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Review article

Micronutrients in the life cycle: Requirements and sufficient supply

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ABSTRACT

Macronutrients (fat, protein, carbohydrates) deliver energy and important material to ensure the entire body composition. Micronutrients are needed to keep this process of continuous construction and re-construction running. Consequently, the requirement for micronutrients will differ depending on the individual need which is related to the different metabolic conditions within the life cycle. Within the first 1000 days of life, from conception to the end of the second year of life the requirement for micronutrients is high and if the supply is inadequate that might have consequences for physical and at least cognitive development. In particular, iron, iodine, vitamin D and folate are micronutrients which might become critical during that period. Due to the fact that clinical symptoms of deficiencies develop late, but inadequate supply of one or more micronutrients may have consequences for health the term hidden hunger has been introduced to describe that situation. In particular the time period of pregnancy and early childhood is critical and hidden hunger is a worldwide problem, affecting > 2 billion people, primarily females and children. The importance of different requirements during the life cycle is usually not considered. In addition, we do not really know what the individual requirement is. The estimation of the requirement is based on studies calculating the supply of a micronutrient to avoid a deficiency disease within a healthy population and is not based on sound scientific methodology or data. We need to consider that at different moments in the life cycle the supply might become critical in particular in case of a disease or sudden increase of metabolic turnover. In this narrative review we summarize data from studies dealing with different micronutrient requirements in pregnancy, exercise, vegan diet, adolescents and elderly. Knowledge of critical periods and related critical micronutrients might help to avoid hidden hunger and its consequences.

1. Introduction

Humans need energy delivering macronutrients (fat, carbohydrate, protein) and no energy-delivering micronutrients. Regarding energy supply one macronutrient can substitute the other for a restricted time period. A life with either low fat or low carbohydrate or low protein supply is possible. To ensure the metabolic pathways and at least function of macronutrients the micronutrients are indispensable. In contrast to the macronutrients they cannot substitute each other and they cannot be synthesized within the body. Consequently we depend on the delivery of all the essential micronutrients via our diet. Whether the micronutrient supply via our diet fulfills our requirement or not depends on a couple of circumstances such as age, life style, hormonal activity or exercise and at least on bioavailability and half-life of the micronutrient.

In general it is claimed that adequate micronutrient supply can be achieved via a mixed diet. But what is adequate? Due to the fact that the metabolic and functional demand of micronutrients might be different, e.g. during childhood growth, adolescence or pregnancy, the requirement may differ and may lead to inadequacy.

We need to understand

- the definition of requirement
- whether there is any risk if a requirement is not achieved
- whether different age groups may have different requirements
- which micronutrients might be critical
- whether inadequate supply may have consequences in the short or long term

The above cited items seem rather simple. However, our knowledge regarding requirement, risk of inadequate supply and impact on health and adequate development is more or less superficial. The existing data show inadequate supply according to the claimed requirement. There might be a harmful impact in particular during pregnancy and early

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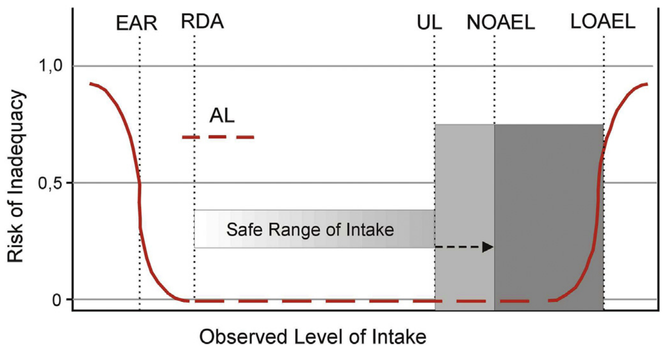

Fig. 1. Definition of different levels of intake: RDA: recommended dietary allowances; AI: acceptable intake (is used if an EAR or RDA could not be calculated); UL: upper level, the amount of a micronutrient below the amount which shows any kind of side effects; NOAEL: pharmacological definition of a no observed adverse effect level, similar to UL; LOAEL: lowest observed adverse effect level, the level which shows side effects.
Source: [1 modfied 3].

childhood but further data regarding long-term health and consequences of not achieving the requirements are needed to estimate the risk of low micronutrient supply. The data analysis below will try to summarize the existing data of micronutrient supply during the life style and some consequences if the intake is low.

