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Pregnancy and supplementation of vitamins and mineral compounds - literature review

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Abstract

Introduction and purpose

Proper nutrition and appropriately chosen supplementation during pregnancy significantly ensure a healthy pregnancy and fetal development. Both nutrient deficiencies and excesses can have negative health effects on both the mother and the child. This article discusses specific active substances that are particularly important in supplementation of pregnant women. The aim of the study is to describe the current state of knowledge about the importance of adequate supply of vitamins and minerals compounds during pregnancy, in order to increase women's awareness and encourage improvement in dietary habits.

Material and methods of research

For this study, a review of literature available on Google Scholar and PubMed was conducted. From the analysis, studies published before 2017 were excluded.

State of knowledge

Based on the current state of knowledge, we know that the nutrition of pregnant women undergoes partial modifications. To ensure a healthy pregnancy, there is an increased energy demand in the body, making appropriate weight gain crucial. Routine use of multivitamin supplements is not recommended for pregnant women, as a balanced diet should be the primary source of macronutrients, micronutrients, and vitamins. Key components that are used in supplementation for pregnant women in specific cases include iron, folic acid, vitamin D, DHA acids, and iodine.

Conclusions

This work emphasizes the significant impact of proper nutrition and appropriately selected supplementation in pregnant women on reducing the risk of various pregnancy complications and fetal developmental disorders. It highlights the importance of deficiencies and excesses of vitamins and minerals compounds in the diet of women during the preconception period, all trimesters of pregnancy and lactation.

Key words: pregnancy; diet; nutrition; supplementation; vitamins; mineral compounds

Introduction

Appropriate nutrition and properly selected supplementation for pregnant women is one of the basic factors that significantly guarantee the proper course of pregnancy and fetal development. It is worth emphasizing that in this case, the nutrition of women in particular trimesters of pregnancy as well as during the preconception period has a significant impact [1]. Women who call their eating habits during planning and during pregnancy "prudent" or "health-conscious" may have significantly fewer pregnancy complications and undesirable effects on the child's health [2]. Inadequate maternal nutrition is associated with unfavorable intrauterine exposure of the fetus, resulting in significant disorders. Both deficiency and excess of nutrients may result in permanent modifications of metabolic and hormonal processes, which are reflected in the form of negative health effects for the mother and child both during prenatal life and in later developmental periods. The most important effects of irrational nutrition of pregnant women include, among others: miscarriages, anemia, preeclampsia, premature births, infections or lactation disorders, and effects directly related to the developing fetus, such as: congenital defects, low birth weight, prematurity, infections, neurological disorders and increased perinatal mortality [3]. Moreover, a relationship has been shown between maternal nutrition not only during pregnancy, but also during lactation and long-term metabolic health disorders in the offspring, molecular changes in the brain and behavioral disorders [4]. That is why a properly balanced diet is so important, being the basic source of minerals and vitamins, additionally taking into account the common problem of inability to obtain a sufficient supply of nutrients solely through the daily diet. Therefore, it is recommended to include selected groups of supplements in optimal doses for the proper growth of the fetus and maintaining the mother's health [5].

The aim of this study is to discuss the current state of knowledge on the importance of appropriate vitamin and mineral supplementation during pregnancy. The information contained therein will be useful for both women planning a pregnancy and pregnant women. The aim of the work is to increase awareness of such an

important topic as proper diet and supplementation and to encourage improvement of eating habits. Thanks to this, it will be possible to reduce the risk of significant pregnancy complications and undesirable effects on the health of the mother and child.

Material and methods of research

For the purposes of this study, a review of the literature available in the Google Scholar (GS) and PubMed (PM) search engines was performed. The review was carried out using the following keywords and their combinations: pregnancy; diet; nutrition; supplementation; vitamins; mineral compounds. Works published before 2017 were excluded from the analysis, in order to use the most current state of knowledge. The review included full original and review works, in Polish and English.

