – | 3 (10.0) | 1 (2.8) | 4 (4.3) |
| UGT1A6 | | | | |
| Wild | 16 (59.3) | 18 (60.0) | 21 (58.3) | 55 (59.1) |
| Mutant | 10 (37.0) | 12 (40.0) | 13 (36.2) | 35 (37.7) |

Table 7. The mean concentration of urinary 1-OHP by genotype. (unit: $\mu\text{mole/mole creatinine}$)

| Genotype | A.M. | S.D. | G.M. | G.S.D. | p value |
|---------------|------|------|------|--------|---------|
| CYP1A1 | | | | | |
| Wild | 2.75 | 4.34 | 1.56 | 2.86 | 0.58 |
| Mutant | 3.25 | 3.25 | 2.68 | 2.84 | |
| CYP2E1 | | | | | |
| Wild | 3.33 | 4.66 | 1.96 | 2.98 | 0.21 |
| Mutant | 2.19 | 2.86 | 2.28 | 2.81 | |
| GSTM1 | | | | | |
| Negative | 2.58 | 3.57 | 1.74 | 2.99 | 0.29 |
| Positive | 3.51 | 4.93 | 2.25 | 2.78 | |
| GSTT1 | | | | | |
| Negative | 3.21 | 4.72 | 2.13 | 2.76 | 0.57 |
| Positive | 2.72 | 3.61 | 1.76 | 3.11 | |
| UGT1A6 | | | | | |
| Wild | 3.26 | 3.88 | 2.38 | 3.02 | 0.31 |
| Mutant | 1.73 | 2.19 | 1.41 | 2.57 | |

A.M.: arithmetic mean, S.D.: standard deviation,
G.M.: geometric mean, G.S.D.: geometric standard deviation

negative was 50.0% and positive was 50.0%. Based on their job, in spray painters, negative was 48.1% and positive was 51.9%. In touch up painters, negative was 56.7% and positive was 40.0%. In the painter assistant group, negative was 44.4% and positive was 55.6% (Table 6). Among the wild type of UGT1A6 gene, P1, P2, P3, and P4 type, the workers involved in the painting process, the four types of wild type, P1, P3, and P4 were detected and P2 was absent. The distribution of the gene of the

Table 8. Regression coefficient between exposure grade and urinary 1-OHP concentration by genetic factor.

| Variables | No. of subject | β | α | γ^2 | p value |
|-----------------------------|----------------|---------|----------|------------|---------|
| CYP1A1 genotype | | | | | |
| Wild | 54 | 1.31 | -0.03 | 0.11 | 0.013 |
| Mutant | 38 | 1.88 | -0.76 | 0.29 | 0.000 |
| CYP2E1 genotype | | | | | |
| Wild | 62 | 1.95 | -0.89 | 0.20 | 0.000 |
| Mutant | 31 | 0.86 | 0.51 | 0.13 | 0.052 |
| GSTM1 genotype | | | | | |
| Positive | 37 | 1.69 | -0.45 | 0.16 | 0.015 |
| Negative | 56 | 1.37 | -0.16 | 0.17 | 0.002 |
| GSTT1 genotype | | | | | |
| Positive | 46 | 1.12 | 0.59 | 0.10 | 0.037 |
| Negative | 46 | 1.89 | -1.27 | 0.23 | 0.001 |
| UGT1A6 genotype | | | | | |
| Wild | 55 | 1.79 | -0.68 | 0.25 | 0.000 |
| Mutant | 38 | 1.10 | 0.23 | 0.07 | 0.101 |
| Age (years) | | | | | |
| < 40 | 18 | 2.56 | -1.15 | 0.32 | 0.014 |
| 40-49 | 62 | 1.55 | -0.51 | 0.17 | 0.001 |
| ≥ 50 | 13 | 0.38 | 1.54 | 0.03 | 0.578 |
| Work duration (year) | | | | | |
| < 10 | 10 | 2.43 | -2.12 | 0.39 | 0.050 |
| 10-14 | 35 | 1.86 | -1.17 | 0.41 | 0.000 |
| ≥ 15 | 48 | 0.98 | 1.12 | 0.05 | 0.111 |
| Alcohol | | | | | |
| Yes | 31 | 1.74 | 0.47 | 0.13 | 0.043 |
| No | 62 | 1.09 | -1.12 | 0.16 | 0.001 |
| Smoking | | | | | |
| Yes | 51 | 1.50 | -0.16 | 0.13 | 0.009 |
| No | 42 | 1.56 | -0.49 | 0.26 | 0.000 |

