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Review Article

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 hypothalamic-pituitary-adrenal activity and regulation of the autonomic nervous system (Mariotti et al. 2015; Akarachkova et al. 2016; Scult et al. 2017). A severe acute and/or long-term negative factor causes disorders of autonomic and hormonal homeostasis, which is manifested by such maladjustment symptoms as growing anxiety and irritability, sleep disturbances and rapid heart rate, gastrointestinal and muscle spasms, increased sweating and fatigue (Akarachkova et al. 2018; Kirkland et al. 2018). In recent years, the role of magnesium deficiency as a trigger factor for hypoxia and energy deficiency of body cells is recognized as underlying the reduction of adaptive capabilities and further occurrence of psychosomatic diseases (Akarachkova et al. 2016; Yamanaka et al. 2016).

The analysis of the molecular biochemistry mechanisms revealed that magnesium belongs to the essential macronutrients that determine the cell vital activity of the whole organism (Costello et al. 2016; Calò et al. 2019). As an activator of numerous enzymes, this element catalyzes more than five hundred intracellular reactions of electrolyte, energy and plastic metabolisms. In the form of magnesium-dependent ATP-ase, it controls the energy supply of all intracellular energy-generating and energy-consuming processes of various organs and systems (Walsh et al. 2015; Van Laecke 2019). It was found that the severity of clinical and physiological maladjustment manifestations is in direct proportion to the total magnesium level in the body (Studenikin et al. 2012; Vyatkina et al. 2014; Akarachkova et al. 2016).

Normal indicators of this element in blood serum, which range from 0.75 to 1.26 mmol/L, do not exclude a general magnesium deficiency and, therefore, its deficiency in the body tissues, because under these conditions, magnesium can be released from the bones, preventing a decrease in its serum concentration. Therefore, the diagnostic significance of determining the content of magnesium ions in blood serum is limited and has value only in hypomagnesemia (Kononova et al. 2017; Shchadneva and Gorbunov 2018; Workinger et al. 2018). Moderate magnesium deficiency corresponds to its level from 0.5 to 0.7 mmol/L, and severe, life-threatening, insufficiency – to below 0.5 mmol/L (Ahmed and Mohammed 2019; Van Laecke 2019). It was proved that a highly sensitive and informative method for determining the magnesium content in tissues is the spectrophotometric measurement of its saliva concentration, which corresponds to the intracellular fluid by the amount of all minerals (Kononova et al. 2017; Machado et al. 2018).

Prevalence of magnesium deficiency is among the leading disorders of elemental homeostasis (Gröber et al. 2015; Spasov and Kosolapov 2017). magnesium deficiency can be either a primary condition or a secondary one (Wolf 2017; Reddy et al. 2018). In the first case, these are genetically determined rare diseases associated with impaired magnesium absorption in the intestine, changes in its transport or its increased excretion. It was found that a decrease in magnesium bioavailability is connected with mutations in the proteins TRPM6 and TRPM7 (Transient Receptor Potential Magnesium) – permeable ion channels that transport divalent cations (Abumaria et al. 2019; Lomelino-Pinheiro et al. 2020). Such protein carriers as Solute Carrier (SLC) are also involved in the ionic transport of magnesium (Tsao et al. 2017; Rodríguez-Ramírez 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 (Alparslan 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 elimination 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 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; Yıldırım and Apaydın 2020). magnesium deficiency occurs against concomitant diseases of the gastrointestinal tract, kidneys, cardiovascular 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, aminoglycosides, and proton pump inhibitors (Spasov and Kosolapov 2017; Gröber 2019).

