

Modern Approaches to Diagnosis and Correcting Magnesium Deficiency in Pregnant Women

Dmytro Gavriushov,^{1*} Anatolii Senchuk,² Tetiana Andriichuk³

¹ – PhD in Medicine, assistant of the Department of Obstetrics and Gynecology, Kyiv medical university; 2, Boryspilska St., Kyiv, 02099, Ukraine.

² – MD, professor, chef of the Department of Obstetrics and Gynecology, Kyiv medical university; 2, Boryspilska St., Kyiv, 02099, Ukraine.

³ – the graduate student of the Department of Obstetrics and Gynecology, Kyiv medical university; 2, Boryspilska St., Kyiv, 02099, Ukraine.

Corresponding author: DmytroGavriushov, 2, Boryspilska St., Kyiv, 02099, Ukraine;
tel. 0502697053; e-mail:gavrushov_d@rambler.ru

Abstract

Background: Maternal and child health, has always been, is and will continue to be a top and overriding priority in obstetric practice. Unfortunately, despite the constant improvement and progress of science and knowledge, preeclampsia remains a threatening (often fatal) factor, for both the future mother and the infant.

Aims of our research are the study of magnesium deficiency: highlighting of patients with clinical signs of magnesium deficiency, study of the use effectiveness of magnesium to prevent preeclampsia.

Materials and Methods: 200 pregnant women participated in the study. 100 respondents were at risk of preeclampsia, the degree of magnesium deficiency was established, and correctional therapy was conducted for them. 50 women formed a control group (magnesium preparations were not injected into their destination list). To correct the magnesium content of the body oral magnesium drugs were used: magnesium oxide light, magnesium carbonate, microgranulated powder magnesium oxide.

Results: preeclampsia risk analysis showed a 100% magnesium deficiency, 76% of women had a significant magnesium deficiency, 24% - moderate. Treatment magnesium oral preparations into pregnant women reduced the risk of pregnancy termination and placenta dysfunction; complications of childbirth and caesarean sections. Prevention of preeclampsia was 96.0%. Kids with magnesium-receiving mothers, were above according to the Apgar scale, there was a decrease in the incidence of nervous system damage.

Conclusions: Treatment magnesium for pregnant women have demonstrated their safety and effectiveness in preventing preeclampsia; reduce the incidence of post-natal complications in newborns.

Keywords: Magnesium, pregnancy, preeclampsia, therapy, postnatal complications.

Introduction

Preeclampsia (PE) is one of the most threatening complications of pregnancy, indicator of both maternal and child pathology and mortality. Sadly, the frequency of PE emergency has no downward trend. Between 1.5 and 23.3% of all pregnancies are registered [1, 2], and the number of maternal deaths PE is second only to thromboembolism [3].

PE is characterized by the complexity of pathogenic development mechanisms, which in turn leads to difficulties in prevention and treatment.

Practitioners report treatment inefficiencies of moderately to severely preeclampsia, therefore, development of preventive measures remains an archival component of the struggle for maternal and child health. This requires, first of all, the timely identification of pregnant women with risk factors and sub-clinical forms of preeclampsia. The next step is an adequate correction of the pathological condition, which will prevent the development of clinical preeclampsia [1, 2, 4].

Oxidative stress in pregnant women is an etiological factor in the development of PE, and the pregnancy, in turn, is a physiological condition, which is characterized by a significant increase in the demand for magnesium (Mg) (for 20-30%). It should be noted that even the laboratory confirmed normal magnesium level in the blood serum of the pregnant woman does not exclude his intracellular deficiency, because in an intercellular substance, Mg is the minimum quantity, its maximum quantity is contained inside the cell. For example, the blood serum contains only 0.3% Mg of its entire body. In 2/3 cases, the pregnancy is accompanied by clinical symptoms of magnesium deficiency, and the leading place in the etopathogenesis of preeclampsia is precisely the magnesium deficiency [5-7].

