Possible prospects for using modern magnesium preparations for increasing stress resistance during COVID-19 pandemic

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Abstract

Introduction: The relevance of the issue of increasing stress resistance is due to a significant deterioration in the mental health of the population caused by the special conditions of the disease control and prevention during the COVID-19 pandemic. Recently, the decisive role in the severity of clinico-physiological manifestations of maladjustment to stress is assigned to magnesium ions.

The aim of the work was to study the magnesium importance in the body coping mechanisms under stress for the pathogenetic substantiation of the magnesium correction in an unfavorable situation of disease control and prevention during the COVID-19 pandemic.

Materials and methods: The theoretical basis of this scientific and analytical review was an analysis of modern Russian and foreign literature data posted on the electronic portals MEDLINE, PubMed-NCBI, Scientific Electronic Library eLIBRARY.RU, Google Academy, and CyberLeninka.

Results and discussion: It was shown that the total magnesium level in the body plays the indicator role of the body functional reserves. Acute and chronic stresses significantly increase the magnesium consumption and cause a decrease in its body content. Magnesium deficiency is one of the main pathogenetic mechanisms of reducing stress resistance and adaptive body reserves. Arising during the COVID-19 pandemic, increased nervous and emotional tension, the lack of emotional comfort and balance can lead to the onset or deterioration of magnesium deficiency, which manifests itself in mental burnout and depletion of adaptive capacities. The inability to synthesize magnesium in the body necessitates including foodstuffs high in magnesium in the population diet during this period. The appointment of magnesium preparations is pathogenetically justified with moderate and severe magnesium deficiency. This therapy should take into account the major concomitant diseases, severity of magnesium deficiency, and a patient’s age.

Conclusion: magnesium correction, carried out during the COVID-19 pandemic, will contribute to increasing stress resistance, preventing mental diseases and improving the population’s life quality.

Keywords

adaptive body reserves, COVID-19 pandemic, literature review, magnesium deficiency, magnesium preparations, disease control and prevention, stress resistance.
Introduction

The relevance of the issue of increasing stress resistance is due to a significant deterioration in the mental health of the population caused by the special conditions of the disease control and prevention during the COVID-19 pandemic (Baloch et al. 2020; Mosolov 2020). The constant flow of negative information, fear of contracting coronavirus infection, an obligatory self-isolation regime and following the necessary sanitary and hygienic requirements lead to increased anxiety and fear in society, which is confirmed by research data from China (Xiang et al. 2020), Japan (Shigemura et al. 2020), Italy (Mazza et al. 2020), and the USA (Schwartz et al. 2020). The exacerbated family problems, worries about the financial position, increased depressive disorders, and alcohol abuse cases occur during the mandatory quarantine (Mosolov 2020; Wang et al. 2020). The complex of identified psychological disorders associated with the impact of the novel coronavirus pandemic was identified as COVID-19 stress syndrome (Taylor et al. 2020). In this connection, the World Health Organization has developed special recommendations for preventing stress and mental disorders in an unfavorable situation of disease control and prevention during the COVID-19 pandemic (World Health Organization 2020).

Limitation of social communication and activity is most difficult for children and the elderly (Jeste et al. 2020; Yang et al. 2020). Acute and chronic stress can not only negatively affect all concomitant diseases in people with low adaptive potential, but can also cause a new chronic psychosomatic pathology (Nagaraja et al. 2016). Recently, a decisive role in stress resistance has been assigned to certain micronutrients, and, first of all, to magnesium ions. Understanding the main pathogenetic mechanisms of the state anxiety and its consequences in the conditions of magnesium deficiency will make it possible to develop therapeutic and prophylactic measures, in which prescribing magnesium preparations will be significant. So the study was aimed to examine the magnesium importance in the body adaptation mechanisms under stress for the pathogenetic substantiation of the magnesium correction in an unfavorable situation of disease control and prevention during the COVID-19 pandemic.

Materials and methods

The theoretical basis of this scientific and analytical review was an analysis of modern Russian and foreign literature data posted on the electronic portals MEDLINE, PubMed-NCBI, Scientific Electronic Library eLIBRARY. RU, Google Academy, and CyberLeninka. Content analysis, structural-logical and systemic methods were used.

Results and discussion

The physiological response to a stressful situation is an allosteric adaptive process that modulates the hypothala-
that transport divalent cations (Abumaria et al. 2019; Lo-
melino-Pinheiro et al. 2020). Such protein carriers as So-
lute Carrier (SLC) are also involved in the ionic transport of
magnesium (Tsoa et al. 2017; Rodriguez-Ramirez et al.
2017). Claudins (CLDN), transmembrane proteins, which are
expressed at tight junctions of renal epithelial cells, play a
significant role in the reabsorption of this element. Mutations in
these genes cause renal hypomagnesemia in combination with
myopia and lens subluxation (Al-
parslan et al. 2018; Perdomo-Ramirez et al. 2019). The
sensitive receptor of the CaSR gene (Calcium-Sensing
Receptor), which is located in the renal tubules and in the
parathyroid gland, also participates in regulating the
magnesium-calcium metabolism. An increased activity of
the CaSR gene reduces phosphorylation of Claudins,
complicates their translocation into lysosomes, resulting in
reduced magnesium reabsorption in the renal tubules
(Agus 2016; Viering et al. 2017).

Secondary magnesium deficiency is primarily due to
an unbalanced diet (Gromova 2014; Kim et al. 2019).
Deterioration in the content and quality of modern regularly
consumed food has a negative effect on the body, reducing
its stress resistance (Akarachkova et al. 2018; Kirkland et
al. 2018; Wallace 2020). The diet currently contains, as a
rule, an insufficient amount of food high in magnesium
(Nielsen 2018; Kim et al. 2019). At the same time, excess
sugar and salt, artificial colors and preservatives used in
popular fast food promote the rapid magnesium elimina-
tion from the body. That is not to deny the negative effect
of heating food processing (Razzaque 2018; Workinger
et al. 2018; Nielsen 2019). Modern methods of softening
and purifying water significantly reduce the magnesium
content in drinking water (Huang et al. 2019; Noy et al.
2020). An unfavourable ecological situation with plenty
of toxins and heavy metals in water, soil, air and food re-
results in these substances displacing magnesium from the
body (Karkashadze et al. 2014; Lopresti 2020).

