RESEARCH ARTICLE

Historical Long-term Exposure to Pentachlorophenol Causing Risk of Cancer - A Community Study

Rui-Zhi Zheng[1&], Qing-He Zhang[1&], Yi-Xin He[2], Qian Zhang[1], Lin-Shen Yang[1], Zhi-Hua Zhang[1], Xiu-Jun Zhang[1], Jing-Ting Hu[2], Fen Huang*

Abstract

Background: Pervious studies suggested occupational workers exposure to pentachlorophenol (PCP) might contribute to increased risk of cancer. However, few studies have focused on associations between PCP and cancer risk at the community level. Objective: The present study was to explore the cancer risk for the community population living long-term in a PCP contaminated area. Methods: All the cancer cases diagnosed in 2009-2011 in Tongling City were collected. The cancer patients' residencies were geo-referenced in each district. The historical PCP usage for each district of Tongling was calculated as the PCP pollution index, which was further used to divide into PCP exposure categories. Standardized rate ratios (SRRs) of cancer incidence were applied to detect the cancer risk as exposure grade elevated. Correlation analysis was performed to analyze the relationship between PCP pollution and cancer incidence. Results: A total of 5,288 cancer cases (3,451 male and 1,837 female) were identified. PCP usage was correlated with the incidence of leukemia (r=0.88, *P*=0.002) for males, and with cancer of the esophagus for males (r=0.83, *P*=0.008) and females (r=0.71, *P*=0.020). Compared with the low exposure category, significant SRRs for total cancer sites was obtained for high PCP exposure category (SRR=1.61, 95%CI=1.59-1.62). Most SRR values of the cancer sites were significantly increased as exposure grade elevated and exposure time extended. Conclusion: The present study found that community residents living in the PCP contaminated area had increased risk of cancers. Leukemias, lymphomas and nasopharyngeal and esophageal cancers are most possibly associated with PCP exposure.

Keywords: Incidence - pentachlorophenol - exposure - cancer risk

Asian Pacific J Cancer Prev, **14 (2)**, 811-816

Introduction

Pentachlorophenol(PCP) has been widely used as wood preservative, herbicide and insecticide in western countries since 1940s; and also it has been used for killing oncomelania in some areas of China where schistosomiasis is epidemic (Zheng et al., 2011). Since the toxicity and carcinogenicity of PCP has been discovered, the International Agency for Research on Cancer (IARC) classified PCP as a group 2B carcinogen in 1991 for inadequate evidence in humans but sufficient evidence in animal studies (IARC, 1991). PCP is restricted or banned to use in many countries in 1990s (Muir et al., 1999).

PCP has been used since 1936, its effect on cancer has been studied in several countries after 1970s. And on account of there is no community population exposing to PCP in western countries, thus the study population are the workers in manuscript plants and sawmills. Case reports and case–control studies of hematopoietic cancers published in the 1980s and 1990s indicated the risk of non-Hodgkin lymphoma, soft-tissue sarcoma and multiple myeloma in relation to pentachlorophenol exposure for occupational workers (Greene et al., 1978; Bishop et al., 1981; Pearce et al., 1986; Smith et al., 1992; Hardell et al., 1994; Hardell et al., 1995; Kogevinas et al., 1995). In the 1990s and 2000s, four cohort studies reported the results between cancer risk and PCP exposure, and most of them reported weak or no risk of exposure to PCP, the authors infer the non-significant results might due to the less study population and healthy worker effects (Hertzman et al., 1997; Demers et al., 2006; Ramlow et al., 1996; Ruder et al., 2011).

After it has been forbidden to use in many countries, a worldwide research suggests that in indoor air, bodies of water, and freshwater sediments around the world, PCP levels has declined over time (Zheng et al., 2011). However, in Chinese surface water/sediments, PCP levels increase over time (Zheng et al., 2012). The causes were that since 1960 the sodium pentachlorophenate(Na-PCP) had been extensively sprayed to control the spread of snailborne schistosomiasis, and also the forbidden using PCP in China is later than other counties. Because of the re-emergence of schistosomiasis causing the adding consumption of PCP in several provinces in China, it

*[1]Department of Epidemiology and Biostatistics, School of Public Health of Anhui Medical University, Hefei, [2]Center for Disease Control and Prevention of Tongling City, Tongling, China [&]Equal contributors *For correspondence: hf0550@yahoo.com.cn*

indicates an aggravating trend of PCP pollution. And also, the Na-PCP is still used for fish pond cleaning in China, in many sampling sites, the long-term using Na-PCP for killing oncomelania and for fish pond cleaning induce a nearly two-fold risk of PCP contamination of the environment (Tan et al., 2008; Yang et al., 1996; Ge et al., 2007). The PCP level is also detected in human body that lives in PCP pollution area. Relatively high concentration of PCP has been found in human urine (Wang et al., 1998), adipose tissue (Zheng et al., 1997), blood lipids (Zhou, 2007), and breast milk fat (Chen et al., 2006). Although Na-PCP has been replaced by some new mollusacides in China, the persistence of PCP and its derivatives has resulted in serious pollution in the schistosomiasis epidemic area, and the human has severely suffered long history of PCP burden. Therefore, even for the populations exposed to low levels of PCP, their health risk is not negligible.

