MYTH OR SCIENCE?
SPILLING THE BEANS ABOUT DIETARY SUPPLEMENTS

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Critical Appraisal

Globally, more than two billion people suffer from at least one, persistent or periodic, micronutrient deficiency [1, 2]. Micronutrients are essential vitamins and minerals, required by the body in small amounts for proper growth and development, disease prevention and wellbeing. Examples of essential micronutrients are zinc, iron, iodine, calcium, vitamins A, B, and D [3]. In the Netherlands, 32.1% of men and 53.6% of women use one or more commercially available dietary supplement(s) containing (multi)vitamins, minerals or a combination of these two [4]. However, the necessity of these supplements in healthy adults remains questionable. Therefore, this article will answer the following question: do dietary supplements really improve your health or are they just a waste of money?

Introduction

All micronutrients must be derived from the diet; therefore, a balanced and varied diet is important. This includes sufficient intake of nuts, fruits, vegetables and whole grains [5, 6]. Also, plant-based foods, lean protein foods and low-fat dairy products are important to meet the Recommended Dietary Allowance (RDA), in µg/d or mg/d, for micronutrients [7].

The RDA is composed by gender and age category and is defined as the mean requirement for a micronutrient plus two times the standard deviation. Therefore, the RDA is a target value that meets the nutrient requirement of almost all healthy individuals [8-10]. However, the personal need of an individual will, in general, be lower than the RDA [9, 11-13]. However, some groups of people have a higher personal need for some micronutrients and, therefore, supplementary advices have been composed. These groups concern babies (vitamin D and when breastfed vitamin K), young children (vitamin D), women who want to become pregnant (folic acid) and during pregnancy (vitamin D and folic acid), elderly (vitamin D), people with dark skin or people who do not have enough sun exposure (vitamin D) and people who do not consume animal products (vitamin B12) [13].

Micronutrient deficiency

Micronutrient availability below the personal need over a longer period (months to years) may result in a deficiency. This process can have two causes: a primary or secondary deficiency [11, 12]. In case of a primary deficiency, micronutrient intake is insufficient due to, for example, a one-sided diet. A secondary deficiency means there is sufficient intake of micronutrients, but it is not available in the right form for the body, for example, due to malabsorption [11]. A secondary micronutrient deficiency is often related to an underlying disease. Regardless of the cause of the micronutrient deficiency, the body will run out of micronutrients. As a result, there will be less synthesis of metabolites and a decrease in the activity of vitamin-dependent enzymes and hormones [11]. This will eventually lead to biochemical and metabolic changes that are detectable in body fluids and tissue by biochemical techniques [11]. This is called a latent deficiency. If the deficiency is not restored, this phase can evolve into a manifest deficiency [11]. During a manifest deficiency, clinical observable, morphological and functional changes will occur, which may even lead to death [11]. For instance, a vitamin D deficiency is associated with impaired bone growth and myopathy [14, 15]. In addition, a deficiency in vitamin A, vitamin E, vitamin C, zinc and selenium might contribute to an impaired immunity and iron deficiency might result in iron deficiency anaemia [16-21]. These possible consequences of micronutrient deficiencies are summarised in Figure 1. In case of a deficiency, dietary supplements can be used to restore micronutrient availability in the body. However, as mentioned before, many healthy people are using dietary supplements as well, even though primary micronutrient deficiencies are rare in healthy adults living in Western countries [22, 11-13]. The most common reasons for using dietary supplements are the improvement of overall health and prevention of health problems [23]. However, a recent study in more than 27,000 adults found that there are beneficial associations with nutrients from foods that are not seen with supplements [24].

In addition, meta-analyses and systematic reviews of the past decade indicate no evidence for the use of dietary supplements for primary or secondary prevention of diseases like cardiovascular events, myocardial infarction, stroke, total death and cardiac death [25-28]. However, a supplement with possible positive health effects is folic acid [28, 29]. In 2015, a large Chinese randomised controlled trial reported that folic acid supplementation may reduce cardiovascular diseases (CVD), and specifically, stroke [28, 29]. Inclusion of this RCT in two recent meta-analysis of folic acid and CVD risk resulted in a 17% reduction in CVD risk and a 20% reduction in stroke [28, 29]. However, more research is needed on these supplements because the results are mainly based on this Chinese study. Therefore, there is no (hard) evidence that an intake of micronutrients above the personal need or RDA does have any additional, positive health effects in healthy adults [11-13, 25-29]. Furthermore, combined calcium plus vitamin D supplementation might increase the risk of stroke. Beta-carotene, vitamin E and high doses of vitamin A seem to increase early mortality [25, 30, 31]. Also, beta-carotene would increase the risk of lung cancer in (ex)smokers and people who worked with asbestos [30, 31].

Micronutrient excess

For different vitamins and minerals, a safe upper limit has been established; the tolerable upper intake level and intake should stay below this level. However, the dose of dietary supplements is often higher than the RDA [11, 32]. Therefore, the use of supplements might result in a micronutrient excess. Especially because supplement users already tend to have higher

