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Pregnancy outcome following various doses of antioxidants such as Vitamin E supplementation – current state of knowledge

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Abstract

Introduction and purpose: Vitamin E is an antioxidant substance. It has been noted that the pathomechanism of many diseases in pregnancy is rooted in oxidative stress. Much of them have an incompletely understood mechanism, and thus treatment is not as effective. Vitamin E is a readily available and important antioxidant. It is reasonable to investigate whether there are links between supplementation with this vitamin and improved outcomes of conditions in pregnant women. Conditions such as preeclampsia (also in a group of women with type 1 diabetes), preterm premature rupture of membranes, spontaneous preterm birth, respiratory diseases were considered.

Material and method: The literature was reviewed in the Pubmed database, GoogleScholar, in the Via Medica journal database, the positions of the Polish gynecological society with the use of keywords.

State of knowledge: According to the cited studies, routine use of vitamin E in combination with other supplements has no discernible benefit. No differences were found in groups taking antioxidants from placebo groups in the context of pregnancy diseases. There were side effects of supplementation and for this reason supplementation with this antioxidant should not be ordered without clear indications.

Conclusions: The information gathered does not indicate the usefulness of vitamin E supplementation in pregnancy. The issue of the use of antioxidants in the fight against diseases that occur during pregnancy requires further research.

Key words: Vitamin E; Pregnancy; Antioxidant

Introduction

Vitamin E is a fat-soluble vitamin, the function of which is chain-breaking antioxidation.[1,2,3] It conditions the normal structure of biological membranes and protects them.[4] Vitamin E, in fact, is a group of organic chemical compounds that includes tocopherols and tocotrienols. In both groups, there are 4 forms: α, β, γ and δ, which differ in the number of methyl substituents at the phenyl ring. Natural sources of vitamin E include oils (wheat germ, sunflower), almonds, hazelnuts, peanuts.[5] Vitamin E deficiency caused by dietary deficiencies in humans is rare[6]. The more common grounds are premature low birth weight, disrupted fat malabsorption, mutations in the tocopherol transfer[7]. Plasma or serum acceptable alpha-tocopherol concertation status is between 11.6-16.2 mumol/l.[8] The average intake is between 5 and 11 mg/day for adults consuming a typical mixed diet.[9] The results of studies conducted in selected population groups showed, in most cases, that vitamin E intake covered the dietary standards for this vitamin.[10]Losses of vitamin E due to pregnancy are minimal, so recommendations for its consumption are usually unchanged.

There is ample evidence that oxidative stress affects the development of conditions such as pre-eclampsia, miscarriage, PROM.[11]

Pre-eclampsia is a condition that occurs during pregnancy, characterized by elevated blood pressure and urinary protein loss. The complicated and incompletely understood pathophysiology of pre-eclampsia prompts exploration of this topic and the search for possible other causes and treatments.[12] Oxidative stress is suspected to be one of the pathomechanisms of the disease.[13]

Pre-eclampsia occurs several times more frequently in pregnant women with type 1 diabetes.[14] Diabetes is associated with increased production of free radicals, depletion of antioxidants.[15]

Premature rupture of membranes (PROM) is the result of collagen damage in the chorionic sac leading to rupture. Isoprostanes (F(2)-IP), produced by the attack of reactive oxygen species (ROS) on polyunsaturated fatty acids, are involved in the mechanism of this reaction and are a reliable predictive indicator of the risk of premature PROM.[16]

Oxidative stress is associated with an increased risk of preterm labor, particularly spontaneous preterm labor, and delivery before 34 weeks of gestation.[17]

Premature infants do not have a well-developed antioxidant defense system and are exposed to increased production of reactive oxygen species.[18]

Oxidative injury is an essential part of lung damage, which begins as acute inflammatory damage in CHD and then evolves into chronic and structural scarring leading to bronchopulmonary dysplasia.

Despite its beneficial antioxidant activities, vitamin E also has side effects, such as nausea, diarrhea, intestinal cramps, fatigue, weakness, headache, blurred vision, etc. Therefore, it is necessary to compare the benefits of its use with the disadvantages.

Vitamin E administration

Table 1. Available capsule size[19]

Capsule size [international units]
100
200
400
600
1000

Table 2. Adult dosing

Vitamin E deficiency	60 to 75 units by mouth per day
Cystic fibrosis patients	100 to 400 units by mouth per day
Tardive dyskinesia (Off-label indication)	1600 units by mouth per day

Table 3. Maximum pediatric dosing

1 month to 3 years of age	200 units daily
4 to 8 years of age	300 units daily
9 to 13 years of age	600 units daily
14 to 18 years of age	800 units daily

Purpose

It has been noted that the pathomechanism of many diseases in pregnancy is rooted in oxidative stress. Vitamin E is a readily available and important antioxidant. It is reasonable to investigate whether there are links between supplementation with this vitamin and improved outcomes of conditions in pregnant women.

The paper presents the current state of knowledge on effect of vitamin E supplementation on the course of pregnancy and the health of the child. The goal was to summarize the data available in the literature, as well as recent reports and studies, that address vitamin E supplementation in pregnancy and to see if there are any benefits or risks associated with this supplementation. Adverse events and side effects were considered.

