

The Influence of Ethanol on Magnesium Body Status

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Abstract

Magnesium (Mg) is the second most important intracellular cation that is needed for a broad variety of physiological functions. Disturbances in Mg body status, which may be induced by environmental contaminants, life style and manner of nutrition, can create serious negative consequences for health. One of the factors affecting Mg homeostasis is excessive ethanol consumption. Interactions between ethanol and Mg can take place at different stages of Mg metabolism (absorption, distribution in the organism and excretion of this element) as well as at the stage of its biological functions. Ethanol ingestion leads to serious disturbances in Mg metabolism on the one hand, while dietary Mg intake has been reported to influence the metabolism and toxicity of ethanol on the other. Experimental data show that Mg supplementation may prevent or reduce adverse effects of ethanol action in animals, whereas its deficiency can intensify ethanol toxicity.

In this review, the interactions between ethanol and Mg in humans and animals are discussed on the basis of the available clinical, epidemiological and experimental data, against the background of common ethanol consumption and insufficient Mg dietary intake in the general population.

Keywords: magnesium, ethanol, interaction, supplementation

Introduction

Magnesium (Mg) is one of the elements essential for the proper function of human and animal organisms. Epidemiological data indicate that dietary Mg intake in the general population is insufficient and that low serum Mg concentration is observed in many people [1-3]. These may result from consumption of soft water that is relatively poor in Mg and calcium (Ca), inappropriate nutrition (the Western diet) and excessive intake of stimulants, including alcohol [2, 4]. Drugs and mental and physical stress are recognized as other major factors leading to disturbances in Mg metabolism [1, 5, 6]. In the modern-day world about 20% of the population consumes less than two-thirds of the recommended dietary allowances (RDA) for Mg (6 mg/kg b.w./day) [3]. Epidemiological data indicate that in Poland 30-60% of the population have inadequate Mg intake and that the mean daily consumption of

this macroelement is about 15% lower than the RDA [7]. The major Mg source for the organism is food, and to a lesser extent drinking water [2]. Epidemiological studies in the United States, Finland, Sweden, France and Taiwan have shown that low Mg concentration in drinking water on these geographical areas contributes to its deficiency in people [2, 3, 8, 9]. Experimental data indicate that Mg concentration in drinking water can be critical for its content in the body, because of its higher bioavailability from water than from eatables [8]. Another factor contributing to Mg deficiency is its low concentration in soil and plants. Some anthropogenic factors (acid rain and fertilization with nitrogen, potassium and sulfur salts) contribute to Mg leaching from the soil and may decrease its concentration in plants [10, 11]. Moreover, the presence of heavy metals in the environment can decrease the uptake and transport of Mg in plants, causing its deficiency in eatables [12].

Mg body status may also be disturbed by numerous chemical contaminants of the natural environment and food, including toxic heavy metals and fertilizers [4, 10]. The disorders may result from its decreased bioavailability, reduced absorption as well as increased elimination as a result of alterations in the metabolism of vitamins and hormones and enhanced formation of free radicals induced by chemical substances [4, 13-15]. Epidemiological data have shown a significant decrease in the concentration of Mg in the hair and serum of workers occupationally exposed to lead [16, 17]. The main causes of Mg deficiency in the organism are summarized in Fig. 1.

Independently of causes, disturbances in Mg homeostasis can create health hazards. Moreover, Mg deficiency makes the organism more susceptible to the action of numerous toxic factors whose detrimental influence is relevant to disturbances in Mg metabolism [4, 17, 18].

Taking into account increasing ethanol consumption and Mg deficiency in a large part of the general population, in the review we discuss the available clinical, epidemiological and experimental data concerning Mg-ethanol interactions.

Magnesium as One of the Most Important Bioelements in the Organism

Mg is the fourth most abundant cation in the organism [1]. It takes part in numerous enzymatic reactions and metabolic processes as well as in the transfer of genetic information [19-21]. Because of its small ion radius, Mg^{2+} ion possesses a great biochemical activity and ability to create complexes with different substances [20]. As an activator of over 300 enzymes, it takes part in proteins, nucleic acids, lipids and carbohydrate metabolism as well as in ion transport across biological membranes [1, 22]. It is involved in the transfer, storage and utilization of intracellular energy through its interaction with adenosinetriphosphate (ATP) [23]. Mg is necessary for cell proliferation, growth and maturation as well as for immunological processes [19]. As a Ca antagonist, Mg decreases muscular contractibility and modulates cytosolic concentration of Ca [23].

