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Assessment of urinary thiodiglycolic acid exposure in school-aged children in the vicinity of a petrochemical complex in central Taiwan

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ABSTRACT

Background: School-aged children living in the vicinity of vinyl chloride (VCM)/polyvinyl chloride (PVC) factories may have an increased risk of exposure to hazardous air pollutants.
Objectives: We aimed to evaluate the urinary thiodiglycolic acid (TDGA) level, as TDGA is a major metabolite of VCM, for students at elementary schools near a petrochemical complex in central Taiwan.
Methods: We recruited 343 students from 5 elementary schools based on distance to the VCM/PVC factory. First-morning urine and blood samples were obtained from our subjects from October 2013 to September 2014. Urine samples were analyzed for urinary creatinine and TDGA using LC/MS–MS. Hepatitis virus infection were assessed using blood samples. We determined their vitamin consumption, resident location, parent's employment, and other demographic or lifestyle characteristics using a questionnaire.
Results: Median urinary TDGA levels for 316 students at 5 elementary schools from the closest (< .9 km) to the farthest (~8.6 km) with respect to the petrochemical complex were 147.6, 95.5, 115.5, 86.8, and 17.3 μg/g creatinine, respectively. After adjusting for age, gender, hepatitis virus infection, vitamin B consumption, passive smoking, and home to source distance, we found that urinary TDGA levels for the closest students was significantly higher than those at other schools. Further, median urinary TDGA levels for students during school time were 4.1-fold higher than those during summer vacation.
Conclusions: After adjusting for confounders, urinary TDGA levels for the school-aged children decreased with increasing distances between the elementary schools and the petrochemical complex.

1. Introduction

Vinyl chloride monomer (VCM) is a colorless gas at room temperature and the major material used to produce ethylene dichloride (EDC) or polyvinyl chloride (PVC) (Sherman, 2009). VCM is less likely to occur naturally or to be present in food and cosmetic products, but it is mostly found in the ambient air in VCM/PVC factories or contaminated ground water (ATSDR, 2006). The No. 6 naphtha cracking complex (namely a petrochemical complex) is owned by the Formosa Petrochemical Corporation (FPC) and is situated in the Mai-Liao Township in central Taiwan (Shie and Chan, 2013; Yuan et al., 2015). For this petrochemical complex, the estimated annual production of VCM and PVC was around 2.76 and 2.93 million tons, respectively, and the estimated annual emission of VCM and 1,2-dichloroethane from the stack and equipment was 24.9 and 11.5 t, respectively.

Since 1987, VCM has been classified as a group 1 human carcinogen by IARC (IARC, 2007). Occupational studies suggested

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Table 4
Multiple regression[a] of urinary TDGA levels for the participating students attending 5 elementary schools in central Taiwan (N=315).

Variables[b]	TDGA (n=315)					TDGA (n=310)[c]				
	β	SE	95% CI	P value	R^2	β	SE	95% CI	P value	R^2
Intercept	2.55	.50	(1.57–3.53)	<.001	.191	2.48	.50	(1.50–3.47)	<.001	.189
Elementary school[d]	−.20	.04	(−.27 to −.13)	<.001		−.20	.03	(−.27 to −.13)	<.001	
Gender[d]	.06	.06	(−.06 to .18)	.344		.07	.06	(−.05 to .18)	.282	
Vitamin B consumption	−.05	.24	(−.52 to .41)	.831						
Passive smoking[d]	−.07	.06	(−.19 to .06)	.283		−.07	.06	(−.19 to .06)	.275	
Father ever employed by a petrochemical complex[d]	.03	.06	(−.09 to .15)	.591		.04	.06	(−.08 to .16)	.525	
Age (y)	−.23	.39	(−.98 to .53)	.558		−.23	.39	(−.99 to .53)	.556	
BMI (kg/m^2)	−.22	.36	(−.92 to .48)	.542		−.17	.36	(−.87 to .54)	.638	
Distance of home to the petrochemical complex (km)	.26	.23	(−.18 to .71)	.246		.26	.23	(−.19 to .71)	.254	

Abbreviation: TDGA, thiodiglycolic acid

[a] Multiple regression adjusted for gender, vitamin B consumption, passive smoking, father ever employed in the petrochemical complex, age, BMI, and distance of home to the petrochemical complex.

[b] Variables were logarithm transformed for TDGA, age, BMI, and distance of their home to the petrochemical complex; 1 subject who had a hepatitis B infection was excluded.

[c] Five participating children had taken vitamin B and were excluded.

[d] Dummy variables: We used school A as a reference and the order of other schools were increased by the increasing distance to the source (km); we also used girl, non-smoker and never served in petrochemical complex as a reference of gender, passive smoking and father's job, respectively.

BMI, vitamin B consumption, passive smoke exposure, their father's employment history, and home to source distance, we found that the median urinary TDGA level for school-aged children was significantly increased with shorter distances of the elementary schools to the VCM/PVC factories. The median urinary TDGA level for the children during school time was significantly 4 times higher than that of summer vacation.