The physiological conditions that require increased
magnesium consumption include the period of growth, high
physical activity and intensive labour, pregnancy and
lactation in women, old age and the convalescence period
(Walsh et al. 2015; Razzaque 2018; Yildirim and Apaydln
2020). magnesium deficiency occurs against concomitant
diseases of the gastrointestinal tract, kidneys, cardiovas-
cular and endocrine systems (Walsh et al. 2015; Wolf
2017; Reddy et al. 2018). Magnesium imbalance in the
body can be also caused by long-term use of primarily
such drugs, as diuretics, cardiac glycosides, aminoglyco-
sides, and proton pump inhibitors (Spasov and Kosolapov
2017; Gröber 2019).

Magnesium is critically important for the normal func-
tioning of the cardiovascular and nervous systems, which
are primarily responsible for the body’s adaptive capaci-
ties (Akarachkova et al. 2018, 2019; Allen and Sharma
2020). The main property of magnesium is the regulation
of the excitation processes of the brain neuronal systems.
Numerous experiments have revealed that magnesium
acts as an excitatory modulator of such aminoacids as as-
partic, glutamic and glycine, the transmitter function of
which is associated with the analyzer function. Magnes-
ium ions are required to stabilize all subtypes of selec-
tive NMDA receptors (receptors that interact with N-meth-
yl-D-aspartate), which are excited during psychogenic
stresses (Hou et al. 2020). In the conditions of magnesium
deficiency, there is overexcitation of these receptors, an
increased transcription of corticotropin-releasing factor
in the hypothalamus, and an increased level of adreno-
corticotropic hormone in blood serum, which leads to the
development of pathological anxiety under stress (Aka-
rahkova et al. 2018; Botturi et al. 2020).

According to the results of studies by other authors, the
ratio of magnesium and calcium ions is of primary im-
portance for controlling the formation and release of all
known neuropeptides and neurotransmitters (Rosanoff et
al. 2012; Botturi et al. 2020). First of all, magnesium limits
the production of catecholamines, the excess of which in
conditions of magnesium deficiency potentiates expressed
vasoconstriction and leads to blood pressure increase. By
participating in the regulation of energy and plastic pro-
cesses in neurons and glia, including glucose utilization,
glycoprotein synthesis, hydrolysis of adenosine triphos-
horic acid, magnesium affects the cells’ membrane poten-
tial and the excitation spread. The magnesium antiasth-
metic properties are associated with its ability to reduce the
lactate concentration and cells oxygen consumption and
to increase glucose utilization (Karkashadze et al. 2014).

Magnesium ions normalize sleep by increasing the
activity of serotonin-N-acetyltransferase involved in the
melatonin synthesis (Gromova et al. 2016b; Cao et al.
2018; Lopresti 2020). It is worthwhile noting that one of
the essential magnesium neuroprotective properties is its
antalgic effect, associated with a decrease in the level of
dangerous peroxynitrite, which triggers a pain reaction
cascade (Dhillon et al. 2011; Andretta et al. 2019; Park et
al. 2020; Shin et al. 2020). Experimental studies showed that
magnesium cations help stabilize neurofilament sub-
bunits in neurons and clear the body of neurotoxic metals
(Karkashadze et al. 2014). Of great interest is the fact that
the magnesium deficiency in neurons is considered to be
the earliest sign of nerve cell apoptosis (Kwashinha 2016).

It has been established that the brain blood vessels are
largely sensitive to the magnesium balance (Akarachkova
2019; Marques et al. 2020). The vasodilating activity of
magnesium is associated with the cyclic adenosine mon-
oposphate synthesis, the accumulation of which inhibits
the effect of the renin-angiotensin system and sympathetic
innervation and is accompanied by vasodilation (Chrysan
t and Chrysant 2020). With a decrease in the concentra-
tion of this cation in the blood serum, the arterial tone in-
creases, and there appear the conditions for ischemic damage
of nerve cells (Kwashinha 2016; Samavarchi Tehrani et al.
2020). Magnesium is also actively involved in the con-
tral of the regular cardiac cycle. So, catalyzing hydrolysis
of adenosine triphosphoric acid, it supplies energy to the
heart systole; and facilitating the calcium release from the
protein troponin, it provides the onset and duration of di-
stole in the heart muscle (Aligieri et al. 2019). Among
the magnesium metabolic actions, its role in maintaining
a normal status of the lipid profile of blood and in maintaining tissue sensitivity to insulin should be especially emphasized, as it is of great importance in preventing the atherosclerotic vascular lesions and the diabetes development (Spiga et al. 2019; Feng et al. 2020; Ponzotto and Figura 2020; Rooney et al. 2020).

Acute and chronic stressful situations significantly raise the magnesium consumption and cause a significant decrease in its body content (Lopresti 2020). An increase in steroids and catecholamines during all kinds of stress causes the active magnesium binding and an increase in its urine excretion, which is accompanied by the magnesium pool depletion with time (Wienecke and Nolden 2016; Nayyar et al. 2017). A "vicious circle" of chronic magnesium deficiency is formed with insufficient magnesium assimilation in the body, which determines low stress resistance and leads to destabilization of the systems responsible for adaptation (Vyatkina et al. 2014; Wallace 2020).