State of knowledge

For many years, there was no access to unified guidelines that would clearly define the scope of proper vitamin and nutrient supplementation during pregnancy. This resulted directly from the insufficient number of clinical studies of the population of pregnant women, mainly for ethical reasons [6]. Based on the current state of knowledge, we know that nutrition during pregnancy is partially modified. Caloric demand during pregnancy is increased in proportion to the gestational age in order to maintain the proper growth of the fetus, placenta and maternal tissues and is closely related to the physiological increase in the basal metabolic rate of the pregnant woman [7]. The basic amount of energy expenditure is influenced by both the energy demand for the tissues being formed, including the embryo, as well as changes taking place in the pregnant woman's body, such as an increase in the volume of the uterus and mammary glands, an increase in the number of red blood cells and plasma volume, as well as the amount of stored fats and proteins. Energy expenditure immediately after conception is relatively small and increases only at the end of the first trimester of pregnancy. Therefore, the energy demand of a pregnant woman during this period does not change dramatically compared to the needs of the body before pregnancy, but the demand for individual nutrients increases. In the second trimester of pregnancy, the daily energy demand increases by an average of 360 kcal, and in the third trimester by an average of 475 kcal compared to the preconception period [8]. An equally important aspect reflecting appropriate nutrition and supplementation in the diet of pregnant women is proper weight gain during pregnancy, which is crucial for the proper growth of the developing fetus. According to research, both too little and too much weight gain during pregnancy results in many negative health consequences for the mother and child. It is worth emphasizing that weight gain of pregnant women is an individual matter and, importantly, depends on the value of body mass index (BMI) before getting pregnant. (Table 1)

Table 1. Appropriate weight gain of pregnant woman depending on the body mass index (BMI) before pregnancy [6]

	body mass index (BMI) value before pregnancy [kg/m2]	weight gain during pregnancy [kg]
underweight	<18,5	12,5-18,0
standard	18,5-24,99	11,5-16,0
overweight	25,0-29,99	7,0-11,5
first degree obesity	30,0-34,99	4,5-11,0
second degree obesity	35,0-39,99	0-4,0
third degree obesity	≥40	weight loss up to 4 kg with a balanced diet

Obesity occurring before pregnancy is associated with a high risk of developing diseases such as hypertension or gestational diabetes, and may also lead to the need to end the pregnancy with a cesarean section and the birth of a newborn with a high birth weight with other accompanying negative health consequences. According to more recent studies, it is very important to personalize the recommendations for weight gain in obese pregnant women, taking into account various classes of obesity (I, II, III), which is significantly related to the proper course of pregnancy and fetal development. It has also been shown that slight weight gain or even loss during pregnancy is directly associated with a high risk of giving birth to a child with a small weight for gestational age [9]. Low BMI and an inadequately balanced mother's diet may significantly impair fetal

development and nutrient supply, leading to adverse perinatal complications, physical and cognitive delays in childhood, and metabolic disorders in adulthood [10].

According to research, there are often significant imbalances in the diet of pregnant women, especially in the field of essential vitamins and minerals. Pregnant women are most often deficient in folic acid, polyunsaturated fatty acids, iron, iodine and vitamin D3 - key ingredients for the mother's health and the proper development of the fetus. Therefore, there are significant benefits associated with the use of optimal doses of selected supplements in pregnant patients with deficiencies of the above-mentioned ingredients [6,11]. However, it is worth emphasizing that in accordance with the position of the World Health Organization (WHO) from 2016 and most scientific societies, the routine use of multivitamin preparations in all pregnant women is not recommended. A properly balanced diet should be the basic source of macro- and microelements and vitamins. Based on the Recommendations of the Polish Society of Gynecologists and Obstetricians (PTGiP) from 2020, the key ingredients used in the supplementation of pregnant women in clearly defined cases include: iron, folic acid, vitamin D, DHA acids (docosahexaenoic acid) and iodine. Other vitamins and minerals are not recommended for supplementing the diet of healthy pregnant women without appropriate medical indications [12]. The following sections will discuss individual vitamins and minerals that are particularly important in supplementation for pregnant women.

