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Effects of coke oven emissions and benzo[a]pyrene on blood pressure and electrocardiogram in coke oven workers

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Abstract: Objective: To evaluate the effects of occupational exposures to coke oven emissions (COEs) and benzo[a]pyrene (B[a]P) on the prevalence of hypertension and abnormal electrocardiogram (ECG) in coke oven workers. **Methods:** We included 880 coke oven workers and 710 oxygen employees in the exposed and control groups, respectively. Blood pressure (BP), ECG, blood lipid levels, and glucose levels of all subjects were measured. COE and B[a]P concentrations at the bottom, side, and top of the oven and control plants were estimated by weighing and high-performance liquid chromatography. **Results:** The COE concentration at the top and side was higher than that at the bottom ($P < 0.05$). The levels of B[a]P at the top and side significantly exceeded the limit value. Abnormal BP, ECG, the detection ratio of hypertension and left ventricular high voltage were significantly greater in the exposed group than in the control group ($P < 0.05$). The logistic regression analysis results revealed that age and B[a]P exposure were risk factors for hypertension in coke oven workers ($P < 0.05$) and both were risk factors for abnormal ECG ($P < 0.05$). Moreover, B[a]P exposure, age, and gender were risk factors for impaired fasting glucose in coke oven workers ($P < 0.05$). **Conclusions:** B[a]P and COE exposures are risk factors for hypertension and abnormal ECG in coke oven workers.
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Introduction

Coke oven emissions (COEs) are produced in the absence of oxygen during high temperature carbonization and contain a variety of toxic substances, including coal dust, coal tar, sulfur oxides, sulfur dioxide (SO_2), nitrogen oxides (NO_x), ammonia, benzene, phenolic compounds, polycyclic aromatic compounds, and carbon monoxide (CO)[1,2]. COEs are major occupational hazard factors of the steel industry, and chronic exposure of coke oven workers to COEs through the respiratory tract, mouth, or skin may cause conjunctivitis, dermatitis, and respiratory and digestive system injuries[3]. However, although previous studies mainly focused on the carcinogenicity of COEs[4,5], the cardiotoxicity of COEs remain elusive.

Polycyclic aromatic hydrocarbons (PAHs) are the main harmful components of COEs. More than 16 types of PAHs are present in COEs, such as benzo[a]pyrene (B[a]P), benzoanthracene, and phenanthrene[6-9]. Coke oven workers are directly exposed to PAHs through the respiratory tract or skin[10]. As a representative PAHs, B[a]P has many toxic effects on human health. Both epidemiological and animal studies have confirmed that chronic exposure to B[a]P can cause various types of cancers, including lung cancer, kidney cancer, liver cancer, and even brain tumor[11]. Nonetheless, the non-carcinogenic toxicities of B[a]P, such as the adverse effect on the cardiovascular system, are also worthy of attention.

In recent years, several studies have shown that B[a]P can not only cause cancers but also lead to cardiovascular injury[12]. Workers exposed to COEs may have remarkable increase in the risk for cardiovascular-related diseases[13-15], and some other studies have further reported that there is a dose-response relationship between COE exposure and decreased heart rate variability[16-18]. Importantly, animal experiments also demonstrated that chronic exposure to B

[a]P is related to changes in blood pressure (BP) rhythm and an abnormal electrocardiogram (ECG)[12,19,20]. These studies together suggest that the presence of COEs in workplaces associated with coke is closely related with the high prevalence of a cardiovascular disease in coke oven workers. However, whether occupational exposures to COEs and B[a]P can affect BP and ECG in humans, particularly coke oven workers, has not been revealed. In addition, the risk factors associated with COE- and B[a]P-induced hypertension or abnormal ECG remain unclear.

Therefore, this study aimed to evaluate the adverse effects of occupational exposures to COEs and B[a]P on the prevalence of hypertension and abnormal ECG in coke oven workers, and the influence factors associated with COE- and B[a]P-induced hypertension or abnormal ECG. Our findings will provide new evidence that occupational COEs and B[a]P may enhance the prevalence of hypertension and abnormal ECG and will be helpful for investigating potential strategies for preventing COE and B[a]P cardiotoxicities in coke oven workers.

