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REVIEW ARTICLE

Vitamins, minerals and other micronutrient supplementations in pregnancy

Suplementación con vitaminas, minerales y otros micronutrientes durante el embarazo

Suplementação com vitaminas, minerais e outros micronutrientes durante a gravidez

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ABSTRACT

Introduction: adequate nutrition in pregnancy depends not only on a healthy diet, but also on the most effective way of taking vitamins, minerals and other nutrient supplementations. **Objective:** to describe aspects related to supplementation with folic acid, iron, iodine, calcium, vitamin B12 and omega-3 in pregnancy. **Method:** a systematic review was conducted between May 2022 and March 2023, concerning supplementation intake of vitamins and minerals in pregnancy. Electronic databases of biomedical scientific literature were reviewed such as: UpToDate, Science Direct, SciELO, PUBMED and LILACS. The search included articles published from 2016 to 2022. The key terms for searching in databases were: supplements "Vitamins", "Micronutrients", "Minerals", and "Pregnancy", in English and Spanish. **Results:** vitamin, minerals and different nutrients intake requirements has increased in pregnancy. An appropriate diet and the consumption of micronutrients in the form of supplements are the basic support for an adequate health status of the mother and the development the fetus; on the other hand, an adequate nutrition reduces the risk of congenital malformations, obstetric, fetal and perinatal complications. Not all pregnant women need the same amount of supplements, so it is necessary to identify those with a highest risk of presenting deficiency. **Conclusions:** supplementation of vitamins, minerals and other micronutrients in pregnancy is very important to reduce the risk of obstetric complications and fetal or perinatal anomalies.

Keywords: pregnancy; minerals; maternal nutrition; supplementation; vitamins

RESUMEN

Introducción: la adecuada nutrición en el embarazo depende no solo de la correcta ingesta de alimentos, sino también de una apropiada administración de vitaminas, minerales y otros nutrientes en forma de suplementos. **Objetivo:** describir aspectos relacionados sobre la suplementación con ácido fólico, hierro, yodo, calcio, vitamina B12 y omega-3, durante el embarazo. **Método:** se realizó una revisión sistemática entre mayo de 2022 y marzo de 2023 sobre la suplementación con algunas vitaminas y minerales durante el embarazo. Se revisaron bases de datos electrónicas de literatura científica biomédica como: UpToDate, Science Direct, SciELO y PUBMED, LILACS. Se realizó la búsqueda de artículos desde el 2016 hasta 2022. Los términos de búsqueda en las bases de datos fueron: suplementos "Vitaminas", "Micronutrientes", "Minerales", y "Embarazo", en inglés y en español. **Resultados:** los requerimientos de vitaminas, minerales y diferentes nutrientes aumentan en el embarazo. Una apropiada alimentación y el consumo de micronutrientes en forma de suplementos son el soporte básico para un adecuado desarrollo de la madre y del feto; por otra parte, una nutrición adecuada reduce el riesgo de malformaciones congénitas, complicaciones obstétricas, fetales y perinatales. No todas las embarazadas necesitan la misma cantidad de suplementos, por lo que es necesario identificar aquellas con mayor riesgo de presentar alguna deficiencia. **Conclusiones:** la suplementación de vitaminas, minerales y otros micronutrientes durante el embarazo es muy importante para disminuir el riesgo de complicaciones obstétricas y anomalías fetales y perinatales.

