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SM Journal of Public Health and Epidemiology

Special Article- Heavy Metals and Health, Editorial

Heavy Metal and Cancer Risk

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Abstract

I summarize our work over the past decade to illustrate how improper management of heavy metal in manufacturing has caused pollution to the environment and as a result, has negatively influenced the health of local people in Changhua, a county in central Taiwan.

Our study found a frightening 5.3-fold increase in the incidence of male oral cancer from 1982 to 2001 in Taiwan. Changhua, one of the 23 counties in Taiwan, ranked first in the list of oral cancer incidence. The incidence of male oral cancer in Changhua was also leading in the world (45.07/100,000/year in 2001).

Heavy metal contained in waste water from electroplating factories was released into the environment and polluted farm soil. The incidence and prognosis of oral cancer in Changhua was strongly correlated with the densities of electroplating factories and the levels of heavy metal in the farm soil. In addition, the levels of heavy metal in the blood from the patients correlated strongly with the levels in the farm soil of their residence areas. Moreover, the patients had higher levels of heavy metal in their blood, compared with the blood levels in controls. Evidence shows that the detrimental effects from the environmental pollution can persist for generations.

Article Information

Received date: Dec 23, 2015
Accepted date: Dec 27, 2015
Published date: Dec 29, 2015

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Introduction

Fortunately, Humans are possessed of the abilities to explore and exploit the environment. Modern civilization depends on our abilities to utilize all kinds of materials on and in the earth, including heavy metals for our purposes. The use of heavy metal has contributed significantly to the convenience of our daily life.

However, the wide applications of heavy metal in all aspects of our lives have at least one dark side: the pollution to the environment resulting from mining, purification, manufacturing and waste management.

Here, I will summarize our work over the past decade to illustrate how improper management of heavy metal in manufacturing has caused pollution to the environment and negatively influenced the health of local people at Changhua, a county in central Taiwan.

Heavy Metal Pollution at Changhua

Taiwan is a small island at the rim of western Pacific, and known for its rapid and successful modernization in the second half of the last century. Before World War Two, Taiwan had been the number one producer of sugar from the sugar cane in the world. The quality and taste of its green tea has been loved by people world-wide. No industries were present except those for simple processing of agricultural products for export.

The picture has been changing since the 1960s. The government established many industrial parks in the neighborhood of harbors, and these parks attracted many foreign companies and investments. As a result, people in Taiwan have witnessed a course of rapid industrialization over the ensuing 30 years.

For Changhua, many factories were established to make parts for automobiles, house wares and machines. Most of these products were made of heavy metal, specifically, iron, and electroplating of the products was required to prevent them from rusting.

Because of lack of regulations and help from the government, large amounts of waste water containing heavy metal from these factories were released into the environment. This is the background of our research.

Epidemiology of Oral Cancer at Changhua and in Taiwan

Taiwan established a national cancer registry in the 1970s. This database gave us an opportunity to look for any peculiarities in the health conditions of local people at Changhua.

The initial survey showed that Changhua stood out among all cities/counties in Taiwan for its high incidence of oral cancer. Based on these results, we began to study the relationships between local pollution and oral cancer. In Taiwan, oral cancer is one of the malignancies showing rapid increase in annual incidence [1]. From 1982 to 2001, Taiwan had an unprecedented 5.3-fold increase in the incidence of male oral cancer. Among the 23 counties, Changhua was the leading county

in oral cancer incidence in recent years. The incidence of male oral cancer in Changhua (45.07/100,000/year in 2001) was also leading in the world. More than 90% of patients with oral cancer have squamous cell carcinoma. The most common site of involvement in Changhua was the buccal mucosa. In contrast, the most common site was the tongue for people in other counties of Taiwan.