Firstly, there happens sensitization of hypothalamic-pituitary-adrenal activity, which determines constantly increased anxiety and depressive disorders (Karkashadze et al. 2014; Serefko et al. 2016; Botturi et al. 2020). The stress influence during the COVID-19 pandemic can be already realized in the conditions of hyperergy due to an unfavourable environmental situation, improper diet, chronic stress situations, the effect of concomitant diseases and taking medications, which is reflected in deterioration of the clinical manifestations of impaired vegetative and hormonal homeostasis, as well as in a significant decrease in the patient’s life quality (Akarachkova et al. 2018; Wallace 2020).

The conducted analytical review makes it possible to identify pathogenetic mechanisms of the magnesium action on adaptation mechanisms and stress resistance (Botturi et al. 2020). Increased nervous and emotional tensions, arising during the COVID-19 pandemic, lack of peace of mind and serenity can lead to the onset or deterioration of magnesium deficiency, which manifests itself in mental burnout and depleted adaptive capacities (Akarachkova et al. 2016, 2019; Fessell and Cherniss 2020). The main symptoms of this condition include constant tiredness, rapid fatigue, blood pressure fluctuations, headaches, cardiovascular and digestive systems diseases, neurological problems and insomnia (Pfefferbaum and North 2020; World Health Organization 2020).

The inability to synthesize this element in the body necessitates its constant intake into the body in sufficient quantities (Gröber et al. 2015). This indicates the feasibility of including foodstuffs high in magnesium in the population diet in an unfavorable situation of the disease control and prevention during the COVID-19 pandemic. So, one should eat more dried fruits, nuts, cereals, groats, green fruits and vegetables, in combination with products rich in vitamin B6, which promotes the magnesium absorption. The inclusion of mineral water providing inorganic magnesium salts is also of great importance. The moderate and severe magnesium deficiencies make it necessary to additionally prescribe magnesium-containing drugs, which are very important for increasing stress resistance and correcting adaptive capacities during the COVID-19 pandemic, being, in fact, a pathogenetic method of therapy. The average values of the daily magnesium requirement, dependent on the age, sex and physiological state of the organism, are presented in Table 1.

Table 1. Recommended Average Values of Daily Magnesium Intake (According to The Federal Research Center of Nutrition and Biotechnology)

| Age, yrs | Male | Female | Pregnancy | Lactation |
|----------|------|--------|-----------|-----------|
| 1-3      | 90 mg/day | 140 mg/day | 420 mg/day | 430 mg/day |
| 4-8      | 140 mg/day | 250 mg/day | 420 mg/day | 410 mg/day |
| 9-13     | 360 mg/day | 320 mg/day | 420 mg/day | 420 mg/day |
| 14-18    | 420 mg/day | 320 mg/day | 420 mg/day | 420 mg/day |
| 19-30    | 320 mg/day | 320 mg/day | 420 mg/day | 420 mg/day |
| over 30  | 330 mg/day | 330 mg/day | 430 mg/day | 420 mg/day |

Currently, several generations of magnesium-containing preparations depending on their pharmacological properties are distinguished (Trisvetova 2012). It was proved that the first-generation drugs, represented by inorganic magnesium compounds, have little effect on the balance of this element in the body (Ates et al. 2019; Uysal et al. 2019). Magnesium oxide, diox ide, carbonate and phosphate exhibit primarily antacids properties, and are not used in correcting magnesium deficiency. Magnesium sulfate taken orally is poorly absorbed, but causes an osmotic pressure increase in the gastrointestinal tract, vascular leakage in the intestinal lumen and increased peristalsis. In addition, it has many side effects, such as a metallic taste in the mouth, nausea and vomiting, which limits this way of its introduction. This drug is used mainly parenterally due to its anticonvulsant, vasodilator, sedative and hypotensive effects (Avg erinos et al. 2019; Soliman et al. 2019).

Second-generation drugs, represented by organic magnesium salts, are well absorbed in the gastrointestinal tract and rarely cause side effects (Gröber et al. 2015; Ates et al. 2019; Gromova et al. 2019). This group of magnesium-containing compounds is represented by such salts as magnesium malate, magnesium gluconate, magnesium orotate, magnesium citrate, magnesium pidolate, and magnesium lactate (Table 2). The content of magnesium included in these preparations is very different. Thus, for example, the amount of this element in magnesium citrate is 24.3 mg, in magnesium gluconate – 27.0 mg, in magnesium orotate – 32.8 mg, in magnesium lactate – 48.0 mg, in magnesium pidolate – 100.0 mg (Studenikin et al. 2012; Trisvetova 2012; Spasov and Kosolapov 2017; Akarachkova 2019).

An obligatory component of the third-generation drugs is magnesiofixers or magnesium protectors, which significantly improve the magnesium bioavailability from organic compounds, provide its permeation into cells and increase its effectiveness. So, calcium, potassium, riboxin, carnitine, vitamin C, vitamin A and vitamin E have a positive effect on the magnesium assimilation; vitamin D (calcitrol) increases its adsorption, and vitamins B1 and B2 improve its metabolism. Vitamin B6, forming a bio-
Table 2. Magnesium Preparations Depending on the form of included magnesium and the type of magnesium-protector

