

Association of p-phenylenediamine exposure with alterations of pulmonary function, pruritus and health-related quality of life in hair dye manufacturer workers: a cross-sectional study

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Abstract

Background p-Phenylenediamine (PPD) is a common component of hair dye, indicating the clinical characteristics of skin contact allergy and asthma with impaired pulmonary function. However the adverse effects of PPD occupational exposure was rarely mentioned. The purpose of this study was to explore the PPD-induced pulmonary function, pruritus and health-related quality of life (HRQOL) of industrial workers of hair dye. **Methods** We recruited 124 workers from a hair dye manufacturer exposed to PPD. Individual PPD exposure and pulmonary function of workers were measured. The quality of life and subjective pruritus of workers was also assessed by SF-36 and VAS of pruritus, respectively. **Results** In the high PPD-exposed group, FVC% (percentage of forced vital capacity) was higher, while FEV1/FVC% (ratio percentage of forced expiratory volume) was lower than that in the low PPD-exposed group ($P < 0.05$). In terms of the HRQOL, the scores of mental health and vitality of the high PPD-exposed group were the lowest of all groups ($P < 0.05$), while the score of VAS was significantly higher than that of other two groups ($P < 0.001$). PPD levels were negatively correlated with vitality and mental health ($P < 0.01$). Higher PPD exposure level was correlated with a significantly higher VAS level (OR 9.394; 95%CI: 1.710, 51.622; $P = 0.010$). The structural equation model provided a good fit to the data ($\chi^2/df = 1.607$, GFI = 0.901, AGFI = 0.934, RMSEA = 0.007, IFI = 0.977, CFI = 0.960, PGFI = 0.615). And showed that PPD exposed level have positive effects on VAS level ($\beta = 0.213$, $P < 0.001$). Then PPD exposed level partly via lack total score of SF-36 ($\beta = -0.465$, $P = 0.002$); on negative effects on VAR level ($\beta = -0.110$, $P < 0.001$). **Conclusion** Occupational PPD exposure might be associated with pulmonary function impairment, poor HRQOL, and subjective pruritus of workers.

1. Background

p-Phenylenediamine (PPD), a derivative of p-nitroaniline, is found in the plastic and chemical industries as byproducts of manufacturing. Due to its low molecular weight (108 kDa), PPD has a strong protein binding ability to penetrate deeply into the hair. It is widely used as an oxidizable hair dye for its free availability and low cost. In addition, this chemical is used as a substitute for henna and in the manufacturing of rubber and certain polymers. It also acts as a developing agent in color photographic film [1].

PPD is highly toxic with local and systemic toxic effects when taken by mouth, and the outcome depends mainly on the dose taken. Many studies have shown that PPD has multiple organ system toxicity, which can cause skin allergies and itching, cardiotoxicity, and urinary toxicity. Among these health hazards, the most common is the skin toxicity and respiratory damage in low-dose exposure of PPD. In addition, PPD use in hair dyes can lead to skin allergy including severe contact dermatitis, and PPD is considered an important cause of hair dye allergy [2, 3].

In 1939, PPD was first defined as a strong allergen and included in the standard antigen group of the North American and European epidermal patch tests. According to European Cosmetic Directive (76/768/EEC), PPD's maximum permissible concentration in hair coloring is 2%. The serious level of PPD allergy is mostly determined by the exposure concentration and duration [4]. It is reported that PPD causes erythema, scaling, itching or edema in less than 1% individuals of the general population after dyeing the hair [5]. Occupational exposure to PPD foam, during its production or application in manufacturing of various products, may result in health problems affecting airway and skin. Both allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD) have been reported [6]. The incidence of PPD related ACD, an occupational-related, positive patch test reaction to PPD, is about 4.80% in outpatients who workers occupational exposed to PPD such as hairdressers, barbers [7]. PPD may also cause damage to the lungs. Induction routines and challenge patches with 0.001–10% PPD sensitized 56–100% of guinea pigs on test. Massive peribronchial infiltrates of eosinophils were observed in guinea pigs after intrapulmonary injection of an aqueous solution containing 1% PPD. Antigen-induced infiltrates were limited to the injected lung, and no eosinophilic infiltrates were detected in the untreated lung, which served as the control [8]. According to European Cosmetic Directive (76/768/EEC), PPD's maximum permissible concentration in hair coloring is 2%. The serious level of PPD allergy is mostly determined by the exposure concentration and duration [9]. It is reported that PPD causes erythema, scaling, itching or edema in less than 1% individuals of the general population after

dying the hair [5]. Moreover, long-term occupational exposure to PPD may lead to chronic renal impairment in workers, and the serum creatinine, proteinuria and hematuria were correlated with their working age [10]. Oxidized products of PPD might also have potential carcinogenicity to humans. Association has been observed between hair dye use and non-Hodgkin's lymphoma, multiple myeloma, acute leukemia and bladder cancer [11, 12, 13].

