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Hypo- and hypermagnesemia of the Hungarian population

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1. Abstract

Reviewing the international scientific literature, it seems that in a large part of the world hypomineralemia is present. Based on the sales figures of dietary supplements in Hungary, one can assume that Hungarians suffer from severe hypomineralemia. Epidemiological data show, however, that the Hungarian population in general, does not suffer from hypomineralemia. Interestingly, in contrast to the western pattern, in Hungary lower potassium and calcium levels are typical and instead of hypomagnesemia, mild hypermagnesemia is common. Thus, in this country supplementation of individual deficiency as well as increased support in case of hypermineralemia is recommended. These targets could be reached by preventive interventions, such as with proper selection of daily consumed food and nutrients. Improper consumption of dietary supplements causes harm therefore ion-supplementation should be done carefully and must be based on laboratory verified deficiency.

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2. Introduction

Hypo- and hypermineralemia means that the patient's blood parameters of minerals are out of the normal range (**Table 1**.). Minerals are indispensable components of the body, they take out ca. 6% of body weight. These elements are present in soluble form as in electrolytes and participate in the acid-base homeostasis and ion-regulation but in bound form they participate in almost all biochemical reactions. Their quantity and interrelations are standard within a narrow range, this is ensured by food uptake and regulated by hormone systems, metabolic processes, as well as by excretion. Based on these, we can state that minerals are essential nutrients and their deficit (even partial deficit), as well as excess, results in complaints and deficiency symptoms. Development of deficiencies can be avoided with consumption of diverse diet and, if necessary, by taking medicines and/or dietary supplements. In our present study we aim to present physiological impact, development of deficits and excess as well as the avoidability of such deviations of the main cations Na^{+}, K^{+}, Ca^{++} and Mg^{++}, with special attention tomagnesium.

Table 1. Main minerals in the adult body

Minerals	Quantity*	Plasma levels**
sodium	92 g	136 – 144 mmol/L
potassium	140 g	3,7 - 5,1 mmol/L
calcium	1300 g	2,2 - 2,6 mmol/L
magnesium	25 g	0,7 - 1,2 mmol/L

Explanation:

* Quantity = Total average amount in the body (in grams)

** Plasma levels = average mineral content in plasma: the normal range in mmol/L (Canada et al., 2015)

It is important to mention that signs and symptoms of mild deficiency or excess of these elements are scarcely specific therefore diagnosis of such ailment should based on laboratory blood tests. Consequently hidden hypo- or hypermineralemia can often be transiently present in the population even if the dynamic balance is within the norm.

3. The applicable epidemiological data and their impact

Survey of the international scientific literature shows that one meets with hypomineralemia all over the world. Approximated incidence of hypomineralemias is presented in **Table 2**. It is visible that incidence increases by ageing and that higher values are found due to the disabled (hospitalized) patients displaying less compensatory capacities.

Table 2. Incidence of hypomineralemia (according to international literature)*

a) according to age

Minerals	Under 65 years	Above 65 years
sodium	4%	25%
potassium	14%	2%
calcium	28%	61%
magnesium	2%	15%

b) according to population

Minerals	Ambulatory	Hospital
sodium	4%	9% (30-40%)
potassium	14%	18% (15-20%)
calcium	1%	28% (18-85%)
magnesium	2%	20% (7-47%)

* Presented data were calculated by the author based on 38 different publications. The data in parentheses originate from the handbook of ASPEN (American Society of Parenteral and Enteral Nutrition (Canada et al., 2015))

Let's focus on the 'healthy' population. Their supply of minerals is, in general, within the normal range but, as seen in **Table 2**, certain proportions of them lie under the normal values. What is the reason for deviations like these? Maybe, in some cases unrevealed disease is in the background, but majority of such ion-deviations are attributed to undernutrition of these minerals. The latter is affirmed by the NHANES study in the USA (Fulgoni

III, V.L., 2011). The data of the Hungarian National OTÁP2019 Survey and the 'Nutritional habits of Hungarian older adults' study corroborate the figures as well [OTÁP2019, Zámbó et al. 2021, Soós et al. 2024].