Subjects and Methods

Subjects

The coke oven plant located in the Chongqing area was chosen as the research site. The bottom, side, and top of the coke plant were selected as the exposed sampling sites, and an oxygen plant at least 4-km upwind from the coke plant was selected as the control site. Subjects for this study were recruited using the cluster sampling method, and after screening, 880 coke oven workers and 710 oxygen employees were included. Subjects were excluded if they had hypertension, a heart disease, and/or severe psychological pressure in the recent 3 months, and employees of the control had not visited the coke plant in the previous 3 months. A standardized occupational questionnaire was used to collect data regarding demographic characteristics, smoking and drinking history, and the number of service years in the plant. The research protocols were approved by the ethics and human subject committees of the Chongqing Medical University, and all subjects signed the written informed consents.

Measurement of B[a]P concentration

Three sampling sites were placed in the bottom, side, and top of the oven plant and at the height of personal breathing zone in oxygen plant. Specifically, three air sampling pumps (FC-2B, Wuhan Analytic Instrument Factory, Wuhan, China) containing glass fiber membrane were placed at each sampling site, and they functioned at a flow rate of 2 *l*/min for continuous 4 h during working hours for 3 consecutive days. The filters were removed and sealed in a clean container and then stored at 4℃ in the laboratory before sampling. High-performance liquid chromatography (HPLC; 1100, Agilent, Palo Alto, CA) was performed to analyze airborne B[a]P concentrations. Retention time and peak area were recorded and further used to identify the analyte, and the ratio of the peak area of a standard sample was used to quantify the analyte.

Measurement of COE concentration

As a substitute of COEs, the concentrations of benzene soluble fraction (BSF) were measured in representative personal samples, and the individual cumulative and permissible exposure limit was 0.15 mg/m^3 [21]. Total particulate matter at the workplace was collected using a dust sampler at a flow rate of 20 *l*/min for continuous 4 h. The glass fiber filter paper was placed in a conical flask, 5 m*l* benzene was added, and then ultrasonic for 10 min. Subsequently, the filtrate was collected in a tube and placed in the flask with a fiber filter paper for drying with nitrogen. This filtration step was repeated twice, and the filtrate was together collected in the same tube. Benzene was further added in the tube until the total filtrate volume was 10 m*l*. Next, 5 m*l* of benzene was added in the weighing bottle and then placed in a vacuum drying box at 60℃ until benzene was evaporated to dryness. The blank control was determined by the method described for samples.

The COE concentration was calculated using the following formula:

$$V_0 = V \times \frac{273}{273 + t} \times \frac{p}{101.3} \quad \text{(A1)}$$

$$C = (m_1 - m_2) / V_0 \quad \text{(A2)}$$

V_0 is the volume of the sample under standard conditions (m^3), V is the measured volume of the sample (m^3), t is the temperature (℃), p is the atmospheric pressure (kPa), C represents COE concentration (mg/m^3), and m_1 and m_2 are the sample and blank quantities (mg), respectively.

ECG test

Data regarding age, gender, personal disease history, occupational history, education, and family cardiovascular disease history of all subjects were collected. In addition, I, II, III, avR, avL, avF, V1-V6, and 12 lead were traced by Cardico of Type 601 (Kenz, Japan).

BP detection

Before measuring the BP levels, subjects were rested in a quiet, comfortable, temperature-suitable environment for at least 5 min, and smoking and drinking tea or coffee was prevented. The BP levels were measured according to the WHO criteria, tests were repeated twice, and the mean value of two measurements was adopted. Subjects with systolic BP of >140 mmHg and/or diastolic BP of >90 mmHg were diagnosed with hypertension.

Table 1. General characteristics of the coke oven workers and control group

Items	Exposed Group (*n*=880)	Control (*n*=710)	*P* Value
Gender (male/female)	648/232	489/221	0.721
Age (means±SD)	39.1±11.32	38.06±11.54	0.071
Service years (means±SD)	9.52±1.74	9.73±2.27	0.079
Smoking (Yes/No)	517/363	426/284	0.633
Drinking (Yes/No)	650/230	328/382	0.714

Table 2. The concentrations of B[a]P and BSF in working environment

Sampling Site	B[a]P concentration (μg/m^3)	COEs concentration (mg/m^3)
Top	2.794±0.335	0.455±0.039
Side	0.788±0.064	0.170±0.032
Bottom	0.029±0.002	0.109±0.015
Control	0.003±0.001	-

Abbreviations: B[a]P, benzo[a]pyrene; COEs, coke oven emissions; BSF, benzene soluble fraction.
"-" BSF at the control' workplace did not detect. The resulting values were represented as means±SD.