| Magnesium form                  | Preparation                                                                 |
|---------------------------------|-----------------------------------------------------------------------------|
| Magnesium citrate               | KAL, Magnesium Citrate (USA)                                               |
| Magnesium citrate + B2          | Magnesium B2 (Slovenia)                                                    |
| Magnesium citrate + B6          | Magnesium B6 forte (Russia)                                                |
| Magnesium bisglycinate           | Magnesium B6 Renewal (Russia)                                              |
| Magnesium lactate                | Magnesium Lysinate + Magnesium B6                                          |
| Magnesium glycinate             | Magnesium L-glutamate + Magnesium B6                                       |
| Magnesium oxalate               | Magnesium Oxalate + Magnesium B6                                          |
| Magnesium aspartate             | Magnesium Aspartate + Magnesium B6                                         |
| Magnesium taurate               | Magnesium Taurate + Magnesium B6                                          |
| Magnesium threonate             | Magnesium Threonate + Magnesium B6                                         |
| Magnesium carbonate             | Magnesium Carbonate + Magnesium B6                                         |
| Magnesium citrate + B6 + E      | Magnesium B6 + Magnesium E (Finland)                                       |
| Magnesium gluconate             | Magnesium Gluconate + Magnesium B6                                        |
| Magnesium lactate               | Magnesium Lactate + Magnesium B6                                           |
| Magnesium asparaginate          | Magnesium Asparaginate + Magnesium B6                                      |
| Magnesium taurate               | Magnesium Taurate + Magnesium B6                                           |
| Magnesium threonate             | Magnesium Threonate + Magnesium B6                                         |
| Magnesium carbonate + B6        | Magnesium Carbonate + Magnesium B6                                         |
| Magnesium lactate + B9, B12     | Magnesium Lactate + Magnesium B9, B12                                       |
| Magnesium asparaginate          | Magnesium Asparaginate + Magnesium B6                                      |
| Magnesium taurate               | Magnesium Taurate + Magnesium B6                                           |
| Magnesium threonate             | Magnesium Threonate + Magnesium B6                                         |
| Magnesium carbonate + B6, B9, B12| Magnesium Carbonate + Magnesium B6, Magnesium B9, Magnesium B12            |
| Magnesium lactate + B6 + B9     | Magnesium Lactate + Magnesium B6, Magnesium B9                             |
| Magnesium asparaginate          | Magnesium Asparaginate + Magnesium B6                                      |
| Magnesium taurate               | Magnesium Taurate + Magnesium B6                                           |
| Magnesium threonate             | Magnesium Threonate + Magnesium B6                                         |
| Magnesium carbonate + B6, B9, B12| Magnesium Carbonate + Magnesium B6, Magnesium B9, Magnesium B12            |
| Magnesium lactate + B6 + B9     | Magnesium Lactate + Magnesium B6, Magnesium B9                             |
| Magnesium asparaginate          | Magnesium Asparaginate + Magnesium B6                                      |
| Magnesium taurate               | Magnesium Taurate + Magnesium B6                                           |
| Magnesium threonate             | Magnesium Threonate + Magnesium B6                                         |
| Magnesium carbonate + B6, B9, B12| Magnesium Carbonate + Magnesium B6, Magnesium B9, Magnesium B12            |
| Magnesium lactate + B6 + B9     | Magnesium Lactate + Magnesium B6, Magnesium B9                             |
| Magnesium asparaginate          | Magnesium Asparaginate + Magnesium B6                                      |
| Magnesium taurate               | Magnesium Taurate + Magnesium B6                                           |
| Magnesium threonate             | Magnesium Threonate + Magnesium B6                                         |

According to some research data, magnesium preparations, in the descending order of their value to make up for systemic alimentary magnesium deficiency in erythro-
cytes, are arranged as follows: magnesium asparagine + B6 > magnesium lactate + B6 = magnesium aspartate > magnesium taurate > magnesium asparagine > magnesium aspartate + potassium aspartate > magnesium pyroglutamate (pidolate) > magnesium glycinate > magnesium citrate > magnesium orotate > magnesium lactate (Spasov and Kosolapov 2017; Ahmed and Mohammed 2019; Ates et al. 2019; Eremenko et al. 2019).

When choosing the optimal magnesium-containing preparation, a number of important criteria should be taken into account, the most important of which are the major comorbidities, the magnesium deficiency severity, and the patients’ age. Magnesium citrate is a highly soluble and assimilable magnesium form, which is a unique compound by its effectiveness, as the citric acid anion takes part in the main biochemical process of all cells – the Krebs metabolic cycle (Ates et al. 2019; Eremenko et al. 2019). Citric acid promotes fat splitting, speeds up metabolism, and eliminates hunger (Schutten et al. 2019). In this connection, that organic magnesium salt can be recommended for use in cases of combined magnesium deficiency and obesity. In addition, optimal concentrations of citrate anions reduce the risk of any type of kidney stone formation, and therefore this drug is highly effective in the prevention and treatment of urolithiasis (Grases et al. 2015). World experience in the use of a synergistic combination of magnesium citrate with pyridoxine indicates their effectiveness in normalizing bone density, treating vascular diseases, restless legs syndrome, bronchial asthma, and preventing convulsions and spontaneous miscarriages in pregnant women (Gromova 2014; Gromova and Limanova 2014). The safety of this magnesium compound makes it possible to prescribe it both for adults and children (Trisvetova 2012; Karkashadze et al. 2014; Kvashmina 2016; Gromova et al. 2019).

Magnesium malate is a magnesium salt of malic acid, which, besides transporting magnesium ions into cells, plays a significant role in cellular respiration and providing cells with energy; therefore, it can be recommended for patients with easy fatigability (Younes et al. 2018; Ferreira et al. 2019).

Oral intake of magnesium pidolate (pyroglutamate) significantly increases the magnesium level in the blood serum within the first 2 hours ($T_{max}$=15–30 minutes), which is especially important for the rapid correction of magnesium deficiency. Such a quick therapeutic effect is necessary to stop tics, seizures and tension headaches. The predominant accumulation of L-pyroglutamic acid in the brain and skin tissues determines the main areas of its application. It was shown that pyroglutamate, maintaining a special neuropeptide conformation, takes part in the vascular tone normalization and neuroprotection mechanisms, and exhibits nootropic and antidepressant properties. In the skin, pidolate anion substantially accelerates wound healing processes, whilst significantly improving the scar quality. The possibility of using this magnesium compound in children over one year old, its convenient form as a solution and a caramel flavor determine its application in combination with vitamin B6 in young children as a drug of choice for magnesium deficiency. As magnesium pidolate is the only sugar-free form of organic magnesium, it can be recommended for diabetic and obese patients (Gromova et al. 2016a).

