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A Review on Maternal Folic Acid and Supplementation

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ABSTRACT

Folate (vitamin B9) is a necessary nutrient for DNA replication as well as a variety of enzymatic processes involved in amino acid synthesis and vitamin metabolism. Because folate is necessary for the fetus's growth and development, demand for it rises throughout pregnancy. Folate deficiency has been linked to birth defects in both mothers and babies (anaemia, peripheral neuropathy) (congenital abnormalities). The metabolism of folic acid, the appropriate use of folic acid supplementation in pregnancy, and the potential benefits of folic acid are discussed in this article, as well as the use of l-methyl folate supplementation for the prevention of pregnancy-related complications other than neural tube defects.

Keywords: DNA, Folic Acid Supplementation, Congenital Abnormalities, Anaemia, Peripheral Neuropathy

I. INTRODUCTION

Folate is required for physiological nucleic acid synthesis and cell division, gene expression regulation, amino acid metabolism, and neurotransmitter synthesis in the one-carbon metabolism [1]. Increased folate intake is essential during pregnancy for the uterus' and placenta's rapid cell proliferation and tissue growth, as well as the foetus' growth and expansion of the maternal blood volume [2]. Pregnant women's folate requirements are 5- to 10-fold higher than non-pregnant women's [3].

As a result, folate insufficiency in pregnant women is a possibility.In human health, adequate periconceptional folate supply is critical; the link between maternal folate status and foetal neural tube abnormalities (NTDs) and other congenital deformities is widely recognised. In most countries, women are advised to take folic acid supplements during the periconceptional stage at a dose of 0.4 mg per day if they are considering a pregnancy and 4 mg per day if a prior pregnancy was affected by NTD [4]

Natural folate in foods, folic acid dietary supplements, and folic acid-fortified foods are the main sources of folate. Since 1998, folic acid has been added to cereal grain products in the United States [6]. This fortification initiative has been extremely effective in reducing the prevalence of NTDs in the US population, even when no additional folic acid supplements are used [5,6].

Impaired neurodevelopment and/or autism in children have significant emotional, societal, and

economic consequences. Specialized education and other community resources will be required for these children. Although these newborns' chances of survival and life expectancy are unlikely to be harmed, many of them will require treatment throughout their lives, at a significant expense to the public health care system. When they reach adulthood, they become more productive. Indirectly, the societal burden is often higher than in people with normal development. [7]

Folic acid and neural tube defects

Birth defects are a serious public health concern, with the Centers for Disease Control and Prevention (CDC) estimating that one out of every 33 infants in the United States has a birth defect, accounting for more than 20% of all infant deaths [8,9]. The neurulation of the brain and spinal cord develops between 21 and 28 days after conception in humans, and neural tube abnormalities (NTDs) are prevalent complicated multifactorial disorders [10]. The prevalence has been observed to range between 1 and 10 in every 1000 births or established pregnancies worldwide, depending on ethnic grouping and geographic region [11]. While we are still learning about the underlying causes, data suggests that both genetic and non-genetic variables, such as maternal nutritional status or obesity, have a role in the emergence of NTDs [12-13]. Several research, including community-based trials, have suggested that NTDs are vitamin deficiency illnesses and that exogenous or periconceptional maternal FA supplementation can reduce the incidence of NTDs in children [14].

History and impact of folic acid on public health

Callender [15] proposed a link between apparent folate insufficiency and an increased incidence of preterm as early as 1944. This was later confirmed by Gatenby and Lillie [16], and in the 1960s, Richard Smithells and Elizabeth Hibbard hypothesized that undernutrition or impaired folate status could be a significant factor in the origin of NTD based on significant observations that women who had given birth to children with birth defects such as anencephaly and spinabifida have an altered formiminoglutamic acid compared to women who had given birth to unaffected children had an altered form [17]

Folate metabolism

FA is essential for folate-dependent one-carbon metabolism, which is involved in a variety of cellular activities. Amino acid metabolism, purine and pyrimidine biosynthesis (the building blocks for DNA and RNA synthesis), and the creation of the principal methylating agent S-adenosyl-methionine (SAM), which is the universal methyl donor for DNA, histones, proteins, and lipids, are all involved. [18] Both receptors and specialised carriers that are active across cell membranes [19] aid in the transport of transmembrane folate. Natural dietary folate is absorbed in the intestine and/or liver under normal conditions and converted predominantly to 5-methyl tetrahydrofolate (5-methylTHF), which is then polyglutamated for cellular retention. FA eaten in fortified foods/supplements, on the other hand, is first transformed to dihydrofolate by the liver enzyme dihydrofolate reductase and then to tetrahydrofolate (THF), the substrate for polyglutamate synthetase. The primary folate acceptor molecule in the one-carbon cycle is the polyglutamyl form of tetrahydrofolate (THF), which can be made from FA or normal dietary folate. Following that, vitamin B6-dependent serine hydroxy methyltransferase converts THF to 5,10-methyleneTHF, which is subsequently permanently reduced to 5-methylTHF by methylenetetrahydrofolate reductase (MTHFR). For the remethylation of homocysteine to methionine, 5-Methyl-THF serves as a major methyl donor. S-adenosylmethionine (SAM) is a major substrate for DNA methyltransferases (DNMTs), which catalyse the methylation processes that result in 5-methylcytosine [20-22]. Several folate coenzymes so control the overall FA metabolism. The essential job

