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Dietary Folic Acid Supplementation and its Role in the Prevention of Neurological Developmental Disorders

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Abstract

The promotion folic acid role as well as the consumption of folate rich foods for the prevention of congenital malformations of the neural tube is of particular importance. A large number of women who are not aware that the consumption of one of the following foods is as important as the medical supplementation of folic acid; wheat, soy, vegetables and dried fruits, whole grain bread, barley, lentils, ripe beans, beer yeast, sprouts, asparagus, broccoli, peas, tomatoes, cabbage, cauliflower, as they contain natural folate's that could reduce the risk of NDT as well as promote health fetal development as well as the mother in the weeks to come.

Keywords: Prevention; Dietary; Folic acid; Congenital malformations; Medical supplementation; Fetal development

Abbreviations: NTD; Neural-Tube Defects; MTHFR: Methylene Tetra Hydrofolate Reductase; NMDA: N-Methyl-D-Aspartate; AFP: Alpha-Fetoprotein

Introduction

In the human body, the folate is involved in enzyme reactions in the form of coenzymes, the active form of which is 5 methyl-tetrahydrofolic acid, involved in the construction of purine and pyrimidine bases in the conversion of serine to glycine and homocysteine to methionine which is an essential process in the human organism allowing DNA synthesis to take place [1]. Folic acid is a water-soluble vitamin from the B complex group. Our body is unable to produce folic acid nor can it store reserves for long periods of time. Natural folate's found organically are unstable and quickly lose their activity during food processing and storage. Absorbed folate's are transported to the liver and plasma as well as red blood cells, where folic acid is bound to glutamate and iron to form haemoglobin. Natural reserves of folate in the body are relatively short-lived and run out quickly.

Our minimum daily need for folic acid is 50-100mg. Blood reference range is from 7 to 15ng/ml. During pregnancy, folic acid needs double as compared to the normal physiological needs due to increased maternal erythropoiesis, as well as fetal needs and fetal tissue growth.

Discussion

In 1968, Hibbard et al. found that malformations of the central nervous system, and in particular neural tube defects, were due to disorders in the metabolism of folic acid [2]. Its deficiency is associated not only with Neural-tube defects (NTD), such as spina bifida, anencephaly, encephalocele, craniorachischisis, etc., but also with other fetal developmental disorders such as stillbirths and premature birth, spontaneous abortions, preeclampsia, placental abruption, hydrocephalus, cleft lip, cleft palate, Down syndrome, mental retardation, heart defects [3].

Neural tube defects occur at the 3rd and 4th weeks of the embryonic development due to defects in the closure of the neural tube. The risk of pregnancy with NTD is higher in families with history of NDT's (the risk of recurrence is estimated at 1 in 35) but can be reduced by changing the environmental factors - such as taking folic acid and other vitamins in the pre-conception period and the first 3 months of pregnancy [4].

The onset of NTD is associated with both genetic and environmental factors. Recently, a link between NTD and the enzyme methylene tetra hydrofolate reductase (MTHFR) have been suspected. Some authors assume that the thermo labile form of (MTHFR) is a risk factor for the onset of NTD due to decreased enzyme activity which increases the plasma homocysteine in pregnant women. To date, 24 mutations have been detected in the gene that codes this enzyme and polymorphism with the gene variants C677T and A1298C.

In recent years a lot of attention was given to neural tube defects and their association to an increase in serum homocysteine in pregnant women. Methylation of homocysteine to methionine

requires: 5-methyltetrahydrofolate, methionine synthase and its co-factor vitamin B12. Therefore, Mills assumes that maternal hyperhomocysteinemia is due to an enzyme dysfunction [5]. Animal studies show, methionine synthase being the responsible enzyme for these effects. It is also thought that a disfunction in the cystine synthesis gene - CBS, 236200 had coronation to NDT's but Ramsbutton et al. [6] couldn't find significant evidence for such correlation in Ireland [6].

Rosenquist presents two hypotheses that explain the relationship between folate's and malformations of the first states that direct decrease in the supply of folic acid to embryonic tissue disrupts tissue limiting the proliferation of neuroepithelial cells [7].

The second hypothesis is based on an indirect and genetic cause associated with a metabolic disorder of methionine as a consequence of folate deficiency. This disorder results in an increase in maternal homocysteine, which in turn inhibits the function of a whole group of N-methyl-D-aspartate (NMDA) neuropeptide levels. This disorder affects the gene receptors of folate, the regulatory genes of methionine homocysteine and the NMDA gene receptors.

Numerous studies highlight the role of folic insufficiency in the development of NTD during the first trimester and the importance of its supplementation in pregnancy to avoid the development of NTD. After folic acid supplementation started in the period 1996-2006, there was a reduction of anencephaly by 32%, spina bifida by 23% and encephalocele by 34% compared to the period 1980-1992 [8].

Alcohol is known to inhibit methionine mediated folic acid synthesis by cutting off methylation processes. According to Liu Y, the most prominent changes are in the genes of chromosomes 7, 10 and X [9]. Early diagnosis and prophylaxis are essential in the fight against NDT and should include the testing of alpha-fetoprotein (AFP) in pregnant women's serum. AFP is a glycoprotein of fetal origin that is synthesized from the yolk and liver. It is transported through the placenta to the mother's blood. Its concentrations in amniotic fluid and maternal serum are highest at around 13 weeks. AFP levels are examined between 15 and 19 weeks using a blood sample taken from the mother.

Early prenatal diagnosis for the detection of fetal abnormalities is performed by trans-vaginal ultrasound with a special transducer at 6-7, 18-20g. w. of pregnancy. The combination of these two methods allows detection of NTD in 90% of cases. Prophylaxis of congenital CNS abnormalities includes supplementation with folic acid, 400 micrograms per day at least 3-4 months before conception and until the end of the first trimester.

Modern trends in dietetics explain the importance of healthy diets containing enough natural folate's which are very important in the fight against congenital abnormalities of CNS [10]. Recent studies confirm the high biological content of natural folate in food. For example, low levels of spina bifida in some southern European countries are explained by their-Mediterranean diet, which is naturally rich in folate, the diet consists of vegetables, different types of beans, grains, fruits, vegetable fats, nuts, wines and fish, and less potatoes and sugar [11]. A risk factor for spina bifida and encephalocele are caffeinated beverages and the development of caffeine tolerance [12]. A protective effect is attributed to tea as an anti-oxidant for the flavanols, catechin and epicatechin, but according to some authors, caffeine-containing tea is associated with an increased risk of encephalocele [13].

Conclusion

The promotion of the role of folic acid as well as plant foods for the prevention of congenital malformations of the neural tube is of particular importance. There is a large number of women who are not aware that the consumption of one of the following foods is as important as the medical supplementation of folic acid ; wheat, soy, vegetables and dried fruits, whole grain bread, barley, lentils, ripe beans, beer yeast, sprouts, asparagus, broccoli, peas, tomatoes, cabbage, cauliflower, as they contain natural folate's that could reduce the risk of NDT as well as a healthy diet is important for the development of the fetus swell as the mother in the weeks to come [14].

Conflict of Interest

All authors declare no economic interest or any conflict of interest.

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