Most studies reported cancer risk of exposing to PCP for occupational workers, but few studies detect the cancer risk for community population who long term lived in PCP contaminated area. To perform a risk assessment of cancer for community population, we collect all the cancer cases in a PCP contaminated area and calculate the cancer incidences. PCP pollution is assessed by collecting the data of PCP usage, so as to investigate the link between human environmental exposing to PCP and risk of cancer.

Materials and Methods

Study area

Tongling was the smallest prefecture-level city in China, located in the east longitudes 117°42'00''-118°10'6" and north latitude 30°45'12''-31°07'56". It comprised 720 thousands inhabitants living in an area of 1113 km^2. Its geographic character was locating in south-side of the midstream and downstream of Changjiang River. And the suitable environment gave rise to abundantly snail propagation, which further led to the schistosomiasis epidemic.

Digital map of the regionalism of Tongling

The 1:200,000 digital map of Tongling were provided by State Bureau of Surveying and Mapping. Our purpose of the study was to detect the correlation between the PCP pollution and the cancer incidences in each district, thus the digital map was simply divided by administrative district boundaries. The Tongling City was divided in ten districts, including an urban area and nine countries (Datong, Wusong, Xilian, Donglian, Xuba, Laozhou, Tianmen, Shunan, Zhongming).The location of the districts had been labeled on the map. Each district was treated as a unit and processed in Geographic Information System in the analysis.

The collection of case records

This study utilized cancer registry system which had collected cancer cases in Tongling city. The cancer registry system was implemented in 2007. The registries identified new cancer cases from all hospitals, community health centers, death registries. The study population included all cancer patients in Tongling city. The database of cancer registry contained individual level data of cancer patients, including name, date of birth, race, sex, county, residence address and cancer site (coded using ICD-10). If some information of cancer cases was unavailable, households interview or telephone call were applied to investigate the information. And all the cancer cases had been localized in each district according to their residence addresses (if the patient had two or more residences in the past, we chose the address which he or she had lived for longer time). Population information of each district was obtained from official registration records.

Owning to the population in the involved district was small, and cancer was a rare disease, we merged cancer data from 2009 to 2011 and calculated average cancer incidence, in order to obtain a relatively stable incidence rate for each district. This study applied incidence data rather than mortality data because incidence data was more closely related to the cause and was not influenced by different effects due to the progress of treatment in different places.

Exposure assessment

We interviewed the Schistosomiasis Control Centre of Tongling, and obtained the historical data of PCP usage in killing oncomelania. According to the PCP usage data, it had been used to kill oncomelania for all the districts in Tongling City, and it was almost constantly sprayed in each district from 1960 to 2002.

We used the PCP usage per square meter as the pollution index. Firstly, we calculated the average usage of PCP per year for each district. Next, the PCP usage per square meter in each district was computed as index to categorize the exposure grade. Exposure categories based on quartiles of reported PCP spray were created. The <25th percentile of PCP pollution index (corresponding to <2.117 mg/m^2 per year) was designated the "low" exposure category, and districts that were in the >75th percentile of PCP pollution index(corresponding to >34.002 mg/m^2 per year) were designated as "high" exposure category. The rest districts that were between 25th percentile and 75th percentile were designated as "medium". According

