

Magnesium Supplementation with Special Reference to the Treatment of Alcoholism

Keywords: Magnesium; Alcoholism; Hypomagnesemia; Infusion therapy

Abstract

Supplementation of various substances is sometimes recommended without sufficient indications. To decide whether a supplementation is needed, the question should be answered whether there is a deficiency, and if there is, whether it can be compensated by diet. Magnesium (Mg) deficiency has been associated with cardiovascular diseases, hypertension, stroke, certain neuropsychiatric and metabolic conditions. Hypomagnesemia is above-average in alcoholism; however, alcoholics should not be a priori assumed to have Mg deficiency. Mild depletion does not necessarily require specific therapy. Wherever possible, the oral route of supplementation is preferable. The parenteral route is mandatory in severe Mg deficiency. Hypermagnesemia may result from excessive supplementation. Intravenous infusions of Mg-containing solutions and some other invasive procedures have been used in the former Soviet Union without sufficient indications. The infusion therapy has been recommended also in moderately severe alcohol withdrawal syndrome. In conditions of suboptimal procedural quality assurance, endovascular and other invasive manipulations can lead to the transmission of viral hepatitis, which occurred to treated alcoholic patients. A combination of viral and alcoholic liver injury is unfavorable. It has been suggested to include Mg in routine blood ionograms. Mg contents in different foodstuffs should be taken into account in patients at risk of deficiency for better adjustment of diets.

Introduction

Supplementation of various substances is sometimes recommended these days without sufficient indications. To decide whether a supplementation is needed, the question should be answered whether there is a significant deficiency, and if there is, whether it can be compensated by diet. A stereotype is observed in some papers: an important role of a metabolite, food component or microelement is discussed; after that, a supplementation is recommended, although it is often unclear, whether it is indicated in a particular case. The theme of this review is a part of the broader topic: invasive procedures applied with questionable clinical indications in the former Soviet Union (fSU) [1-3]. According to the author's estimates following his practice as pathologist in some countries of Europe and Africa, an average size of malignant tumors in surgical specimens was larger in Moscow than abroad. Obviously, it reflects the efficiency of cancer diagnostics. Outside fSU, almost all mastectomy specimens were without muscle. The worldwide tendency towards more conservative breast cancer treatment remained unnoticed in fSU for decades. In the 1980s and decreasingly during the 1990s, the Halsted operation was the widespread method of breast cancer management; it was presented as the main treatment modality in some textbooks edited in the 21st century [4,5]. The Halsted operation is known to be associated with complications; during the Soviet era millions of women of different ages underwent this procedure. Even more radical procedures were recommended and applied [6]. When the nuisance started to be realized, leading surgeons proposed as alternative the



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Jargin SV*

Department of Pathology, People's Friendship University of Russia Russian Federation, Russia

*Address for Correspondence

Jargin SV, Department of Pathology, People's Friendship University of Russia, Clementovski per 6-82, 115184 Moscow, Russia, Tel: 7 495 9516788; Email: sjargin@mail.ru

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modified radical mastectomy of Patey with the removal of pectoralis minor muscle [7]. The latter procedure is also associated with complications; it has been broadly used in Russia during last decades. Furthermore, the cauterization or cryodestruction of endocervical ectopies (pseudo-erosions) independently of the presence of epithelial dysplasia has been applied routinely. Ectopies were detected at mass examinations and treated by coagulation. This generally disagrees with the international practice. At the same time, Pap-smears have been rare and technically suboptimal, cervical cancer being detected averagely late [8]. There are numerous other examples discussed previously [1-3]. Some papers containing questionable recommendations have remained without due commentaries, so that a continuation of suboptimal practices or reversion to them is not excluded. It should be mentioned here that this review is incomplete because some journals, books and dissertations are not given out to readers under technical pretexts e.g. at the Central Medical Library in Moscow. Potential motives of the unhelpful attitude have been discussed elsewhere [9].

Dietary and metabolic role of magnesium

Magnesium (Mg) deficiency has been associated with a number of conditions: cardiovascular disease, hypertension, stroke, neuropsychiatric, metabolic disorders such as diabetes and osteoporosis, migraine headaches, Alzheimer's disease, and alcoholism. A variety of drugs - some antibiotics, diuretics, digitalis, proton-pump inhibitors, chemotherapeutic agents may cause Mg wasting [10-19]. Among causes of Mg deficiency in chronic alcoholism are inadequate nutritional status, malabsorption, diarrhea, vomiting and enhanced renal excretion [11,20,21]. Mg deficiency may develop in diseases interfering with Mg absorption/excretion (renal, gastrointestinal) [12,22,23]. The prevalence of hypomagnesemia varied from 7% to 11% in hospitalized patients [13]; in those critically ill it ranged from 20% to 65% [14]. The overall prevalence of hypomagnesemia among geriatric patients reached 36%; in diabetes mellitus it ranged from 19% to 29% [15]. Hypomagnesemia is above-average in alcoholism: ~30% [13]. Alcoholics should not be a priori assumed to have hypomagnesemia requiring supplementation. For example, in a study of 129 chronic alcoholics, 84 (65.11%) had