Magnesium is involved in more than 350 physiological processes, stabilization of the DNA molecule, promotes nucleic acid integrity, proteins and mitochondria. Separately, its participation in cell fission mechanisms (mitosis and meiosis processes), that during pregnancy can lead to genetic pathologies of the fetus [7-9]. Plus, hypomagnemia, reducing the placenta's proliferation capacity, results in the fetus's pituitary condition [10]. On the other hand, magnesium is the calcium antagonist, and his or her insufficiency in the body can cause hypertension in the muscle tissue (including the placenta) and which can cause premature termination of pregnancy [11]. In biochemical processes, this microelement is necessary for energy exchange. Magnesium deficiency leads to increased aldosterone concentrations fluid retention and edema. Relative hyperestrogenemia occurs, that causes angiotensin hyperproduction in the liver, increased level of aldosterone in blood and blood pressure (BP), which is a dangerous syndrome during pregnancy [12-14].

Mg influences the synthesis of protein and nitrogen oxide, lowers her uterus, stimulates vasodilation, improving blood flow in the placenta vessels, and also reduces platelet aggregation, increasing prostacycline activity and by reducing A2 thromboxane activity. This helps prevent endothelial dysfunction and its consequences (hypercoagulation, gestosis and placental dysfunction), adequate functioning of the central and peripheral nervous system, normalization of vascular tone, increased resistance of fetal tissues to hypoxia, lowers the incidence of fetal delay syndrome. Magnesium therapy reduces the risk of haemorrhaging to the brain tissue of a child. Implementation of the mechanism for energy support of central nervous system (CNS), the incidence of sudden neonatal death syndrome is reduced, resistance of tissues to hypoxia increases [5, 7, 15-16].

Bullarbo et al. [5] showed that due to the effect of muscle relaxation magnesium prevents convulsions and, like the calcium antagonist, lowers elevation and normalizes BP during pregnancy.

Since laboratory diagnosis of Mg deficiency can be poorly informative more attention should be paid to identification clinical signs of a deficiency in this element, in particular states of increased nervous and mental excitement (irritability, stress, anxiety, depressiveness, sleep-deprivation, asthenia), as well as increased muscular arousal (back pain, muscle cramps, increased uterine tone, urinary pain).

The purpose of our research was to study magnesium deficiency: highlighting of patients with clinical signs of magnesium deficiency, study of the effectiveness of magnesium in their use to prevent preeclampsia.

Materials and Methods

Study of the effectiveness of magnesium in their use to prevent pre-eclampsia, follow-up of pregnancy through detection and correction (magnesium prophylaxis) late gestosis (preeclampsia) in the group of women - 100 pregnant, who formed I Group. Risk identification and basic prevention

were conducted under the Protocol “Hypertensive disorders during pregnancy”, Decree № 676 HM of Ukraine [17]. All respondents had written consent to participate in the study. The results were compared with observations of 50 pregnant women (Group II) at risk of preeclampsia, which oral magnesium preparations have not been added to the prophylactic complex. The Control Group (KG) comprised 50 healthy women with the physiological course of pregnancy.

The presence of magnesium deficiency was determined by examination of the survey data, as recorded in our questionnaire for the study of magnesium deficiency in pregnant women. The questionnaire contained evidence of somatic pathology in the patient, pathology of the nervous system, aggravated obstetric-gynecological anamnesis, data on nutrition, lifestyle and general well-being. We developed the questionnaire based on the questionnaire materials, Proposed by O.O. Gromova and O.A. Limanova (2014), UNESCO Institute for Microelements RRC [18].

The results of the questionnaire were evaluated in terms of: 0 points feature missing; 1 point appearing periodically, mild flow observed; 2 marks of late gestosis present continuously. After the questionnaire, according to the results, patients requiring correction of Mg in the body, were divided into three groups. Patients in the first group required emergency magnesium therapy, lifestyle and nutritional changes (there was a significant magnesium deficiency) (31-132 points). Second group patients (11-30 points) there was a moderate deficiency requiring magnesium drugs, lifestyle and nutrition adjustments. For third-group patients (5-10 points) with Mg's marginal deficit, a correction of diet and lifestyle was sufficient. Magnesium monoprohylaxis was performed by:

1. Magnesium oxide light (342 mg) and magnesium carbonate (670 mg), which equals to 365 mg Mg²⁺ ions: 1 powdered pill per day with intermittent courses of 10-12; 22-26; 30-32 weeks of pregnancy.
2. Microgranulated magnesium oxide powder (535 mg), which equals to 300 mg of magnesium and light oxide magnesium 403.0-435.2 mg equivalent to 243 mg Mg²⁺.