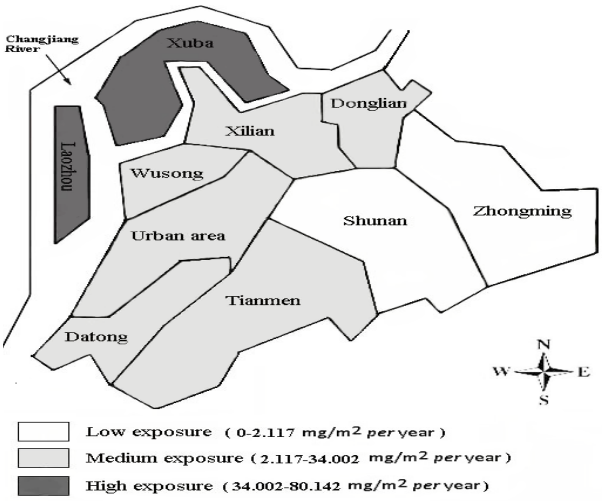

Figure 1. The PCP Exposure Categories Classified by PCP Usage in Each District

Table 1. Cancer Incidences in Males and Females in Tongling City

Cancer sites	Male		Female		Standardized
	Cancer incidence rates*	Cancer standardized incidence rates**	Cancer incidence rates*	Cancer standardized incidence rates**	incidence ratio(male:female)
Oral Cavity, Pharynx (C00-10,C12-14)	1.71	1.33	0.57	0.43	3.09(0.62-15.51)
Nasopharynx (C11)	3.15	2.40	1.42	0.99	2.42(0.71-8.52)
Esophagus (C15)‡	51.99	36.16	11.80	8.36	4.33(3.21-5.83)
Stomach (C16)‡	77.67	54.06	29.26	21.00	2.57(1.99-3.33)
Colon, Rectum, Anus (C18-21)	28.11	20.35	21.42	15.30	1.33(0.86-2.05)
Liver (C22)‡	25.59	18.67	7.64	5.53	3.38(2.20-5.17)
Gallbladder (C23-24)	3.60	2.55	6.23	4.43	0.58(0.17-1.93)
Pancreas (C25)	6.49	4.52	5.57	3.99	1.13(0.45-2.85)
Trachea, Bronchus, Lung (C33-34)‡	65.23	45.82	23.12	16.46	2.78(2.11-3.67)
Breast(C50)‡	0.54	0.46	22.08	16.13	0.03(0.00-0.17)
Ovary (C56)	-	-	4.34	3.29	-
Kidney, Urinary Organs (C64-66,68)	4.23	3.17	1.51	1.13	2.81(0.98-8.04)
Bladder (C67)‡	6.40	4.50	1.70	1.26	3.57(1.50-8.48)
Brain, Central Nervous System (C70-72)	4.32	3.26	2.45	1.70	1.92(0.66-5.57)
Thyroid Gland (C73)	0.36	0.29	2.27	2.01	0.14(0.01-3.29)
Lymphoma (C81-85, 88, 90, 96)	5.23	4.01	3.87	3.06	1.31(0.49-3.48)
Leukemia (C91-95)	3.69	3.18	4.06	3.51	0.91(0.30-2.72)
Total (C00-C97)‡	308.96	219.77	182.05	138.63	1.59(1.39-1.81)

‡Significant different incidences between men and women, $P<0.05$; * per 100000 population; ** World population per 100000

Table 2. Standardized Rate Ratios and 95% Confidence Intervals of Cancer Incidence with the Low Exposure Category as the Reference

Cancer sites	Male				Female				Combined			
	Medium†		High‡		Medium		High		Medium		High	
Oral Cavity, Pharynx (C00-10,C12-14)	2.72	2.36-3.13	2.01	1.73-2.34	-	-	-	-	3.63	3.00-4.40	2.01	1.64-2.48
Nasopharynx (C11)	0.71	0.64-0.79	0.33	0.28-0.37	0.77	0.65-0.91	5.21	4.76-5.71	0.69	0.61-0.78	1.55	1.41-1.70
Esophagus (C15)	0.91	0.89-0.92	2.36	2.32-2.39	1.27	1.23-1.31	4.51	4.38-4.65	0.93	0.91-0.95	2.73	2.69-2.78
Stomach (C16)	0.89	0.87-0.90	1.46	1.44-1.48	1.20	1.17-1.24	1.87	1.83-1.91	0.91	0.90-0.93	1.60	1.57-1.62
Colon, Rectum, Anus (C18-21)	1.14	1.11-1.18	0.94	0.91-0.97	0.90	0.87-0.92	0.53	0.51-0.55	0.94	0.91-0.97	0.75	0.73-0.78
Liver (C22)	0.89	0.86-0.91	1.13	1.09-1.16	1.13	1.07-1.20	0.93	0.88-0.99	0.90	0.87-0.93	1.14	1.10-1.19
Gallbladder (C23-24)	0.70	0.66-0.75	-	-	1.32	1.26-1.38	2.36	2.27-2.46	0.90	0.85-0.95	1.27	1.21-1.34
Pancreas (C25)	1.89	1.80-1.99	0.86	0.80-0.93	2.32	2.19-2.46	2.85	2.57-3.16	1.90	1.80-1.23	1.83	1.67-2.00
Trachea, Bronchus, Lung (C33-34)	1.17	1.15-1.19	1.50	1.48-1.53	1.61	1.57-1.65	1.19	1.15-1.24	1.21	1.18-1.23	1.45	1.42-1.48
Breast(C50)	-	-	-	-	1.84	1.76-1.92	0.92	0.87-0.97	1.57	1.48-1.67	1.09	1.02-1.17
Ovary (C56)	-	-	-	-	0.88	0.81-0.96	1.30	1.21-1.39	0.73	0.64-0.82	1.40	1.27-1.54
Kidney, Urinary Organs (C64-66,68)	0.85	0.79-0.91	0.63	0.59-0.67	2.75	2.39-3.17	-	-	1.04	0.96-1.14	0.55	0.51-0.59
Bladder (C67)	1.34	1.27-1.40	2.87	2.76-2.98	1.51	1.37-1.67	-	-	1.32	1.24-1.40	2.18	2.08-2.29
Brain, Central Nervous System (C70-72)	1.19	1.09-1.30	3.81	3.51-4.14	0.79	0.73-0.85	1.86	1.70-2.05	0.94	0.86-1.03	2.99	2.74-3.25
Thyroid Gland (C73)	0.37	0.30-0.46	2.01	1.73-2.34	0.89	0.79-1.01	0.96	0.85-1.08	0.67	0.58-0.78	1.21	1.06-1.38
Lymphoma (C81-85, 88, 90, 96)	0.46	0.43-0.49	1.10	1.05-1.16	3.15	2.85-3.47	9.37	8.41-10.45	0.73	0.68-0.78	2.23	2.10-2.37
Leukemia (C91-95)	5.75	4.94-6.70	27.97	24.60-31.79	0.69	0.63-0.75	1.58	1.47-1.70	1.04	0.95-1.15	4.11	3.79-4.45
Total (C00-C97)	1.00	0.99-1.01	1.62	1.61-1.63	1.38	1.36-1.39	1.45	1.43-1.47	1.01	1.00-1.02	1.61	1.59-1.62