As aforementioned, occupational exposure to PPD can result in health problems such as skin allergies and pulmonary function changes [7]. These problems may lead to a decline in their quality of life, and then interfere with their activities of daily living and work. However, previous studies have mostly conducted research on ordinary people or emergency patients, and the studies of occupational groups only focused on individual case reports of hairdressers. So far, no research has been conducted on workers who are working on exposure PPD. In addition, there are few studies evaluating the effect of the PPD exposure on the itching of the skin and the quality of life for the workers. In order to evaluate skin discomfort and correlate it with the effects on the individual, there is also a need for methods to determine the clinical severity of people. Compared with patch-test to PPD allergy in previous research, the Visual analogue scale (VAS) could evaluate the skin discomfort without an obvious allergic reaction [7, 14]. And examination including peripheral blood, pulmonary function has been presented as an easily-used method reflecting the physical condition. Health-related quality of life (HRQOL) is a broad and multidimensional measure that assesses an individual's perception of physiological function, mental ability and social adaptability. HRQOL can be influenced by health status, medical interventions, personal beliefs, social environments, economic circumstances and cultural backgrounds [15]. Therefore, another aim of the present study is focused on the dimensions of subjective quality of life by using the short form 36 health survey (SF-36) to evaluate the HRQOL of PPD-exposed workers in hair dye production.

2. Methods

2.1 Study Population

The cross-sectional study was based on data from a hair dye company containing PPD in Zhejiang Province of PR China. The occupational health management in this company is standardized, possessing protective measures that can prevent contact with dangerous substance includes masks, protective clothing, boots and overshoes. The participants were enrolled using a simple random method who are engaged in configuring raw material (n = 9), adding chemical (n = 9), adding material into the jar (n = 28), packaging and transporting (n = 50), laboratory staffs (n = 4), accounting (n = 6), cleaning and logistics (n = 13) and managing (n = 5). The sample had 68 men and 56 women. All subjects had a convincing history of no allergic reaction. They were asked to fill out a demographic questionnaire which included the age, gender, area of residence, telephone number, working age, educational status, smoking status and hair dye use status. All participants have signed informed consent, and ethical approval was granted by the Ethics Committee of Tianjin Center for Disease Control and Prevention.

2.2 Measurement of PPD concentration

Referenced to the method 5013 of the U.S. National Institute for Occupational and Safety (NOISH) [16], the PPD in the air of various working environments and workers of different types (simple random sampling of 3 ~ 5 individuals per type of work) were sampled, and then determined samples by high performance liquid chromatography (HPLC) with the analytical column of Eclipse SB-C18 (150 mm × 4.6 mm × 5 μm) and the mobile phase of mixed solution of disodium hydrogen phosphate solution and acetonitrile with a flow rate of 2.0 mL/min. The detection wavelength was 240 nm and the injection volume was 5 μL.

2.3 Self-reported measures of life condition

The subjects completed two self-reported assessment for life condition: SF-36 and VAS of pruritus.

The quality of life was assessed by SF-36, derived from the health survey results of the Medical Outcomes Study (MOS) in 1988. It has been translated into Chinese in 1991 and its reliability and validity has been verified in Chinese population after considering cultural adaptation, validation, and normalization [17]. SF-36 measured eight dimensions of health including physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health. In addition to these dimensions, SF-36 also considered reported health transition scaled scores [18]. Each scale was directly transformed into a score from 0 to 100 after modifying the weighing coefficient in each question. The lower score meant the worse health status, whereas the higher the score the less possible disability [19]. The Cronbach's α values for each dimension of SF-36 were calculated to be greater than 0.7, indicating that the internal consistency of the scale is good in occupational workers. After factor analysis, the KMO value was 0.625 and Bartlett's test result show P value was less than 0.001, indicating that the structural validity was good. Therefore, this scale had suitable reliability and validity for the occupational population.