The medication was administered from 10 weeks for the duration of the pregnancy one pill per day.

Results and Discussion

Testing of 100 studied patients at risk of preeclampsia showed, that 76 respondents (76.0%) had a significant Mg deficit, requiring emergency magnesium therapy, lifestyle and nutrition (result of questionnaire from 31 to 132 points). 24 pregnant women were in the group with moderate deficiency Mg (11-30 points).

It should be noted that hypomagnemia is a common phenomenon in the world. Most pregnant women require additional doses of magnesium (300 mg of magnesium citrate per day) [19]. For example, according to Rocha et al. among 52 pregnant women examined in São Paulo (Brazil), where the magnesium content of erythrocytes and blood serum was in the physiological subdivision, 39% of patients with reduced excretion Mg with urine and in need of magnet therapy have been identified [20].

For each of the patient categories identified in the survey, appropriate therapy was administered, aimed at correcting the concentration of Mg in the body. Results of oral magnesium prophylaxis were high, the harmlessness and good tolerance of the proposed therapy compared to the generally accepted approaches [17].

Our results (**Table 1**) show that, in the group of pregnant women taking magnesium (Group I) the threats of pregnancy termination and placental dysfunction were significantly lower. Prevention of pre-eclampsia was 96.0% in group I and only 68.0% in group, prevention of preeclampsia according to The Protocol (Group II). The percentage of obstetric complications and the frequency of caesarean sections were twice as high among women, for prophylaxis and treatment of preeclampsia.

Table 1.Incidence of complications of pregnancy and childbirth (P±m)

The studied parameter	Control Group (n=50)	I Experimental Group (n=100)	II Experimental Group (n=50)
Miscarriagerisk.	12,0±4,6*	17,0±3,8 ^Δ	44,0±7,0**
Placentaldysfunction	6,0±3,4*	11,0±3,1 ^Δ	32,0±6,7**
Preeclampsia	-	4,0±2,0 ^Δ	32,0±6,7
Obstructedlabour	8,0±3,8*	12,0±3,2 ^Δ	30,0±6,5**
Caesareansections	8,0±3,8*	15,0±3,6 ^Δ	32,0±6,7**

Notice: * – p<0,05between the CG and the I Group;** – p<0,05between the CG and the II Group;Δ – p< 0,05between the first and second groups.

Although international studies have shown that, the effect of adding magnesium drugs does not necessarily have a 100% positive effect. So de Araújo et al. indicates the inefficiency of oral treatment for 2 weeks for treatment of increased nervous and psychiatric excitement in (leg cramps) [21].

We also noted that positive effects of magnesium, are not only related to spasmolytic properties, as well as with a favourable impact on the woman's emotional state which reduces the negative effects of stressful situations.

Research results of Japanese scientists [22] indicate a decrease in toxicological effects on the fetus if pregnant magnesium sulfate is introduced into the prescription sheet.

To determine the effect of the oral treatment with Mg drugs on the development of the fetus, we have monitored newborn patients in both groups (**Table 2**).

Table 2. Newborn conditions of patients under examination (P±m)

The studied parameter	Newborns from the Control Group (n=50)	Newborns from the I Experimental Group (n=100)	Newborns from the II Experimental Group (n=50)
Grade according Apgar scale 7 points and less	2,0±2,0	9,0±2,9*	22,0±5,9**
Incidence	2,0±2,0	13,0±3,4*	20,0±5,7**
Nervous system lesions,	-	7,0±2,6	18,0±5,4

Notice: * – p<0,05 between the CG and the I Group;** – p<0,05 between the CG and the II Group.