†Medium, medium exposure category; ‡High, high exposure category

to the exposure categories, the districts of Shunan and Zhongming were defined as "low" exposure; six districts, including urban area, Datong, Wusong, Donglian, Tianmen and Xilian, were "medium"; and the rest two districts, Xuba and Laozhou were in "high" exposure category. To better interpret the PCP exposure categories, we used the map with different grey scales to represent the PCP exposure grade in Figure 1.

The overall distribution of exposure for the patients lived in each districts was similar with PCP pollution. Subjects had a cumulative exposure from 1 year at least to approximately 10-40 years. According to the lengths of living in the PCP polluted area for each case, we classified the exposure time grades as <10 years, ≥10 years, ≥20 years, ≥30 years and ≥40 years.

Statistical analysis

We firstly calculated the average age-standardized incidence rates for each district and for each exposure categories, using the world population in 2000-2025 as the standard population. Pearson correlation analysis was conducted to test the association between PCP usage and cancer incidences. And then the standardized rate ratios(SRR) of the cancer incidence for PCP exposure category of medium and high were calculated relative to low exposure category. Statistical stability was evaluated with a 95% confidence interval (CI). The data analysis was completed using Stata11.0 Software.

Results

For the study period a total of 5288 cases (3451 male and 1837 female cases) were collected. The age distribution was skewed, the median was 65 year-old, and the 25 percentile and 75 percentile of age distribution was 55 and 73 year-old, respectively.

The results of the incidence for the cancers grouped by pathogenetic site between 2009 and 2011 in Tongling

Table 3. The Standardized Rate Ratio for Medium Exposure Category Relative to Low Exposure Category

Cancer sites	Exposure ≥ 10 years	Exposure ≥ 20 years	Exposure ≥ 30 years	Exposure ≥ 40 years
Oral Cavity, Pharynx (C00-10,C12-14)	3.13(0.65-15.0)	3.13(0.79-12.4)	3.13(0.88-11.1)	4.97(2.38-10.4)
Nasopharynx (C11)	0.78(0.22-2.75)	0.72(0.23-2.27)	1.09(0.39-3.06)	6.98(3.93-12.4)
Esophagus (C15)	0.95(0.68-1.32)	0.95(0.71-1.27)	1.10(0.86-1.42)	1.96(1.70-2.27)
Stomach (C16)	0.92(0.71-1.88)	0.93(0.75-1.16)	1.08(0.89-1.31)	2.02(1.81-2.26)
Colon, Rectum, Anus (C18-21)	0.95(0.66-1.36)	0.94(0.69-1.30)	1.15(0.87-1.51)	2.09(1.77-2.46)
Liver (C22)	0.93(0.60-1.45)	0.96(0.65-1.42)	1.15(0.82-1.62)	2.34(1.92-2.86)
Gallbladder (C23-24)	0.88(0.39-2.01)	0.88(0.43-1.82)	1.00(0.54-1.88)	1.87(1.30-2.68)
Pancreas (C25)	1.87(0.94-3.73)	1.88(1.02-3.44)	2.18(1.31-3.64)	3.81(2.87-5.07)
Trachea, Bronchus, Lung (C33-34)	1.23(0.94-1.60)	1.23(0.97-1.55)	1.45(1.19-1.78)	2.70(2.41-3.02)
Breast (C50)	1.62(0.96-2.74)	1.57(0.98-2.52)	1.94(1.27-2.96)	6.74(5.30-8.58)
Ovary (C56)	0.65(0.18-2.39)	0.82(0.26-2.60)	0.76(0.25-2.28)	1.55(0.76-3.15)
Kidney, Urinary Organs (C64-66, 68)	0.89(0.31-2.57)	0.89(0.35-2.26)	0.90(0.38-2.10)	1.55(0.92-2.62)
Bladder (C67)	1.29(0.54-3.09)	1.26(0.58-2.75)	1.45(0.75-2.82)	2.46(1.68-3.61)
Brain, Central Nervous System (C70-72)	1.00(0.35-2.83)	1.00(0.40-2.50)	1.32(0.60-2.89)	2.80(1.75-4.46)
Thyroid Gland (C73)	0.64(0.13-3.29)	0.50(0.10-2.51)	0.57(0.12-2.74)	1.42(0.48-4.16)
Lymphoma (C81-85, 88, 90, 96)	0.79(0.32-1.96)	1.03(0.46-2.30)	1.11(0.54-2.26)	2.23(1.46-3.39)
Leukemia (C91-95)	0.85(0.30-2.35)	0.84(0.31-2.27)	1.01(0.41-2.46)	2.18(1.28-3.71)
Total (C00-C97)	1.02(0.90-1.14)	1.02(0.92-1.14)	1.20(1.10-1.31)	2.28(2.16-2.40)