Magnesium is critically important for the normal functioning of the cardiovascular and nervous systems, which are primarily responsible for the body's adaptive capacities (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 aspartic, glutamic and glycine, the transmitter function of which is associated with the analyzer function. Magnesium ions are required to stabilize all subtypes of selective NMDA receptors (receptors that interact with N-methyl-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 adrenocorticotropic hormone in blood serum, which leads to the development of pathological anxiety under stress (Akarachkova 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 importance for controlling the formation and release of all known neuropetides 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 processes in neurons and glia, including glucose utilization, glycoprotein synthesis, hydrolysis of adenosine triphosphoric acid, magnesium affects the cells' membrane potential and the excitation spread. The magnesium antiasthenic 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 worthshile 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 subunits 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 (Kvashnina 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 monophosphate synthesis, the accumulation of which inhibits the effect of the renin-angiotensin system and sympathetic innervation and is accompanied by vasodilation (Chrysant and Chrysant 2020). With a decrease in the concentration of this cation in the blood serum, the arterial tone increases, and there appear the conditions for ischemic damage of nerve cells (Kvashnina 2016; Samavarchi Tehrani et al. 2020). Magnesium is also actively involved in the control 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 diastole in the heart muscle (Algieri 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; Ponzetto 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			
4-8	140 mg/day			
9-13	250 mg/day			
14-18	420 mg/day	360 mg/day mg/day		
19-30	400 mg/day	320 mg/day	420 mg/day	410 mg/day
over 30	450 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, dioxide, carbonate and phosphate exhibit primarily antacid properties, but are not used in correcting magnesium deficiency. Magnesium sulfate taken orally is poorly adsorbed, but causes an osmotic pressure increase in the gastrointestinal tract, vascular leackage 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 (Avgerinos 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 (calcitriol) 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	Magne Express (Austria)
	Solgar, Magnesium Citrate (USA)
	Life Extension (USA)
	Now Foods (USA)
	Natural Vitality, Natural Calm (USA)
	CGN, Magnesium Powder Beverage (USA)
	ChildLife, Liquid Calcium with Magnesium (USA)
	Nature's Plus, Animal Parade, MagKidz (USA)
	Vitables, Chewable Magnesium for Children (USA)
	Nature's Plus, "Animal Parade" Mag Kidz (USA)
	Citramag (UK)
Magnesium citrate + B2	Magnesol B2 (Slovenia)
	Magnesium Diasporal 300 (Germany)
Magnesium citrate + B6	Magnelis B6 forte (Russia)
	Magnesium B6 Renewal (Russia)
	Magnecit Magnesiumsitraati + B6 (Finland)
Magnesium citrate + B6 + E	ZdravCity Magnesium B6 (RF)
Magnesium gluconate	Ritmokor (Ukraine)
	Magnesium Gluconate (USA)
	Almora (Greece)
	Magonate, Mag-G (USA)
Magnesium hydrocitrate + Magnesium gluconate	Floradix Magnesium (Germany)
Magnesium Malate	KAL, Magnesium Malate (USA)
	Source Naturals Magnesium Malate (USA)
	Now Foods, Magnesium Malate (USA)
Magnesium malate + B6	Jarrow Formulas, Magnesium Optimizer (USA)
Magnesium citrate + Magnesium malate	Magnesium Chelate NSP (USA)
Magnesium glycinate+ Magnesium bisglycinate	Magnesium chelate Evalar (RF)
	KAL, Magnesium Glycinate 400 (USA)
	BioSchwartz, Maximum Absorption Magnesium Bisglycinate (USA)
	Natural Vitality, Calm, Magnesium Glycinate Capsules (US)
	Country Life, Chelated Magnesium Glycinate (USA)
	Metabolic Maintenance, Magnesium Glycinate (USA)
	Now Foods, Magnesium Glycinate (USA)
	Solaray, Magnesium Glycinate (USA)
	KAL, Magnesium Glycinate 400 ActivMix (USA)
	Thorne Research, Magnesium Bisglycinate (USA)
	Now Foods, Magnesium Bisglycinate Powder (USA)