Analysis of the data received indicates that, newborn babies who have given birth to magnesium prophylaxis drugs, were rated higher on the Apgar scale. For example, in the fifth minute, 22.0 % of children had a grade of 7 or lower, of mothers in the group, receiving treatment under the Protocol [17]. In a group of patients who were taking magnesium to prevent preeclampsia, the rate was 9.0%, which is 2.5 times less than the number of patients per group, that didn't add magnesium to the prophylactics. Neonatal morbidity and perinatal disorders of the nervous system were also significantly higher in the group of patients without magnesium prophylaxis (Table 2). Neonatal nervous system damage is a critical health parameter in post-natal period. The percentage of resuscitation is increasing significantly, in case of convulsions in newborns. 60% Mg in newborn is in bones, the rest is mostly intracellular, therefore, diagnosing Mg deficiency in newborns is problematic. In addition, use of oral medication for children in the post-natal period must be conducted with caution, especially if it is performed before the birth of the pregnant woman. The onset of convulsions is also influenced by the development of the child on the Apgar scale. Ball below 7 according to neonatologists exacerbates postnatal cramping [23-24]. According to Aditiawarman et al.

[25] introduction of Magnesium sulfate in pregnancy prescription, reduces cerebral palsy in premature babies.

Conclusions

Pregnancy magnesium deficiency is a common pathology. In our study, 100.0% of patients at risk of developing preeclampsia, hypomagnesemia was found. At the same time, 76.0 per cent of patients have a significant deficiency, requiring emergency magnesium therapy (31-132 points) in combination with lifestyle correction, and nutrition. 24.0% moderate, requiring magnesium nutritional and lifestyle corrections (11-30 points). Preventive treatment of magnesium by patients at risk of developing pre-eclampsia has demonstrated its effectiveness and safety, according to the analysis of pregnant women and newborns. Prevention of preeclampsia was 96.0%.

The percentage of complications among pregnant women receiving magnet therapy has decreased during delivery and the frequency of caesarean sections.

Perinatal outcomes are more favourable for newborns, mothers who received pre-eclampsia prophylaxis with magnesium drugs.

Practical applications

Based on the results of our research, we consider it appropriate to use magnesium preparations for the prevention of preeclampsia, as basic drugs with the means, improving micro-circulation (aspirin, curantyl, Tivatortin, etc.). This combination is synergistic, which has a positive effect on PE therapy.

References

1. Verentskovski BM, Zaporozhan VN, Senchuk AY, Skachko BG. 2005. Gestosis. A guide for doctors. Moscow: Meditsinskoye informatsionnoye agentstvo. 312 p. (in Russian).
2. Veropotvelyan PN, Veropotvelyan NP, Smorodskaya EP, Lazaren AT. A modern view of the gestosis problem. *Medical aspects of women's health*. 2006; 6(46):43-52. (in Russian).
3. Aksenova AN. Preeclampsia and modern methods its predicting. *FORCIPE*. 2020; 3(S): 44-45.
4. Rambaldi MP, Weiner E, Mecacci F, Bar J, Petraglia F. Immunomodulation and preeclampsia. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2019; 60: 87-96. doi: <https://doi.org/10.1016/j.bpobgyn.2019.06.005>.
5. Bullarbo C, Ödman N, Nestler A et al. Magnesium supplementation to prevent high blood pressure in pregnancy: a randomised placebo control trial. *Arch Gynecol Obstet*. 2013; 288(6):1269-1274. doi: <https://doi.org/10.1007/s00404-013-2900-2>.
6. Chiarello, Abad C, Rojas D et al. Oxidative stress: Normal pregnancy versus preeclampsia. *Biochimica et Biophysica Acta (BBA) – Molecular Basis of Disease*. 2020; 1866(2): 165354. doi: <https://doi.org/10.1016/j.bbadis.2018.12.005>.
7. Vasilyeva MV, Degtyareva MV, Sankevich OA et al. Homeostasis of minerals and trace elements in newborns. Part 2. Clinical role of magnesium balance in the body of newborn. *Neonatologiya: novosti, mneniya, obuchenie [Neonatology: News, Opinions, Training]*. 2020; 8(1): 22-33. doi: 10.33029/2308-2402-2020-8-1-22-33. (in Russian).
8. Dadak K. Magnesium deficiency in obstetrics and gynecology. *Obstetrics, gynecology, reproduction*. 2013; 7(2): 6-14. (in Russian).
9. Balan VE, Zhuravel AS. Modern view of the need to correct magnesium deficiency during pregnancy. *Medical advice*. 2017; 20: 198–202. doi: 10.21518/2079-701x-2017-20-198-202. (in Russian).
10. Dikke GB. The role of magnesium in physiological pregnancy: controversy and evidence.