Due to the critical importance of Mg in modulating numerous biological functions and processes, all disorders in its body status create a health hazard [3, 19, 21]. Mg deficiency contributes to cardiovascular diseases,

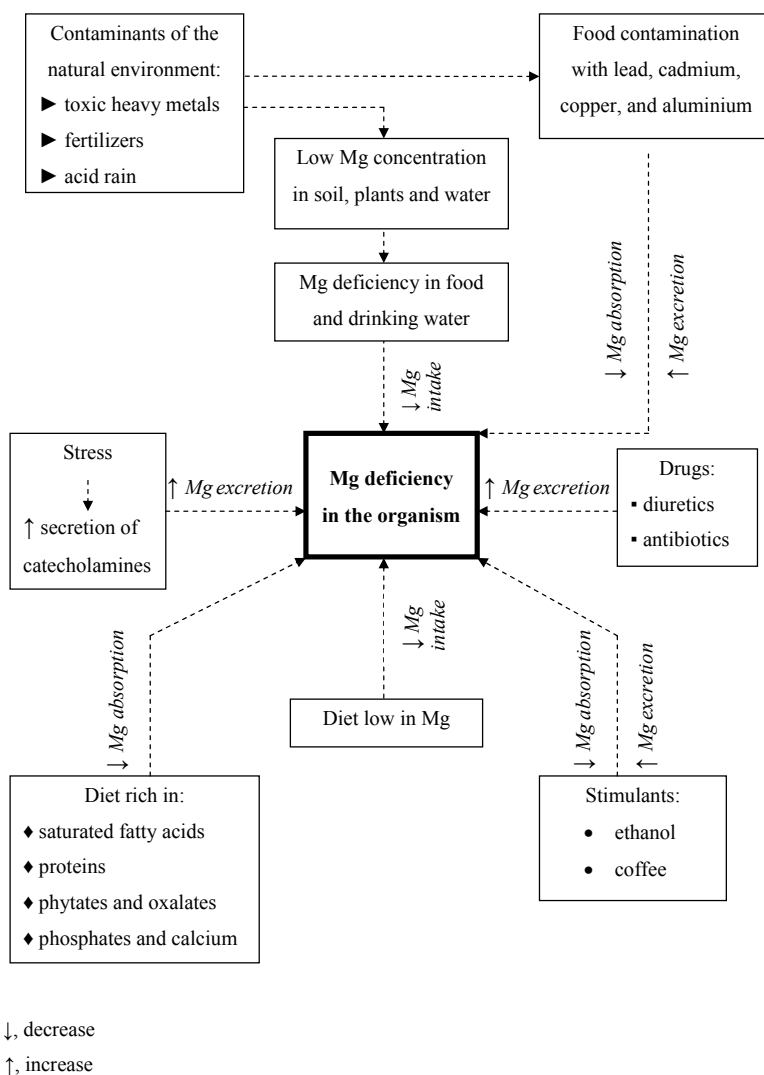


Fig. 1. The main causes of Mg deficiency in the human organism.

osteoporosis, and disorders in electrolyte balance, as well as disturbed integrity and functions of cell membranes, increased susceptibility to oxidative damage and cancer [20, 24, 25].

Toxicity of Ethanol

Ethanol poisonings result from its large consumption as a stimulant by millions of people over the world and from its common and wide usage in industry as an organic solvent [26]. Toxicity of ethanol in humans and experimental animals has been well known and widely reported [27-31]. It results from the action of its toxic metabolites such as acetaldehyde and acetic acid [27, 32]. Accumulation of reduced nucleotides and H⁺ ions in cytosol as well as the generation of reactive oxygen species during ethanol biotransformation is also responsible for its toxic action [33, 34]. These chemical compounds are capable of interacting with and damaging proteins, nucleic acids, and membrane lipids, inducing a number of alterations in the structure and biological functions of many tissues [27, 28, 34].

Consumption of large quantities of ethanol leads to Mg depletion [14, 35-37]. In 1954, Flink et al. [38] reported for the first time excessive alcohol consumption as a cause of Mg deficiency in an organism.

Ethanol-Magnesium Interactions at the Toxicokinetic Phase in Humans and Animals

Ethanol-induced disorders in body Mg status have been confirmed by numerous epidemiological and experimental studies [5, 6, 14, 39]. However, the causes of the decrease in tissue Mg content remain unclear. Ethanol as well as its toxic metabolites can influence the absorption, tissue distribution and excretion of Mg [25, 35, 39] (Fig. 2). Chronic alcohol abuse causes primary malnutrition by insufficient dietary Mg intake and may result in secondary malnutrition from impaired intestinal absorption, utilization, storage and accelerated excretion of this macroelement [40, 41]. On the other hand, increased Mg intake influences ethanol metabolism and affects its toxic action (Fig. 3) [35, 42-46].

