LETTERS TO THE EDITOR

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Occupational metal exposures, smoking and diabetes

Dear Sir,

Yang *et al*. investigated the effect of occupational exposure to metals and smoking on the risk of diabetes and prediabetes in male workers [1]. The authors adopted Poisson regression analyses to estimate the interaction of metal exposures and smoking on the prevalence of diabetes. Adjusted prevalence ratio (PR) (95% CI) of workers with >40 pack-years of smoking and with smelting/refining work (the highest metal exposures) for diabetes was 3.6 (2.4–5.4). In patients with prediabetes, significance of PR and significant interaction disappeared. I have some queries on their study.

First, Kuo *et al*. conducted a systematic review on the association between environmental chemicals and type 2 diabetes, by considering obesity and metabolic syndrome [2]. From the view point of consistency, temporality, strength, dose–response relationship and biological plausibility, arsenic, cadmium, mercury, persistent organic pollutants, phthalates and bisphenol A showed no clear association with type 2 diabetes. Although the difference of the level of exposure and the type of metal would affect the risk of diabetes, Yang *et al*. should conduct quantitative evaluation on metal exposure and also consider the relationship between specific metal and diabetes with a sufficient number of samples.

Second, Le Boudec *et al*. assessed the association between smoking cessation and incidence of type 2 diabetes and impaired fasting glucose by a 5.5-year follow-up study [3]. They concluded that adjusted odds ratio of recent quitters and long-term quitters for the incidence of type 2 diabetes and for impaired fasting glucose did not become significant. Pan *et al*. conducted a meta-analysis of prospective studies on smoking behaviours and diabetes risk [4]. Active and passive smoking were associated with increased risks of type 2 diabetes. About smoking cessation, the risk of diabetes increased in new quitters but decreased substantially as the time since quitting increased. Subjects with impaired fasting glucose can be considered as a state of prediabetes, and there was no significant effect of smoking cessation on the risk of diabetes and prediabetes, which should be confirmed by further study.

Finally, Moon conducted a cross-sectional study on the association of heavy metals, including lead, mercury and cadmium, with diabetes [5]. Blood lead, mercury and cadmium had no significant relationship with diabetes by adjustment for age, sex, region, smoking, alcohol consumption and regular exercise, and the sum of heavy metal mixture with prevalent diabetes did not significantly relate with diabetes. The level of metal exposure would be lower than workers with occupational exposure, and independent variables for predicting diabetes and prediabetes should be handled quantitatively to confirm the association.

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Reply

Dear Sir,

We thank Dr Kawada for the interest in our study regarding exposure to heavy metals and smoking with risk of diabetes among occupational workers [1].

Although the study of heavy metals on diabetes development is currently under-researched, there is growing epidemiological evidence linking environmental chemicals, particularly heavy metals, to diabetes. Among heavy metals associated with the risk of

diabetes, arsenic has received special attention and increasing prospective evidence is generally consistent with an increased diabetes risk. Dr Kawada stated that there is no clear association between arsenic and risk of type 2 diabetes (T2D) in the systematic review cited in the letter [2]. However, the authors of this review had concluded that the evidence is suggestive but not sufficient for the relationship. Several other toxic metals and essential trace metals have also been linked to T2D, prediabetes and metabolic syndrome as recently reviewed by others [3,4]. A relationship between heavy metal exposure and increased T2D risk is biologically plausible [5–7]. It has been recognized that large longitudinal studies that prospectively investigate the role of multiple metal exposures and their independent and joint effects on T2D are urgently needed to further evaluate heavy metal exposures as risk factors for diabetes [8,9].

We are particularly encouraged that Dr Kawada recognized the need to conduct quantitative evaluation on specific metal and diabetes risk. In our recent study [10], we had performed an exploratory analysis with 464 metal-exposed workers to directly evaluate the dose–response associations between urinary levels of multiple metals and fasting plasma glucose (FPG) and dysglycemia. We found that increased level of nickel and imbalanced levels of zinc were positively associated with elevated FPG and dysglycemia while cobalt was negatively associated with risk of high FPG and dysglycemia. Our preliminary results support the notion that metal exposure may play an important role in the risk T2D in humans.

We fully agree that further studies are needed to examine the relationship between tobacco smoking cessation and the risk of diabetes and prediabetes, and the joint effects between tobacco smoking and heavy metal exposures on the risk of T2D.

Considering that T2D and its complications is a major public health problem worldwide, it is critical to understand the preventable determinants of this disease in order to establish appropriate interventions to assist with prevention efforts. Of the known risk factors for T2D, obesity is considered to play a significant role in the risk of the disease [11]. Body mass index, however, varies widely in patients with T2D indicating that other factors unrelated to obesity are likely implicated in the risk of T2D [12,13]. Recent experimental and epidemiological studies indicate that heavy metal exposure deserves consideration as a risk factor for T2D and this association is biologically plausible. Due to the inconclusive nature of the reported epidemiological association and the widespread exposure to heavy metals, there exists an urgent need for larger, more rigorous epidemiologic studies to investigate the alleged association and to determine the optimal levels of essential metals in reducing the toxic metal impacts on T2D. We are currently conducting a large prospective cohort study with over 45 000 participants—The China Metal-exposed Workers Cohort Study (Jinchang Cohort) [14]—and one of the major aims of the study is to investigate the role of multiple heavy metal exposures on the risk of T2D.

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