of this coenzyme in the metabolic pathway is to control it by receiving or giving one-carbon units [23]. Methylenetetrahydrofolate reductase (MTHFR), methionine synthase reductase (MTRR), reduced folate carrier (RFC), and vitamin B12-dependent methionine synthase (MTR) are key genes in this pathway that are involved in transferring the methyl group to homocysteine and have been extensively studied [24].

Folate intake and concern about potential adverse effect

The clinical significance of a chronic or high FA intake has yet to be determined. Epidemiological studies after fortification have found that FA intake increased by around twice as much as previously predicted. Concerns have been raised about the potential health impacts, because, in addition to fortified food, broad supplementation is common, including over-the-counter prenatal vitamins and energy drinks that are significantly supplemented with multiple vitamins. [25,26] In a recent mouse investigation, we discovered that a ten-fold increase in maternal FA supplementation during pregnancy changed the expression of numerous genes in the frontal cortex of day-old pups [27]. Furthermore, offspring from moms who received lower doses of prenatal FA supplementation showed behavioural changes in the post-weaning period as compared to offspring from mothers who received higher doses of gestational FA supplementation. Such behavioural changes could be the result of abnormalities in gene expression as a result of abnormal methylation, according to the mechanism.

Maternal folate intake and health outcomes in children

Effects of dietary fatty acids on the health of newborn newborns [28] While the findings of a number of cohort and observational research in the United States and Canada. Although clinical relevance of FA supplementation has been recorded in Chile, Australia, and other European and Asian nations, the direction of the therapeutic impact has not always been Favourable. As a result, numerous governments have mandated FA fortifications, and despite their effectiveness, there is no general agreement based on published evidence [29]. The issue of the proper dose and possible adverse effects is still being debated [13,30]. Because maternal FA can have potential epigenetic effects on the offspring's DNA, which can vary depending on metabolic aptitude, sex, geographic location, or interactions with other nutrients, one possible reason for disagreement between research could be changes in study design.

Additional Benefits of Folic Acid Supplementation

In addition to preventing NTD, folic acid supplementation during pregnancy appears to have a number of other advantages, including the protection of congenital heart disease and oral clefts [31-34], as well as perhaps premature birth. The method by which folic acid protects the foetus from structural abnormalities is unknown, however it may involve homocysteine metabolism regulation. [35] Folic acid supplementation may have extra benefits on pregnancy outcome, according to several researchers. Pregnancies exposed to folic acid antagonists have significantly increased risks of placenta-related pregnancy problems, according to epidemiologic research. [36-39] Folic acid antagonists are a class of medications that are used to treat a wide range of clinical conditions, including seizure disorders, mood disorders, and urinary tract infections. Folic acid antagonists are divided into two categories: (a) DHFR inhibitors (e.g., sulfamethoxazole-trimethoprim), which prevent folate from being converted to more active metabolites (Figure 1), and (b) other folic acid antagonists, which include anticonvulsant medications (phenobarbital, phenytoin, primidone, and carbamazepine), as well as Spasmophen (Pregnancies exposed to DHFR inhibitors (n = 12,546) or other folic acid antagonists (n = 1565) were shown to have a higher chance of developing preeclampsia

(adjusted odds ratio [OR] 1.52; 95 percent confidence interval [CI], 1.39–1.66), according to one study. [38] These negative outcomes have one thing in common: they all appear to be caused by early-stage implantation and placentation problems. Because folic acid has been found to influence trophoblast invasion, [40] it is theoretically feasible that a lack of folic acid could disrupt early stages of placental development, resulting in difficulties later in pregnancy.

II. CONCLUSION

Folate (vitamin B9) is a necessary nutrient for DNA replication as well as a variety of enzymatic processes involved in amino acid synthesis and vitamin metabolism. Because folate is necessary for the fetus's growth and development, demand for it rises throughout pregnancy. Folic acid supplementation during pregnancy protects against foetal structural abnormalities such as NTD and congenital heart problems. It may also protect against preterm birth, according to new research. The impact of genetic variants in genes that regulate folate metabolism (especially the MTHFR gene) and how they affect l-methylfolate bioavailability and hence folate supplementation techniques is not well understood. Although further research is needed to better identify the exact timing, dose, and formulation, current evidence suggests that dietary folic acid supplementation is beneficial to all reproductive-aged women. Direct supplementation with l-methylfolate may help women with known MTHFR mutations, but there is currently insufficient data to make that judgement firmly.

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