The extent of subjective pruritus was assessed by VAS of pruritus [20]. It has been widely used because of a simple structure and flexible operation. Participants could mark a score for a 100 mm horizontal line on the questionnaire to represent their subjective feelings of cutaneous itching. The benchmark descriptors for each level were as follows: 1 level: 0 mm to 10 mm (i.e., no itching symptoms), "no or almost no itch"; 2 level: 10 mm to 40 mm (i.e., slight itching symptoms), "occasional restless sensations that do not necessarily induce scratching behavior"; 3 level: 40 mm to 70 mm (i.e., moderate itching symptoms), "significant scratching and the itch disrupts sleep, and although the patient can go back into sleep after scratching"; 4 level: more than 70 mm (i.e., fierce itching symptoms), "unbearable itch causes scratching and scratching almost deprived of sleep, the patient keeps scratching ceaselessly".

2.4 Biochemical detection

The levels of alanine transaminase (ALT), aspartate aminotransferase (AST), total protein (TP), albumin (ALB), alkaline phosphatase (ALP), total bilirubin (TBI) in serum were detected using commercial test kits (Jiancheng Bioengineering Ltd., Nanjing, China).

2.5 Hematologic detection

Red blood cell (RBC), white blood cell (WBC), hemoglobin (HGB) and platelet (PLT) were detected using commercial test kits (Jiancheng Bioengineering Ltd., Nanjing, China).

2.6 Pulmonary function examination

The pulmonary function test was obtained for all workers to evaluate the capacity and the volume of lungs, by forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and ratio of FEV1 to FVC (FEV1/FVC).

2.7 Statistic analysis

Statistical analysis was conducted using SPSS package (Version 20.0) unless otherwise specified. Numerical variables were reported as mean \pm SD. The Chi-square test and Chi-square after Yates continuity correction test were used to compare the differences of demographic situation and working age, educational, smoking and hair dye use between different groups. The covariance analysis and Bonferroni test were performed for comparing interesting variables in different groups after controlling for the confounding factors, and $P < 0.017$ (two-tailed) was considered statistically significant, taking the multiple comparisons into consideration. Covariates included gender, nation, working age, education condition and recent hair dye history. Due to the co-linearity of working age and age, this study only adjusted working age as a covariate. Study on the influencing factors of VAS level by logistic regression. Before the multivariate analysis, the Variance Inflation Factor (VIF) was calculated to rule out the effects of multicollinearity. We used logistic regression to estimate the odds ratio (OR) and its 95% confidence interval (95% CI) for the association of VAS level with hematologic indexes and some factor scores in SF-36. $P < 0.05$ (two-tailed) was considered statistically significant in the final models. Structural equation modeling (SEM), which can evaluate the relationship between variables, was performed with the AMOSE software. Cutoff criteria for good

model fit were attained from extant literature; Satorra-Bentler χ^2 / df values < 3.0 were considered good; GFI values > 0.90 and AGFI > 0.90 were considered reasonable; RMSEA values < 0.10 , IFI and CFI values > 0.90 , PGFI > 0.50 were considered good. $CAIC_{\text{default}} < CAIC_{\text{independence}}$ and $CAIC_{\text{default}} < CAIC_{\text{saturated}}$ were considered good [21]. Missing data was replaced by means of the scores in the different groups.

3. Results

3.1 General characteristics of investigated population

According to the PPD exposure concentrations, each worker was divided into three levels (1st level: $< 0.00001 \text{ mg/m}^3$; 2nd level: $0.00001 \sim 0.00033 \text{ mg/m}^3$; 3rd level: $0.00033 \sim 0.047 \text{ mg/m}^3$). Subsequently, 124 subjects were divided into exposed groups and non-exposed control group, the former further divided into high and low concentration groups of PPD exposure. The non-exposed control group included financial staffs, support staffs, administrative personals and cleaners ($< 0.00001 \text{ mg/m}^3$). The workers who were involved in raw material, adding chemical, adding material into the jar, and laboratory staffs were designated as the high concentration group ($0.00089 \sim 0.19 \text{ mg/m}^3$), while the packaging workers were designated as the low concentration group ($0.00001 \sim 0.00089 \text{ mg/m}^3$) (Supplemental Table 1).