The combination of magnesium with gluconic acid to form magnesium gluconate provides good absorption of this element. The metabolic effect of this organic salt is characterized by a growing activity of cell enzymes, an increased concentration of adenosine triphosphoric acid and body’s working capacity. Its combination with potassium gluconate exhibits antiarrhythmic properties and potentiates the effect of antiarrhythmic drugs (Shkolnik et al. 2014; Trivedi et al. 2017).

The organic salt of magnesium orotate is widely used in cardiac practice for the prevention and treatment of magnesium deficiency. It was established that orotate anions promote the accumulation of magnesium ions in cells due to the formation of its combination with adenosine triphosphoric acid (Trisvetova 2012; Gromova et al. 2016a). Orotic acid (vitamin B13) has an expressed metabolic effect, manifested in the stimulated synthesis of nucleic acid, enhancement of regenerative processes in tissues, metabolism activation and an increased albumin formation in the liver. The cardioprotective properties of this compound are expressed in the increased cardiac muscle resistance to ischemia and in its enhanced regeneration after infarction (Trisvetova 2012, 2018; Loginova et al. 2018). The use of magnesium orotate in cardiovascular diseases makes it possible not only to correct magnesium deficiency, but also to normalize blood pressure, increase myocardial contractile function and reduce the heart failure risk (Trisvetova 2012; Shekhyan et al. 2017; Gilyarevskij et al. 2019).

Recently, magnesium taurate has become increasingly important in the therapy of cardiovascular pathology with underlying magnesium deficiency and reduced stress resistance. The inclusion of this compound in the complex chronic heart failure treatment improves myocardial contractility and hemodynamics, contributing to the blood pressure normalization (Teplova et al. 2017; Waldron et al. 2018, 2019). The magnesium taurate intake is of great importance in stabilizing the heart rate and decreasing the thrombus formation risk (Ra et al. 2019). It was established that high levels of magnesium and taurine in urine correlate with a significantly lower risk of cardiac complications (Basalaj et al. 2017). Long-term use of this drug in the treatment of type II diabetes improves the parameters of carbohydrate and lipid metabolisms (Ametov and Soluyanova 2011; El Idrissi et al. 2017; Ribeiro et al. 2018). High tolerability of magnesium taurate and no side effects are also important (Basalaj et al. 2017).

Magnesium lactate therapy in combination with vitamin B6 is advisable with spastic contractions of the uterus, the gastrointestinal tract and limb muscles caused by magnesium deficiency, and is applied in obstetrics and gynecology, gastroenterology and neurology (Gröber et al. 2015; Gromova et al. 2016a; Globa 2019). The inclusion of this magnesium compound in the therapy of patients with osteoarthritis made it possible to slow down the bone
tissue remodeling and reduce the joint syndrome symptoms (Kolomiietys and Mailian 2016).

Magnesium and potassium aspartate preparations not only compensate for the lack of these electrolytes, but also have an antarrhythmic effect, which combines the calcium channel blockers action and the properties of membrane stabilizing drugs. Asparaginate ion, being included in the tricarboxylic acid cycle, normalizes their ratio and the synthesis of adenosine triphosphoric acid, promoting the magnesium and potassium entry into cells. Magnesium, preserving potassium inside cells, regulates the QT interval length variability, a decrease in which is a prognostically unfavorable factor for developing fatal arrhythmias. In addition, magnesium reduces sympathetic effects on the heart, thereby eliminating the damaging effect of catecholamines on the myocardium (Gröber et al. 2015; Trisvetova 2018). As a result, magnesium aspartate has an adaptogenic effect, increasing the body’s resistance and endurance to various stressful influences (Baryshnikova et al. 2019).

Magnesium glycinate is a compound of magnesium with glycine, which, being an inhibitory mediator, significantly enhances the magnesium effects, contributing to muscle relaxation and sleep normalization (Gromova and Limanova 2014; Gröber et al. 2015; Ates et al. 2019). Due to hyperpolarization, glycine protects the nervous tissue from possible damage under conditions of intoxication, hypoxia, and reperfusion. This magnesium preparation is mainly prescribed for cerebral circulation disorders, headaches, anxiety-depressive states, seizures, and sleep disorders (Shchekina and Usanova 2019).

Magnesium threonate is unique in its ability to cross the blood-brain barrier and accumulate in brain tissues. The special feature of this compound is an increase in the intracellular magnesium content predominantly in neurons, which makes it especially effective in the treatment of neuropsychic disorders and reduced stress resistance (Kim et al. 2020; Surman et al. 2020). By activating the neurotrophic factor of the brain, mitochondrial functions and neuroplasticity, this drug has an expressed neuroprotective effect and significantly improves the cognitive functions (Liu et al. 2016; Vink 2016).

The combination of several magnesium organic salts and aminoacid complexes with magnesium protectors significantly increases the bioavailability of this element and a spectrum of its positive clinical effects (Spasov and Kosolapov 2017; Ates et al. 2019). A treatment with magnesium-containing preparations has to be provided for at least three months until magnesium homeostasis is normalized and the clinical symptoms of impaired adaptation to stress are reduced (Trisvetova 2018). It should be taken into account that the magnesium absorption is impaired with food containing proteins and saturated fats, dietary fiber, alcohol, manganese, caffeine, vitamin B1, calcium and phosphorus excess (Kim et al. 2019; Kuleshova and Karpova 2019). Increasing stress resistance in an unfavorable situation of disease and control prevention during the COVID-19 pandemic is the key to preservation of the population mental health (Mosolov 2020).