Folic acid

Folic acid (also known as pteroylmonoglutamic acid, vitamin B9) is a water-soluble vitamin from the B group. This compound has a pteridine base, p-aminobenzoic acid (PABA), and glutamic acid in its structure. Folates, i.e. salts of folic acid, take part in various chemical reactions as carriers of one-carbon groups (OCM, one carbon metabolism). These are extremely important reactions in the processes necessary for the synthesis of proteins, nucleic acids, reactive oxygen species and epigenetic regulation, and include processes such as folate metabolism, methylation and transsulfuration of homocysteine. Folic acid is a key compound for the body with multidirectional biological effects, playing an important role in the tissues of the fetus, the hematopoietic system and the epithelium of the gastrointestinal tract, where cell division takes place, and its appropriate amounts ensure the proper functioning of cells and maintaining homeostasis [12, 13]. Similar to some vitamins, it is impossible to synthesize folates in human cells, which is why they are supplied exogenously, mainly from food and intestinal microflora [14]. The foods richest in folate are lettuce, spinach, cabbage, broccoli, whole grains, liver, eggs, nuts and cheese. During pregnancy, the demand for folic acid increases and can only be partially met by the supply of appropriate products in the diet. Folate deficiency increases the risk of neural tube defects in the fetus, as well as heart and urinary tract defects, cleft lip and palate, and Down syndrome. In case of abnormal folate metabolism, hyperhomocysteinemia may occur and, consequently, there is an increased risk of serious pregnancy complications such as recurrent miscarriages, preeclampsia or inhibition of intrauterine growth of the fetus. Studies have shown that in order to obtain the appropriate level of folate in the body, folic acid supplementation is necessary for at least 12 weeks before the planned pregnancy [15]. On the other hand, due to the global popularization of the recommendation to take a synthetic form of vitamin B9 during pregnancy, the recommended dose is sometimes exceeded in pregnant women even several times, and this is related to the consumption of folic acid contained in the daily diet and its simultaneous supplementation [16] . According to research, excessive concentration of folates in the mother's body may have a harmful effect on the developing fetus, disturbing its neurodevelopment and, consequently, increasing the risk of, among others: autism. Therefore, it is extremely important to assess the impact of both deficiency and excess of the synthetic form of vitamin B9 on the development of fetal organs [17]. According to current guidelines, it is recommended to take folic acid at a dose of 0.4 mg/day for all women of reproductive age, in order to supplement the basic diet that includes large amounts of products rich in folates. For pregnant women up to the 12th week of pregnancy, a dose of 0.4-0.8 mg/day is recommended, and from the 12th week and during breastfeeding in the absence of concomitant risk factors, a dose of 0.6-0.8 mg/day. Patients with a fetal neural tube defect confirmed in a previous pregnancy should take folic acid at a dose of 4 mg/day for at least 4 weeks preceding the planned pregnancy and for the first trimester of pregnancy, and after that period the dose should be reduced to that recommended in the general population. An increased amount of supplemented folate is recommended for women at high risk of folic acid deficiency and neural tube defects, i.e. patients with type I or II diabetes before pregnancy; taking antiepileptic drugs, metformin, methotrexate, sulfasalazine or cholestyramine during pregnancy or the preconception period; using stimulants such as smoking or alcoholism; obese (BMI over 30); with kidney or liver failure; after bariatric surgery or with diseases that interfere with absorption from the gastrointestinal tract, including: ulcerative colitis, Crohn's disease, celiac disease [12]. It is also worth mentioning that it is estimated that approximately 50% of women have reduced activity of the enzyme methylenetetrahydrofolate reductase (MTHFR), which may significantly affect the poorer absorption of folic acid. In such a case, the calcium salt of N5-methyl-TH-folate is used, i.e. the active form of folate, which bypasses a number of enzymatic reactions and is directly transported to

the circulatory system. This form of folic acid directly participates in cellular processes and allows for the assessment of bioavailability in a more precise and controlled way [18].