Palabras clave: embarazo; minerales; nutrición materna; suplemento; vitaminas

RESUMO

Introdução: a nutrição adequada durante a gravidez depende não só da ingestão correta de alimentos, mas também da administração adequada de vitaminas, minerais e outros nutrientes na forma de suplementos. **Objetivo:** descrever aspectos relacionados à suplementação com ácido fólico, ferro, iodo, cálcio, vitamina B12 e ômega-3, durante a gestação. **Método:**foi realizada uma revisão sistemática entre maio de 2022 e março de 2023 sobre a suplementação com algumas vitaminas e minerais durante a gravidez. Bases de dados eletrônicas de literatura científica biomédica como: UpToDate, Science Direct, SciELO e PUBMED, LILACS foram revisadas. A busca dos artigos foi realizada no período de 2016 a 2022. Os termos de busca nas bases de dados foram: suplementos "Vitamins", "Micronutrients", "Minerals" e "Pregnancy", nos idiomas inglês e espanhol. **Resultados:** as necessidades de vitaminas, minerais e diferentes nutrientes aumentam na gravidez. Uma dieta adequada e o consumo de micronutrientes na forma de suplementos são o suporte básico para um desenvolvimento adequado da mãe e do feto; por outro lado, uma nutrição adequada reduz o risco de malformações congênitas, complicações obstétricas, fetais e perinatais. Nem todas as gestantes precisam da mesma quantidade de suplementos, por isso é necessário identificar aquelas com maior risco de apresentar deficiência. **Conclusões:** a suplementação de vitaminas, minerais e outros micronutrientes durante a gravidez é muito importante para reduzir o risco de complicações obstétricas e anomalias fetais e perinatais.

Palavras-chave: gravidez; minerais; nutrição materna; suplemento; vitaminas

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INTRODUCTION

Micronutrients are vitamins and minerals needed by the body in very small amounts, but vital for normal functioning, growth and development. During pregnancy, women begin to have more deficiencies, due to the need to provide nutrition to the fetus as well. This is why there is a significant increase in maternal nutritional requirements[12,3,4] and both nutritional deficiencies and excesses can have an impact on pregnancy outcomes, milk quality and maternal-fetal health.[1,4]

Adequate nutrition in pregnancy depends not only on the correct intake of food, but also on the appropriate administration of vitamins, minerals and other nutrients in the form of supplements.[4]

On the other hand, nutritional deficiencies, even in pregnant women with adequate and varied diets, may appear selectively, due to low dietary protein contents and individual capacity for absorption and metabolism of nutrients.

The main deficiencies that may appear are: vitamins (folic acid, vitamin D, vitamin A and E), minerals (iron and iodine), macroelements (magnesium and calcium) and polyunsaturated fatty acids. Nutritional studies have shown that the diet of pregnant women, in general, lacks sufficient amounts of vitamins, minerals and other micronutrients.[5,6,7,8,9,10]

The World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics stress the importance of providing early care to all pregnant women with a focus on nutrition, health and lifestyle. Counseling on healthy eating should be provided to ensure adequate gestational weight gain, as well as nutritional treatment for conditions that may jeopardize the outcome of their pregnancy.[4]

The objective of the review is to describe related aspects of folic acid, iron, iodine, calcium, vitamin B12, and omega-3 supplementation during pregnancy.

METHOD

A systematic review was conducted between May 2022 to March 2023 on supplementation with some vitamins and minerals during pregnancy.

Electronic databases of biomedical scientific literature such as UpToDate, ScienceDirect, SciELO, PUBMED and LILACS, between others, were reviewed.

A search was made on systemic reviews, original articles, among others, from 2016 to 2022. In addition, information was obtained from clinical guidelines of the American College of Obstetrics and Gynecology and the Royal College of Obstetrics and Gynecology of the United Kingdom. The search terms in the databases were: supplements "Vitamins", "Micronutrients", "Minerals", and "Pregnancy", in English and Spanish.

The most relevant contributions on consumption and supplementation during pregnancy with folic acid, iron, iodine, calcium, vitamin B12 and omega-3 were included in this review.

From a total of 33 published articles, 27 were chosen for the review.

DEVELOPMENT

Vitamins and minerals are indispensable compounds for the growth, development and maintenance of the human organism, which need to be acquired through food. Plasma concentrations of many vitamins and minerals decrease during gestation, perhaps due to hemodilution; others are sensitive to heat, light, air and are eliminated by sweat. The most frequent deficiencies are of vitamin A, folate and iron.[4]

Folic acid (FA)

FA is responsible for the regulation of cell growth and division, especially in the digestive, nervous and hematopoietic systems. Its absorption occurs in the small intestine and it subsequently binds to plasma proteins and is converted into a coenzyme involved in nucleic acid synthesis.[10]

Folate deficiency both preconception and during the first 10 weeks of pregnancy is associated with cardiac malformations and neural tube defects.[4]