Table 4. The Standardized Rate Ratio for High Exposure Category Relative to Low Exposure Category

Cancer sites	Exposure ≥ 10 years	Exposure ≥ 20 years	Exposure ≥ 30 years	Exposure ≥ 40 years
Oral Cavity, Pharynx (C00-10,C12-14)	2.32(0.36-15.0)	2.32(0.45-12.0)	2.70(0.68-10.8)	4.82(2.28-10.2)
Nasopharynx (C11)	1.90(0.86-4.21)	1.90(0.94-3.83)	3.17(1.78-5.63)	20.9(16.0-27.5)
Esophagus (C15)	2.81(2.34-3.38)	2.82(2.39-3.31)	3.32(2.90-3.80)	5.91(5.49-6.37)
Stomach (C16)	1.59(1.32-1.92)	1.63(1.38-1.92)	1.93(1.67-2.21)	3.67(3.39-3.97)
Colon, Rectum, Anus (C18-21)	0.72(0.48-1.09)	0.73(0.51-1.04)	0.84(0.61-1.17)	1.60(1.32-1.93)
Liver (C22)	1.18(0.80-1.74)	1.22(0.86-1.72)	1.43(1.06-1.950	2.91(2.44-3.47)
Gallbladder (C23-24)	1.23(0.61-2.47)	1.23(0.67-2.27)	1.43(0.85-2.41)	2.74(2.05-3.66)
Pancreas (C25)	1.55(0.72-3.32)	1.18(0.54-2.56)	1.09(0.52-2.28)	1.69(1.07-2.66)
Trachea, Bronchus, Lung (C33-34)	1.43(1.12-1.83)	1.43(1.16-1.78)	1.64(1.36-1.98)	2.93(2.63-3.26)
Breast(C50)	1.13(0.60-2.13)	1.13(0.64-1.97)	1.40(0.85-2.32)	3.57(2.50-5.12)
Ovary (C56)	1.42(0.59-3.43)	1.80(0.83-3.88)	2.09(1.09-4.00)	4.26(2.87-6.33)
Kidney, Urinary Organs (C64-66,68)	0.51(0.13-2.01)	0.51(0.15-1.71)	0.59(0.21-1.67)	1.18(0.65-2.17)
Bladder (C67)	2.02(1.01-4.01)	2.02(1.10-3.69)	2.35(1.41-3.91)	4.19(3.17-5.54)
Brain, Central Nervous System (C70-72)	2.73(1.49-5.00)	2.73(1.61-4.65)	2.51(1.45-4.35)	4.26(2.96-6.12)
Thyroid Gland (C73)	0.47(0.07-3.09)	0.47(0.09-2.47)	0.70(0.17-2.93)	2.41(1.08-5.39)
Lymphoma (C81-85, 88, 90, 96)	1.81(1.00-3.270	2.39(1.43-3.99)	2.52(1.60-3.98)	4.65(3.55-6.10)
Leukemia (C91-95)	3.30(2.03-5.39)	3.53(2.25-5.55)	3.21(2.01-5.15)	5.51(4.06-7.48)
Total (C00-C97)	1.59(1.45-1.75)	1.60(1.47-1.74)	1.87(1.74-2.01)	3.56(3.42-3.71)

were summarized in Table 1. The age-standardized incidence in males was greater than that in females with a sex standardized incidence ratio(SIR) of 159 males per 100 female. And significant incidence ratios were also detected in the cancer sites of breast, liver, stomach, lung and esophageal, bladder.