Iron

Iron is the most abundant chemical element on Earth, classified as a microelement, which plays an extremely important role in organic biological processes occurring in the body. The fundamental task of iron is to support erythropoiesis, i.e. the process of creating red blood cells. Every cell in the body requires iron for proper development and to achieve proper metabolic function. This element supports enzymatic processes crucial for the metabolic functions of cells, including the reactions necessary for the supply of oxygen and the production of cellular adenosine triphosphate [19]. Additionally, it has a positive effect on cholesterol levels in the body and plays an auxiliary role in the metabolic processes of the liver. The richest in iron are products such as offal, red meat, eggs, parsley, kale, spinach, legumes, pumpkin seeds, sunflower seeds and dried apricots. It is worth mentioning that iron contained in animal products (heme iron) is better absorbed than iron from plant foods (non-heme iron) [6]. The degree of iron storage is reflected in the value of ferritin, which is also an acute phase protein that increases in response to existing inflammation in the body - then the lower limit of normal ferritin concentration is 100 mcg/l. In such a situation, it is advisable to measure transferrin saturated with iron (TSAT), which indicates iron deficiency at a value < 20%.

As we know, pregnant women physiologically increase blood volume by an average of 50% and red blood cell mass by approximately 25%. An increase in plasma volume results in a decrease in hemoglobin concentration. Moreover, additional total iron loss is observed during pregnancy and lactation, which is related to the development of the fetus and placenta, an increase in erythrocyte mass and perinatal blood loss [20]. According to research, of pregnant and breastfeeding women, the demand for iron increases on average by 1–2.5 mg in the first trimester of pregnancy and 6.5 mg/day in the third trimester of pregnancy. It is worth emphasizing that iron deficiency occurs when the amount of iron supplied to the body is insufficient to cover the current demand and this condition does not always equate to anemia. Iron deficiency may occur in pre-latent, latent and overt stages (with symptoms of anemia). According to WHO criteria, anemia in a pregnant patient is diagnosed when the hemoglobin (Hb) value drops below 11 g/dl (in each trimester of pregnancy) and below 10 g/dl in a patient in the postpartum period. The clinical picture of women with iron deficiency or iron deficiency anemia is characterized by symptoms such as fatigue, pallor, shortness of breath, palpitations, weakness, headaches, dizziness, hair loss, leg cramps, cold intolerance, irritability and poor concentration, and also the patient may experience reduced milk production and depletion of iron stores in the postpartum period. Anemia during pregnancy is very dangerous and increases the risk of many complications, such as circulatory system failure, eclampsia, hemorrhagic shock and increased susceptibility to infections. Importantly, if left untreated, it causes an increased risk of low birth weight and premature delivery, especially if the patient was deficient in this microelement in the first two trimesters of pregnancy. When talking about iron deficiency, it is also worth mentioning the potential effects of its excess, which may lead to the development of insulin resistance and reduced insulin secretion by pancreatic B cells, the occurrence of gestational diabetes or an increased risk of preeclampsia, especially in women who supplemented iron before the 16th week of pregnancy. without reduced hemoglobin concentration (hemoglobin>13.2 g/dl at the beginning of the second trimester) [21,22]. Taking into account the negative impact of both iron deficiency and excess in pregnant women, it is recommended to systematically monitor the morphology and ferritin concentration throughout pregnancy. It is recommended to take iron preparations before the 16th week of pregnancy for women with iron deficiency anemia (i.e. with Hb <11g/dl and reduced ferritin concentration). After week 16, iron supplementation is possible at a dose of up to 30 mg/day in women without anemia and with a ferritin concentration below 60 mcg/day. In the treatment of anemia, it is recommended to use low doses of oral iron for a longer period of time, and if there is no response, treatment modifications and further observation of the patient. In the absence of the intended therapeutic effect on large oral doses of iron or Hb below 7 g/dl, the need for transfusion of packed red blood cells (RBC) should be considered [12].