- Medical advice. 2016; 19: 96-102.doi: 10.21518/2079-701x-2016-19-96-102. (in Russian).
11. Petrova AE, Solomeina ES, Kiseleva MK, Bakurinskih AB. Influence of magnesium deficiency on the outcome of pregnancy and labors. *Topical issues of modern medical science and health care.* 2020; 1: 110-115. URL: <http://elib.usma.ru/handle/usma/2139> (in Russian).
 12. Shifman EM. 2002. Preeclampsia, eclampsia, HELLP syndrome. Petrozavodsk: IntelTEK. 432 p.
 13. Shechter M, Saad T, Shechter A, Koren-Morag N, Silver BB, Matetzky S. Comparison of magnesium status using X-ray dispersion analysis following magnesium oxide and magnesium citrate treatment of healthy subjects. *MagnesRes.* 2012; 25(1): 28-39. doi:10.1684/mrh.2012.0305.
 14. Reznichenko GI, Bessarabov YuM, Potrebnaya VYu, Kovalenko KI. The effectiveness of the drug Bioelectra Magnesium Direct in treatment and prophylactic measures in pregnant women with preeclampsia. *Medical aspects of women's health.* 2015; 6(102): 105. (in Russian).
 15. Grober U., Schmidt J., Kisters K. Magnesium in Prevention and Therapy. *Nutrients.* 2015; 7(9): 8199-226. doi: <https://doi.org/10.3390/nu7095388>.
 16. Selihova MS, Smolyaninov AA, Kalacheva LS. (2019). Women's Reproductive Health and Magnesium Deficiency. *Bulletin of the Volgograd State Medical University.* 2019; 4(72): 3-8. doi: 10.19163/1994-9480-2019-4(72)-3-8. (in Russian).
 17. On approval of clinical protocols for obstetric and gynecological care. *Dirrection 676 MOZ of Ukraine.* Jan. 12.2004. (in Ukrainian).
 18. Gromova OA, Limanova OA. Magnesium deficiency and muscle cramps in pregnant women: treatment options (clinical and pharmacological lecture). *Gynecology.* 2014; 16(2): 70-77. (in Russian).
 19. de Araújo CAL, Ray JG, Figueiroa JN, Alves JG. BRAZIL magnesium (BRAMAG) trial: a double-masked randomized clinical trial of oral magnesium supplementation in pregnancy. *BMC Pregnancy and Childbirth.* 2020; 20(234): 1-7. doi: <https://doi.org/10.1186/s12884-020-02935-7>.
 20. Rocha VS, Lavanda I, Nakano EY, Ruano R, Zugaib M, Colli C. Calcium and magnesium status is not impaired in pregnant women. *Nutr Res.* 2012; 32(7): 542-6. doi: <https://doi.org/10.1016/j.nutres.2012.05.010>.
 21. de Araújo CAL, de Lorena SB, de Sousa Cavalcanti GC, de Souza Leão GL, Tenório GP, Alves JGB. Oral magnesium supplementation for leg cramps in pregnancy—An observational controlled trial. *PLoS ONE.* 2020; 15(1): e0227497. <https://doi.org/10.1371/journal.pone.0227497>.
 22. Kino E, Ohhashi M, Kawagoe Ya, Sameshima H, Kamitomo M, Suga S, Yasuhi I, Funakoshi T. Impact of tocolysis-intent magnesium sulfate and beta-adrenergic agonists on perinatal brain damage in infants born between 28–36 weeks' gestation. *Obstetrics Gynaecology Research.* 2020; 46(10): 2027-2035. doi: <https://doi.org/10.1111/jog.14364>.
 23. Prutkin ME. Parenteral nutrition protocol in neonatal intensive care unit practice. *Intensive care bulletin.* 2004; 3: 56-61.
 24. Safarova A.G. Features of risk of neonatal seizures in premature infants. *Intern J Clin Fundament Research.* 2020; 8: 27-31.
 25. Aditiawarman, Selean JT, Sampurna MTA, Ernawati, Joewono HT. Comparison of short-term outcome and serum magnesium levels in premature infants of mothers after magnesium sulfate therapy. *Eurasian Journal of Biosciences.* 2020; 14(1): 1863-1867.