At present, women during the preconception stage have an inadequate intake of vegetables, cereals and FA.[5] Therefore, consumption of FA in the preconception period, during pregnancy and during lactation is essential.[4,10]

Adequate PA supplementation is associated with a decreased risk of neural tube defects (NTDs), fetal congenital heart and urinary disorders. It also reduces the risk of spontaneous abortion and maternal thrombosis. Supplementation during the second and third trimesters of pregnancy prevents megaloblastic anemia secondary to vitamin B12 and folate deficiency.[10]

Hernandez, *et al.*[11] states that in the international guidelines proposed by the WHO, the use of FA supplementation is recommended at a dose of 400 mcg/day. Mejía[10] describes that its consumption should be initiated 6 weeks before conception.

In women with a history of NTD in previous pregnancies, 4 mg/day is recommended. The optimal dose of FA that reduces the risk of NTD and other congenital defects is still unknown.[12]

It is worth noting that co-administration with vitamins (B6, B12 and C) facilitates its absorption.[10]

The Society of Obstetricians and Gynecologists of Canada also states that in all women at low risk of developing NTDs and with a low-risk partner (no personal or family history of folic acid-sensitive birth defects), 400 mcg/d of folic acid should be supplemented starting 3 months before conception. This should be maintained during pregnancy and up to 4 to 6 weeks postpartum or for the duration of breastfeeding. It is important to emphasize that in addition to supplementation, counseling should be provided to women to increase their consumption of foods that are good sources of folate.[12]

However, the Royal College of Obstetricians and Gynecologists (RCOG) recommends that women with obesity [body mass index (BMI) greater than or equal to 30, starting at least 1 month before and continuing during the first trimester of pregnancy] and with hereditary anemias (thalassemia or sickle cell disease, starting 3 months before pregnancy) should be supplemented with 5 mg/day of folic acid[12,13].

The authors of the present study are of the opinion that since malformations occur during the first 28 days of gestation, when the woman may be unaware that she is pregnant, it is advisable to increase the consumption of green leafy vegetables prior to pregnancy.

Iron

The increased demand for iron during pregnancy may not be sufficiently met by dietary intake alone, which regularly provides between 10 mg - 15 mg of the mineral. As a consequence of this, and in the absence of supplementation therapy, a negative balance of body iron levels will occur: unless body iron stores are greater than 200 mg, iron depletion will occur, and anemia will set in.[14]

In pregnant women, given their greater need for iron due to the presence of the fetus, a requirement of 2 to 4.8 mg/day is suggested. Based on this, it is assumed that a woman should consume between 20 and 48 mg of iron in the diet to absorb this daily amount, on the hypothesis that from food consumption only 10% of the iron contained will be absorbed in the enterocytes.[8]

At present, there is abundant literature describing that both iron deficiency and iron overload are associated with undesirable health effects.[4,9] In Germany, for example, as in other developed countries, iron supplements are only recommended for pregnant women diagnosed with iron deficiency/iron deficiency anemia.[9] This contrasts with the regulations in Peru, where the Ministry of Health orders mandatory compliance with iron supplementation for pregnant women, whether or not they are anemic.[8]

It is estimated that 1.62 billion people suffer from anemia, of which the most vulnerable populations are pregnant women and children between 6 and 59 months of age.[8] In pregnant women, it is estimated that 41.8 % of them suffer from anemia.[4,11]

Gonzales and Olavegoya[8] state, according to WHO, that iron deficiency is the main cause of anemia, particularly in countries of medium and low economic development.

Iron deficiency anemia has been related to prematurity, intrauterine growth restriction, low birth weight, deficits in cognitive development of newborns, infectious diseases and increased perinatal and maternal morbidity and mortality.[4,11,15]

The WHO recommends that pregnant women should supplement with 30-60 mg/day of elemental iron and that those who are anemic should preferably supplement with 60-120 mg/day of iron.[11]

Silva, *et al.*(14) highlight the emergence of Trofín® as an antianemic that delivers heminic iron, is immediately absorbable and has enjoyed high therapeutic tolerance.