Should we look at the data of the National OTÁP2019 Survey, we may observe some interesting facts. All figures originate from healthy adults taking nutrients, including minerals, from regular daily meals only and display the quantitative uptake of minerals and their relations to each other. In order to understand the figures, we should know that not only ion-concentration is important in evaluation of the actual health situation but the balance of ions as well. For example take the relation of sodium to potassium. The former cation is an extracellular ion and the other is an intracellular one, i.e. most of the ions are outside the cells and, in the cells, respectively. The constant proportion is ensured by membrane-transporters, chiefly the enzyme Na^+, K^+-ATPase and this creates the electrochemical potential of the cell membrane. It means, the above mentioned enzyme pumps Na^+ out and K^+ into the cell (Fedosova et al. 2021). Similar ion-pairs are Ca^{++} and Mg^{++}. These bivalent cations are responsible for the signal transmission of neural cells via the membrane-enzymes Ca^{++}-ATP-ase and Mg^{++}-ATPse, respectively. For any stimulus, the ratio of Ca^{++} and Mg^{++} between the two sides of the cell membrane changes and results in action potential (Maier et al., 2023). Thus, apart from the absolute quantity of the ions, their constant ratios are of importance in maintaining the healthy function of the body.

Now, let's review the epidemiologic characters of the mentioned cations on the local and international level. It should be anticipated that for the recommended daily allowance (RDA) of this particulate case different authorities and institutions set different levels, thus in **Table 3**. we listed the RDA-s of Hungarian (RDAHu) and European (RDA) Authorities as well the recommendations of one of the leading prestigious healthcare institutions, Harvard University (Harvard1, Harvard 2 and Harvard3).

Table 3. Recommended daily allowance in milligramms

Ions	AI*	RDAHu**	Harvard***	NRV****
sodium	2000	2000	1500	none
potassium	3500	3500	4700	2000
calcium	750/950	800	1000/1200	800
magnesium	350/300	300	420	375

* AI = EFSA Adequate Intake = daily intake of a healthy person per day in milligrams (male/female)

**RDAHu = Hungarian daily recommendation according to the Hungarian Food Book [Codex Alimentarius Hungaricus] (Magyar Élelmiszerkönyv 1-1-90/496 sz. (2002) melléklete)

***Harvard = recommendation of the Harvard Medical School, USA

****NRV = Daily reference value according to the Regulation (EU) No 1169/2011 of the European Parliament and of the Council

Should we compare the OTÁP2019 data to the Hungarian RDAs, we see the landscape of **Figure 1** and **Figure 3**.

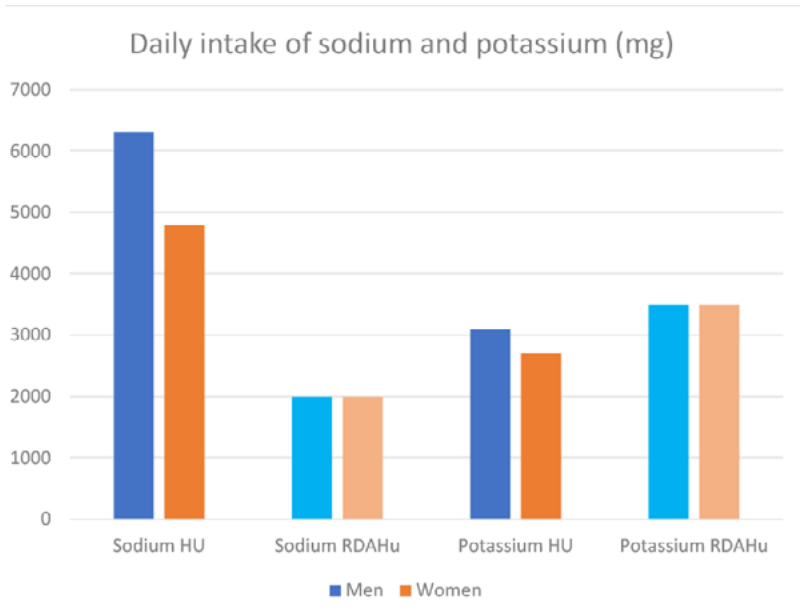

Figure 1. Measured (dark color) and recommended (light color) daily intake of sodium and potassium