Ethanol-Mg Interactions at the Intestinal Absorption Stage

Efficiency of Mg absorption in the gastrointestinal tract depends on its amount in the diet [21, 22]. Clinical studies have revealed that the percentage of Mg absorbed is from 27% on a high Mg diet (640 mg/day) to 79% on a low Mg

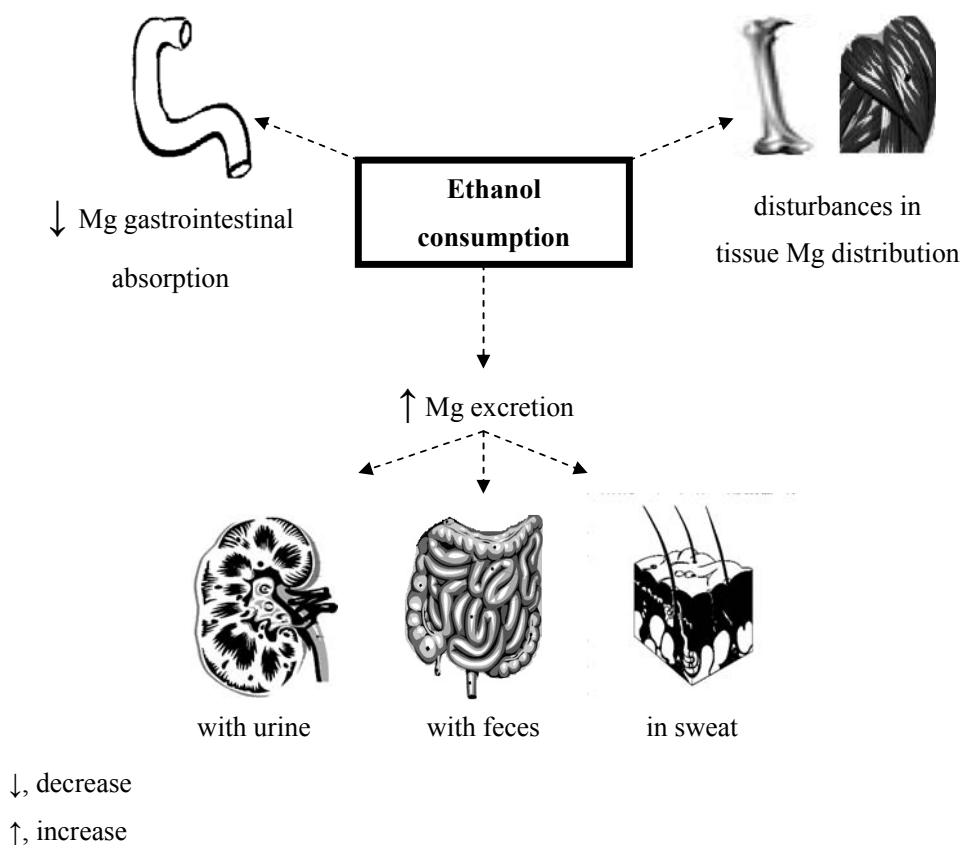


Fig. 2. Schematic presentation of ethanol influence on Mg metabolism.

diet (36 mg/day) [22]. Mg^{2+} ions, unlike the other divalent cations, are absorbed equally well in ileum and jejunum by a passive leak, active extrusion and the involvement of the sodium/magnesium antiporter ($2Na^+/Mg^{2+}$ antiporter), and the jejunal absorption appears to be vitamin D-dependent [23].

Ethanol may diminish gastrointestinal absorption of Mg through several mechanisms [4, 19, 40, 47]. Clinical evidence indicates that chronic ethanol intake leads to functional and structural disorders in the gastrointestinal tract that result from its direct action on the gastrointestinal tract and damage to the liver and pancreas [5, 35, 36]. Mg losses may then occur via the alimentary tract where absorption may be compromised with or without ethanol-induced vomiting, diarrhea, gastroenteritis, ulceration and bowel inflammation [5, 40]. Functional and structural disorders in the cellular membrane of enterocytes due to interactions of free radicals (generated by cytochrome P4502E1) with $2Na^+/Mg^{2+}$ antiporter in the basolateral membrane may also diminish Mg absorption [19, 23]. Our own experimental studies on rats confirmed a disturbing ethanol impact on Mg gastrointestinal absorption [48]. We have noted that administration of 10% ethanol in drinking water for 12 weeks resulted in a decrease in apparent Mg absorption by 28%.