Model : 1-OHP= β *exposure grade+ α

entire painters was that the wild type was 59.1%, P1 type was 31.2%, P3 type was 2.2%, and P4 type was 4.3%. Among spray painters, P3 and P4 type were absent, the wild type was 59.3%, and P1 type was 37.0%. In touch up painters, the wild type was 60.0%, P1 type was 26.7%, P3 type was 3.3%, and P4 type was 10.0%. In the painter assistant group, the wild type was 58.3%, P1 type was 30.6%, P3 type was 2.8%, and P4 type was 2.8% (Table 6).

The Distribution of the Concentration of PAH Metabolites According to Genetic Polymorphism

In regard to CYP1A1 genotype, the concentration of urinary 1-OHP in the wild type was lower than other genotypes, however, it was not significant. Concerning the CYP2E1 genotype, the wild type was

Table 9. Multiple regression analysis of urinary 1-OHP concentration.

| Co-variate | β (SE) | t-value | p value |
|----------------|----------------|---------|---------|
| Exposure grade | 0.876 (0.133) | 6.60 | .001 |
| CYP1A1 | 0.891 (0.568) | 1.56 | .121 |
| CYP2E1 | -0.496 (0.594) | -0.83 | .406 |
| GSTM1 | -0.307 (0.586) | -0.52 | .602 |
| GSTT1 | -0.090 (0.572) | -0.15 | .875 |
| UGT1A6 | -1.003 (0.597) | -1.68 | .091 |
| Age | 0.001 (0.049) | 0.02 | .979 |
| Smoking | 0.609 (0.717) | 0.84 | .399 |
| Alcohol | -0.632 (0.595) | -1.06 | .292 |
| Intercept | -0.003 | | |
| R-square | 0.478 | | |

Coding : genotype of CYP1A1 (Ile/Ile=0, Ile/Val & Val/Val=1), genotype of CYP2E1 (c1/c1=0, c1/c2 & c2/c2=1), genotype of GSTM1 & GSTT1 (positive=0, negative=1), genotype of UGT1A6 (Wild=0, Mutant=1), age (years), drink (no=0, yes=1), smoking habits (no=0, yes=1)

3.33 ± 4.66 μ mole/mole creatinine and other genotype was 2.19 ± 2.86 μ mole/mole creatinine, and it was not significant. Among the concentration of GSTM1, GSTT1, and urinary 1-OHP, a statistically significant difference was not detected. In the case of UGT1A6 genotype, 1-OHP concentration of the wild type was higher than mutant types, but it was not significant (Table 7).

The Comparison of Regression Coefficient by the Job-exposure Matrix and Multiple Regression Analysis

The regression of urinary 1-OHP concentration in the semi-quantitative job-exposure matrix prepared based on the job of painters, the sealing status of working space, and the status of the use of protective equipment was stratified to each genotype and regression coefficient was obtained, and it was found that it was not significant in the mutation type of CYP2E1 gene and the mutation type of UGT1A6 gene, however, it was statistically significant in CYP1A1, GSTM1, and GSTT1 genotype. It was also significant in the wild type of CYP2E1 gene and the wild type of UGT1A6 gene. In addition, the regression coefficient of age, drinking on the day before, and smoking was statistically significant, and the age of over 50 years and the working period over 15 years were not statistically significant (Table 8). In multiple regression analysis of urinary 1-OHP, the regression coefficient of job grade was statistically significant ($p < 0.05$) and UGT1A6 was not significant but a trend ($p < 0.1$) (Table 9).