Many studies have indicated that urinary TDGA was a good biomarker of VCM for workers (Heger et al., 1982; Cheng et al., 2001; Kim et al., 2006). However, some confounders should be noted if applying to a general population. The exposure sources for the presence of urinary TDGA in children could result from different exposure routes including inhalation and ingestion. Some studies revealed that VCM, EDC, and ethylene oxide were possible sources for subjects having the presence of TDGA in their urine (ATSDR, 2006). We examined the annual monitoring data from the local EPA for air pollution inside and outside the petrochemical complex. We found that the annual mean VCM level was 2.2 ppb, with a maximum level of 165 ppb at school A. The EDC level in ambient air was around one-fifth that of the VCM level at school A. Some air monitoring stations near schools C, D, and E also indicated a similar phenomenon (supplementary Table 3 and supplementary Fig. 1). Although we could not rule out the possibility of exposure from other air pollution sources, it is less likely that our subjects were exposed to those chemical compounds in a special location, such as ethylene oxide, in the hospital. Reports have indicated that frequent and constant VCM and EDC emissions occurred in the surrounding area of the petrochemical complex and could possibly lead to our subjects' urinary TDGA levels.

Occupational studies indicated that a hepatitis virus infection and active or passive cigarette smoking might affect the metabolism of VCM and TDGA in male VCM and PVC employees (Cheng et al., 2001; Kim et al., 2006). Our subjects were tested for HBV and HCV infections using blood examinations and a questionnaire, and we found only 1 student who was positive for HBV and was excluded from further analysis. Although low VCM levels have been reported in tobacco smoke (5–30 ng/cigarette) (ATSDR, 2006), no participant was an active smoker, but a number of our participants reported passive smoking. Therefore, we included passive smoking in our statistical model; passive smoking did not significantly affect the urinary TDGA level in the children. It is possible that our subjects did not reside with smokers or avoided them. Therefore, a hepatitis virus infection and smoking status were less likely to bias our results. Some studies reported that consumption of specific anti-tumor medications or nutritional supplements in humans or rodents, such as ifosfamide, cyclophosphamide (the oxazaphosphorine class of chemotherapeutics), vitamin B, folate, and creatine, increased the urinary TDGA level (ATSDR, 2006; Li et al., 2010, 2011; Navrátil et al., 2007, 2010). None of our subjects were undergoing cancer treatment; their medical history was confirmed using a questionnaire. We found that only 5 subjects had consumed vitamin B the month prior to the survey and were excluded from further analysis; none were taking any specific medications, folate, creatine, or any other nutrition supplement. Hence, it is less likely that the source of TDGA exposure for our subjects was the consumption of a specific medication or nutritional supplement.

We found that the median level of urinary TDGA for the children during school time was significantly *higher* (4-fold) than that of summer vacation. The exposure scenario for the students was quite different between school time and summer vacation. During school time, the elementary school students regularly attended school on weekdays, while they did not attend school during summer vacation. Therefore, the TDGA exposure leading to the urinary TDGA levels observed in our participants on summer vacation should be close to the background level of the study area. Our data indicated that students might be exposed to certain chemicals, possibly VCM and PVC or related VOCs, and experienced increased exposure levels, leading to urinary TDGA excretion. Because of the results of our investigation, Yun-Lin County Government (the local authority), the Ministry of Health, Welfare, and Ministry of Education in Taiwan (central governments) decided to temporarily relocate the students attending elementary school A to school C, which is located about 5.5 km from the petrochemical complex, on September 2014. Further study is ongoing to assess the changing exposure profile of TDGA in these students.

The current study had some interesting findings, in our opinion. We investigated and controlled or adjusted for several important confounders such as HBV, smoking status, vitamin B, and medication consumption to elucidate the potential sources of urinary TDGA in school-aged children. We used a relatively specific biomarker, urinary TDGA, to evaluate the potential exposure of children to certain VOCs. Further, we assessed different exposure scenarios for the urinary TDGA levels between school time and summer vacation in a subgroup of students.

There were some limitations in the current study regarding data interpretation. First, we did not measure the ambient air levels of VCM or EDC in any subject during our sampling period. Further, we cannot provide direct evidence regarding the sources of TDGA in the school-aged children. Secondly, although we collect urine samples of our subject at the same time of individual elementary school, we did not collect all the urine sample at the same day. Third, the wind direction during our sampling period, autumn and spring, was similar, and we used repeated sampling for TDGA in a subgroup of participating children to compare differences in TDGA exposure between school time and vacation. Fourth, we did not utilize a detailed food questionnaire to evaluate the possible effects of food products or containers. Fifth, we could not rule out potential exposure from drinking water. Drinking water might contain VCM released from contact with polyvinyl pipes, from contaminated underground water, or a microbial degradation product of trichloroethylene in groundwater. Lastly, the air inside new cars could emit trace levels of VCM, mainly from the new plastic parts. However, it is less likely that this was the major source for urinary TDGA in our subjects.

5. Conclusions

We concluded that a majority of children living and studying in the neighborhood of about 9 km away from the petrochemical complex have been possibly exposed to VCM, a class I carcinogen, to some extent. We concluded there is an environmental injustice issue related to children's exposures to the industrial carcinogen as children of poor family tend to live near the pollution source and possibly experience higher VCM exposures than those living farther away. Action has been taken by the authorities to relocate children of School A to School C in September, 2014 as our preliminary data surfaced in July, 2014. A follow-up study is on-going to further investigate exposure levels and potential health effects of VCM after such relocation for School A children, in particular, and for all children of all schools in general.

Conflicts of interest

The authors declare that no competing interests exist.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.envres.2015.11.027.

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