Total cholesterol and fasting blood glucose detection

A 5-m*l* venous blood was collected from each subject after a 12-h fasting. The blood was anticoagulated using ethylenediaminetetraacetic acid, and biochemical indexes, such as total cholesterol (TC) and fasting blood-glucose (FBG) were analyzed using the Nissan 7020 biochemical analyzer (Hitachi, Japan). TC level of >5.72 mmol/*l* was regarded as dyslipidemia, and normal reference values of FBG were set from 3.89 to 6.10 mmol/*l*. According to the diagnostic criteria of diabetes (ADA, 1997), FBG values of >6.10 mmol/*l* and <7 mmol/*l* were defined as impaired fasting glucose (IFG).

Statistical analysis

All statistical analyses were conducted using the SPSS version 19.0 (SPSS Inc., Chicago, Illinois, USA). Student's *t*-test was used to compare the mean value of two numerical variables, and the ANOVA test was used to analyze multiple numerical variables. The chi-square test was used to analyze categorical variable data, and the rank sum test was used to evaluate two ordinal variables. The OR values of different variables were obtained and analyzed by logistic regression analysis. A *P* value of <0.05 was considered to be statistically significant.

Results

General data

Coke oven workers were divided into three groups according to the type of work and workplace, and 285 workers (32.39%) worked at the bottom of the oven, 353 (40.11%) at the side, and 242 (27.50%) at the roof. There were no significant differences with respect to gender (*P* = 0.721), age (39.1 ± 11.32 years and 38.06 ± 11.54 years; *P* = 0.071), smoking (*P* = 0.633), and drinking alcohol (*P* = 0.714) between the exposed and control groups. Furthermore, the number of service years of subjects in the exposed and control groups were 9.52 ± 1.74 years and 9.73 ± 2.27 years, respectively, showing no significant difference between the two groups (*P* = 0.793; Table 1).

Results of measuring B[a]P

The B[a]P concentrations in the working environment were 2.794 ± 0.335, 0.788 ± 0.064, and 0.029 ± 0.002 μg/m^3 at the top, side, and bottom of the oven, respectively, and 0.003 ± 0.001 μg/m^3 at the oxygen plant (Table 2). The B[a]P concentrations at the top and side of the oven were 17.63 and 4.25 times, respectively, above the maximum allowable airborne B[a]P concentration (0.15 μg/m^3) in a workplace.

Results of measuring COEs

The COE concentration was indirectly reflected by the BSF concentration. The BSF concentration was detected at each sampling site, and there were significant differences in the BSF concentrations among both groups (*P* < 0.05). The BSF concentrations in the working environment were 0.455 ± 0.039, 0.170 ± 0.032, and 0.109 ± 0.015 mg/m^3 at the top, side, and bottom of the oven, respectively. However, the BSF concentration in the working environment at the oxygen plant was not detected

Table 3. Differences in the physical examination between exposed group and control group

Items	Exposed Group (n=880)		Controls (n=710)		*P* Value
	Cases	Detection Rate (%)	Cases	Detection Rate (%)	
Abnormal Blood Pressure					0.049
Stage 3 Hypertension	10	1.14	12	1.69	0.347
Stage 2 Hypertension	32	3.64	19	2.68	0.28
Stage 1 Hypertension	114	12.95	69	9.72	0.044
Abnormal ECG					0.033
Block	15	1.7	8	1.13	0.337
Left Ventricular High Voltage	27	3.07	9	1.27	0.016
Premature Beat	13	1.48	7	0.99	0.382
Preexcitation Syndrome	5	0.57	3	0.42	0.738
Electrical Axis Deflection	2	0.23	1	0.14	0.999
ST-T Segment Change	9	1.02	8	1.13	0.841
Ventricular Hypertrophy	5	0.57	1	0.14	0.234
Sinus Arrhythmia	1	0.11	5	0.7	0.095
IFG	90	10.23	66	9.3	0.540
Abnormal TC	50	5.68	26	3.66	0.610

Workers with SBP of 140 to 159 mm Hg and/or DBP of 90 to 99 mm Hg was defined as stage 1 hypertension. Moreover, SBP of 160 to 179 and over 180 mm Hg and/or DBP of 100 to 109 and over 110 mmHg are defined as stage 2 and stage 3 hypertension, respectively. P<0.05 was considered to be of statistical significance.