Conclusions

The bioinformatic analysis carried out as part of this literature review showed that the total magnesium level in the body plays a role of the indicator of the body’s functional reserves. Acute and chronic stressful situations significantly increase the magnesium consumption and cause a decrease in its body content. Magnesium deficiency is one of the main pathogenetic mechanisms of reducing stress resistance and body’s adaptive reserves. Increased nervous and emotional tension, lack of emotional comfort and balance due to the COVID-19 pandemic can lead to the onset or deterioration of magnesium deficiency, which manifests itself in mental burnout and depletion of adaptive capacities. The inability to synthesize magnesium in the body necessitates including foodstuffs high in magnesium in the population diet during this period. The appointment of magnesium preparations is pathogenetically justified with moderate and severe magnesium deficiency. This therapy should take into account the major concomitant diseases, severity of magnesium deficiency and a patient’s age. Magnesium correction, carried out during the COVID-19 pandemic, will contribute to increasing stress resistance, preventing mental diseases and improving the population’s life quality.

Conflict of interests

The authors declare no conflict of interests.

References

- Abumaria N, Li W, Clarkson AN (2019) Role of the chanzyme TRPM7 in the nervous system in health and disease. Cellular and Molecular Life Sciences 76(17): 3301–3310. https://doi.org/10.1007/s00018-019-03124-2 [PubMed]
- Agus ZS (2016) Mechanisms and causes of hypomagnesemia. Current Opinion in Nephrology and Hypertension 25(4): 301–307. https://doi.org/10.1097/MNH.0000000000000238 [PubMed]
- Ahmed F, Mohammed A (2019) Magnesium: the forgotten electrolyte – a review on hypomagnesemia. Medical Sciences 7(4): e56. https://doi.org/10.3390/medsci7040056 [PubMed] [PMC]
- Akarachkova ES (2019) Magnesium in the treatment and prevention of cerebrovascular diseases. Human and Medicine. Kazakhstan [Chełovek i Lekarstwo. Kazachstan] 112(1): 21–26. [in Russian]
- Akarachkova ES, Blinov DV, Kotova OV, Kadyrova LR, Lebedeva DI, Mel’nikova IM, Sorokina AS, Travnikova EV, Careva EV (2018) Stress in children: how to activate adaptive reserves in a child. Russian Medical Journal [Rossiiskii Meditsinskii Zhurnal] 26(9): 45–51. [in Russian]
- Akarachkova ES, Shavlovskaya OA, Vershinina SV, Kotova OV, Ryabokon’ IV (2016) The magnesium deficiency role in the formation...
of stress clinical manifestations in women. Human and Medicine. Kazakhstan [Chelovek i Lekarstvo. Kazakhstan] 70(9): 48–54.

Algeri C, Trombetti F, Pagliarani A, Ventrella V, Bernardini C, Fabbrini M, Forni M, Nesci S (2019) Mitochondrial Ca2+ -activated F1 FO -ATPase hydrorizes ATP and promotes the permeability transition pore. Annals of the New York Academy of Sciences 1457(1): 142–157. https://doi.org/10.1111/nyas.14218 [PubMed]

Allen MJ, Sharma S (2020) Magnesium. StatPearls. Treasure Island (FL): StatPearls Publishing, January 20. https://www.ncbi.nlm.nih.gov/books/NBK519036/[PubMed]

Alparslan C, Öncel EP, Akbay S, Mutlubas F, Taflı M, Konrad M, Yavaşçı O, Kasap-Demir B (2018) A novel homozygous W99G mutation in CLDN-16 gene causing familial hypomagnesemic hypercalciuric nephrocalcinosis in Turkish siblings. The Turkish Journal of Pediatrics 60(1): 76–80. https://doi.org/10.24953/turkped.2018.01.011 [PubMed]

Ametov AS, Soluyanova TN (2011) Taurine in the diabetes treatment. Medical Councilium [Meditsinski Sovet] 1–2: 54–58. [in Russian]

Andretta A, Dias Batista E, Madalozzo Schieferdecker ME, Rasmussen Petterle R, Boguszewski CL, Dos Santos Paiva E (2019) Relation between magnesium and calcium and parameters of pain, quality of life and depression in women with fibromyalgia. Advances in Rheumatology 59(1): e55. https://doi.org/10.1186/s42358-019-0099-5 [PubMed]

Ates M, Kizıldag S, Yuksel O, Hosgorler F, Yuce Z, Guvendi G, Kandis S, Karakılıçe A, Koc B, Uysal N (2019) Dose-dependent absorption profile of different magnesium compounds. Biological Trace Element Research 192(2): 244–251. https://doi.org/10.1007/s12011-019-01663-0 [PubMed]

Averinov KI, Chatsisiotiriou A, Haidich AB, Tsapons A, Lioutas F (2016) Magnesium. Advances in Osteoarthritis 2016: 1–20. https://doi.org/10.1155/2016/716303 [PubMed]

Botturi A, Ciappolino V, Delvecchio G, Boscutti A, Viscardi B, Delvecchio G, Boscutti A, Viscardi B, Botturi A, Ciappolino V, Delvecchio G, Boscutti A, Viscardi B (2019) Magnesium and drugs. International Journal of Clinical Practice 73(1): 10(1): e1354. https://doi.org/10.3390/nu10101354 [PubMed] [PMC]

Chrysant SG, Chrysant GS (2020) Adverse cardiovascular and blood pressure effects of drug-induced hypomagnesemia. Expert Opinion on Drug Safety 19(1): 59–67. https://doi.org/10.1080/14740338.2020.1700228 [PubMed]

Costello R, Wallace TC, Rosanoff A (2016) Magnesium. Advances in Nutrition 7(1): 199–201. https://doi.org/10.3945/an.115.008524 [PubMed] [PMC]

Dadak K (2013) Magnesium deficiency in obstetrics and gynecology. Obstetrics, Gynecology and Reproduction [Akusherstvo, Ginekologiya i Reproduktivsa] 7(2): 6–14. [in Russian]