Smoking, alcohol drinking and betel nut chewing are known risk factors for oral cancer [2]. We used statistical methods, including regression models to assess the strength of these factors on the incidence of oral cancer. As expected, betel nut chewing is the most dominant factor in predicting oral cancer. Unexpectedly, Changhua was the only outlier in our regression model, meaning betel nut chewing is not the most important risk factor for the incidence of oral cancer in Changhua, compared with other counties. It also indicates that risk factors other than betel quid chewing may exist in Changhua.

We first documented that there was an extremely high incidence of oral cancer in Changhua and the location was the buccal mucosa in preponderance, which was different from that in other counties. Lack of a close relation with betel quid chewing provided us a clue that other unknown etiologic factors may be present locally [1].

Age at Diagnosis and Prognosis of Oral Cancer in Relation to the Densities of Electroplating Factories in Patient's Residential Area

Smoking and betel quid chewing are two established risk factors for oral cancer in Taiwan [2]. The prevalence of these risk factors in Changhua ranked in the mid-range nationally, yet the county has the highest incidence of oral cancer in Taiwan.

We next explored whether any environmental factors might explain the lack of association between betel quid chewing and the incidence of oral cancers in Changhua.

We did a retrospective review of medical records between 1994 and 2005for oral cancer patients in Changhua. These patients were all treated at the Changhua Christian Hospital (CCH) [3]. We examined the association between patients' residences, ages at diagnosis, and overall prognoses. Totally, 1363 patients with oral cancer were recruited. There was a constant increase in the number of patients diagnosed with oral cancer annually. The tongue and buccal mucosa were the two most common sites, constituting 56% of cases, while squamous cell carcinoma was diagnosed in 80% of the cases. The mean ages at diagnosis were 53.1 and 52.8 years for patients living in the northern and central parts of Changhua, and 55.1 years for those living in the south. Moreover, patients living in the northern and central parts of Changhua had poorer long-term prognoses, compared with the prognosis for patients in the south. The density of electroplating factories in northern and central parts of Changhua is significantly higher than in the south. We concluded that factors related to electroplating factories may play a role in the differences in the prognosis of oral cancer patients living in different parts of Changhua.

Incidence of Oral Cancer in Relation to Heavy Metal Concentrations in Farm Soil of Patients' Residential Areas in Taiwan

To explore if exposure to heavy metals in the environment is a new risk factor of oral cancer, we did an observational study [4]. We first calculated the age-standardized incidence rates of oral cancer in the 316 townships and precincts of Taiwan. We also collected information about prevalence rates of cigarette smoking and betel quid chewing, and concentrations of heavy metal in farm soil in these townships [5]. There were 22,083 patients with oral cancer in this study.

The results established the incidence of oral cancer was geographically related to the concentrations of arsenic and nickel in the patient's residential areas, with the prevalence of cigarette smoking and betel quid chewing as controlled variables.

We concluded that beside the two important risk factors, cigarette smoking and betel quid chewing, heavy metals, including arsenic and nickel in farm soil are highly likely new risk factors for oral cancer.

Association between Blood Nickel and Blood Chromium and Oral Cancer: A Case-Control Study in Changhua

To elucidate the relationship between heavy metals and oral cancer in Changhua, we recruited 101 oral cancer patients and 104 controls from the Changhua Christian Hospital. All subjects completed a questionnaire containing demographic information; uses of cigarette, alcohol, and betel nuts; environmental and occupational exposure history. Blood samples were collected for measurement of metals with inductively coupled plasma mass spectrometry. We found a strong association between the blood levels of nickel and chromium and oral cancer (both with $P<0.0001$) [6]. This study highly supported these two metals play a role in the development of oral cancer.

A Strong Association between Blood and Farm Soil Chromium Concentrations among Oral Cancer Patients in Changhua

We also studied the association between the metal concentrations in the farm soil and in the blood of oral cancer patients.

We recruited 79 oral cancer patients from Changhua County. Some of the lifestyle factors, including smoking and betel nut chewing were adjusted in regression analyses. The results showed that the chromium concentration in the blood of the patients is significantly higher than the background value, and is positively associated with the chromium concentration in the soil in their residing towns (p-value < 0.023) [7].