From **Fig. 1.** we can read, that in Hungary there is no lack of sodium in the young population but the Na^+ uptake – predominantly resulting from the daily diet – is much higher than recommended. A similar finding is seen in the study of Sarkadi-Nagy (Sarkadi-Nagy et al, 2021). This leads to increased fluid-retention and a concomitantly high risk for development of hypertension. Astonishingly, it is more common in the elderly, as demonstrated in **Figure 2**. due to the age-dependent physiological and pathophysiological changes. While hyponatremia is dangerous in the elderly (Ganguli et al., 2015), high sodium-levels, which are a consequence of e.g. inadequate fluid intake or kidney disease, due to the diminished compensatory mechanisms, more frequently increase the morbidity and mortality of the elderly (Shah et al., 2014).

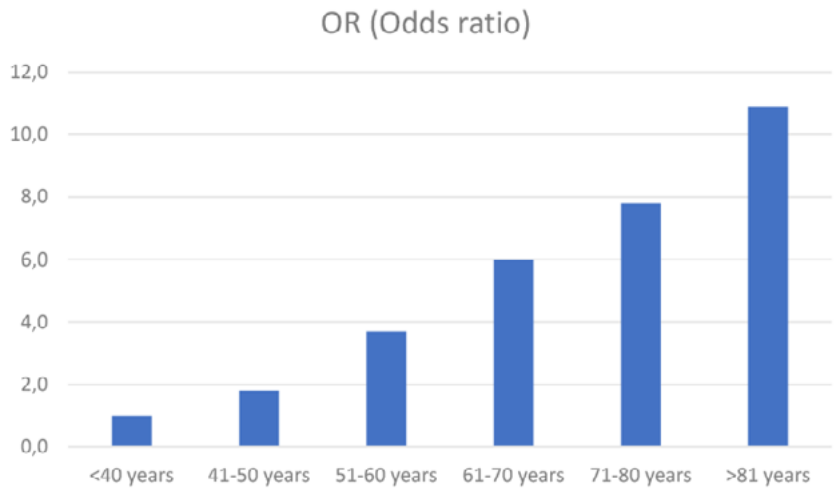

Figure 2. The odds for medium severe hypernatremia according to years of age. (Based on data of Upahyay et al. 2006)

In contrast, as also demonstrated in **Figure 1**., daily uptake of potassium from daily meals lags behind the recommendations. This is in corcondance with the survey of Sun et al (2021) which demonstrated that the USA population takes up less and less potassium from their daily food and this is attributed to changes in dietary habits, i.e. more processed foods are consumed (Sun, H. et al., 2021). This may cause symptoms in the form of hypokalaemia, characteristically in the form of muscle cramps, cardiac arrhythmias, low blood pressure, weaknes, and increased thirst. In the elderly, cardiac functions are overloaded which elevate hospitalization costs and increase mortality figures (Bardak et al., 2017). Moreover, the fall of hypokalemic patients is doubly as frequent as in normokalemic patients (Tachi, T. et al., 2015). Supplementation of these ions are, however not a priority for Hungarians, or – according to my suspicion – due to misdiagnosis they ascribe night cramps of the lower limbs/calf to magnesium deficiency and therefore take magnesium containing dietary supplements without medical consultation.