Discussion

During painting processes in shipbuilding work, the variables affecting the exposure level are very diverse, hence, to consider the concentration of working environment at one time as the representative exposure concentration of the group is not reasonable. For example, comparing the exposure concentration of PAH according to the job, spray painters were highest with the mathematical mean $12.79 \mu\text{g}/\text{m}^3$, and painter assistant job showed the lowest exposure $1.60 \mu\text{g}/\text{m}^3$. But, the evaluation of urinary 1-OHP was high in the order of touch up painters, spray painters, and painter assistants, which shows an aspect discordant from the evaluation of the PAH in air. Thus, the result of the evaluation of external exposure is the result measured from the outside of protective equipment, hence it requires a caution to compare with the evaluation of internal exposure markers (1-OHP). Because, the exposure level is different dependent on the status of the wear of protective equipment, and the skin is a more important the absorption route of polycyclic aromatic hydrocarbon than the respiratory system⁴. Therefore, not only environmental concentration, by considering the condition of working place, the level of shut tight, the exposure probability, the wear of protective equipment, and other important factors, a meaningful exposure level could be estimated. In our study, as a solution, the job-exposure matrix was applied. Bouyer *et al.*⁵ have suggested that the entry to the job-exposure matrix cell must have two dimensions, and that one reflects exposure intensity or exposure frequency and another represents the exposure probability. To meet such conditions, the estimated exposure level of the worker designated as a similar exposure group was scored according to the job and the sealing condition of working place, and as the evaluation of exposure, it was assessed according to the status of wearing protective equipment. Therefore a semi-quantitative evaluation that scores the multiplication of job score and exposure level by dividing to several categories^{3,6,7} was applied.

In this study, 1-OHP was selected as a biomarker and the sensitivity markers CYP1A1, CYP2E1, GSTM1, GSTT1, and UGT1A6 pertinent to PAH were analyzed together. In our study, urinary 1-OHP concentration in the indirect exposure group was average $0.96 \mu\text{mole}/\text{mole}$ creatinine, which was substantially higher than the workers not exposed to PAH, $0.08\text{--}0.14 \mu\text{mole}/\text{mole}$ creatinine, reported by Ovrebo *et al.*⁸ For the exposure group, Ovrebo *et al.*⁸ have reported that urinary 1-OHP of the workers exposed to PAH was the mathematical mean 6.98

$\mu\text{mole}/\text{mole}$ creatinine, Petry *et al.*⁹ have reported $0.5\text{--}61.8 \mu\text{mole}/\text{mole}$ creatinine in the workers in carbon electrode manufacturing business, and Angerer *et al.*¹⁰ have reported $0.5\text{--}61.8 \mu\text{mole}/\text{mole}$ creatinine. In our study, it was average $4 \mu\text{mole}/\text{mole}$ creatinine, which was a slightly low value, and in the range reported by other investigators, it was in the lower side.

The research on the genotype of metabolic enzymes and the metabolites is not abundant. Because, PAH is diverse chemicals and thus the possibility of influenced by different metabolic enzymes is high. In this study, a statistically significant result was not detected in the phase I enzymes, and in the workers whose exposure grade was high, it has been suggested that the concentration of 1-OHP can be influenced by CYP1A1 genotype. In the case of the phase II enzymes, it has been reported that GSTM1 negative type is related to the PAH-DNA adduct concentration¹¹, on the other hand, it has been reported that urinary 1-OHP, GSTM1, and GSTT1 are not related or shown to be very low¹². In our study, a significant result was not observed. In the UGT1A6, when exposed to a low level of PAH only, UGT1A6 is involved in the metabolism of pyrene, however, when exposed to a high concentration, for example cokes workers, a significant result was not observed. In this study, a significant result was detected in the worker group with high grade exposure. In multiple regression analysis, adjusted the variables that may affect urinary 1-OHP, the possibility of UGT1A6 was suggested, nevertheless, metabolic enzymes were not significant and the exposure grade was the only significant predictive variable.

In conclusion, the factor that influences the greatest effect on urinary 1-OHP concentration was the grade of exposure, and among the metabolism processes of exposed PAH, UGT1A6 appears to be involved in more than CYP1A1, CYP2E1, GSTM1 and GSTT1 genotype, and the activation of glucuronidation is believed to mediate a large effect. Further investigation of genetic polymorphism with large sample size is needed.

Methods

The Study Population

The study population was recruited from shipyard company. The workers who work in the paint process exposed to PAHs were total 93, and in regard to their job type, spray paint was 27 persons, touch up paint was 30 persons, and paint assistants were 36 persons. Among them, we classified spray painter and touch

up painters as the direct exposure group, and paint assistants as the indirect exposure group.

Questionnaire and the Job-exposure Matrix

As a questionnaire survey, by using a questionnaire containing age, gender, working period, the department of work, work contents, working place, the wear of protective equipment and its type, past history and medication history, drinking, smoking habit, etc., it was recorded as a self-writing type. Among the study population, as the evaluation of the exposure to harmful factors, the analysis of the process in working places, working place, working frequency, name of substances, and harmful factors were examined, and the working load of workers, exposure frequency, exposure condition, and the wear of protective equipment were assessed.