normal, 37 (28.68%) subnormal and 8 (6.21%) elevated blood Mg level [16]. Some dietary surveys suggested that nearly two-thirds of the population in the Western world is not achieving the recommended daily allowance for Mg [22-24]. Considering that chlorophyll (and thus green vegetables) is the major source of Mg [12], a significant deficiency in conditions of diversified diet is deemed improbable [13]. Unprocessed grains, nuts, seeds and some vegetables are also rich sources of Mg. Phytic acid present in some seeds, including grains, nuts and pulses, interferes with the Mg absorption [18]. Drinking water is a source accounting for ~10% of Mg intake [12]. The total body Mg depletion may coexist with normal serum concentrations, while hypomagnesemia can persist without Mg deficiency [13]. Although some limitations apply, the serum Mg concentration is used as a standard for evaluation of the Mg status [14]. Wherever possible, more than one marker should be taken into account by researchers [17]. The supplementation is deemed necessary only in patients with demonstrably low Mg levels. Considering favorable effects of Mg in conditions of insulin resistance, a Mg-rich diet is recommended in type 2 diabetes mellitus and metabolic syndrome [25]. High-risk patients e.g. those with chronic diarrhea, receiving parenteral nutrition, long term diuretic and other therapies causing Mg loss, as well as chronic alcoholics, should have their serum Mg tested and, if necessary, supplemented [12,13]. Mild Mg depletion does not necessarily require specific therapy. Doubts remain about supplementing the general population as an excess of Mg may have detrimental effects [26-29]. Wherever possible, the oral route of replacement is preferable. When hypomagnesemia is severe and symptomatic, the parenteral route is mandatory. In order to avoid an overdose, attention should be given to tendon reflexes, respiration, and serial serum Mg levels [21]. The evidence-based use of Mg preparations, e.g. cathartic or antacid agents [14,22], is beyond the scope of this review. Some experimental and epidemiological studies indicated that both low and high Mg levels may be unfavorable for bone metabolism and parathyroid gland function, leading to mineralization defects [28,30]. High Mg levels potentiated osteoclast and hampered osteoblast differentiation in vitro [26,31]. Along with the evidence showing that Mg is generally beneficial for the skeleton, the data were reported that postmenopausal women with the highest quintile of Mg intake had the highest incidence of wrist fracture [27,28]. According to another research, Mg consumption slightly greater than the Recommended Dietary Allowance was associated with increased lower-arm and wrist fractures [32]. These results are in keeping with the data showing that elevated Mg may have unfavorable effects on the osseous metabolism and parathyroid gland function, leading to mineralization derangements. High bone Mg inhibits the formation of hydroxyapatite crystals by competing with calcium. The above mechanisms may contribute to osteomalacic renal osteodystrophy and adynamic bone disease [30]. Hypermagnesemia should be commented here, as it is sometimes iatrogenic as a result of excessive supplementation. Besides, it can be caused by a kidney disease, hypothyroidism and adrenocortical insufficiency. Hypermagnesemia may interfere with cell and organ functions, leading to various disorders [19]. Among others, it interferes with the blood clotting [13]. The prevalence of hypermagnesemia in hospitalized patients varied from 5.7% to 9.3% [14], being associated with an increased risk of in-hospital mortality [19].

Magnesium and the treatment of alcoholics

Excessive infusions of Mg-containing solutions can lead to adverse effects also in alcohol consumers. The differential diagnosis between hangover and alcohol withdrawal syndrome [33] is of importance in this connection. Both conditions have not always been clearly distinguished in fSU; more details are in [34]. The recommended duration of detoxifying treatment was irrationally long: 10-12 days [35]. Note that alcohol and its derivatives are eliminated spontaneously while rehydration is often achieved per os. The following treatments have been applied in alcohol withdrawal syndrome: intravenous drip infusions of 25% Mg sulfate, sodium chloride and thiosulfate, potassium permanganate, glucose, dextran and other solutions (7-10 infusions daily, alternating with intramuscular injections according to some instructions) [36-40]. The infusion therapy has been recommended also in moderately severe withdrawal syndrome [36]. Besides, intramuscular injections were applied: 10-15 ml 25% Mg sulfate together with 10 ml 40% glucose, 10 ml 30% sodium thiosulfate solutions, Unithiol, strychnine; subcutaneous infusions of up to one liter of isotonic saline, sorbent hemo- and lymphoperfusion, detoxification of cerebrospinal fluid by sorbents ("cerebrospinal fluid perfusion" or "liquorosorption" [41,42]), extracorporeal ultraviolet irradiation of blood etc. [35,40-44]. The above is generally at variance with the international practice. According to a Cochrane review, there is insufficient evidence to determine whether Mg is beneficial or harmful for the treatment or prevention of alcohol withdrawal syndrome. Existing evidence is also insufficient for Mg treatment or prophylaxis in people with low serum Mg experiencing or at risk of withdrawal syndrome. The current guidelines recommend that fluid status and electrolyte levels to be monitored with abnormalities corrected [45]. As mentioned above, over 70% of chronic alcoholics had normal or elevated blood Mg levels in the study [16]. In delirium tremens hypomagnesemia was detected in 42.3% [16]. Other authors reported similar or higher percentages [46,47]. The concentration of serum Mg may return to normal spontaneously by the time the patient develops delirium tremens [21,48]. As delirium is difficult to differentiate from Wernicke encephalopathy, oral Mg was recommended in case of severe withdrawal symptoms [49]; but routine administration of parenteral Mg was not recommended [48]. The treatment of delirium and other alcohol-related psychoses is beyond the scope of this review. Administration of electrolytes must be governed by laboratory findings. Apropos, correction of low sodium concentrations must be carried out with caution, lest a central pontine myelinolysis be induced [21]. Furthermore, the following treatments were applied to alcoholics in fSU: pyrotherapy with sulfozine (1% oil solution of sulfur for intramuscular injections), subcutaneous injections of oxygen (200-500 ml, 10-15 procedures pro course), endolymphatic and endobronchial drug delivery, biopsies of internal organs, angiography and cholangiopancreatography sometimes without clear indications [35-37,40,50-52]. Note that repeated intravenous infusions are associated with risks and discomfort especially for people with narrow, collapsed veins. Some patients regarded compulsory treatments as punishments; the latter ideation has apparently been present in some personnel [53]. In conditions of suboptimal procedural quality assurance, endovascular and other invasive manipulations can lead to a transmission of viral hepatitis and other infections, which occurred to treated alcoholics.