Another mechanism of the diminished intestinal absorption of Mg in alcoholics could be related to the ethanol-induced deficiency of vitamins B₆, D and selenium (Se) that take part in Mg absorption by enterocytes [1, 47, 49]. Moreover, Mg absorption may be influenced by the ethanol-induced hypofunction of the parathyroid gland, resulting in a decrease in the serum parathyroid hormone (PTH) concentration [4, 5]. Deficiency of PTH inhibits the activity of 1- α -hydroxylase of 25-hydroxyvitamin D in the kidney and as a result decreases conversion of 25-hydroxyvitamin D (25(OH)D) to 1,25-dihydroxyvitamin D (1,25(OH)₂D) in the mitochondria of renal tubular cells [19]. Moreover, low circulating levels of 25(OH)D observed in chronic alcoholics, even in the absence of liver disease, may also contribute to the decreased production of 1,25(OH)₂D [50]. This vitamin D active metabolite stimulates Mg absorption through epithelium of intestinal villi, and thus in the case of its deficiency intestinal Mg absorption may be diminished [19].

Alcohol-induced hyperglycaemia and insulin deficiency, associated with pancreas damage, may further diminish Mg absorption from the alimentary tract, because insulin participates in its transport across biological membranes [4].

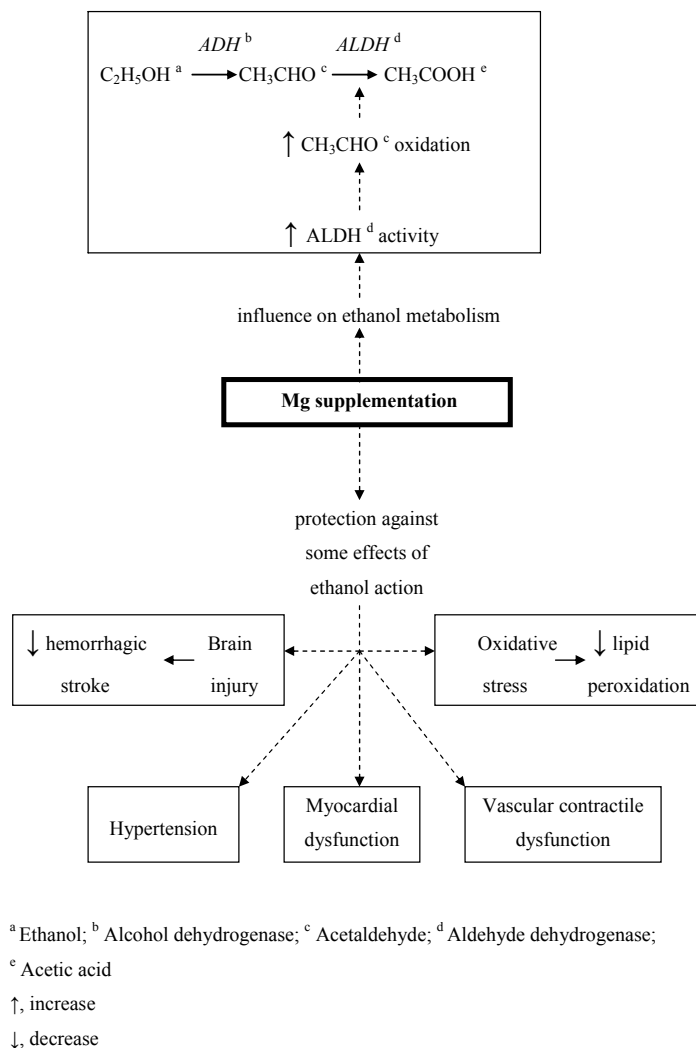


Fig. 3. Schematic presentation of Mg influence on ethanol metabolism and its toxic action.