Based on this, the relative job score according to the job title of workers and the sealed level of working space was assessed. Job score was based on the TLV to the harmful factors that can be exposed during performing job, and the method according to Astrakianakis *et al.*⁶ that designates without the exposure as 0 point, lower than 10% of TLV as 1 point, 10-25% of TLV as 2 points, 25-100% of TLV as 3 points, 100-200% of TLV as 4 points, and over 200% of TLV as 5 points was used.

In addition, according to the status of protective equipment, it was evaluated as the use of appropriate protective equipment continuously as 1 point, intermittent use as 2 points, and the use of inappropriate protective equipment or not use as 3 points. And by multiplying the job score and the use of protective equipment point, a semi-quantitative job-exposure matrix was established, and this value was presented as the pattern of exposure grade.

Exposure grade = job score × protective equipment point.

The Evaluation of the Exposure of Painters

Personal air sample were collected over 6 hour per day from the breathing zone of painting workers before urine sample were collected. The method evaluating PAHs in the air was performed according to the NIOSH method 5515.

Determination of Genetic Polymorphism

The genotypes of CYP1A1, CYP2E1, GSTM1, GSTT1 and UGT1A6 were investigated by using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) methods with DNA extracted from venous blood.

Statistical Analysis

The descriptive analysis on the general characteristic, working place, the status of using protective equipment of the study population was performed. The level of metabolite according to the general characteristic and the occupational characteristic was obtained by mathematical mean, standard deviation, geometric mean, geometric standard deviation and presented, statistical significance between two groups was evaluated by t-test and among more than three groups was evaluated by ANOVA. The distribution of the genetic polymorphism of the study population according to their job was presented by using a crosstab table. Finally, multiple regression analysis was performed by considering each genotype as a dummy variable and the metabolites in urine as a dependent variable, and age, drinking, smoking, genotype and the level of exposure as an independent variable, the factors that have influence on the metabolites in urine were examined.

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References

1. International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risk of chemicals to human; polynuclear aromatic compounds. *IARC* (1983).
2. Cralley, L.V., Woolrich, P.F, Mutchler, J.E. & Caplan, K.J. In plant practices for job related health hazards control. *John Wiley & Sons, New York* (1989).
3. Koh, S.B. *et al.* The similar exposure group and exposure variation in shipbuilding painters. *Korean J Occup Environ Med.* **13**, 413-422 (2001).
4. Van Rooij, J.G.M., Van Lieshout, E.M.A., Bodelier-Bade, M.M. & Jongeneelen, F.J. Effect of the reduction of skin concentration on the internal dose of Cresote workers exposed to polycyclic aromatic hydrocarbons. *Scand J Work Environ Health* **19**, 200-207 (1993).
5. Bouyer, J. & Hemon, D. Retrospective evaluation of occupational exposure in populational-based case-control studies; general overview with special attention to job exposure matrices. *Int J epidemiol.* **22**, (Suppl) 57-S64 (1993).
6. Astrakianakis, G. *et al.* Job exposure matrixes and retrospective exposure assessment in the pulp and paper industry. *Appl Occup Environ Hyg.* **13**, 663-670 (1998).
7. Susi, P. & Schneider, S. Database needs for a task-based exposure assessment model for construction.

- Appl Occup Environ Hyg.* **10**, 394-399 (1995).
8. Ovrebo, S. *et al.* Biologic monitoring of exposure to polycyclic aromatic hydrocarbons in an electrode paste plant. *J Occup Med.* **36**, 303-310 (1994).
 9. Petry, T., Schmid, P. & Schlatter, C. Airborn exposure to polycyclic aromatic hydrocarbon and urinary 1-hydroxypyrene of carbon anode plant workers. *Ann Occup Hyg.* **40**, 345-357 (1996).
 10. Angerer, J., Mannschreck, C. & Guumlndel, J. Occupational exposure to polycyclic aromatic hydrocarbons in a graphite electrode producing plant; biological monitoring of 1-hydroxypyren and monohydroxylated metabolite of phenanthrene. *Int Arch Occup Environ Health* **69**, 323-331 (1997).
 11. Shields, P.G. *et al.* Polycyclic aromatic hydrocarbon-DNA adduct in human lung and cancer susceptibility genes. *Cancer Res.* **53**, 3486-3492 (1993).
 12. Gabbani, G. *et al.* GSTM1 and NAT2 genotype and urinary metabolite in coke oven workers. *Carcinogenesis* **17**, 1677-1681 (1996).