The Pearson correlation analysis showed that the PCP usage was correlated with leukemia (r=0.88, *P*=0.002) for male, and with cancer of esophageal for male (r=0.83, *P*=0.008) and female (r=0.711, *P*=0.020).

Standardized rate ratios(SRR) was calculated according to the age-standardized incidences by using the incidence in the low PCP spray districts as the reference. Without considering the exposure time, significant SRRs for total cancer sites was obtained with high exposure category (SRR=1.61, 95%CI=1.59-1.62). As shown in Table 2, we detected that most SRR values of cancer sites were significantly increased as exposure grade elevated. The SRRs of leukemia in high exposure for male (SRR=27.97, 95%CI=24.60-31.79) and lymphoma in high exposure for female (SRR=9.37, 95%CI=8.41-10.45) indicated strong association between leukemia of male and lymphoma in female with PCP exposure.

Most of the cancer incidences appeared to increase consistently with the SRR grouped by exposure time (Table 3 and Table 4). And it also corroborated the association between leukemia and lymphoma with PCP. In the longer term exposed strata some prominent elevated cancer incidences were observed for nasopharyngeal cancers that were less considered a priori to be associated with PCP. Of these, nasopharyngeal cancer exhibited the most consistent pattern as exposure time extended and exposure level rose.

Discussion

Different with the results of previous similar studies of occupational workers exposing to PCP, the present study detected significant cancer risk for community population long term exposed to PCP. The occupational workers in former studies were almost male and in the middle-age, which contained healthy worker effect. That might limit those studies to obtain statistical significant result. The present study was to detect the cancer incidence of the

whole city residents in all age groups. And by dividing exposure categories, we had found that the people lived in PCP pollution area had excess risk of occurring cancers.

The present study discovered the PCP exposure was associated with cancer of esophageal, which had not been found in previous studies. The significantly raised SRR values of cancer in esophageal also indicated the risk when people exposing to higher concentration of PCP. And, the incidence ratio of cancer of esophageal (male: female=4.33, 95%CI=3.21-5.83) indicated the higher incidence was more attributed to male. The standardized cancer incidences of esophageal (29.66 per 105) and stomach (50.13 per 105) in Tongling were almost twice than that in national average level. Although the correlation analysis did not show PCP exposure was significant associated with cancer of stomach, the SRR values of it suggested more than two-fold risk in high exposure category. We surmised the PCP might contribute to the results. As we investigated to all the area of Tongling, its geographic character was that the communities and countries were surrounded by natural water networks, such as rivers, ponds and ditches. And the PCP was sprayed into these water networks which were also used as drinking water for the local residents. This might provide the direct pathway of exposing and ingesting to PCP, which was different with mainly though inhalation and less from dust deposition in occupational workers (Greene et al., 1978). In addition, many studies regarded that PCP was persistent, toxic, anthropogenic chemicals. Its bio-accumulate in humans, because humans resided at the top of the ''food chain'', thus mostly (>90%) intake of PCP was through contaminated foods, such as meat and fish, and particularly from food of animal origins (Hong et al., 2005).

The PCP exposure was also associated with incidence of leukemia in male. The PCP associated with the leukemia in male were much evident (high exposure category SRR=27.97, 95%CI=24.60-31.79). The association with female was significant in lymphoma (high exposure category SRR=9.37, 95%CI=8.41-10.45). To explain the association, we interviewed the staff of Schistosomiasis Control Centre and local residents of high exposure category districts. These districts were almost farmland, and the farmers used the water of Changjiang River, which was contaminated by PCP, to irrigate the field. PCP was also sprayed along the canals and ditches around the field. People were undertaken the agricultural work which provided the opportunity to directly expose to PCP. Especially, when PCP is exposure to intense solar radiation, it could result to even greater toxicity and carcinogenicity (Agbo et al., 2011). There was one cohort study had similar result with us, it reported increased risk of leukemia associated with people directly exposing to PCP in occupational workers (Ruder et al., 2005). They discovered that among the male workers, except white races, had increased leukemia mortality (SMR=4.57, 95%CI=1.25-11.7).

Since 1980s, the descriptive and analytical epidemiology of exposure to PCP causing human cancer had been extensively studied in developed countries. Most population-based studies conducted in developed countries used occupational workers as the study population to analysis the relationship between PCP exposure and cancers. The previous case-control studies and recent cohort studies were mainly concerning to lymphoma, and strong evidence had been provided to substantiate the association between exposure to PCP and Non-Hodgkin's lymphoma (Demers et al., 2006). In our study, we also detected the statistical significant SRRs for lymphoma as exposure grade elevated. And a similar study conducted in Finland observed increased incidence of Non-Hodgkin's lymphoma in community population who lived in PCP-contaminated area (Lampi et al., 1992).