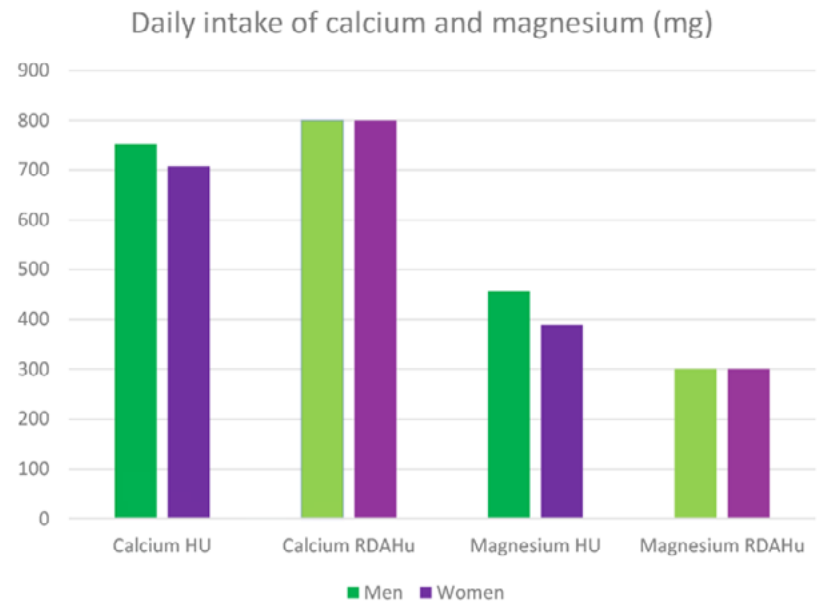

Fig. 3. The calcium and magnesium provision of the Hungarian population (measured values are in dark columns, recommended values in light columns)

Figure 3. presents the provision of local population with calcium and magnesium in contrast to the recommended values. As visible, calcium intake is less than needed, conversely, natural magnesium intake is more than recommended. This is worrisome! Direct hypermagnesemia usually does not results in toxicological consequences, however, there are some examples for this as well. Its negative ionotropic and chronotropic effect worsens cardiac insufficiency and may provoke paralytic ileus, too (Eiraku, K.,2022, Aydin, K., 2020). Magnesium stands in a pair with calcium, thus in order to maintain healthy ion-relations calcium intake should be increased and magnesium intake decreased, viz. a population with diverse and healthy diet patterns are able to ensure the uptake of needed amounts of magnesium and will not overintake calcium, which is desirable in order to maintain optimal ion-balance. Not so in the case of calcium where daily uptake from average diet is less than recommended by the local as well as international guidelines. The continuous hiperalimentation with magnesium and hypoalimentation with calcium can alter the Ca^{++}/Mg^{++} intake ratio and this may result in pathophysiological consequences (Dai et al. 2013). Here should be mentioned that absorption and bioavailability of these ions are influenced by several other parameters as well, e.g. the Ca^{++} and the Mg^{++} are absorbed via the same transmembrane transporters in the gut thus the local concentration of one of them alters absorption of the other one due to the competition for the transporters' capacity. Therefore if Mg-supplementation is recommended, it should be done with small amounts but frequently, instead of one big dose per day. On the population level, the moderate overingestion of magnesium is obviously not the reason for hypocalcemia but due to the huge amounts of sales of Mg-containing dietary supplements, in some cases this may contribute to the observed hypocalcemia. The putative hypocalcemia on a population level is worth considering because of the increased risk for osteoporosis and the consequent fractures, as does hypomagnesemia and the resulting deficient vitamin D levels (Capozzi et al., 2020).

4. Present situation of foods and dietary supplements containing minerals

Regarding the sales figures of dietary supplements containing minerals it seems the Hungarian population suffers from several and different deficiency syndromes. The Hungarian survey on consumption of dietary supplements also supported the steady increase in sales figures (OTÁP2019 report). If the deficit were a true deficit and the people realized the imperfect intake of certain minerals and had taken mineral-containing dietary supplements in response, it would be gratifying! The pity is, that there are very few supplementations based on ion-diagnostics.Mineral deficiencies have unspecific symptoms and patients of hidden mineral deficits rarely turn to MDs with these complaints. Moreover, actual laboratory data seldom show alarming signs. In the case of Mg^{++}, just 0.3% of the total magnesium is present in the serum and it does not represent the true intracellular value. Especially if an individual takes dietary supplements only occasionally and the measurement is done within some hours of the Mg^{++} -administration; in this situation serum-Mg levels are much higher than that in other tissues. Reliable measurement of how tissues are loaded with magnesium is the measurement of excretion: if the 60-70% of a certain dose of Mg^{++} was excreted by urine within 24 hours, it alludes to a well-loaded body. Also alarming that ca. half of the population exclusively follows the recommendations of the manufacturers, if dietary supplements are in question (NEBIH, 2021).