Animal Model of Oral Cancer Induced by Chronic Chromium Intake

We designed experiments to test the carcinogenic effects of chromium on oral cancer in mice. Mice were given different doses of chromium, with the highest dose making mouse blood chromium levels up to 10 fold of the levels found in oral cancer patients living in Changhua. These mice were fed with chromium for 12 months and then sacrificed for cancer detection. The results are that we failed to find any malignancy in the oral cavity or other organs studied. However, another study done by researchers at NIH, USA successfully induced oral cancer in mice and rats after two years of administration of chromium [8].

Chronic Exposure to Heavy Metals and Risk of Oral Cancer in Taiwanese Males

We used chart records from the Taiwan Cancer Registry and found 21,135 male patients diagnosed with oral cancer from 1983 to

2002. The age-period-cohort model was used to analyze information from these records. Although the incidence increased in both Changhua and Taiwan overall, Changhua had a similar incidence to that in Taiwan as a whole until 1990, when the incidence in Changhua began to speed up, leaving a marked difference with Taiwan in general. After 10 years' exposure to the heavy metal pollution, it begins to impact the incidence of oral cancer. This novel factor can explain the extremely high incidence in Changhua [9].

Reduction in Arsenic Intake from Water Has Different Impacts on Lung Cancer and Bladder Cancer in an Arseniasis Endemic Area in Taiwan

How long the detrimental effects from exposure to heavy metal will persist after the environmental pollution is cleared? Our studies showed the incidence of oral cancer in Taiwan is associated with the levels of arsenic and nickel in farm soil. The Blackfoot disease, a severe endemic disease on the southeast coast of Taiwan, was caused by arsenic, too. People were exposed to excessive amounts of arsenic in the drinking water from artesian wells, which was the major source of water for local people. This problem was solved 3 decades ago with the supply of clean municipal water to local residents.

Researchers in Taiwan have established that excessive arsenic intake has a detrimental effect on human health, as reflected by an increase in cancer incidence [10]. We explored the impacts of reduction in arsenic intake from water on lung cancer and bladder cancer in the arseniasis endemic area in Taiwan. The results can give us an answer to the above-mentioned question.

We retrieved chart records of 23,013 patients with bladder cancer and 93,633 patients with lung cancer from 1979 to 2003 from the Taiwan Cancer Registry Center. We used the age-period-cohort model to study the changes in the incidence of both cancers in the arseniasis endemic area and the rest of Taiwan.

The results show three decades after municipal water supply to the arseniasis endemic area, there was a marked decrease in the incidence of bladder cancer and lung cancer in the area, especially for those in the later cohorts. The Relative Risk (RR) of getting a bladder cancer for people living in the arseniasis endemic area compared with those in the rest of Taiwan has dropped from 20 for the early cohorts to 5 for the late cohorts. As to lung cancer, the RR has decreased from 8 to between 1.5 and 2.

We conclude that reduction in arsenic intake from water has a positive impact on the incidence of both lung and bladder cancer; however, while RR for lung cancer has dropped to below 2, RR for bladder cancer has remained at around 5. The difference may be caused by presence of other risk factors beside the well-water intake or a longer latency period for bladder cancer than for lung cancer. More studies are required to understand the causes behind the difference. However, this study confirms our fear that the detrimental effects from environmental metal pollution can persist for generations.

Conclusion

Our studies have clearly demonstrated that environmental pollution, specifically farm soil pollution with heavy metal, can have a detrimental effect on the health of people feeding on crops and vegetables on these farms.

Industrialization may be a path no country can circumvent for modernization. However, cautions and regulations must be strictly applied for industries managed by people who are liable to near sightedness and sheer profit-making.

Acknowledgement

I thank Dr. Susan Olmstead-Wang at the Johns Hopkins University for her help in editing the manuscript.

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