(Table 2). The COE concentration at the top of the oven was 1.70 times over the maximum allowable airborne BSF concentration (0.15 mg/m^3) in a workplace as specified by the Occupational Safety and Health Act (OSHA).

Results of physical examination

The physical examination results revealed that 573 subjects of the exposed group had abnormal states (Abnormal BP, Abnormal ECG, Abnormal TC and IFC) (65.11%), while 444 subjects of the control group had abnormal states (62.53%). The detection rate of BP abnormalities of the exposed group was significantly higher than that of the control group (P = 0.049). Our results also showed that the prevalence of hypertension (stage 1) in the exposed group was significantly higher than that of the control group (P = 0.049), while the proportion of undetected hypertension was remarkably lower in the exposed group than in the control group (P < 0.05). Moreover, the detection rate of abnormal ECG in the exposed group was significantly higher than that in the control group (P = 0.033). Moreover, the detection rate of the left ventricular high voltage in the exposed group was also markedly higher than that in the control group (P < 0.05). No significant difference was observed between the two groups with respect to IFG and TC (Table 3).

Logistic regression analysis results of hypertension, abnormal ECG, TC, and IFG

To further reveal the risk factors associated abnormal examination, age, gender, smoking, and B[a]P exposure were introduced in the logistic regression analysis. Compared with the control group, results showed that low and high exposures to B[a]P, age, and smoking were all risk factors for hypertension in the exposed group. Moreover, subjects with high exposure to B[a]P were 1.819 times at a risk for hypertension compared with those with low exposure to B[a]P. The results also showed that age and high exposure to B[a]P were both risk factors for abnormal ECG, and subjects with high exposure to B[a]P were 1.978 times at a risk for abnormal ECG compared with those with low exposure to B[a]P. However, low and high exposures to B[a]P, drinking, and gender were protective factors for IFG, while age was a risk factor for IFG. Logistic regression analysis results of abnormal TC revealed that age was the only risk factor (Table 4).

Discussion

Cardiovascular disease is the leading health problem globally. Previous investigations have demonstrated that age, gender, family history, and habits (such as smoking and drinking) are closely related to the occurrence of a cardiovascular disease. Importantly, the hazards in an oc-

Table 4. Analysis of the factors associated with hypertension by logistic regression in coke oven workers

Factors	Hypertension				ECG				IFG				TC			
	P Value	OR	OR (95% CI)		*P*	OR	OR (95% CI)		*P* Value	OR	OR (95% CI)		*P* Value	OR	OR (95% CI)	
B[a]P medium-exposure	0.728	1.082	0.694	1.686	0.205	1.492	0.803	2.771	0.377	0.794	0.475	1.325	0.787	1.069	0.661	1.728
B[a]P high-exposure	0.011	1.819	1.148	2.883	0.041	1.978	1.030	3.800	0.013	0.454	0.243	0.848	0.823	1.062	0.627	1.799
Smoking	<0.001	1.146	1.052	1.241	0.733	1.028	1.011	1.045	0.067	1.257	1.108	1.406	0.756	1.136	1.067	1.205
Drinking	0.167	1.853	1.589	2.11	0.694	0.967	0.794	1.141	0.037	0.686	0.432	0.94	0.377	0.871	0.649	1.093
Sex	0.118	0.610	0.328	1.134	0.737	0.872	0.393	1.938	0.040	0.418	0.182	0.962	0.218	0.665	0.348	1.272
Age	<0.001	1.067	1.048	1.087	<0.001	1.036	1.012	1.060	<0.001	1.103	1.072	1.135	<0.001	1.054	1.033	1.075

Abbreviations: ECG, electrocardiogram; IFG, impaired fasting glucose; TC, total cholesterol.
According to the monitoring results of B[a]P and COEs, the lowest concentration of the coke oven was at bottom, which was considered as B[a]P low-exposure monitoring point and set as the indicator for contrast. While beside and top of the coke oven were considered as B[a]P medium-, high-exposure monitoring point. Compared with B[a]P low-exposure point, $P<0.05$ was considered have statistical significance.

cupational environment can also increase the prevalence of a cardiovascular disease[22,23]. In this study, we observed a significant increase in the BP levels of smokers ($P <$ 0.001) compared with that of non-smokers (data not shown). Furthermore, our finding revealed that B[a]P and COE exposures were risk factors for hypertension and abnormal ECG in coke oven workers.