Media often deals with changes in the mineral content of the diet but the professional approach is scarce. The fact is, that alterations in eating habits – increase in proportion of processed and ultraprocessed food in the daily meal – influence the total mineral intake as well intake of vitamins and trace elements. It is known that for exampe white rice contains 4.5-times less magnesium and 3-times less potassium, than brown rice (Farthing, 2020). But there are documents that even raw materials (vegetables, fruits) contain less minerals today, than some decades ago. This is presented in **Table 4.** The data originated from the laboratory of Pharmakonzern Geigy from 1985 and the Food Laboratory of the Karlsruhe, Germany, from 2002 (Gräber, 2022).

Table 4. Change in ion content of vegetables and fruits between 1985 and 2002 in mg/100g

Raw material	Ions	1985	2002
Broccoli	Ca	103	28
	Mg	24	11
Beans	Ca	56	22
	Mg	26	18
Potato	Ca	14	3
	Mg	27	14
Banana	Ca	8	7
	Mg	31	24
Strawberry	Ca	21	12

A similar decrease has recently been published by an Australian research group, too (Rangan et al., 2022). Differences are appreciable, even if we take into consideration the accidental change of strains. The population has hardly any information about this, with especially no information on the specific food he/she purchases in the supermarket. The reasons for the loss of content are not to be discussed in this article. However, it can be stated that fortification of certain foods with minerals and vitamins has raison d'étre and, in certain individuals, administration of dietary supplements is also a reasonable assumption.

5. On the physiological role of magnesium and its supplementation

As the sales of magnesium-containing dietary supplements are the highest of all mineral-containing supplements, we are motivated to discuss the situation and the prospective consequences.

Magnesium is a cofactor of ca. 600 enzymes, being chiefly active in energy production and energy utilization, and where iontransports are involved in the biochemical processes (Adamako et al., 2024). Magnesium has a role in the maintenance of the human genome (DNA repair, replication, transcription, translation), further it has a function in structure-stabilization in the case of nucleic acids as well as proteins. This cation is important in electrophysiological processes where the proper function of Ca^{++}- and K^{+}-channels depends on the presence of Mg^{++} (Plichova et al., 2017). Consequently, hypomagnesemia plays a role in the pathophysiology of cardiovascular disease, Type-2-diabetes mellitus, osteoporosis, and mental diseases, etc. All of these underline the necessary presence of magnesium in a complicated physiological-biochemical network. Here should be recalled the impact of ion-balance, viz. hypomagnesemia induces hypokalemia and hypocalcemia and these affect hormonal systems (parathyroid-, antidiuretic system and insulin) as well (Ehrenpreis et al., 2021). If anyone really had low Mg-levels, it should be corrected. The first step in this direction is to explore the reason for the deficit. Should pathophysiological reasons be in the background, it must be treated. If pathophysiological problems were excluded, low intake should be corrected, at first with analysis of the eating habits. For example, in Hungary there is a high rish for non-communicable diseases due to an unhealthy diet on a population level: Hungarians consume less than the EU average of vegetables, fruits, nuts, and whole grain products (Tufts University, 2022).