In the large cohort study of Demers et al., 2006, the sawmill workers exposed to PCP with 2-5 exposure years had an increased risk of liver cancer(RR=8.47, 95%CI=2.21-32.45). In present study, the significant SRRs value of liver cancer also showed increased risk as the exposure time extended. But the effect-response relationship between PCP exposure and liver cancer might be confounded by other factors, which weakened the association. In schistosomiasis epidemic area, the schistosomal infection could promote developing liver cancer. It could accelerate progression to hepatitis C-associated fibrosis and made quicker progression to Hepatocellular carcinoma (Kamel et al., 1992; Hassan et al., 2001). But we had not collected the clinic data of the liver cancer patients, in further investigation with detailed exposure information would be helpful to detected the association between PCP exposure and liver cancer.

The study found significant association with nasopharyngeal cancer. When the exposure over 40 years, for high exposure category the SRR was 20.98 (95%CI=16.04-27.46). Evidence of an excess of nasal and nasopharyngeal cancer had been observed in another study of chlorophenol and wood preservative exposed workers (Mirabelli et al., 2000). They obtained elevated risk for nasopharyngeal who held jobs assigned high intensity chlorophenol exposure (OR=9.07, 95%CI=1.41-42.9).

We recognized that the study had several limitations. Firstly, imprecision existed in calculating average cancer incidences. The development of cancer from exposure to environmental pollutants was a long-term event, and yet in this study the number of cancer cases for the years 2009-2011 collected from available sources was slightly insufficient. And this might be the reason of failing to detect significant SRRs value of soft-tissue sarcoma and multiple myeloma which were considered to be associated with PCP exposure. In addition, the small population in this city might be another reason for the fewer cases.

The exposure occurred during 1960-2002. Changes in population characteristics due to migration or other dynamics might influence cancer estimates separately from PCP pollution. However, that might not have impact on our study. As we interviewed bureau of census, we were told that there was no large-scale migration happened in the history of Tongling City after 1960.

Lastly, the study was also limited by the ecological design, because no direct person-level measures of environmental exposure were available. And all individuals in a given district were assigned to the same exposure category, without regard for proximity to other

carcinogens exposure and individual behavior, which could cause individual variations. For instance, commercial grade PCP contained a variety of contaminants and by-products of the manufacturing process, the primary contaminants were hexa-, hepta-, and octa-chlorinated dibenzodioxins, and higher-chlorinated dibenzofurans. In Canada, polychlorodibenzo-p-dioxins and furans (PCDD/Fs) were detected in the place where emission from pentachlorophenol (PCP)-treated wooden poles in service (Bulle et al., 2010). And in further study, the measurement of PCP concentration and other carcinogens in human body and environment would be advantageous to better realize the carcinogenicity of PCP to the community residents who were long-term living in PCP pollution area.

In summary, by assessing the PCP pollution for the districts in Tongling city, we had established a practical approach to reveal the impact of environmental PCP exposure on community population developing cancers. Study results suggested that community residents living in the PCP contaminate area had increased risk of developing cancers, and also the PCP exposure might associate with the leukemia, lymphoma, esophageal and nasopharyngeal cancer.

Acknowledgements

The present study was supported by the Grants for Scientific Research of BSKY(XJ200908) from Anhui Medical University.

References

Agbo SO, Küster E, Georgi A, et al (2011). Photostability and toxicity of pentachlorophenol and phenanthrene. *J Hazard Mater*, **189**, 235-40.

Bishop CM, Jones AH (1981). Non-Hodgkin's lymphoma of the scalp in workers exposed to dioxins. *Lancet*, **2**, 369.

Bulle C, Samson R, Deschênes L (2010). Enhanced migration of polychlorodibenzo-p-dioxins and furans in the presence of pentachlorophenol-treated oil in soil around utility poles: screening model validation. *Environ Toxicol Chem*, **29**, 582-90.

Chen JW, Wang SL, Yu HY, Liao PC, Lee CC (2006). Body burden of dioxins and dioxin-like polychlorinated biphenyls in pregnant women residing in a contaminated area. *Chemosphere*, **65**, 1667-77.

Demers PA, Davies HW, Friesen MC, et al (2006). Cancer and occupational exposure to pentachlorophenol and tetrachlorophenol(Canada). *Cancer Causes Control*, **17**, 749-58.

Ge J, Pan J, Fei Z, Wu G, Giesy JP (2007). Concentrations of pentachlorophenol (PCP) in fish and shrimp in Jiangsu Province, China. *Chemosphere*, **69**, 164-9.