Hypertension is the most important risk factor for a cardiovascular disease. Coke oven workers exposed to COEs and B[a]P via the respiratory tract may have a higher risk for high BP and easily induced cardiovascular disease[24]. As we know, the age of the onset of hypertension usually ranges from 40 to 60 years, particularly stage 1 hypertension[25,26]. In this study, we also found a significant increase in the BP levels of the exposed group compared with those of the control group ($P = 0.049$), and the logistic regression analysis further confirmed that B[a]P exposure was a risk factor for hypertension in coke oven workers, indicating that B[a]P exposure may enhance the prevalence of a cardiovascular disease by affecting BP.

At present, there is still no provision of an allowable airborne B[a]P concentration in a workplace in China, which mainly refers to the standard of the ex-Soviet Union, i.e., 0.15 $\mu g/m^3$. Moreover, the BSF concentration is typically used to reflect the COE concentration in a workplace according the criterion of OSHA (0.15 mg/m^3). Our study showed that B[a]P and COE concentrations were significantly higher in the coke oven plant than in the oxygen plant. The mean B[a]P concentrations at the top and side of the oven were 17.63 and 4.25 times, respectively, above the maximum allowable airborne B[a]P concentration in a workplace as set by the ex-Soviet Union. These results were also in line with those of a previous study[2]. Our results also revealed that occupational exposure to COEs affected the prevalence of hypertension in coke oven workers. Although age was a risk factor for hypertension, there was no obvious influence of age on other indices. In the logistic regression analysis, the side and top of the oven were considered as dummy variables, while the bottom of the oven was used as a comparison indicator; the results revealed that workers at the top of the oven had a higher risk for abnormal BP than those at the side and bottom of the oven.

By analyzing the association between B[a]P exposure and abnormal ECG, we found that age was statistically associated with ECG, but the correlation between them was very low ($P < 0.001$, $OR = 1.036$). Moreover, the workers at the top of the oven had approximately two times the risk for abnormal BP compared with those at the bottom of the oven. Altogether, these results indicate that age has a positive association with abnormal ECG, and it was also a risk factor for IFG and abnormal TC. It appears that drinking is a protective factor for IFG ($P =$ 0.037, $OR = 0.686$), but because of the finite number of subjects in this study, the association between drinking

and IFC required more investigation for confirmation.

Coke oven workers are regularly exposed to COEs, which mainly comprise a variety of volatile organic compounds and particulates, particularly PAHs[2]. It has been widely studied that B[a]P is typically considered as a representative substance of PAHs (accounted for 10%-20%)[9]. Considering this, B[a]P may also play an important role in estimating the health risk of coke oven workers. By measuring COE and B[a]P concentrations in different workplaces, we found that the side and top of the coke oven were the main sites of pollution, which were similar to the results of previous studies[9,27]. Our study also demonstrated that COE concentrations increased from the bottom to the top of the oven, and the concentration at the roof significantly exceeded that specified by OSHA (0.15 mg/m^3). In addition, the detection rates of abnormal BP and ECG in the exposed group were significantly higher than those in the control group. There was statistical relevance of COE and B[a]P exposures with hypertension and abnormal ECG.

The limitation of this study was that only few workers wore protective equipment (face mask or respirator) while working because of an uncomfortable feeling and inconvenience faced while using them. Among the coke oven locations, the COE concentration at the top and side was higher than that at the bottom. Thus, improving the protection of coke oven workers, particularly those working at the top and side, and increasing occupational health knowledge propaganda are even more important. Furthermore, because of the finite number of subjects involved in this study and to avoid the increase in type II errors in statistics, it is difficult for us to divide the groups with respect to gender, particularly for abnormal ECG. Thus, we did not compare gender as a single factor and the association with gender needs to be evaluated in future studies.

In conclusion, our results suggest that COE and B[a]P exposures influence hypertension and abnormal ECG in coke oven workers. Further studies should be devoted to understand the pathophysiological mechanism of B[a]P- or COE-induced cardiovascular system impairment.

Conflicts of interest: We declare that there is no conflict of interest of the authors.

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