For supplementation of magnesium there are medicines, nutraceuticals, and dietary supplements available. All of them are suitable, however only medicines guarantee their content and bioavailability due to authorization conditions. According to the EU regulations, dietary supplements containing minerals are subject to food regulations and the specific tolerated manufacturing deviation limits of mineral content ranges from -45 to +25% (Directive, 2002)! Disintegration of tablets, absorption of the content, and bioavailability are not regulated. This has an impact from a patient-safety point of view because, as mentioned above, many Hungarians take magnesium-containig dietary supplements as if they were a part of the daily meal or due to misdiagnosis (leg cramps). Usually, surplus excretes but a regularly overladen Mg-pool may cause pathological deviations in ion-homeostasis. According to the present understanding the healthy Ca^{++}: Mg^{++} ratio is between 2.5 and 3.0. The deviation of this range may result in pathological consequences.

Dai and co-workers assessed nearly 75,000 Chinese females and 61,500 Chinese males and found in contrast to the USA that high intake of magnesium (i.e. low Ca:Mg ratio) resulted in an increase in the risk of total mortality (Dai, 2012).

Then again, neither is too high a ratio of Ca:Mg beneficial: in the study of De Luccia at al. Ca:Mg ratio in 56 adults was 3.37 (18-29 years of age) and 3.58 (30-39 years of age) and this high ratio was in significant correlation with elevated levels of inflammatory parameters (e.g. IL-6) in the blood. (DeLuccia et al., 2019).

Another study points out that in 1977 the measured 2.3 – 2.9 Ca:Mg ratio increased to 2.9 – 3.5 in 2007/2008 and this correlated with an elevated incidence and prevalence of Type-2-diabetes mellitus as well as colon carcer (Rosanoff, 2010).

The NHANES study (USA) shows that from 2007 the Ca:Mg ratio increased due to the excessive use of Ca-containing supplements and if it was above 3.0 (i.e. relative Mg-deficit) the risk fordevelopment of certain types of cancer increased(Costello et al., 2021). In Hungary, it is just the opposite: the Mg-supplementation is in dominance. Thus, if the Ca:Mg ratio falls under 1.7, i.e. the Mg comes to relative excess, the cardiovascular risks and cancer probability increases (Li et al., 2020).

6. Discussion

According to the Hungarian dietary and food survey data Hungarians have no general mineral-deficiency. However, food consumption measurements demonstrate that Hungarians take in less calcium and potassium, but more sodium and magnesium from daily meals, than recommended. These deviations are worsened by voluntary and groundless consumption of magnesium, but non-consumption of K^{+} and Ca^{++} containing, supplements. This can be attributed to advertisements as well as to free access to these products. The best

(ideal) solution would be an altered eating habit: the increased consumption of ion-rich nutrients (vegetables, fruits) and avoiding ultraprocessed food. Unfortunately, supplementation based on medical examination and/or laboratory tests is scarce.

Following the Guideline of the European Parliament Hungarian legislation abolished the former registration process for dietary supplements. This brings about that consumers get formal information only about products. The market regarded this change as the arrival of freedom, not risk and the number as well as consumption of dietary supplements increased dramatically. Regrettably, the advertisements increased exponentially as well and urged people to irresponsible consumption, even consumer groups like athletes who usually are considered more health-conscious customers (Daher et al. 2022). The referred publication also attracted attention to the potential contamination and other risks associated with dietary supplement consumption.

As it is generally accepted, the intake of common salt (NaCl) should be reduced in order to improve health-related quality of life. To target the same goal, in the future Hungary should rationalize the use of drugs and dietary supplements, including magnesium-containing drugs and dietary supplements. This can be achieved via education in schools as well as adult education, and by enabling free consultation with healthcare professionals for the whole population.

7. Summary and conclusions

Based on the population-wide survey of Hungarian ion-status, general deficiencies or excesses can not be determined. Still, inadequate potassium intake and overconsumption of magnesium can be detected in a propertion of the population. The deficit or relative deficit of minerals seldom precipitates symptoms for individuals. However, these deficiencies, due to their complicated role in the maintenance of normal health, may contribute to generally poor health-related figures (Hungary, 2023). The estimation of the individual ion-supply, proper explanations of the signs and symptoms, and further extensive education may lead to a healthy diet and to avoiding erroneous or needless ion-supplementation.

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