The use of Trofín® derivatives as part of new antianemic preparations in Cuba is an additional gain on the technological development that has resulted from the appearance of this drug. Such is the case of CombiFer®, which has been specifically designed to meet the iron needs generated during pregnancy.[14]

The greater effectiveness of CombiFer® was evident from the first sampling time of the trial, done between 28 - 30 weeks of pregnancy. Treatment with this compound produced increases in mean hemoglobin (Hb) values and in the number of pregnant women with Hb ≥ 110 g.L-1. Women treated with CombiFer® always showed higher Hb values. In addition to the above, the excellent tolerance observed after its use would support the systematic use of this antianemic preparation.[14]

Iodine

Iodine is essential for the formation of thyroid hormones. Iodine deficiency during pregnancy and lactation affects the thyroid function of the mother and the neonate, as well as the neuropsychological development of the child. In this sense, it has been related to the development of maternal goiter, spontaneous abortions, perinatal mortality, congenital anomalies, growth restriction, alterations in fetal and neonatal brain and neurological development.[10,15]

It should be noted that even with the consumption of iodized salt used universally, the desired iodine levels are not reached, so in some countries it is administered in the form of supplements. The American Thyroid Association (ATA) recommends taking 150 µg/day of iodine as a supplement. In Spain, they recommend the consumption of iodine supplements of 200 µg/day in those women who do not reach the recommended daily amounts.[11] The requirements during pregnancy are 160 µg/day.[10]

The present authors, in the searches performed, identified that the Royal College of Gynecology and Obstetrics of the United Kingdom is not in favor of recommending iodine supplements, because it refers that in its population the required daily levels are reached through the intake of foods containing this trace element.[11,13]

Calcium

Calcium is the most abundant mineral in the body and is essential for several processes, such as: bone formation, muscle contraction and enzymatic and hormonal function.[11] Its deficiency states are related to osteopenia, muscle cramps and preeclampsia. Given that its absorption is increased in pregnancy, supplementation is not recommended for mothers with adequate intakes (three dairy products/day) but should be reserved for pregnant women with insufficient intakes and/or at risk of preeclampsia.[4,16]

A systematic review identified the effects of calcium and vitamin D supplementation on preeclampsia and the risk of gestational hypertension or pregnancy-induced hypertension. It is suggested that calcium supplementation could cause a significant reduction in the risk of preeclampsia, gestational hypertension, or pregnancy-induced hypertension in approximately 50% and 25% of cases, respectively, compared with placebo administration.[17,18]

Another systematic review, cited by the Pan American Health Organization (PAHO)[17], identified that low-dose calcium supplementation caused a reduction in the incidence of preeclampsia, with a relative risk (RR) of 0.36 (95% confidence interval [95% CI95%]: 0.23 - 0.57); in another group, calcium supplementation with or without additional supplementation reported a RR of 0.38 (95% CI: 0.28 - 0.52), low-dose calcium supplementation plus linoleic acid a RR of 0.23 (95% CI: 0.09 - 0.60), and low-dose calcium supplementation plus vitamin D a RR of 0.49 (95% CI: 0.31 - 0.78).

Based on these considerations, it becomes necessary to establish guidelines to indicate calcium supplementation in women, in particular: those who intend to become pregnant, those with a higher risk of hypertensive disorders associated with pregnancy and pregnant women, for the prevention of preeclampsia and its complications.[17]

Calcium supplementation during pregnancy for the prevention of preeclampsia and its complications in populations with low dietary intake should be 1.5 g - 2 g of oral elemental calcium[11,17]; whereas before pregnancy it is recommended only in the context of rigorous research.[17]

The authors, in their search, found out that the total calcium dose should be divided into three doses with the main meals, which would provide in each one, 500 mg of elemental calcium. In the same way, they suggest that calcium intake should be separated from iron intake, so as not to decrease iron absorption.