Ethanol-Mg Interactions at the Stage of Tissue Distribution

Mg deficiency has been well documented in chronic alcoholics [5, 6, 51]. It has been estimated that 25-30% of them have low Mg concentrations in the serum [47]. Epidemiological data also indicate decreased Mg concentration in muscles, while no changes in Mg concentration in bone tissue were observed [6]. Acute ethanol ingestion also decreases the serum Mg concentration in humans [47, 52]. Pasternak et al. [52] have shown that a single dose of ethanol (0.84 g/kg b.w.) in the form of vodka decreased Mg concentration in the serum, whereas ethanol at the same dose but in the form of wine or beer did not change the serum Mg concentration. Slight effects of dependence period, family history of alcoholism and drinking of non-consumption alcohols on the serum Mg concentration were also observed in alcoholics [51]. Alcohol withdrawal syndrome is associated with a further decline in the serum Mg concentration [5].

Experimental data also show that acute or chronic ethanol administration results in alterations in tissue Mg distribution [14, 53-55]. As can be seen from the data in Table 1, changes in tissue Mg concentration (decrease or increase) or lack thereof were observed dependent on ethanol dose and administration duration as well as tissue type.

Our own observations from experimental studies did not reveal disturbing ethanol impact on tissue Mg distribution [13, 48]. We have noted that neither administration of 10% ethanol in drinking water for 12 weeks nor 1.25 g/kg b.w./24 h of 25% alcohol intragastrically for 5 days did not result in any alterations in tissue Mg contents. The lack of ethanol influence on tissue Mg distribution might result from short duration and low doses of alcohol administration. Trevisiol et al. [30] have reported that administration of ethanol contributing 35% of daily caloric intake for 6 weeks did not alter the bone Mg content in rats. Church et al. [56] have shown that prenatal ethanol exposure at a dose of 3 g/kg b.w. via oral gavage twice a day for 2 weeks was associated with a significant elevation in total body Mg concentration in male rat fetuses, whereas female fetuses had significantly lower Mg concentration in the body. These differences might result from the sex-dependent differences in the hormonal status. Yet, the mechanisms by which ethanol administration depletes tissue Mg content are not fully elucidated.

The body status of Mg in chronic alcoholics may also be influenced by the ethanol-induced disturbances in acid-base balance [57]. Ketoacidosis caused by catecholamines surge associated with alcohol withdrawal syndrome results in an increase in free non-esterified fatty acid concentration [22]. They probably temporarily bind Mg, decreasing

Table 1. The influence of oral ethanol exposure on Mg concentration in various tissues of experimental animals.

Ethanol intake (dose, time and manner of administration)	Species of animals	Tissue Mg concentration ^a									References
		blood (plasma or serum)	liver	kidney	spleen	heart	brain	muscle	bone	lung	
1.25 g/kg b.w./24h of 25% (w/v) ethanol, 5 d ^e	rats	↔ ^b	↔	↔	↔	↔	↔	↔	↔	↔	[13]
2 g/kg b.w./24h of 20% (w/v) ethanol, 5 d ^e	mice	↓ ^b	↑	↓	↑	↔	↓	↑		↓	[54]
5% (w/v), 6 wk ^f 20% (w/v), 6 wk	rats	↔ ^b ↔	↔ ↓	↔ ↓	↔ ↓	↔ ↓	↔ ↓	↔ ↓		↔ ↓	[53]
2.5% (w/v), 8 wk ^f 5% (w/v), 8 wk 10% (w/v), 8 wk	rats	↔ ^c ↔ ↓	↔ ↔ ↓	↔ ↔ ↔			↔ ↔ ↔				[14]
10% (w/v), 12 wk ^d	rats	↔ ^b	↔	↔	↔	↔	↔	↔	↔	↔	[48]
6% ethanol (67 ml of ethanol/l), 4 wk ^g	rats	↔ ^b /↓ ^c	↓	↓	↓	↓	↔	↓		↓	[41]

wk, weeks; d, days; b.w., body weight; ml, milliliter; l, litre; (w/v), weight/volume solution of ethanol;

^a ↔, no change; ↑, increase; ↓, decrease; ^b serum; ^c blood; ^d ethanol as the only drinking fluid;

^e ethanol was given intragastrically (by a stomach tube); ^f ethanol was administered in drinking water; ^g ethanol was administered in liquid diet.

the total and ionized Mg concentration as well [58]. This is accompanied by a state of catecholamines-induced lipolysis with subsequent intracellular precipitation of insoluble Mg-fatty acid complexes [59]. Alkalosis may be responsible for shifting Mg^{2+} ions out of the extracellular fluid space, resulting in augmentation of hypomagnesaemia [5]. Respiratory alkalosis associated with the withdrawal syndrome also shifts Mg and phosphorus intracellularly in patients who are commonly phosphorus deficient due to alcoholism [22]. Increased demands and loss of Mg can be compensated through tissue shifts, especially from its body stores into the bloodstream [53]. This is connected with the necessity of maintaining constant Mg concentration in the serum [6, 48].