The distributions of demographic characteristics among the three groups were showed in Supplemental Table 2. High concentration group, low concentration group and control group statistically differed in gender, nation, working age, education condition and hair dye history ($P < 0.05$). The male constituent ratio was higher in the high concentration group (82%) than in the low concentration group (36%) and the control group (37.5%). Among the three groups, the proportion of the Han nationality in low concentration group (80%) was lower than other groups. The number of workers with working age less than 5 years was the highest in low concentration groups (54%). In the term of educational condition, the proportion of primary school and lower level was lower in control group than the other two groups. The hair dye history in the control group (16.67%) had a lower constituent ratio than the high concentration group (54%).

3.2. Changes of hematologic indexes of the study participants

The hematologic indexes results among the three groups were in the normal count ranges. After adjustments for gender, nation, working age, education condition and recent hair dye history, the covariance analysis showed that in the high concentration group, white blood cell count was lower ($P < 0.001$), while basophils and eosinophils were higher ($P < 0.05$) than that in the control and low concentration groups. Besides, compared to the low concentration group, workers in the high concentration group presented a higher neutrophil and hemoglobin level. No differences were observed for other hematologic indexes indices among the three groups (Table 1).

Table 1
Covariance analysis results of serum biochemical indexes (mean \pm SD)

Variable	Control group	Low concentration group	High concentration group	F	P value
White blood cell count($10^9/L$)	6.929 \pm 1.243	6.656 \pm 1.088 [#]	5.206 \pm 1.209 [*]	8.569	< 0.001
Neutrophil($10^9/L$)	3.951 \pm 0.914	3.423 \pm 0.291 ^{*#}	3.949 \pm 0.911	2.803	0.010
Lymphocyte($10^9/L$)	1.839 \pm 0.489	1.836 \pm 0.480	1.925 \pm 0.541	0.706	0.667
Basophils ($10^9/L$)	0.015 \pm 0.010	0.015 \pm 0.014 [#]	0.040 \pm 0.015 [*]	16.053	< 0.001
Monocytes ($10^9/L$)	0.350 \pm 0.078	0.342 \pm 0.050	0.334 \pm 0.063	0.718	0.657
Eosinophils ($10^9/L$)	0.157 \pm 0.112	0.212 \pm 0.078 ^{*#}	0.363 \pm 0.102 [*]	16.505	< 0.001
Red blood cell count($10^{12}/L$)	5.017 \pm 0.392	5.122 \pm 0.413	5.080 \pm 0.420	0.379	0.913
Hemoglobin(g/L)	142.920 \pm 13.247	140.780 \pm 12.621 [#]	148.160 \pm 13.577	13.364	< 0.001
Mean corpuscular volume(fL)	85.670 \pm 10.516	86.380 \pm 10.463	85.560 \pm 10.695	0.643	0.720
Mean corpuscular hemoglobin concentration(g/L)	340.880 \pm 11.449	339.540 \pm 8.779	338.400 \pm 7.902	0.756	0.625
Mean platelet volume(fL)	9.370 \pm 1.075	9.650 \pm 0.497	9.480 \pm 0.945	1.065	0.391
Platelet volume distribution width	11.996 \pm 2.146	11.770 \pm 1.668	11.796 \pm 1.897	0.849	0.549
The average amount of Hb in red blood cells(pg)	28.920 \pm 4.106	28.940 \pm 4.043	29.720 \pm 3.552	0.486	0.843
Platelet count($10^9/L$)	234.040 \pm 45.108	237.940 \pm 45.488	238.320 \pm 43.507	1.105	0.365
Plateletcrit(PTC)	0.271 \pm 0.042	0.258 \pm 0.042	0.261 \pm 0.045	0.639	0.723
* P < 0.05,there were statistical differences between exposed groups and control group by Bonferroni method.					
[#] P < 0.05,there were statistical differences between high concentration group and low concentration group by Bonferroni method.					
The covariant variables including gender, ethnic group, working age, education condition and recent hair dye history.					

3.3 Alteration of Pulmonary function of the study participants

After adjustments for gender, nation, working age, education condition and recent hair dye history, the spirometry parameters of the three groups were significantly different. The pulmonary function indices like FEV1% and FEV1/FVC% of the high concentration group were significantly lower than those of control group (P < 0.05). In the high concentration group,

FVC% was higher, while FEV1/FVC% was lower than that in the low concentration group ($P < 0.05$). In addition, compared to control group, workers in the low concentration group presented the lower FVC% and FEV1% ($P < 0.05$) (Table 2).