Vitamin B12

It is related to folate and homocysteine metabolism and is involved in cell metabolism and DNA synthesis.[19]

A systematic review of longitudinal cohort studies reported that low maternal vitamin B12 levels were associated with an increased risk of preterm delivery. In the United States, the recommended daily allowance of vitamin B12 is 2.6 µg/day in pregnancy and 2.8 µg/day during lactation. Most pregnant women in the United States ingest the daily requirement of vitamin B12, so they do not need supplements.[20]

It should be noted that only foods of animal origin, such as fish, meat, poultry, animal offal, eggs, and dairy products contain vitamin B12; thus, pregnant women who eat a vegetarian diet or who do not consume the above-mentioned foods are at increased risk for vitamin B12 deficiency and should take a supplement.[21]

The main author refers that, in many sectors of Ecuador, the consumption of foods rich in vitamin B12 is deficient, so it should be administered in the form of a supplement.

In the search carried out, no articles were found that reflected the doses of vitamin B12 supplementation in pregnancy.

Omega-3

Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are two long-chain polyunsaturated fatty acids (LCPUFA n-3) also known as omega-3, obtained mainly from fish or sea products. DHA is necessary for normal brain and retinal development in the fetus, as well as favorable cognitive development in offspring. LCPUFA n-3 have anti-inflammatory effects that have been associated with a reduction in preterm birth.[10]

Among the omega-3 polyunsaturated fatty acids, DHA is the most important for pregnancy and lactation. Different researchs have shown that they have beneficial effects on the obstetric-perinatal outcome: increased newborn weight (without increasing the risk of macrosomia), reduced risk of preterm delivery and correct psychomotor development of children in the first years of life. Adequate intake in the maternal diet reduces the risk of alterations in oxidative stress and inflammatory markers.[10]

Foods rich in polyunsaturated fatty acids are: fish and other seafood (tuna, herring, and sardines), nuts and seeds (flaxseed and chia) and plant oils (flaxseed, and soybean). The recommended dose is 600 mg/day (preferably before 20 weeks of pregnancy and during lactation). In case of insufficient intake from natural sources, low unsaturated fatty acids diet or high risk of preterm delivery, it can be increased up to 1,000 mg/day. To date, there are no reports of symptomatology related to omega-3 fatty acid overdose.[10]

Dietary guidelines recommend that pregnant women consume 8 to 12 oz of seafood per week. The number of weekly servings of fish needed to achieve the DHA intake target of 200 to 300 mg/day depends on the type of fish. It is important to note that pregnant women and those planning to conceive should choose fish with low mercury content.[20]

Omega-3 fatty acid and choline are two micronutrients that are being recommended in recent times in some countries; however, there is some controversy in their use. The American College of Gynecology and UpToDate recommend them, in contrast to the Royal College of Gynecology of the United Kingdom, which does not advise their use; although it is reported in the literature that they are two micronutrients that are related to the improvement of cognitive development in the newborn.[21,22,23,24]

The present authors emphasize that when pregnant women cannot consume fish in adequate amounts, supplementation with LCPUFA n-3, consumption of ground flaxseed or flaxseed oil, which is also a good source of this micronutrient should be recommended. Other sources of this fatty acid include broccoli, cantaloupe, beans, spinach, cauliflower and nuts.

Regarding vitamins and micronutrients in general, Kominiarek,[23] Güler[25] and Xiang[26] agree that iron, folic acid and calcium are essential during pregnancy. They also state that there are other supplements with more controversy in their use, such as iodine, vitamin B-12, omega-3 and choline, which have recently begun to be recommended for pregnant women.

The consumption of micronutrients increases the possibility of good obstetric outcome and reduction of the risk of complications.[27] Nutritional studies show that about a quarter of pregnant women admit to using different supplements during gestation, despite the lack of medical recommendations for their consumption.[10,27]

FINAL CONSIDERATIONS

The authors reaffirm the importance of micronutrient supplementation during pregnancy under medical prescription to avoid overdose. They also claim that since the diet in several cases is not balanced and nutritional needs are not met, vitamin and mineral supplementation is necessary, especially folic acid, iron and calcium, to provide adequate levels and thus avoid maternal, fetal and perinatal complications.

Supplementation of vitamins, minerals and other micronutrients during pregnancy is very important to reduce the risk of obstetric complications and fetal and perinatal anomalies.

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Conflict of interest:
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