A combination of viral and alcoholic liver injury is known to be unfavorable. Other therapies of alcoholic patients potentially at variance with medical ethics have been reviewed previously [3].

Informed consent and overtreatment of alcoholics in Russia

The compulsory treatment in fSU was endorsed by regulations e.g. [35]. In 1974, chronic alcoholism was declared to be a ground for compulsory treatment; the regulations were hardened in 1985, making the forced hospitalization and treatment of chronic alcoholics independent of antisocial behavior. This practice has been designated in 1990 as contradictory to human rights [54]. “Labor-and-Treatment Prophylactoriums” (abbreviated LTP also in Russian) were a form of detainment from 6 months to 2 years. Alcohol was available for many LTP inmates: excursions to retail outlets through loopholes “unnoticed” by the administration could be regularly observed. LTPs have been abolished in Russia per Presidential Decree in 1993. In Belarus, these institutions have been preserved. Reportedly, in 1994 about 60% of patients of one of the “phthisio-narcological” institutions for compulsory treatment of alcoholic patients with tuberculosis (Tb) broke out; a half of them were returned by the police (militia) [55]. The duration of compulsory treatment in such institutions was up to 1 year or longer [35,55]. According to recommendations by the Health Ministry, indications for surgery were broader in alcoholics than in other Tb patients. Lung resections have been prevailing modality. The surgical treatment of Tb was recommended to be implemented earlier i.e. after a shorter period of medical therapy [43,56,57]. Among others, vocal cord injuries were observed after repeated bronchoscopies sometimes performed in conditions of suboptimal procedural quality assurance. Besides, it was noticed that vigorous apomorphine-induced vomiting as emetic or aversive therapy of alcohol dependence provoked hemoptysis in some Tb patients [58]. The system of compulsory treatment was largely dismantled during the 1990s, but some experts recommended its restoration and further development [59,60]. It is known that the concept of informed consent has not been uniformly accepted in fSU. The factors contributing to the persistence of suboptimal practices included a partial isolation from the international scientific community, authoritative management style, disregard for the rules of scientific polemics, paternalistic attitude to patients, former party and military functionaries, their helpers and protégées in leading positions of the healthcare, science and education [1-3,61]. The training of medical personnel may be a motive behind the excessive use of invasive procedures. Alcohol abusers are a group of risk for such procedures performed without sufficient indications.

Conclusion

Mg deficiency has been associated with cardiovascular diseases, hypertension, stroke, some metabolic and neuropsychiatric conditions. Hypomagnesemia is above-average in alcoholism; however, alcoholics should not be a priori assumed to have Mg deficiency. To decide whether a supplementation is needed, the question should be answered whether there is a deficiency, and if there is, whether it can be compensated by diet. A regular intake of drugs or dietary supplements can be more expensive than a diet modification. The Mg supplementation by oral drugs is generally well tolerated but may cause gastrointestinal symptoms [12]. With regard to topical treatments, the propagation of transdermal Mg is not scientifically

supported [62]. Further studies are needed, with participation of patients and volunteers, as well as animal experiments, determining serum Mg concentrations and using other tests (Mg content in red blood cells, 24h urinary excretion, Mg loading test etc.) [13,14,63], comparing dietary and pharmacological Mg supplementation especially in conditions of deficiency. It has been suggested to include Mg in routine blood ionograms [19]. Mg concentrations in different foods should be taken into account in patients at risk for better adjustment of diets [64]. Intravenous infusions of Mg-containing solutions, as well as other invasive procedures, have been used for the treatment of alcoholics in fSU without sufficient indications.

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