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Editorial

Does vitamin supplement use reduce serum levels of some heavy metals and/or trace inorganic elements in pregnant women?

Adequate nutritional support for pregnant women is an important issue, not only to help such women maintain peak health and performance, but also as it indirectly affects fetal growth and the minimization of adverse fetal outcome risks.[1] Among those nutritional components that are integral to this support, adequate protein-containing calories are most frequently discussed. Unquestionably, some essential minerals and chemical elements are generally considered to be of greater concern for pregnant women. At least nine trace elements, including selenium, zinc, copper, manganese, chromium, iron, molybdenum, iodine, and fluoride are important for maintaining physiological functions in human.[2] Additionally, vitamin D_3 is not only essential for bone health but also associated with improved absorption of essential elements such as calcium, magnesium, iron, phosphate, zinc, and copper.[3] However, higher levels of vitamin D_3 have been linked to enhanced absorption of toxic elements, including aluminum, cadmium, cobalt, and lead, as well as radioactive isotopes such as cesium and radioactive strontium.[3] It is well-recognized that bioaccumulation of such toxic metals in turn appears to disrupt physiological function in humans.

In this issue of the *Journal of Chinese Medical Association* by Huang et al[4] from one main medical school-associated hospital in southern Taiwan, the authors performed a cross-sectional study to investigate the blood concentration of mercury, manganese, iron, and copper in paired maternal/fetal blood samples from 145 pregnant women, and found that prenatal vitamin use (>3 times/wk) was significantly associated with lower maternal mercury (heavy metals) and copper (essential trace elements) serum levels.[4] The authors also found that there was a positive correlation of mercury and copper in paired maternal/fetal blood samples,[4] suggesting that maternal serum level of these elements could reflect intrauterine fetal serum levels. This raised an important issue, namely: "does the vitamin supplement reduce serum levels of some heavy metals and/or trace inorganic elements in pregnant women?"

Mercury, a common heavy metal and inorganic element, is often considered to be a poison; yet other heavy metals such as iron, copper, and zinc, are essential for living. In fact, healthy levels of minerals are a requisite for proper physiological function. However, in human physiology, these inorganic elements are found in low concentrations in body tissues and fluids, and are generally termed "trace elements," contributing to increasing attention which is being directed towards important areas of nutritional biochemistry and toxic bioaccumulation as they are linked to various adverse health outcomes.[4]

Copper is recognized as an essential trace element for many normal functions, such as neurotransmitter synthesis, antioxidant defense, mitochondrial respiration, iron metabolism, pigmentation, and connective tissue formation. Yet uncertainty remains regarding verifiable copper reference value for humans.[5] There are several gaps and unresolved issues which make it difficult to know the relationship between copper intake, copper balance, biomarkers of copper status, and health.[5] Increased tissue copper level may induce a series of harmful biochemical reactions, including oxidative stress, damaging the structure and integrity of mitochondria, and subsequently leading to cell injury.[6] However, low tissue copper levels impair immune and neurological function.[7] It is well-known that there are two hereditary defects in copper metabolism which result in disorders with severe clinical courses. One is Wilson's disease, which is a status of copper overload where mutation of those genes encoding the P-type ATPase copper transporters, ATP7B, are linked to impaired copper excretion, leading to abnormal deposition of copper in the target organs. The other condition is Menkes disease, a copper deficiency which results from impaired activity of copper-dependent enzymes and is caused by alterations in the genes encoding the P-type ATPase copper transporters, ATP7A in the target organs, contributing to a neurodegenerative disorder.[6,7]

Therefore, if appropriate vitamin supplement (>3 times/wk) for pregnant women would reduce the serum levels of copper, which has been demonstrated in the current issue of the *Journal of Chinese Medical Association*,[4] is it possible that the fetus might escape a potentially toxic bioaccumulation of mercury and copper? Of course, the fetus might also be at risk for complications arising from low serum levels of copper in a similar situation. It remains unclear why frequent use of a vitamin supplement is associated with decreased serum levels of mercury or copper. Before attempting to answer this question, two basic inquiries should be considered. First, it is unclear that pregnant women in southern Taiwan are at risk for multiple-micronutrient deficiencies. It is not clear which

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components and contents of the "vitamin (multiple-micronutrient)" are associated with blocking the absorption of mercury and copper as shown in the current study by Huang et al.[4] In fact, multiple-micronutrient deficiencies often coexist among women of reproductive age in low- to middle-income countries and are frequently exacerbated during pregnancy.[8] In general, it is difficult to accept Taiwan as a low- to middle-income country. As previously shown, vitamin D_3 is associated with enhancing trace element absorption, and evidence confirms the potential harms associated with vitamin D_3 deficiency, displaying the enormous benefits of supplementation to replenish and maintain adequate vitamin D indices.[3] However, uncertainty has arisen regarding levels that are considered adequate because, as shown above, elevated levels of vitamin D3 are linked to enhanced absorption of toxic elements. Taken together, these trace elements and nutrition might have a U-shaped phenomenon of benefits and risks, since the asserted benefits exist only within a specific range, and the risks present outside of this range.

In conclusion, adequate and balanced nutritional support, including adequate amount of trace elements, are important for the human body, regardless of the nature of the observed population (men or women; or pregnancy or not).[9,10] If pregnant women undergo proper dietary assessment and nutritional education to increase their own nutritional awareness, this could help such women decide whether extra vitamin supplements could be beneficial.[11]

Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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