Table 2
Covariance analysis of FVC%, FEV1%, FEV1/FVC% in different PPD-exposure group (mean \pm SD)

Variable	Control group	Low concentration group	High concentration group	F	P value
FVC%	103.044 \pm 9.498	89.076 \pm 11.806*#	101.399 \pm 9.409	7.519	< 0.001
FEV1%	104.665 \pm 12.289	91.772 \pm 6.261*	92.483 \pm 10.300*	8.791	< 0.001
FEV1/FVC%	102.215 \pm 14.040	104.700 \pm 14.779#	91.889 \pm 12.737*	6.855	< 0.001
* $P < 0.05$, there were statistical differences between exposed groups and control group by using Bonferroni method.					
# $P < 0.05$, there were statistical differences between high concentration group and low concentration group by Bonferroni method.					
The covariant variables including gender, ethnic group, working age, education condition and recent hair dye history.					

3.4 Self-reported of physical subjective feelings of the study participants

After excluding the influence of gender, nation, working age, education condition and recent hair dye history, covariance analysis indicated that means for role-physical ($P = 0.023$), bodily pain ($P < 0.001$), general health ($P < 0.001$), vitality ($P < 0.001$), mental health ($P < 0.001$), health transition ($P < 0.001$) and total scores were all significantly different among the three groups (Table 3). The means for bodily pain, general health and health transition in low concentration group were lower than the control group and the high concentration group ($P < 0.05$). Besides, the mean for mental health in the high concentration group and role-physical in the low concentration group was lowest of all groups ($P < 0.05$). High concentration PPD also resulted in a decreased vitality score compared to the control group. For the total score, the score for control group was higher than the exposure groups, and the high concentration group was higher than the low concentration exposure group ($P < 0.05$).

Table 3
Covariance analysis results of SF-36 (mean ± SD)

Variable	PF	RP	BP	GH	VT	SF	RE	MH	HT	Total score
Control group	98.13 ± 2.88	96.09 ± 6.60	97.25 ± 8.77	92.0 ± 10.62	72.08 ± 9.55	92.71 ± 9.69	93.06 ± 9.08	61.5 ± 5.25	85.40 ± 24.36	788.32 ± 48.52
Low-concentration group	97.40 ± 3.81	94.88 ± 9.25#	83.60 ± 21.01*#	78.4 ± 13.93*#	65.30 ± 14.16	91.20 ± 12.94	95.83 ± 8.29	59.04 ± 6.18#	59.50 ± 19.49*#	725.29 ± 47.11*#
High-concentration group	98.50 ± 2.31	96.87 ± 5.54	97.37 ± 5.23	88.20 ± 16.96	62.30 ± 11.91*	87.25 ± 15.04	94.3 ± 10.84	55.12 ± 8.68*	72.50 ± 22.73	752.45.32 ± 47.52*
F	1.276	2.444	8.972	6.983	5.51	1.632	0.617	4.477	6.163	3.780
P	0.268	0.023	< 0.001	< 0.001	< 0.001	0.133	0.741	< 0.001	< 0.001	0.026
* P < 0.05, there were statistical differences between exposed groups and control group by Bonferroni method.										
# P < 0.05, there were statistical differences between high concentration group and low concentration group by Bonferroni method.										
SF-36: the short form 36 health survey; PF: physical functioning; RP: role-physical; BP: body pain; GH: general health; VT: vitality; SF: social functioning; RE: role-emotional; MH: mental health; HT: health transition.										
The covariant variables including gender, ethnic group, working age, education condition and recent hair dye history.										

The results of multivariable logistic regression analysis for VAS levels with some demographic variables, SF-36 factors were showed in Table 4. It found that men were less likely to present high VAS levels than women (OR 0.114, 95%CI: 0.027, 0.482, P = 0.003). The worker who works in a high concentration PPD atmosphere significantly increased the probability of VAS level (OR 9.394, 95%CI: 1.710, 51.622, P = 0.010). Individuals without a hair dye history had almost one tenth the probability of not (OR 0.091, 95% CI: 0.021, 0.385, P = 0.001). And workers with senior middle school and higher education have lower level of VAS (OR 0.041, 0.033 respectively; both P < 0.05). As for SF-36 scores, workers with the higher BP score have higher VAS level (OR 1.056, 95% CI: 1.008, 1.106, P = 0.021), and with higher GH score have lower VAS level (OR 0.950, 95% CI: 0.904, 0.998, P = 0.040).