Docosahexaenoic acid (DHA)

Docosahexaenoic acid belongs to the group of long-chain omega-3 polyunsaturated fatty acids. Even though it does not belong to the groups of vitamins or minerals, its inclusion in this study was important from the point of view of its necessity for supplementation in pregnant women in accordance with current recommendations. Its appropriate level plays an extremely important role in supporting the course of pregnancy and child development [23]. DHA is an important structural element of the nervous system and retina, contributing largely to the proper development and functioning of the brain and visual acuity in the fetus and child in the first years of life.

Docosahexaenoic acid also affects the birth weight of the newborn and the optimal duration of pregnancy, reducing the risk of premature birth. Moreover, ensuring appropriate DHA supplementation in a pregnant woman's diet may significantly reduce the likelihood of postpartum depression [24]. Foods rich in polyunsaturated fatty acids include marine fish (such as mackerel, salmon, tuna, halibut, sardines and herring) and marine algae [25]. However, it should be remembered that sea fish may be a source of environmental pollution, therefore their consumption may involve exposure to methylmercury, dioxins and polychlorinated biphenyls, which often leads to adverse neurological effects in the child [26]. Taking into account the available information on the role of docosahexaenoic acid during pregnancy, in accordance with current recommendations, DHA supplementation is recommended for all pregnant women at a dose of not less than 200 mg. Women in the preconception period and during pregnancy whose diet does not provide an adequate supply of DHA, i.e. contains small amounts of fish, should consider taking higher doses of supplemented polyunsaturated fatty acids. In patients at risk of premature birth, a DHA supply of 1000 mg/day is recommended [12].

Vitamin D

Vitamin D is a group of fat-soluble steroid organic chemicals. It comes in two main isoforms, vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol). Vitamin D3 comes mainly from ultraviolet (UV)-induced cutaneous synthesis from its precursor 7-dehydrocholesterol in the skin and, to a lesser extent, from the consumption of foods rich in this vitamin, such as fatty fish, cod liver oil, or egg yolk. Vitamin D2 comes from consuming products such as mushrooms and yeast. Both vitamins have a similar metabolism. An additional source of vitamin D, apart from its synthesis in the skin and consumption through natural foods, are supplements and foods synthetically enriched with this vitamin [27]. As a result of hydroxylation of previtamin D in the liver, the main circulating form is formed, i.e. 25-hydroxyvitamin D [25(OH)D]. It may be bound to vitamin D binding protein (DBP), albumin, or free. 25-hydroxyvitamin D is converted to the active metabolite, i.e. 1,25-dihydroxyvitamin D [1,25(OH) 2D], mainly in the proximal tubules of the kidneys, but also in the bones, parathyroid glands and, in the case of pregnancy, in the placenta [28]. The main task of vitamin D is to regulate the calcium-phosphate metabolism by controlling the absorption of calcium in the small intestine and interacting with parathyroid hormone (PTH) in the process of mineralization of skeletal bones and stabilizing the level of calcium in the bloodstream. Additionally, it has been shown that this vitamin may contribute to improving the body's immunity, muscle cell contractility, cognitive abilities and cardiometabolic health. Its immunomodulatory and anti-inflammatory properties play a special role in conditions of chronic low-grade inflammation, such as type 2 diabetes or heart failure, as well as in autoimmune diseases. The demand for vitamin D increases during pregnancy, which is related to the physiological processes taking place in the mother's body, including supporting the maintenance of an environment of tolerance to fetal tissues and the accompanying alloantigens and the formation of the fetal skeleton [29]. Vitamin D deficiencies often lead to bone mineralization disorders, including osteoporosis, immune disorders and the development of hypertension. Reduced levels of vitamin D may lead to gestational diabetes, preeclampsia and the birth of a child with a weight that is too small in relation to the duration of pregnancy or a low birth weight (below 2500g). Moreover, a significantly increased risk of abnormal fetal growth, childhood eczema, severe hypocalcemia and rickets has been demonstrated [30]. Therefore, according to current recommendations, the recommended dose for women during pregnancy and lactation who have a normal BMI and do not have any risk of vitamin D deficiency is 1,500-2,000 IU/d. It is suggested to adjust the dose individually, taking into account the concentration of vitamin D in the blood. For obese women (BMI >30 kg/m2), the recommended dose is 4000 IU/d [12].