Magnesium bisglycinate + B6	Natural Factors, WomenSense, MoodSense (USA)
Magnesium malate + Magnesium bisglycinate	Nature's Answer (USA)
Magnesium lactate	Promagsan (Czech Republic)
	Mg-Tab SR (Spain)
Magnesium lactate + B6	Complivit Magnesium (Russia)
	Magnelis B6 (Russia)
	Magne B6 (France) tablets
	Magnistad (Vietnam)
	Magnesol (Belarus) tablets
Magnesium lactate + Magnesium carbonate + B6, B9, B12	Magnesium plus (Poland)
Magnesium pidolate (pyroglutamate)	Magne B6 (France) ampoules
+ Magnesium lactate + B6	Magnesol (Belarus) solution
Magnesium Orotate	Magnerot (Germany)
	KAL, Magnesium Orotate (USA)
	AOR, Cardio Mag 2.0 (USA)
	Res-Q, Orozin, Cell Repair Formula (USA)
	Magnemax (Russia)
Magnesium asparaginate	Mg 5-Long Oral (Germany)
	Magnesiocard (Germany)
	Emgecard (Austria)
	Trofocard (Greece)
	Magnesit (South Africa)
	Maginex (USA)
Magnesium asparaginate + Potassium aspartate	Panangin (Hungary)
	Panangin Forte (Hungary)
	Asparkam (RF)
	Kudesan with potassium and magnesium (Russia)
	Pamaton (USA)
Magnesium asparaginate + Potassium aspartate + E	Potassium + Magnesium with vitamin E (Russia)
Magnesium asparaginate +B6	Magnesium B6 Evalar (Russia)
	Laktomag B6 (England)
	FILOMAG B6 (Poland)
Magnesium taurate	KAL, Magnesium taurate+, 400 (USA)
	Cardiovascular Research, Magnesium Taurate (USA)
	Cardiovascular Research, Magnesium+Potassium Taurate (USA)
Magnesium threonate_	Life Extension, Neuro-Mag, Magnesium L-Threonate (USA)
	Dr. Mercola, Magnesium L-Threonate (USA)
	Doctor's Best, Magnesium for the Brain (USA)
	KAL, Magnesium L-Threonate for Brain Improvement (USA)
	Jarrow Formulas, MagMind (USA)
	Now Foods, Magtein (USA)
	Source Naturals, Magtein, Magnesium L-Threonate (USA)
Magnesium l-lysinate + Magnesium l-glycinate	Doctor's Best, 100% Chelated Highly Absorbable Magnesium with Albion Minerals (USA)
Magnesium citrate + Magnesium_succinate + Magnesium lysyl glycinate chelate + Magnesium oxide	Life Extension, Magnesium Capsules (USA)
Magnesium citrate + Magnesium_aspartate + Magnesium oxide	Now Foods, Magnesium Capsules (USA)
Magnesium citrate + Magnesium oxide	Nature's Way, Magnesium Complex (USA)
Magnesium Amino Acid Chelate + Magnesium Oxide	Country Life, Chelated Magnesium (USA)
Magnesium Biglycinate Chelate + Magnesium Oxide	Bluebonnet Nutrition, Buffered Magnesium Chelated (USA)
Magnesium Citrate + Magnesium_Carbonate + Magnesium Amino Acid Chelate	Garden of Life, Dr. Formulated (USA)
Magnesium Aspartate + Magnesium_Oxide + B6	Bluebonnet Nutrition, Magnesium Plus B6 (USA)
Magnesium Citrate + Magnesium_succinate + Magnesium glycinate + Magnesium malate + Magnesium_taurinate + B6	Source Naturals, Ultra-Mag (USA)

coordinate bond with four magnesium atoms at once, promotes its permeation into cells and intensifies its action (Trisvetova 2012; Dadak et al. 2013; Pouteau et al. 2018).

The fourth-generation drugs include magnesium complexes with aminoacids: magnesium_asparaginate, magnesium lysinate, magnesium threonate, magnesium taurate, magnesium glycinate and magnesium bisglycinate (Table 2). Such aminoacid complexes (chelates) provide the maximum absorption of magnesium ions, as the mineral in the aminoacid shell is completely ready for absorption by the small intestine cells. In addition, the chelated form is able to cross the placental barrier and provide fetal nutrition. It is important that such compounds neither affect the gastric acidity nor the digestive processes (Trisvetova 2012; Dadak et al. 2013; Ates et al. 2019).

According to some research data, magnesium preparations, in the descending order of their value to make up for systemic alimentary magnesium deficiency in erythrocytes, are arranged as follows: magnesium asparaginate + B6 > magnesium lactate + B6 = magnesium aspartate > magnesium taurate > magnesium aspartate > 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; Kvashnina 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 (Kolomiyets and Mailian 2016).

Magnesium and potassium aspartate preparations not only compensate for the lack of these electrolytes, but also have an antiarrhythmic 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.

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