Ethanol may also directly or indirectly modify mechanisms that control cellular Mg^{2+} homeostasis and/or transport across cell plasma membranes. Experimental evidence suggest that acute administration of ethanol mobilizes a considerable amount of Mg^{2+} from perfused rat livers and isolated hepatocytes in a dose-dependent manner [55]. The increased extrusion of this macroelement correlated well with a concomitant decrease in cytosolic ATP levels, indicating that a decreased buffering capacity of cytosolic Mg-ATP complex was responsible for the increase in cytosolic-free Mg^{2+} concentration and, consequently, extrusion of this element due to activation of the Na^+/Mg^{2+} exchanger in the cell membrane [33, 55]. The possible mechanism by which acute and chronic alcohol administration would result in a loss of Mg^{2+} from the Mg-ATP pool involves alteration in the nicotinamide-adenine dinucleotide/reduced nicotinamide-adenine dinucleotide ratio ($NAD^+/NADH$ ratio), as a result of oxidation of ethanol to acetaldehyde. The increase in NADH content would favor the formation of glyceraldehyde 3-phosphate (GAP), which acting as a trap for intracellular phosphorus (P_i), would decrease the cellular P_i content and remove the inhibitory effect of this moiety on adenosinemonophosphate (AMP) deaminase, allowing the degradation of ATP to proceed to uric acid and allantoin [41]. It is considered that prolonged exposure to ethanol may also markedly affect the hormone-modulated Mg transport mechanisms. It may exert alterations in various elements of the adrenergic signaling cascade, including membrane-bound G proteins and phosphodiesterase, as well as disorders in protein kinase C and Ca^{2+} signaling pathways [60]. This hypothesis is corroborated by the decrease in glucose output, cyclic adenosinemonophosphate (cAMP) production, and binding of G protein with the cell membrane, which was observed after acute ethanol administration to rats [33]. Slightly less clear is how alcohol inhibits the adrenoceptor-mediated Mg^{2+} extrusion, but most likely this inhibitory effect can be explained by changes in G protein activation/coupling, and Ca^{2+} cycling between the endoplasmic reticulum and cytoplasm [60]. In addition, ethanol administration affects the Mg^{2+} transport mechanisms in the plasma membrane, either directly (alcohol-related modification of the phospholipid environment or acetaldehyde-protein interaction) or indirectly (via the decrease in cellular ATP content), decreasing the cytosolic and intraorganelle Mg content [55].

Experimental data indicate that chronic ethanol administration may also markedly impair the ability of hepatocytes, and possibly other tissues, to accumulate Mg^{2+} from the extracellular compartment, which prevents the liver cells from restoring cellular Mg homeostasis [41]. These results provide a novel and basic understanding of the mechanisms by which ethanol decreases tissue Mg content.

Ethanol-Mg Interactions at the Excretion Stage

One of the major reasons for ethanol-induced hypomagnesaemia in alcohol abusers is increased urinary Mg excretion [4, 35, 40, 57]. The main cause for hypermagnesuria may be impaired renal Mg reabsorption because of damage to the renal proximal tubules and the Henle loop directly induced by ethanol [5, 23]. It is believed that the ethanol-induced decreased Mg tubular reabsorption may also result from increased tubular filtration rate [22]. Clinical studies indicate that renal Mg losses may result from acidosis as well as volume expansion due to aldosterone excess or inappropriate secretion of antidiuretic hormone (vasopressin) and increased taurine concentration in urine of alcoholics [5, 61]. Increased renal loss of Mg in chronic alcoholics may be due to an elevation of the blood lactate concentration during metabolism of alcohol, as lactate is known to increase Mg excretion [57]. In studies conducted on both healthy volunteers and ethanol addicted patients it has been noted that urinary Mg excretion increases together with the increase in ethanol concentration in blood [62]. Secondary hypoaldosteronism related to chronic alcoholic liver disease may also cause urinary loss of Mg. The acute ingestion of ethanol results in decreased vasopressin secretion followed by diuresis [61]. Chronic alcoholics have been shown to have increased concentration of vasopressin and may be overhydrated [40]. Ethanol-induced liver cirrhosis may lead to secondary magnesuria because of hyperammoniaemia. Hormonal disorders in alcoholics like hypofunction of the parathyroid gland or excessive function of the thyroid gland may also induce Mg loss through the kidney [4, 35]. Contrary to the above-mentioned effects, Majdanik et al. [63] have noted low Mg concentration in urine of drunk victims, which may indicate blood Mg deficiency during acute ethanol intoxication and reduction in glomerular filtration rate. Our own observations from experimental studies also indicate that exposure to ethanol may alter urinary Mg excretion. We have noted that administration of 25% ethanol by a stomach tube in a dose of 1.25 g/kg b.w./24 h for 5 days did not influence urinary Mg excretion in rats [13]. The lack of ethanol influence on the urinary Mg excretion noted in our study might result from short duration of alcohol administration. Choi et al. [64] have also reported unaffected urinary Mg concentration in rats receiving alcohol contributing 15% of daily caloric intake for 6 weeks. However, in our another experiment administration of 10% ethanol in drinking water for 12 weeks resulted in a decrease in urinary Mg excretion by 67% [48]. This might be the result of compensation