Iodine

Iodine is a chemical element necessary for the production of thyroid hormones, and its deficiency is still a significant public health problem in many regions of the world [31]. During pregnancy, the demand for iodine increases, and this is due to its increased loss by the kidneys, the activity of type 2 and type 3 deiodinase in the placenta, and an increase in the level of human chorionic gonadotropin and circulating estrogens, which lead to an increase in the level of thyroxine-binding globulin [32] .

Hormones produced by the thyroid gland are an essential factor supporting brain development, therefore, since the thyroid function in the fetus begins only in the middle of pregnancy, it is extremely important for the mother to ensure their appropriate level. Maternal T4 (thyroxine) crosses the placenta and is converted to the active form T3 (triiodothyronine), which plays an important role in the neurodevelopment of the fetus. Therefore, low thyroxine levels caused by hypothyroidism may lead to impaired brain development and cause functional deficits in the child. Hormones produced by the thyroid gland are an essential element in the process of neurogenesis, axon and dendrite growth, synapse formation, myelination and neuronal migration [33]. Symptoms that may occur in the event of significant iodine deficiency in pregnant women include:

hypothyroidism, increased serum TSH level, enlargement of the thyroid gland and goiter. However, iodine deficiency in the fetus significantly increases the risk of mental retardation, miscarriage, intrauterine fetal death and increased perinatal and neonatal mortality, as well as congenital hypothyroidism [34]. The main sources of iodine in the diet are iodized salt, dairy products, fish and eggs. It should also be borne in mind that not only deficiency, but also excess of this element may lead to negative health effects, including: hyperthyroidism or hypothyroidism, gastrointestinal disorders, heart rate disorders, and in severe cases of poisoning - coma. Taking into account the effects of inadequate iodine supply, it is currently recommended to supplement it for all pregnant women without a positive history of thyroid diseases at a dose of 150-200 mcg/d, while in the case of pregnant women with thyroid diseases, the dose of supplemented iodine should be adjusted based on test results for thyroid hormones and antithyroid antibodies [12,35].

Conlusions

This study highlights the significant impact of appropriate nutrition and properly selected supplementation of pregnant women on reducing the risk of numerous pregnancy complications and fetal development disorders. It draws attention to the importance of deficiencies and excesses of vitamins and minerals in the diet of women during the preconception period, all trimesters of pregnancy and lactation. During pregnancy, the body's energy demand and demand for individual nutrients increase. Correct weight gain during pregnancy is extremely important, as it is crucial for the proper development of the fetus. It was emphasized that both too low and too high an increase in the BMI value has negative consequences for the course of pregnancy and the developing child. Supplementation should be individually tailored to the patient and only complement her basic, well-balanced diet. The role of key ingredients used in the supplementation of pregnant women, i.e. iron, folic acid, vitamin D, DHA and iodine, was discussed. Supplementation of other vitamins and minerals is not routinely recommended to pregnant women without specific medical indications.

Author's contribution

Conceptualization, Samanta Gawryszczak, Justyna Górska; methodology, Izabela Halczuk, Bartłomiej Stachura; software, Anna Gliwa; check, Anna Gliwa, Katarzyna Nowak; formal analysis, Samanta Gawryszczak, Justyna Górska; investigation, Katarzyna Nowak, Samanta Gawryszczak; resources, Izabela Halczuk; data curation, Bartłomiej Stachura; writing-rough preparation, Katarzyna Nowak; writing–review and editing, Anna Gliwa, Justyna Górska; visualization, Samanta Gawryszczak; supervision, Bartłomiej Stachura; project administration, Samanta Gawryszczak; receiving funding, Justyna Górska.

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