Greene MH, Brinton LA, Fraumeni JF, D'Amico R (1978). Familial and sporadic Hodgkin's disease associated with occupational wood exposure. *Lancet*, **2**, 626-7.

Hardell L, Eriksson M, Degerman A (1994). Exposure to phenoxyacetic acids, chlorophenols, or organic solvents in relation to histopathology, stage, and anatomical localization of non-Hodgkin's lymphoma. *Cancer Res*, **54**, 2386-9.

Hardell L, Eriksson M, Degerman A (1995). Meta analysis of 4 Swedish case-control studies on exposure to pesticides as risk-factor for soft-tissue sarcoma including the relation to tumor-localization and histopathological type. *Int J Oncol*, **6**, 847-51.

Hassan MM, Zaghloul AS, El-Serag HB, et al (2001). The role of hepatitis C in hepatocellular carcinoma: a case control study among Egyptian patients. *J Clin Gastroenterol*, **33**, 123-6.

Hertzman C, Teschke K, Ostry A, et al (1997). Mortality and cancer incidence among sawmill workers exposed to chlorophenate wood preservatives. *Am J Public Health*, **87**, 71-9.

Hong HC, Zhou HY, Luan TG, Lan CY (2005). Residue of pentachlorophenol in freshwater sediments and human breast milk collected from the Pearl River Delta, China. *Environ Int*, **31**, 643-9.

International Agency for Research on Cancer (1991). IARC monographs on the evaluation of carcinogenic risks to humans, Vol. 53; International Agency for Research on Cancer, Occupational exposures in insecticide application, and some pesticides, Lyon.

Kamel MA, Ghaffar YA, Wasef MA, et al (1992). High HCV prevalence in Egyptian blood donors. *Lancet*, **340**, 427.

Kogevinas M, Kauppinen T, Winkelmann R, et al (1995). Soft tissue sarcoma and non-Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols, and dioxins: two nested case-control studies. *Epidemiology*, **6**, 396-402.

Lampi P, Hakulinen T, Luostarinen T, Pukkala E, Teppo L (1992). Cancer incidence following chlorophenol exposure in a community in southern Finland. *Arch Environ Health*, **47**, 167-75.

Mirabelli MC, Hoppin JA, Tolbert PE, et al (2000). Occupational exposure to chlorophenol and the risk of nasal and nasopharyngeal cancers among U.S. men aged 30 to 60. *Am J Ind Med*, **37**, 532-41.

Muir J, Eduljee G (1999). PCP in the freshwater and marine environment of the European Union. *Sci Total Environ*, **236**, 41-56.

Pearce NE, Smith AH, Howard JK, et al (1986). Non-Hodgkin's lymphoma and exposure to phenoxyherbicides, chlorophenols, fencing work, and meat works employment: a case-control study. *Br J Ind Med*, **43**, 75-83.

Ramlow JM, Spadacene NW, Hoag SR, et al (1996). Mortality in a cohort of pentachlorophenol manufacturing workers, 1940-1989. *Am J Ind Med*, **30**, 180-94.

Ruder AM, Yiin JH (2011). Mortality of US pentachlorophenol production workers through 2005. *Chemosphere*, **83**, 851-61.

Smith JG, Christophers AJ (1992). Phenoxy herbicides and chlorophenols: a case control study on soft tissue sarcoma and malignant lymphoma. *Br J Cancer*, **65**, 442-8.

Tan YM, Liu YQ, Su F, Hu K, Feng Y (2008). Investigation of endocrine disrupting chemicals in source water and tap water in a city. *J Environ Health*, **25**, 232-5 (in Chinese).

Wang XH, Qian S, Yang R, Yang P (1998). Exposure level of pentachlorophenol in environment in human body. *J Environ Health*, **15**, 24-6 (in Chinese).

Yang R, Yang P, Qian S, Jiang XF (1996). Investigation on environmental exposure level of PCP in population. *Admin Technol Environ Monitor*, **8**, 19-21 (in Chinese).

Zheng M, Bao Z, Wang K, Yang H, Xu X (1997). Polychlorinated dibenzo-p-dioxins and dibenzofurans in lake sediments from Chinese schistosomiasis areas. *Bull Environ Contam Toxicol*, **59**, 653-6.

Zheng W, Wang X, Yu H, et al (2011). Global trends and diversity in pentachlorophenol levels in the environment and in humans: a meta-analysis. *Environ Sci Technol*, **45**, 4668-75.

Zheng W, Yu H, Wang X, Qu W (2012). Systematic review of pentachlorophenol occurrence in the environment and in humans in China: not a negligible health risk due to the re-emergence of schistosomiasis. *Environ Int*, **42**, 105-16.

Zhou Y (2007). Study on the revision for health limited value of pentachlorophenol in drinking water. Shanghai: Fudan University, (Post Doctor Report) (in Chinese).