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Original Article

Incidence of sicca syndrome is 3.6 fold higher in areas with farm soils high in chromium and nickel[☆]

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Received 25 October 2017; received in revised form 21 February 2018; accepted 19 April 2018

KEYWORDSSicca syndrome;
Chromium;
Nickel;
Epidemiology

Background/Purpose: Chromium and nickel are important soil pollutants in Taiwan. Previously, we showed that blood chromium levels correlated strongly with soil chromium levels. Our observation that many patients with dry eyes or a dry mouth came from areas where soils contain high chromium levels prompted us to investigate whether incidence and prevalence of SS are higher in areas where soils contain high levels of heavy metals.

Methods: We used a database from national health insurance (NHI) to study the epidemiology of SS. It was ascertained by at least 3 hospital visits with the diagnosis within 12 months. We then compared the results with the information about heavy metal contents in farm soils.

Results: The incidence of SS was significantly increased (3.6 fold) in the areas where soils contained high levels of chromium and nickel. In contrast, lead, copper, or arsenic did not show such a strong association.

Conclusion: Both the prevalence and incidence of SS are significantly increased in areas where soils contain high levels of chromium and nickel. Whether heavy metal, particularly chromium or nickel is a novel environmental risk factor for sicca syndrome needs more studies to confirm. Copyright © 2018, Formosan Medical Association. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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Introduction

Chromium is the second most abundant inorganic contaminant in the world, only next to lead.¹ Hexavalent chromium is the form of chromium commonly found in contaminated soils.¹ It is known to be toxic, even in very low concentrations in the water.^{2,3} Chromium can act as an allergen or carcinogen,^{4–6} causing tumor development, tissue inflammation and hypersensitivity.^{7–9} In addition, chromium can activate genes involved in inflammation, immunity and apoptosis.¹⁰

Heavy metal pollution in farm soils is a great concern in Taiwan. Because of loose regulations and public ignorance, many farm soils were polluted by wastes from factories during the early industrialization in Taiwan. Fortunately, the government recognized the problem and stipulated strict regulations. On the background, several nation-wide surveys on heavy metal contents in the farm soils were carried out from 1989 to 2002. Data from these surveys enable us to study the effects of heavy metal pollution in the farm soils on people's health in Taiwan. Previously, we found Changhua, a county in Taiwan and has a severe problem of heavy metal pollution in farm soils had the highest incidence of oral cancer in Taiwan.¹¹ The incidence of oral cancer was statistically associated with the levels of heavy metals in the farm soils.¹² Furthermore, the blood from oral cancer patients contained higher levels of certain heavy metals than the blood from controls.¹³ Other researchers also found that people living in the polluted areas of Changhua had higher levels of urine nickel and blood chromium.^{14,15} Moreover, we found a strong correlation exists between blood chromium levels and chromium levels in the farm soils.¹⁶

Besides cancer, we also found a strong correlation between disease activities and copper levels in farm soils for patients with rheumatoid arthritis.¹⁷ In addition, we observed many patients with dry eyes or a dry mouth came from areas where farm soils were contaminated with heavy metals. This observation prompted us to investigate whether heavy metals are risk factors for sicca syndrome (SS).

Taiwan began a compulsory NHI program in 1995. More than 95% of the medical institutes in Taiwan are contracted with the NHI, and more than 99% of the general population is covered by the program. This database gives us an opportunity to study the epidemiology of SS in Taiwan.

Materials and methods

Study population

The prevalence and incidence of SS in Taiwan were calculated using the National Health Insurance Research Database (NHIRD), which is managed by the National Health Research Institute of Taiwan. The NHIRD provides details of demographic data including healthcare services for outpatient visits, hospitalizations, prescriptions, and place of registration. We analyzed the healthcare records from a sample of exactly one million Taiwanese residents (more than 4% of the total population) randomly selected from the

NHIRD of persons enrolled in 2005. We studied only those older than twenty in 2005.

Definition of the patients with SS

SS is defined by at least 3 records (inpatient admissions or outpatient clinic visits) with a diagnosis of SS (ICD-9 code: 710.2) within any 12-month interval during the study period from 2005 to 2009. Standardization of the incidence and prevalence were done by the year 2000 world standard population by World Health Organization (WHO).

Definition of the place-of-residence

The address for a specific insured individual is not available in this database; however, the locations of the hospitals visited, and the location of registration are available. We decided the place-of-residence at the county level for each individual based on the location of hospitals or clinics visited for common colds and/or dental diseases. When the medical records were not available, the registered location of the insured is defined as the place-of-residence.

Incidence and prevalence of SS

The incidence of SS is defined as the newly diagnosed cases with the disease in a fixed number of population during a specific year. For prevalence, it is defined as the actual number of cases alive with the disease during a particular year. The age-standardized incidence or prevalence were standardized according to age distribution based on year 2000 world standard population by WHO.

We used ArcGIS with GiZScore statistics to characterize areas with a significantly high incidence rate of SS (hot spot) or a significantly low incidence rate of SS (cold spot) in Taiwan. The null hypothesis (H_0) for testing spatial autocorrelation is that the SS incidence rate for a specific region is unassociated with neighboring regions, whereas the alternative hypothesis (H_a) is that the neighboring regions have similar SS incidence rates. When a region has significant spatial autocorrelation, the null hypothesis is rejected and a region is defined as a hot spot or a cold spot.

Geographic distribution of heavy metals in farm soils

Heavy metal concentrations in farm soils were derived from several nationwide surveys that determined the concentrations of arsenic (As), cadmium (Cd), chromium (Cr), copper (Cu), mercury (Hg), nickel (Ni), lead (Pb) and zinc (Zn) in the agricultural topsoil (0–15 cm), conducted by the Environmental Protection Administration (EPA) in Taiwan from 1989 to 2002.¹⁸ The area-weighted mean was used to represent the level of heavy metal in each township. Based on these data, maps of Taiwan with concentrations of a specific metal in farm soils for each township were made.

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