Table 4

Multiple Logistic regression analysis of VAS level with hematologic indexes and some factor scores in SF-

36

	β	S^2_x	Wald χ^2	P value	OR	95%CI
Intercept	8.271	5.182	2.548	0.110		
PPD exposed levels						
Control = 0					1	
Low = 1	0.230	0.893	0.066	0.797	1.259	(0.219,7.240)
High = 2	2.240	0.869	6.640	0.010	9.394	(1.710,51.622)
Working age	0.031	0.042	0.553	0.457	1.031	(0.951,1.119)
Gender						
Female = 0					1	
Male = 1	-2.170	0.735	8.721	0.003	0.114	(0.027,0.482)
Hair dye history						
Yes = 0					1	
No = 1	-2.399	0.737	10.598	0.001	0.091	(0.021,0.385)
Ethnic group						
Han = 0					1	
Others = 1	-1.648	0.874	3.555	0.059	0.192	(0.035,1.067)
Educational condition						
Primary school and lower level = 1					1	
Junior high school level = 2	-1.242	1.127	1.214	0.271	0.289	(0.032,2.632)
Senior middle School level = 3	-3.197	1.337	5.718	0.017	0.041	(0.003,0.562)
College and higher level = 4	-3.418	1.544	4.904	0.027	0.033	(0.002,0.675)
SF-36						
RP	-0.034	0.047	0.519	0.471	0.967	(0.883,1.059)
BP	0.055	0.024	5.337	0.021	1.056	(1.008,1.106)
GH	-0.052	0.025	4.206	0.040	0.950	(0.904,0.998)
VT	-0.007	0.031	0.051	0.821	0.993	(0.935,1.054)
MH	-0.008	0.042	0.038	0.845	0.992	(0.914,1.076)
HT	-0.017	0.015	1.389	0.239	0.983	(0.955,1.012)

3.5 Structural equation model for SF-36, VAS level and PPD exposed concentrations

A model with PPD exposed level predicting VAR level through SF-36 scores evidenced reasonable fit across indices (Table 5). All indicators meet the reasonable reference value of the model ($\chi^2/df = 2.215$, GFI = 0.901, AGFI = 0.927, RMSEA

= 0.092, IFI = 0.972, CFI = 0.969, PGFI = 0.593). The model with standardized path coefficients is presented in Supplemental Fig. 1. Direct paths were significant, PPD exposed level have positive affect on VAS level ($\beta = 0.213$, $P < 0.001$). Then PPD exposed level partly via lack total score of SF-36 ($\beta = -0.465$, $P = 0.002$); on negative affect on VAR level ($\beta = -0.110$, $P < 0.001$). The indirect path of hair dye history has negative affect on VAS level ($\beta = -0.221$, $P = 0.002$), and PPD exposed levels via white blood cell count ($\beta = -0.952$, $P < 0.001$), basophils ($\beta = 0.015$, $P < 0.001$), eosinophil ($\beta = 0.110$, $P < 0.001$) and hemoglobin ($\beta = 3.349$, $P = 0.036$) were all significant ($P < 0.001$), while neutrophil was nonsignificant ($\beta = 0.080$, $P = 0.388$). In the model, the indirect paths of PPD exposed level via pulmonary function indices showed FEV1% ($\beta = -5.051$, $P < 0.001$) and FEV1/FVC% ($\beta = -6.333$, $P < 0.001$) were significant, while FVC was nonsignificant ($\beta = 1.188$, $P = 0.418$). The model with standardized path coefficients is presented in Supplemental Fig. 1.

Table 5
Summary of model fit

Adaptability index	χ^2/df	GFI	AGFI	RMSEA	IFI	CFI	PGFI	CAIC
Reference value	1–3	> 0.90	> 0.90	< 0.10	> 0.90	> 0.90	> 0.50	$CAIC_{\text{default}} < CAIC_{\text{independence}}$ and $CAIC_{\text{default}} < CAIC_{\text{saturated}}$
Model test value	2.29	0.901	0.934	0.099	0.979	0.907	0.593	$488.056 < 1432.971$ and $890.503 < 890.503$

4. Discussion

In our study, pulmonary function index like FEV1/FVC% were lower in high PPD concentration group, and FVC% was lower in low PPD concentration group than other two groups. In terms of the HRQOL, mental health and vitality of the high PPD-exposed group were the lowest of all groups ($P < 0.05$), while the score of VAS was significantly higher than that of other two groups ($P < 0.001$). Higher PPD exposure level was correlated with a significantly higher VAS level (OR 9.394; 95%CI: 1.710, 51.622; $P = 0.010$). Occupational PPD exposure might be associated with pulmonary injury, poor HRQOL, and subjective pruritus of workers.