Material and methods

A review of the available literature in the Pubmed database, GoogleScholar, in the Via Medica journal database, the positions of the Polish gynecological society was performed. The articles were searched based on keywords “Vitamin E”, “pregnancy”, “preeclampsia”, “antioxidant”, “oxidative stress”, “PROM”. The search provided 2553 scientific papers, of which, after rejecting papers that did not meet the authors' criteria, were included 19 research in this paper.

State of knowledge

Supplying vitamin E to the fetal-placental unit

The first issue that needs to be checked is whether the vitamin E could be delivered to the fetal-placental unit through maternal oral supplementation. It has been proven[20] that maternal

plasma vitamin E levels increase with oral supplementation. Maternal plasma vitamin E concentrations correlate with vitamin E in the chorioamnion.

Preeclampsia

Four[21,22,23,24] papers examined the effect of supplemental antioxidant vitamins on the rate of preeclampsia in high-risk pregnant women. The incidence of preeclampsia was not significantly different between the groups of women taking antioxidants and the placebo groups.

One study[25] compared women who were at high risk and who were taking vitamin supplements with 2 other groups of women: one who took a placebo and one who had a low risk of preeclampsia. The aforementioned supplementation in women at higher risk of preeclampsia was associated with improved biochemical indices of the disease.

In women at low risk of preeclampsia, the results[26] also show that vitamin E supplementation did not reduce the rate of adverse maternal or perinatal outcomes associated with pregnancy-related hypertension.

In a paper that evaluated the benefits of supplementation in the form of prolongation of pregnancy and biochemical assessment of lipid peroxides and antioxidants showed that supplementation had a positive effect on the aspects studied, however these results do not encourage the routine use of antioxidants against pre-eclampsia.

It also assessed[27] the development of superimposed preeclampsia, the severity of hypertension, the need for hospital admission, the need for increased antihypertensive medications, and small size relative to gestational age (<fifth non-standard centile of birth weight). Results did not show any significant benefit of vitamin supplementation. There was some trend in lessening of hypertensive complications of pregnancy.

High doses of antioxidants used during pregnancy also have no proven beneficial effect in preventing preeclampsia in women at risk. They increase the percentage of babies born with low birth weight.[28]

Diabetic pre-eclampsia

The authors of one study[29] tested whether vitamin E supplementation reduces the incidence of preeclampsia in women with type 1 diabetes. Vitamin E supplementation in pregnant women with type 1 diabetes did not reduce the risk of preeclampsia. However, the possibility that vitamin supplementation may be beneficial in women with low antioxidant status at baseline requires further study.

It was discussed[30] whether the Hp phenotype affects the risk of preeclampsia or the effectiveness of vitamin E in preventing preeclampsia in women with type 1 diabetes. The conclusion of the study is that the Hp phenotype did not significantly affect the risk of preeclampsia in women with type 1 diabetes.

Preterm premature rupture of membranes

Another condition being looked at is PROM and PPROM. It has been investigated whether maternal antioxidant supplementation is associated with prolonged pre-pregnancy latency period and occurrence of these diseases. Two studies[31,32] found that there is no proven benefit of antioxidant supplementation in reducing PROM and PPROM in single or multiple pregnancies. It was shown, admittedly, that the use of vitamin E in women with PPROM is associated with a longer latency period before delivery, but adverse neonatal and maternal outcomes were similar between the placebo group and vitamin group.

Spontaneous preterm birth

Both preterm births associated with premature rupture of membranes (PROM) and the total number of spontaneous preterm births (spontaneous preterm birth associated with PROM or spontaneous labor) were examined. The study was conducted in nulliparous women and involved vitamin E supplementation between the 9th and 16th week of pregnancy. Antioxidants did not reduce spontaneous preterm births.[33]

Respiratory diseases

It was tested whether supplementation with high doses of vitamin E in pregnant women would result in subsequent good effects on fetal lung development and growth, as well as reduced infant respiratory morbidity. According to the results[34], high-dose antioxidants not only do not improve infant respiratory outcomes but are also associated with increased health care utilization and costs of care.

Vitamin E supplementation in smoking pregnant women

As with non-smoking pregnant women, vitamin E has no effect on the development of preeclampsia in smoking pregnant women. However, vitamin E supplementation was associated with a reduction in placental abruption and a reduction in preterm labor among smokers.[35]

Discussion and conclusion

According to the cited studies, routine use of vitamin E in combination with other supplements has no discernible benefit. No differences were found in groups taking antioxidants from placebo groups in the context of diseases such as preeclampsia (also in a group of women with type 1 diabetes), preterm premature rupture of membranes, spontaneous preterm birth, respiratory diseases. In women smokers also no advantages were noted. Supplementation was associated with a reduced risk of placental abruption, which requires further study. There were side effects associated with the need for more frequent use of health care services. There was no convincing evidence that vitamin E supplementation in combination with other supplements has any other significant benefits or harms.

The information gathered does not indicate the usefulness of vitamin E supplementation in pregnancy. The issue of the use of antioxidants in the fight against diseases that occur during pregnancy requires further research.

Disclosures

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