Dhillon KS, Singh J, Lyall JS (2011) A new horizon into the pathobiology, etiology and treatment of migraine. Medical Hypotheses 77(1): 147–151. https://doi.org/10.1016/j.mehy.2011.03.050 [PubMed]

El Idrissi A, El Hilali F, Rotondo S, Sidime F (2017) Effects of taurine supplementation on neuronal excitability and glucose homeostasis. Advances in Experimental Medicine and Biology 975: 271–279. https://doi.org/10.1007/978-94-024-1079-2_24 [PubMed]

Eremenko NN, Shikh EV, Serebrova SY, Sizova ZM (2019) Comparative study of the bioavailability of magnesium salts. Drug Metabolism and Personalized Therapy 34(3): e2190004. https://doi.org/10.1015/dmp-2019-0004 [PubMed]

Feng J, Wang H, Jing Z, Wang Y, Cheng Y, Wang W, Sun W (2020) Role of magnesium in type 2 diabetes mellitus. Biological Trace Element Research 196(1): 74–85. https://doi.org/10.1007/s12011-019-01922-0 [PubMed]

Ferreira I, Origoza A, Moore P (2019) Magnesium and malic acid supplement for fibromyalgia. Medwave 19(4): e7633. [PubMed]

Fessell D, Cherniis C (2020) Coronavirus disease 2019 (COVID-19) and beyond: micropractices for burnout prevention and emotional wellness. Journal of the American College of Radiology 17(6): 746–748. https://doi.org/10.1007/jacr.2020.03.013 [PubMed] [PMC]

Gilyarevskij SR, Golshmid MV, Zaharova GY, Kazmina IM, Sincina II (2019) Hypomagnesemia and magnesium deficiency as risk factors for the development of complications of cardiovascular diseases. Cardiology and Cardiovascular Surgery [Kardiologiya i Serdechno-Sosudistaya Khirurgiya] 12(5): 459–466. https://doi.org/10.17111/kardio201912051459 [in Russian]

Globa YUS (2019) The role of magnesium deficiency in the development of premenstrual syndrome clinical manifestations. Journal of Obstetrics and Women’s Diseases [Zhurnal Akusherstva i Zhenshchik Boleznii] 68(S): 20–21. [in Russian]

Grases F, Rodríguez A, Costa-Bauza A (2015) Efficacy of mixtures of magnesium, citrate and phytate as calcium oxalate crystallization inhibitors in urine. The Journal of Urology 194(3): 812–819. https://doi.org/10.1016/j.juro.2015.03.099 [PubMed]

Gröber U, Schmidt M, Kisters K (2015) Magnesium in prevention and therapy. Nutrients 7(9): 8199–8226. https://doi.org/10.3390/nu7095388 [PubMed] [PMC]

Gröber U (2019) Magnesium and drugs. International Journal of Molecular Sciences 20(9): pii: E2094. https://doi.org/10.3390/ijms20092094 [PubMed] [PMC]

Gromova OA (2014) Magnesium deficiency as a modern nutritional issue in children and adolescents. Pediatric Pharmacology [Pediatricheskaya Farmakologiya] 11(1): 20–30. https://doi.org/10.15690/pf.v11i1.891 [in Russian]

Gromova OA, Limanova OA (2014) Magnesium deficiency and muscle cramps in pregnant women: treatment options (clinical and
Sankova MV et al.: Importance of magnesium preparations during COVID-19 period

- Nielsen FH (2019) The problematic use of dietary reference intake to assess magnesium status and clinical importance. Biological Trace Element Research 188(1): 52–59. https://doi.org/10.1007/s12011-018-1573-x [PubMed]

- Noy AF, Zilberman U, Regev N, Moskovitz M (2020) Drinking desalinated water that lack calcium and magnesium has no effect on mineral content of enamel and dentin in primary teeth. The Journal of Clinical Pediatric Dentistry 44(1): 47–51. https://doi.org/10.17796/tjcp.44.1.e14 [PubMed]

- Park R, Ho AM, Pickering G, Arendt-Nielsen L, Mihoud M, Gilron I (2020) Efficacy and safety of magnesium for the management of chronic pain in adults: a systematic review. Anesthesia and Analgesia 131(3): 764–775. https://doi.org/10.1213/ANE.0000000000004673 [PubMed]

- Perdomo-Ramírez A, de Armas-Ortiz M, Ramos-Trujillo E, Suárez-Artiles L, Claverie-Martin F (2019) Exonic CLDN16 mutations associated with familial hypomagnesemia with hypercalcemia and nephrocalcinosis can induce deleterious mRNA alterations. BMC Medical Genetics 20(1): 1–6. https://doi.org/10.1186/s12881-018-0713-7 [PubMed] [PMC]

- Pfefferbaum B, North CS (2020) Mental health and the Covid-19 pandemic. The New England Journal of Medicine 383(6): 510–512. https://doi.org/10.1056/NEJMp2008017 [PubMed]

- Ponsetto A, Figura N (2020) Serum magnesium and the prevalence of peripheral artery disease. Atherosclerosis. 292: e230. https://doi.org/10.1016/j.atherosclerosis.2019.10.020 [PubMed]

- Pouteau E, Kabir-Ahmadi M, Noah L, Mazur A, Dey L, Hellhammer J, Pickering, G, Durbay C (2018) Superiority of magnesium and vitamin B6 over magnesium alone on severe stress in healthy adults with low magnesemia: A randomized, single-blind clinical trial. PLoS ONE 13(12): e0208454. https://doi.org/10.1371/journal.pone.0208454 [PubMed]

- Ra SG, Choi Y, Akazawa N, Kawanaka K, Ohmori H, Maeda S (2019) Effects of taurine supplementation on vascular endothelial function at rest and after exercise resistance. Advances in Experimental Medicine and Biology 1155: 407–414. https://doi.org/10.1007/978-981-13-8023-5_38 [PubMed]