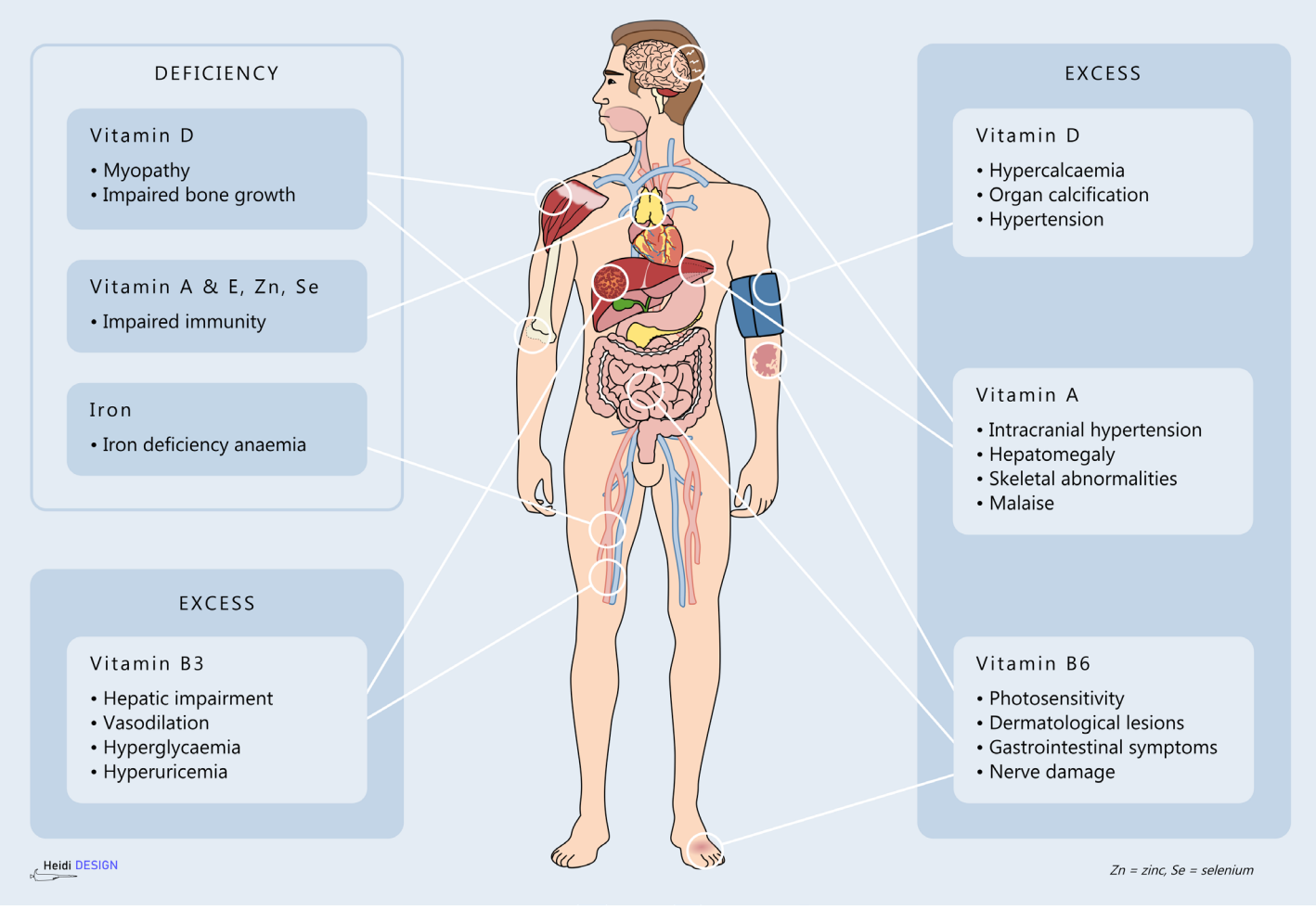

Figure 1: A summary of possible consequences of different micronutrient deficiencies and excesses.

nutrient intake from the diet itself [33-35]. This is probably due to the fact that supplement users have a higher nutrition awareness [35, 36]. As a result of micronutrient excess, micronutrient absorption in the intestinal tract will decrease and fat-soluble micronutrients will be stored in tissues and water-soluble micronutrients will be excreted in urine [11,13]. In addition, excessive intake of micronutrients might disrupt the normal metabolism or even reach toxic doses, which are associated with adverse health effects and deleterious consequences on health and development [11-13]. Especially, high doses of vitamin A, B3, B6 and D can be toxic [11, 37, 38].

A well-known example is the Dutch professional ice skater Sven Kramer, who suffered from nerve damage in his leg after a vitamin B6 excess due to dietary supplement use [32]. These dietary supplements contained 16 times the RDA for vitamin B6, which is equal to 25 mg [32]. Since October 2018, it is included in the Dutch Commodities Act that supplements may not contain more than 21 mg of vitamin B6 [39]. Nerve damage is the main toxicity of vitamin B6, but also gastrointestinal symptoms, photosensitivity and dermatological lesions might occur [37]. In 2014, the 'Gelderse Vallei' Hospital in Ede, the Netherlands, registered 300 vitamin B6 poisonings [32]. In addition, vitamin A excess might result in malaise, intracranial hypertension, hepatomegaly (an enlarged liver) and skeletal abnormalities [11, 38]. Besides, an excess of vitamin D might result in hypercalcaemia (high calcium levels), organ calcification and hypertension [11, 38]. Lastly, an excess of vitamin B3 might result in vasodilatation, hepatic impairment, hyperglycaemia (high blood sugar levels) and hyperuricemia (high uric acid blood levels) [11, 38]. Possible consequences of micronutrient excesses are summarised in Figure 1.

Conclusion

In conclusion, both micronutrient deficiencies and excesses can have negative health effects. However, a normal and varied diet in Western countries will contribute to sufficient intake of micronutrients. Therefore, dietary supplements should be used primarily in risk groups following the supplementary advice. Preventive dietary supplement use in healthy adults is not necessary. Although a multivitamin pill that does not exceed the tolerable upper intake level is a useful and safe supplement, the risk of excess should not be underestimated. If it turns out that you have a micronutrient deficiency, consider changing your diet before taking supplements.

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