FOLIC ACID vs. FOLATE

ESTABLISHING THE IMPORTANCE, BENEFITS AND DIFFERENCES

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INTRODUCTION

The purpose of this paper is to inform women, healthcare professionals and birth workers of the difference between folic acid and folate - to better understand how both forms are metabolised and the impact this has on blood folate levels.

BACKGROUND

Folate, a water-soluble vitamin belonging to the B-complex group, plays a critical role in the proper functioning of various physiological processes in the human body. It is involved in maintaining a healthy nervous system, DNA synthesis, cell division, as well as the formation of healthy red blood cells which carry oxygen around the body.[1] Thus, ensuring an adequate folate intake is crucial for maintaining optimal health.

The biologically active form of folate is called 5-methyltetrahydrofolate (l-methlyfolate or 5-MTHF), and is the predominant physiological form of folate found in blood. It is available in small amounts in foods, mainly in leafy green vegetables.[2]

Folic acid, is a synthetic version of folate commonly used in supplements and food fortification that needs to be converted into the active form l-methylfolate before the body can utilise it.[2] This conversion process occurs in the liver by hepatic reductases. Although folic acid is a precursor to l-methylfolate, it is inactive until it is converted to its active form. It is particularly important for women to consume enough folate before and during pregnancy to aid in the healthy development of the fetus. It is well understood and accepted that adequate levels of folate helps to reduce the risk of development of neural tube defects in the fetus.[3]

FOLATE AND ANAEMIA

Megaloblastic anaemia is a type of blood disorder that results in the production of abnormally large and immature red blood cells that have a reduced ability to transport oxygen.

Megaloblastic anaemia is most often due to hypovitaminosis, specifically vitamin B12 and folate deficiencies.[5] Both these nutrients play a crucial role in the synthesis of both red blood cells and DNA.[6]

Since the metabolism of folate is reliant on B12, a deficiency of either nutrient can cause megaloblastic anaemia. To differentiate between the two, expert clinical evaluation and several lab tests are necessary. In some cases, normal results may be obtained but the patient may appear symptomatic. It is important to be curious about these patients and seek to find answers with further investigations or referrals.

FOLATE INTAKE IN PREGNANCY

During pregnancy, folate requirements increase not only to support embryonic and fetal development and maternal tissue growth, but also may reduce the risk of related adverse pregnancy outcomes.[2]

National Institute of Health (NIH) has found that large amounts of folic acid can mask the damaging effects of vitamin B12 deficiency.[7] Yet it is not uncommon for pregnant women to consume excessive folic acid rather than vitamin B12, leading to normal red blood cells appearing during lab testing. It is important to note that such cases may mask vitamin B12 deficiency[8], which could manifest in neurological or systemic symptoms such as poor memory, muscle cramps, or nerve tingling, as opposed to typical anaemia symptoms. Vitamin B12 is not routinely tested in the UK and will only be promoted by clinical induction. Furthermore, folic acid can correct anaemia caused by vitamin B12 deficiency without correcting the neurological damage that also occurs due to the vitamin B12 deficiency. Some of these risks can be avoided by supplementation with l-methylfolate rather than folic acid. Because l-methylfolate does not accumulate in blood like folic acid does in cases of reduced hepatic transformation.[9]

Daily recommendations for folate/folic acid supplementation[10]:

- Adults and children **over 11 years**: 200 µg
- Anyone **considering pregnancy**: 400 µg
- If you are **pregnant**: 400 µg supplement during the first 12 weeks of pregnancy
- If you are **breastfeeding**: 260 µg

FOOD SOURCES OF FOLATE

Folate intakes are typically poor in many individuals' diets for several reasons. Natural folates are susceptible to oxidation, can rapidly lose activity in foods, and are largely destroyed by cooking.

Some good food sources of folate include sunflower seeds, lentils, chickpeas and other legumes, nuts and seeds, as well as green vegetables such as spinach and asparagus.

FOLIC ACID VERSUS FOLATE

Folic acid and folate differ in structure and function. Folates are natural and come in various forms found in food. Folic acid doesn't occur in nature and has no biological functions until it has been converted by the liver into l-methylfolate.[2] Not everyone can process folic acid effectively.

Evidence suggests that **up to 67% of the worlds population are unable to effectively convert folic acid into a form that is usable in the body**, due to a genetic variation in an enzyme that is involved in the metabolism of folate.[9]

The enzyme, known as MTHFR, plays a crucial role in the metabolic pathways of folate amino acid processing and methylation. It is imperative that MTHFR is functioning correctly to ensure that these metabolic processes occur efficiently. According to the National Institute of Health (NIH), this enzyme converts a form of folate called 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, which is the primary form of folate found in the blood. This conversion is necessary for the multistep process that converts the amino acid homocysteine to methionine. Methionine is used by the body to make proteins and other essential compounds.[4] Studies suggest that folate insufficiency due to MTHFR deficiency is bypassed by supplementation with l-methylfolate.[11]

THE BENEFITS OF ACTIVE FOLIC

Acive Folic contains the active form of folate, l-methylfolate, which bypasses folate metabolisation, a process which is potentially impaired by MTHFR polymorphism. L-methylfolate is directly absorbed to exert the biological activity. Data suggests that supplemental l-methylfolate can effectively improve folate biomarkers in young women in early pregnancy in order to prevent neural tube defects (NTDs).[12]

The benefits of supplementing with Active Folic (l-methylfolate):

- High bioavailability, being in a biologically active form that avoids the need for conversion or activation
- It does not cause unmetabolised folic acid in the body
- It is the main type of folate in our blood (serum and red blood cells) as well as cord blood.
- Unlike folic acid, it does not conceal a vitamin B12 deficiency.

CONCLUSION

In conclusion, folate is a critical nutrient that plays a vital role in the human body. When the body does not get enough folate, it can lead to folate deficiency. Symptoms of folate deficiency include weakness, fatigue, irritability, and difficulty concentrating. Long-term consequences of folate deficiency can include problems with the nervous system, temporary infertility and heart conditions.[13] It is crucial for women to ensure adequate intake of folate before and during pregnancy to support optimal development of the fetus, prevent folate deficiency and ensure optimal health. A balanced diet that includes folate-rich foods is crucial for meeting daily folate requirements and preventing deficiency. However folate intakes are typically poor in many individuals' diets, so supplementation can play a role here. Because the association between the MTHFR polymorphism and a low folate concentration has been assessed, supplementation with an active form, such as Active Folic (l-methylfolate), could be considered as being universally beneficial.[2]

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