- Razzaque MS (2018) Magnesium: are we consuming enough? Nutrients 10(12): piiE1863. https://doi.org/10.3390/nu10121863 [PubMed]

- Reddy ST, Soman SS, Yee J (2018) Magnesium balance and measurement. Advances in Chronic Kidney Disease 25(3): 224–229. https://doi.org/10.1053/j.ackd.2018.03.002 [PubMed]

- Ribeiro RA, Bonfleur ML, Batista TM, Borck PC, Carneiro EM (2018) Regulation of glucose and lipid metabolism by the pancreatic and extra-pancreatic actions of taurine. Amino Acids 50(11): 1511–1524. https://doi.org/10.1007/s00726-018-2650-3 [PubMed]

- Rodríguez-Ramírez M, Rodríguez-Morán M, Reyes-Romero MA, Guerrero-Romero F (2017) Effect of oral magnesium supplementation on the transcription of TRPM6, TRPM7, and SLC41A1 in individuals newly diagnosed of pre-hypertension. A randomized, double-blind, placebo-controlled trial. Magnesium Research 30(3): 80–87. https://doi.org/10.1684/mrh.2017.0426 [PubMed]

- Rooney MR, Alonso A, Folsom AR, Michos ED, Rehbolz CM, Missalek JR, Chen LY, Dudley S, Lutsey PL (2020) Serum magnesium and the incidence of coronary artery disease over a median 27 years of follow-up in the Atherosclerosis Risk in Communities (ARIC) study and a meta-analysis. The American Journal of Clinical Nutrition 111(1): 52–60. https://doi.org/10.1093/ajcn/nqg256 [PubMed]

- Rosanoff A, Weaver CM, Rude RK (2012) Suboptimal magnesium status in the United States: are the health consequences underestimated? Nutrition Reviews 70(3): 153–164. https://doi.org/10.1111/j.1753-4887.2011.00465.x [PubMed]

- Samavarchi Tehrani S, Khataei SH, Saadat P, Sarfi M, Ahmadi Ahangar A, Daroie R, Firouzjahi A, Maniati M (2020) Association of serum magnesium levels with risk factors, severity and prognosis in ischemic and hemorrhagic stroke patients. Caspian Journal of Internal Medicine 11(1): 83–91. https://doi.org/10.22088/cjim.11.1.83 [PubMed] [PMC]

- Schutten JC, Joris PJ, Mensink RP, Danel RM, Goorman F, Hein Er-Fokkema MR, Weersma RK, Keyerza CR, de Borst MH, Bakker SJL (2019) Effects of magnesium citrate, magnesium oxide and magnesium sulfate supplementation on arterial stiffness in healthy overweight individuals: a study protocol for a randomized controlled trial. Trials 20(1): e295. https://doi.org/10.1186/s13063-019-3414-4 [PubMed] [PMC]

- Schwartz BJ (2020) New poll: covid-19 impacting mental well-being: americans feeling anxious. American Psychiatric Association. March 25. https://www.psychiatry.org/newsroom/news-releases/new-poll-covid-19-impacting-mental-well-being-americans-feeling-anxious-especially-for-loved-ones-older-adults-are-less-anxious [PubMed]

- Scult MA (2017) Flexible adaptation of brain networks during stress. The Journal of Neuroscience 37(15): 3992–3994. https://doi.org/10.1523/JNEUROSCI.0224-17.2017 [PubMed] [PMC]

- Sereffko A, Szopa A, Poleszak E (2016) Magnesium and depression. Magnesium Research 29(3): 112–119. [PubMed]

- Shehchekina SA, Usanova TA (2019) Rehabilitation measures in the acute period of ischemic stroke. Norwegian Journal of Development of the International Science 28: 26–28. [in Russian]

- Shekhtyan GG, Yalymov AA, Shchikota AM, Zadionchenko VS, Terp VG, Kabanova TG, Shiroyoka EB (2017) Clinical efficiency of magnesium orotate in the therapy of cardiovascular diseases. Russian Medical Journal [Rossiiskii Meditsinskii Zhurnal] 25(4): 273–278. [in Russian]

- Shigemura J, Ursano RJ, Morganstein JC, Kurosawa M, Benedek DM (2020) Public responses to the novel 2019 coronavirus (2019-nCoV) in Japan: Mental health consequences and target populations. Psychiatry and Clinical Neurosciences 74(4): 281–282. https://doi.org/10.1111/pcc.12988 [PubMed] [PMC]

- Shin HJ, Na HS, Do SH (2020) Magnesium and pain. Nutrients. 12(8): E2184. https://doi.org/10.3390/nu12082184 [PubMed] [PMC]

- Shkolnik VM, Gavalko YuV, Pogorelov AV, Baranenko AN (2014) Use of Magnesium and Potassium gluconate in neurological practice: treatment of residual effects of ischemic stroke (results of open randomized comparative parallel study). International Neurological Journal [Mezhunarodnyy Nevrologicheskii Zhurnal] 1(63): 146–153. [in Russian]

- Soliman R, Nofal H (2019) The effect of perioperative magnesium sulfate on blood sugar in patients with diabetes mellitus undergoing cardiac surgery: A double-blinded randomized study. Annals of Cardiac Anaesthesia 22(2): 151–157. https://doi.org/10.4103/aca.ACA_32_18 [PubMed] [PMC]

- Spasov AA, Kosolapov VA (2017) The use of magnesium L-aspartate and combinations of magnesium salts with vitamin B6 in medicine. Russian Medical Journal [Rossiiskii Meditsinskii Zhurnal] 23(2): 89–95. https://doi.org/10.18821/0869-2106-2017-23-2-89-95 [in Russian]
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