According to the define of health in the World Health Organization, the quality of workers' life is focused not just on the condition of no diagnosed diseases, but on the life [15]. We use two ways for assessing an individual's quality of life; self-administered questionnaire and physiological health examination. The physiological health examination including peripheral blood and pulmonary function. It evaluates the factors that affect an individual's health such as diseases, which affects life quality. The self-administered questionnaire assesses the complex reaction environmental factors such as pruritus subjectively, pressure and working environment that affect the life quality.

Frequent contact with hair dyes production and working in the atmosphere with PPD aerosol can caused widespread health issues such as contact allergy [22]. In the present study, the blood biochemical indices, pulmonary function, HRQOL and VAS of pruritus were compared among the workers who exposed to different concentrations of PPD aerosol. The results of air monitoring suggested that the mean concentration of PPD in different workshops were lower than the threshold-limited value-time-weighted average (0.1 mg/m^3). It puts pressure on the human body health. The workers exposed in high PPD concentration showed a lower white blood cell count and higher basophils, hemoglobin and eosinophils counts. An elevation of basophils, hemoglobin and eosinophils counts was similar to those found in neutrophilic dermatitis, apart from the pronounced eosinophilia. Numerous studies have reported that is a marker of hypersensitivity [23, 24, 25]. Moreover, the results of the present work agreed with most findings of the Sieben's study that both PPD and its auto-oxidation product can stimulate lymphocyte proliferation [26, 27].

In our study, both FEV1% and FEV1/FVC% were lower in high PPD concentration group, and FVC% was lower in low PPD concentration group than other two groups. In addition, the mean of all groups' indices were in the normal range. The

reason may cause this situation was that the hazard of low PPD dose with long-term exposure was relatively weaker. Some case report researches have also indicated that PPD poisoning could lead to respiratory distress [28, 29]. However, these studies have not reported the effects of low PPD concentration on pulmonary function in the workplace. This finding implied that there might be an increased risk of respiratory disorders for workers in response to long-term PPD exposure.

Any health problems can cause a disruption in the normal life and have a substantial impact on the quality of life [30], it seems important to assess the non-organ-specific manifestations such as HRQL. In the present study, we found that not only body pain, mental health and physical role were affected, but also the general health, vitality and reported health transition were affected for all workers. It has been suggested that these effects can have a long term effect of the acquisition of personality and health behaviors. Our results were similar to the conclusions reached by Mohammadi et al., who studied the HRQL of silica-exposed workers [31]. Various studies have showed that age is a risk factor to physical health status [32, 33], because elders were usually affected by one or more chronic diseases and conditions [34]. However, the present study showed that the general health status, vitality and health transition were better in longer work-age workers. It might be explained by the healthy worker effect phenomenon that older workers usually have better health conditions than the general population [35, 36]. People exposed in high PPD levels have lower score in the dimensions of vitality and mental health. One reason for the results might be because they engaged in different types of work that caused different PPD exposed concentration. The other reason for this could be the different ways to select subjects, with studies in this field based on retrospective analysis. The present study proved that smoking was harmful to physical role, it was similar to the previous studies [37, 38]. The current study found that subjective feelings of bodily pain, mental health, and general health are not the same for men and women. As reported by previous study, general health and mental health were significantly associated with gender [9].

In the light of the itching of skin seen as a subjective discomfort, the VAS of pruritus was used in this survey. The results of VAS levels in this survey are related to PPD exposed levels. A similar tendency was found that PPD is responsible for the majority of the allergic reactions to permanent hair color, among which the most common kind of allergic reactions is itchy [39]. It found that women were more likely to feel itching of skin than men. This is partly due to the physiological sensitivity of different gender to PPD. While gender distribution varies among different types of work, we suggest to interpret the presented data considering this gender bias. Because VAS level is also affected by subjective perception, we analyze the impact of health-related quality of life and education condition on VAS level. It found that the higher the level of education, the lower the degree of itching. This may be because that a high level of education will have a more comprehensive understanding of the dangers of PPD. The reciprocal and intricate relationship between the psyche and itch has been widely studied [40]. The augmentation of perception of itch owing to the interplay of psychogenic and emotional factors has been well studied [41]. Although pruritus itself is not recognized as a separate entity as such, DSM-V (Diagnostic and Statistical Manual of Mental Disorders, 5th edition by American Psychiatric Association) has already included a category of physical symptoms and related disorder. Pruritic conditions exacerbate the symptoms of itching [42]. Itching and pain have the same receptors and have much in common [43]. Therefore, there is a certain relationship between the degree of body pain and VAS level.