2. Dietary reference intakes

The Institute of Medicine (IOM) of the US [1] presented the concept of "Dietary Reference Intakes" (DRI). According to the IOM are quantitative estimates of nutrient intakes to be used for planning and assessing diets for apparently healthy people (Fig. 1).

The following terms are used by IOM:

Recommended dietary allowances (*RDA*): the dietary intake level that is sufficient to meet the nutrient requirement of nearly all (97 to 98%) healthy individuals in a particular life stage and gender group.
Adequate intake (*AI*): a recommended intake value based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of healthy people that are assumed to be adequate – used when an RDA cannot be determined.
Tolerable upper intake level (*UL*): the highest level of nutrient intake that is likely to pose no risk of adverse health effects for almost all indviduals in the general population. As intake increases above the UL, the risk of adverse effects increases.
Estimated Average Requirement (*EAR*): a nutrient intake value that is estimated to meet the requirement of half of the healthy individuals in a life stage and gender group.

Very recently the European Food Safety Authority (EFSA) summarized the reports on micronutrient requirements of EFSA scientific panels since 2010 [2].

Instead of RDA the *Population Reference Intake* (PRI) is defined as the level of (nutrient) intake that is adequate for virtually all people in a population group. The term Average requirement (AR) is used instead of EAR and a new term the *Lower Threshold Intake* (LTI) is introduced. The LTI is the level of intake below which, on the basis of current knowledge, almost all people will be unable to maintain "metabolic integrity", according to the criterion chosen for each nutrient.

The differences between the IOM RDA and the EFSA PRI values are not substantial. In some cases the EFSA recommended intakes are slightly lower (e.g. vitamin A, Folate) or slightly higher (vitamin C, vitamin B12). However, because the values are based on either EAR or AR these differences are not really justified.

2.1. Estimated average requirement

To understand the impact of adequate micronutrient supply it is necessary to define the margins of adequate and inadequate and to discuss their impact on health and disease.

This estimation is based on specific indicators which are taken as a criterion of adequacy, e.g. absence of night blindness (vitamin A) or osteomalazia (vitamin D) or anemia (iron) in half of the apparently healthy individuals in a life stage or gender group. In most cases only small studies exist which are the basis for the criteria to calculate the EAR. If an EAR cannot be calculated an acceptable intake (AI) is determined. Consequently an EAR is a population-related value and not an individual one. The aim of the definition of an EAR is to calculate the mean intake based on the diet of a healthy adult population which seems adequate to avoid a micronutrient deficiency in 50% of the population. Individuals on the right side of this Gaussian distribution have a lower risk for a deficiency, those on the left a higher risk (Fig. 1). Thus, the EAR is only useful in populations with similar dietary composition. This explains differences between different populations. Nevertheless in many cases the EAR levels are used without discriminating country and population specific data.

EARs related to either life style, age or gender are extrapolated from the existing EAR for a given micronutrient with regard to the average healthy population without further scientific evaluation.

Based on current data a couple of US citizens (from the age of 1) do not even meet the EAR (Table 1).

Inadequate supply with micronutrients is not only present in low-income countries, it also occurs increasingly in high-income countries, e.g. in the US and Europe [5].

In a recent Europe-wide study, the percentage of healthy people (adults aged 19–64 years) and elderly (aged > 64 years) below the EAR (as defined by IOM [1]) has been reported based on different national surveys (Tables 2a, 2b and 3a, 3b) [6].

The data above show that inadequate micronutrient supply is not only present in low- income countries but also in high-income countries. Depending on the countries the magnitude can differ. This shows that food availability, dietary traditions and behaviors have a strong impact on micronutrient supply. If we consider that the amount of micronutrients which should be supplied (according to RDA) differs with respect to age, gender and life style, the number of people with inadequate supply may even increase.

What does it mean if the population does not reach the EAR for different micronutrients? Supply below EAR increases the risk for a clinical deficiency.

Indeed, based on the definition of the EAR, there might be an increased risk for developing a deficiency disease. This is in particular of importance if the requirement is substantially increased, e.g. in cases of a disease, accelerated growth or pregnancy.

Table 1
Percentage of US citizens not meeting the EAR for selected nutrients.
Source: [4].

Micronutrient	US citizens not meeting the EAR for selected nutrients [%]
Riboflavin	10.9
Niacin	12.7
Thaimin	18.4
Vitamin B12	20.3
Vitamin B6	26.1
Folate	40.3
Vitamin C	49.0
Vitamin A	54.0
Vitamin E	86.4
Zinc	29.2
Magnesium	57.0