Tidsskriftet Tidsskrift for Den norske legeforening

Nutritional status of vitamins and trace elements

FROM THE LABORATORY

PAUL KJETEL SOLDAL LILLEMOEN

Paul Kjetel Soldal Lillemoen, specialty registrar in medical biochemistry in the Department of Medical Biochemistry and Pharmacology at Haukeland University Hospital.
The author has completed the ICMJE form and declares no conflicts of interest.

ANNE-LISE BJØRKE-MONSEN

almo@helse-bergen.no
Anne-Lise Bjørke-Monsen, specialist in paediatrics and medical biochemistry, senior consultant in the Department of Medical Biochemistry and Pharmacology at Haukeland University Hospital and associate professor in the Department of Clinical Science at the University of Bergen. She is a board member of the Norwegian Society of Medical Biochemistry.
The author has completed the ICMJE form and declares no conflicts of interest.

Undernutrition and malnutrition are common among unwell and elderly individuals, but also occur during pregnancy, periods of growth and an unbalanced diet. Correct diagnosis is essential to ensure optimal vitamin and trace element status.

Micronutrients are essential substances needed in small quantities for normal physiological function. Micronutrients comprise nine water-soluble vitamins (vitamin B1, B2, B3, B5, B6, B7, B9, B12 and C), four fat-soluble vitamins (vitamin A, D, E and K), iron and trace elements such as iodine, copper, chromium, manganese, molybdenum, selenium and zinc. Vitamins are antioxidants, prohormones or cofactors in metabolic reactions, while trace

elements are catalytic or structural components in organic molecules. In the most severe cases, deficiencies of micronutrients can cause life-threatening conditions such as beriberi (vitamin B1 deficiency), pellagra (vitamin B3) and scurvy (vitamin C). There are very widespread global deficiencies of, for instance, iron, iodine, zinc and vitamin A, which are associated with increased child mortality, anaemia, reduced psychomotor development, growth retardation, reduced immune function and blindness (1). While severe deficiencies are not disputed, there is generally much disagreement about the consequences of less severe or subclinical deficiencies (2, 3).

Reference ranges

Most micronutrients and several metabolic markers can be measured in blood or urine, but interpretation is often problematic. In medical biochemistry, we often use reference ranges, which should be the central 95 % of analysis results in a healthy population. Reference ranges can be established for different sexes and age groups, and are well-suited for assessing endogenous biochemical parameters such as creatinine and albumin. However, reference ranges for micronutrients depend on external factors such as soil type, solar radiation and diet of the population on which the reference range is based. For instance, the reference range for serum folate (vitamin B9) is 5–29 nmol/l in Norway, but 16–109 nmol/l in the United States, where folic acid is added to flour (4, 5). Another example is vitamin B12, where serum levels reflect the consumption of animal products. In other words, a low folate level in the United States would be in the normal range in Norway, while a low vitamin B12 level in Norway would be in the normal range in India (3, 5).

Cut-offs

Reference ranges describe vitamin and trace element levels in the population, but consequently do not specify adequate or optimal status. The use of cut-offs (also known as clinical decision limits) is preferable for that. Cut-offs are conventionally based on clear signs of depleted stores, but it is increasingly understood that subclinical deficiencies can also impair health (6). For example, it is poor medical practice to wait until iron deficiency has resulted in microcytic anaemia before initiating intervention. In our opinion, diagnostic testing and decision limits should be used that ensure *optimal* vitamin and trace element status.

The challenge is finding appropriate biomarkers and cut-offs. We use assessment of iron status here as an example, but the principles can also apply to other micronutrients.

Diagnostic testing of iron status should include measurement of serum ferritin, serum soluble transferrin receptors or reticulocyte haemoglobin. In children, serum ferritin levels between 5 and 20 µg/l are used as cut-offs for iron deficiency, but many haematological parameters will only be stabilised at

serum ferritin above 30 µg/l for those aged less than 13 years and at serum ferritin above 40 µg/l for those aged between 13 and 19 years (7). Since we know that iron is not only important for haemoglobin levels, but also for normal psychomotor development and function (8), we should consider setting cut-offs for low serum ferritin levels higher than they are currently.

REFERENCES

1. Bailey RL, West KP, Black RE. The epidemiology of global micronutrient deficiencies. Ann Nutr Metab 2015; 66 (Suppl 2): 22–33. [PubMed] [CrossRef]

2. Carleen MH, Weissman N, Owen PS et al. Subclinical vitamin deficiency. Science 1943; 97: 47–9. [PubMed][CrossRef]

3. Sivaprasad M, Shalini T, Reddy PY et al. Prevalence of vitamin deficiencies in an apparently healthy urban adult population: Assessed by subclinical status and dietary intakes. Nutrition 2019; 63-64: 106–13. [PubMed] [CrossRef]

4. Pfeiffer CM, Sternberg MR, Fazili Z et al. Folate status and concentrations of serum folate forms in the US population: National Health and Nutrition Examination Survey 2011-2. Br J Nutr 2015; 113: 1965–77. [PubMed] [CrossRef]

5. Schwettmann L, Berbu S. Reference interval and status for serum folate and serum vitamin B12 in a Norwegian population. Clin Lab 2015; 61: 1095–100. [PubMed][CrossRef]

6. Houston MC. The role of cellular micronutrient analysis, nutraceuticals, vitamins, antioxidants and minerals in the prevention and treatment of hypertension and cardiovascular disease. Ther Adv Cardiovasc Dis 2010; 4: 165–83. [PubMed][CrossRef]

7. Markus C, Saxon B, Metz M. Ferritin as a functional biomarker of iron status in children and young adults. Br J Haematol 2019; 184: 640–2. [PubMed][CrossRef]

8. Barks A, Hall AM, Tran PV et al. Iron as a model nutrient for understanding the nutritional origins of neuropsychiatric disease. Pediatr Res 2019; 85: 176–82. [PubMed][CrossRef]

Publisert: 19 September 2022. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.19.0587