mechanisms, preventing further Mg losses from the organism due to chronic alcohol ingestion. Kreusser et al. [65] have reported that phosphate and potassium ion depletion common in chronic ethanol consumption could cause hypermagnesuria in rats. Mg deficiency itself has been identified as a cause of hyperphosphaturia in experimental animals.

Clinical studies in alcoholics also indicate increased fecal Mg excretion [57]. Because of a decrease in Mg intestinal absorption under ethanol influence the enhanced unabsorbed part of consumed Mg is excreted in feces [13, 48]. Due to increased cellular membranes permeability under ethanol influence, absorbed Mg can be transported from circulation into the lumen of the alimentary tract. Ethanol-induced pancreas inflammation in chronic alcoholics may lead to fatty diarrhoeas that intensify gastrointestinal losses of Mg [6, 57]. Increased excretion of Mg in alcoholics may also occur via sweat, but only during excessive diaphoresis in delirium tremens [4].

Involvement of Ethanol-Mg Interactions in Ethanol Toxic Action

The available experimental, epidemiological and clinical studies have provided evidence that interactions between ethanol and Mg are involved in the mechanisms of ethanol toxic action [27, 35, 39, 62, 66-68]. Moreover, there are data indicating that some adverse effects of acute and chronic ethanol ingestion in humans and experimental animals can be prevented or markedly reduced by concomitant Mg supply [4, 28, 42, 47, 67].

The influence of Mg on some effects of toxic ethanol action is related to its impact on ethanol biotransformation. Mg influences the liver ethanol metabolism via activation of the aldehyde dehydrogenase (ALAD) that oxidizes acetaldehyde to acetic acid [22]. Ethanol-induced Mg deficiency results in a decrease in ALDH activity and leads to acetaldehyde accumulation in the organism. Increased concentration of this toxic metabolite contributes to damage to the liver and central nervous system [35]. The accumulated acetaldehyde interacts with neurohormones in the brain, changes their activity, and stimulates β -endorphin secretion, which may influence development of alcohol addiction [27].

Clinical and experimental data indicate that brain trauma in humans and animals are associated with early falls in the brain total and cytosolic Mg^{2+} ions and in serum Mg^{2+} ions, which is exacerbated by the presence of ethanol [67, 68]. Ethanol-induced brain injury and stroke is preceded by a rapid fall in brain intracellular Mg^{2+} ions [28, 39]. These complications may be related to a decrease in cerebral blood flow, because of ethanol-induced powerful contractions of isolated animal cerebral arteries [69]. These cerebrovasospasms are due to an increase in the cytoplasmic concentration of free Ca^{2+} ions. A number of studies have demonstrated that Mg^{2+} ions can modulate the flux and actions of Ca^{2+} ions across cell membranes of smooth muscle and exert vasodilator actions on arterioles in vivo and

in vitro [22, 62]. One of the most likely mechanisms of alcohol-induced brain damage is due to depletion of Mg^{2+} ions from vascular smooth muscle cell membranes, causing the formation of reactive oxygen species and a consequent elevation of intracellular Ca^{2+} ions which, in turn, activate certain protein kinase C isozymes and promote induction of nuclear transcription factor- κ B (NF- κ B) [68]. Ethanol-induced Mg deficiency may also lead to an electrolytic imbalance contributing to cardiovascular damage, coronary atherosclerosis, heart failure, renal and hepatic damage, increased risk of aneurysms and internal hemorrhages [19, 23, 66].