We found direct paths from PPD exposure level to VAS level outcomes through one variable: lack of SF-36. Specifically, have hair dye history predicted negative affect on VAS level. PPD exposed may cause FEV1% and FEV1/FVC% decreased, and some pressure to blood biochemical index such as white blood cell count, eosinophils, basophils and hemoglobin. The model provided a good fit to the data. Taken together, structural equation model results support the above hypothesis study, and provides with a possible causal relationship between these variables.

There are several strengths of our study. A key strength of our study is that we first studied the workers with the occupational exposure of PPD as the research object, and measured the levels of occupational exposure to PPD in groups. Therefore, the exposure grouping in this study is more accurate and reasonable. An additional strength of our study is the comprehensively consider the physical and mental health of workers. The physical examination indicators and health-

related quality of life of workers exposed to PPD were analyzed, and a structural equation model was established to establish possible causality. We provide scientific basis for proposing the PPD occupational exposure control level to protect the health of the occupational population.

There are some limitations in this study. First, the study is a cross-sectional study. Although a possible causal association has been established through structural equation modeling, further cohort studies and experimental studies are needed to verify these association. Secondly, the study was limited by its small sample size. Thus, large-scale studies seem necessary in PPD occupational exposed workers to gain a better understanding of the physiological and mental state of the workers. Moreover, there were different types of confounding factors for SF-36 scores and VAS levels: the socio-economic status, income, work type, and stress for life, therefore, further comprehensive studies should consider these factors.

Although there is no relatively safe and effective raw material composition that can completely replace PPD during its production or application in manufacturing of various products, the hazard and risk due to PPD emphasize the needs for multifaceted measures to decrease exposure. It is necessary to put forward protective measures and programs for workers with occupational exposure to PPD.

5. Conclusion

Our current study showed that occupational PPD exposure was associated influences on HRQL in workers. PPD exposure levels affect the degree of itching through a partial mediation of health-related quality of life. The means of vitality and mental health were negatively associated with PPD exposure. Workers who exposed to high levels of PPD may cause changes in blood biochemical indicators such as lower white blood cell count and higher basophiles, hemoglobin and eosinophils counts. In response to PPD exposure, workers might have an increased risk of respiratory disorders. Occupational PPD exposure has an effect on subjective itching and health-related quality of life. And health-related quality of life mediates the effects of PPD exposure on subjective pruritus.

Abbreviations

ACD, allergic contact dermatitis; FEV1, forced expiratory volume in one second; FEV1%, percentage of forced expiratory volume in one second; FVC%, percentage of forced vital capacity; FEV1/FVC %, ratio percentage of forced expiratory volume in one second /forced vital capacity; HRQOL, health-related quality of life; HPLC, high performance liquid chromatography; ICD, irritant contact dermatitis; MOS, the Medical Outcomes Study; OR, odds ratio; PPD, p-Phenylenediamine; SF-36, the 36-item Short Form Health Survey; SEM, structural equation modeling; VAS, Visual analogue scale; VIF, variance inflation factor; BP (bodily pain); GH (general health); RP (role-physical); MH (mental health); VT (vitality); HT (health transition); VAS (Visual analogue scale); SF-36 (36-item Short Form Health Survey).

Declarations

Ethics approval and consent to participate

All participants have signed informed consent, and ethical approval was granted by the Ethics Committee of Tianjin Center for Disease Control and Prevention.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors contributions

All authors contributed to the development of this manuscript (LF, MZ, MBZ, BFL and QZ). MZ contributed to the study design. LF, MZ, MBZ, BFL and QZ participate in the investigation, measurements and data collection. LF and QZ conducted the data analysis. LF drafted the original manuscript. MZ reviewed and edited the manuscript. All authors revised and approved the final manuscript.

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