Effects of Mg Supplementation on Ethanol Toxicity

Numerous experimental [4, 28, 67, 70] and some clinical [19, 35, 42] studies suggest that dietary Mg supplementation may be useful in the treatment and prevention of ethanol-induced damage to various tissues and systems. Findings of in vitro studies suggest that Mg supply may prevent ethanol hepatotoxicity [29]. It was found that administration of Mg even in a low dose to rat's hepatocytes incubated with ethanol may decrease malondialdehyde (MDA) concentration compared to hepatocytes incubated with ethanol alone. Protective action of Mg^{2+} ions against ethanol-induced lipid peroxidation could be a consequence of increased ALDH activity, which accelerates oxidation of acetaldehyde. Because increased dietary Mg intake may accelerate oxidation of acetaldehyde, Mg replacement therapy is recommended to prevent and treat toxic effects of ethanol ingestion [5, 35]. Mg supplementation may among others be useful in the treatment as well as prevention of ethanol-induced brain vascular damage and cardiovascular disease, especially in the case when Mg deficiency occurs [28, 47]. Experimental data have shown that even the nonvasodilator doses of magnesium sulfate (1 and 4 μ mol/min) exerted dose-dependent ameliorative actions against the vasculotoxic actions of ethanol (severe vasospasm, ischemia) [67, 69]. Brown et al. [67] have demonstrated that Mg supplementation (0.65 g Mg/dm^3 of drinking water) in ethanol-consuming animals also abolished alcohol-induced hypertension and vascular dysfunction. Compensation of Mg deficiency by its administration in the diet led to a fall in the rate of ventricular arrhythmias [47]. Wold et al. [43] have noted that dietary Mg supplementation (0.52 g Mg/dm^3 of liquid diet) in female rats consuming ethanol contributing 36% of daily caloric intake, may be beneficial to certain cardiac contractile dysfunctions. Mg supply may also prevent ethanol-induced hypertension [44]. These effects can be explained by the fact that Mg plays an important role in the control of vascular smooth muscle function by modulating myogenic tone and the contractile response to the vasodilators (histamine and acetylcholine) and to the vasoconstrictors (5-hydroxytryptamine, angiotensin and noradrenaline) [4, 19]. Birch and Walker [70] have shown that Mg^{2+} ions protect yeast cells by preventing increases in cell membrane permeability elicited by ethanol-induced oxidative stress. The increase in

Mg²⁺ extra- or intracellular concentrations, may afford protection to alcohol-stressed cells by maintaining the structural integrity of membrane and supplying cells with an excess of this ion for repair mechanism and cellular function (enzyme activation). Supplementation with this macroelement may prevent the development of Wernicke–Korsakoff syndrome, closely related to Mg deficiency in alcoholics as well as chronic ethanol ingestion-induced sclerotic artery and gastrointestinal bleeds observed in experimental studies [19, 22, 35]. Gullestad et al. [42] have revealed that a 6-week oral Mg supplementation may improve liver cell function (decreased activity of aspartate and alanine aminotransferase, gamma-glutamyl-transpeptidase, decreased concentration of bilirubin), electrolyte status (increased serum concentration of Ca and Mg) and muscle strength in chronic alcoholics. Aagaard et al. [45] have also shown that the administration of Mg in a daily dose of 12.5 mmol to patients with alcoholic liver disease increased muscle strength and mass. Mg supplementation in chronic alcoholics suffering from withdrawal syndrome also prevented respiratory, muscular and gastrointestinal symptoms due to ethanol-induced hypomagnesaemia [46]. Nowadays it is strongly highlighted that disturbances in Mg homeostasis are involved in the development of ethanol-induced metabolic and neurological disorders, including alcohol addiction [35]. Experimental studies have also shown that Mg deficiency increased animal attraction to alcohol, whereas increased dietary Mg supplementation decreased alcohol demand [6].

Conclusions

Numerous clinical and epidemiological data show that subjects consuming alcohol may be Mg deficient. On the other hand, Mg deficiency makes the human organism more susceptible to the action of ethanol, because it influences ethanol metabolism and may intensify some effects of its toxic action in the organism. Mg deficiency may also result from inappropriate nutrition, low hardness of drinking water as well as from the influence of chemical contaminants of the natural environment (heavy metals, fertilizers). The protective role of dietary Mg intake during chronic ethanol consumption and the potentiation of accumulation and toxicity of its toxic metabolites during Mg deficiency show that it is possible to influence ethanol metabolism and action in the organism by Mg supplementation. Further studies should focus on better understanding ethanol-Mg interactions, which might be used to prevent various body dysfunctions caused by ethanol-induced disturbances in Mg body status in alcohol abusers.

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