Folic acid in pregnancy: MTHFR gene explains why benefits may differ

May 2 2018, by Darya Gaysina

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It's generally recommended that all women should take folic acid, both while they're trying to get pregnant and during the first 12 weeks of pregnancy. This is because folic acid is considered to be very important

for the development of a healthy foetus.

But recently, it has been claimed this "one-size-fits-all" approach may be wrong and that some pregnant women may benefit more from alternatives to folic acid. Specifically, it has been found that forms of a certain gene that vary among people, may affect how the body utilises folic acid.

The terms "folic acid" and "folate" are often used interchangeably to describe Vitamin B9, but they are not exactly the same. Folate is often called the natural form of vitamin B9, which is found in dark green vegetables, including broccoli and spinach and dried legumes. Folic acid is the synthetic form of vitamin B9, found in supplements and also added to processed, or "fortified," foods.

By eating foods that are high in folate regularly, most people should be able to get the necessary amount (200 mcg a day). For some people though, more than this recommended amount of folate is necessary.

It is known that folate or folic acid is very important for the development of a healthy foetus. This is why all pregnant women and women trying for a baby are advised to take double this amount (400 mcg a day) – or even more in certain cases, to help prevent the risk of birth defects in unborn babies.

It would be almost impossible to get this much folate just from natural sources. That's why folic acid is often prescribed to pregnant women in the form of supplements.

It is also the reason why folic acid is added to grains (this process is called fortification) in many countries. Recently, there has been a push to make it mandatory in the UK as well.

Understanding the science

People differ in how much folate they need and receive in their diet, and this can be corrected with supplements. But people also differ in how much folate or folic acid they need for their health – based on the activity of "the MTHFR gene".

To understand why this matters, first of all we need to know a bit more about the science of how our bodies work. There are 20,000 genes in the human genome. Each of these genes provides instructions in the form of a DNA sequence for making a specific protein. Proteins play various important roles in our body: from building our cells through to making our brain function.

One of these genes – the MTHFR gene – provides the instructions for making the protein methylenetetrahydrofolate reductase. This protein is a key player in the complex process of converting folic acid (or folate) that we receive with foods into methylfolate, the form that our body can use.

The MTHFR gene is responsible for how much methylfolate is produced in the body. Our body needs methylfolate for a proper metabolism. If there is not enough methylfolate in the body, it leads to many serious health problems.

MTHFR explained

All people have two copies of the MTHFR gene – one copy is inherited from the mother and another copy is inherited from the father. Each copy of the gene can be normal or can have a defect – a change in DNA sequence that affects how much protein this gene can produce.

These defects are called mutations. The common mutation in the MTHFR gene is a single change in DNA sequence that reduces the activity of the protein produced. About 10-15% of people have both copies of the gene affected by this mutation.

These people have very low activity of the MTHFR protein in the body. This results into a highly reduced ability of the body to convert folic acid into a usable form and can lead to accumulation of the amino acid homocysteine – which is toxic to the body.

The MTHFR gene mutation has been found to be one of the factors that puts people at an increased risk of cancer, cardiovascular disease, infertility, migraine, and foetal development problems. It has also been found to increase the risk of depression, schizophrenia and dementia.

To supplement or not

A diet rich in folate is said to be particularly important for those with the mutation in the MTHFR gene. People with a mutation in the gene may be affected more if they do not receive enough folate with foods.

It has been shown that people with this mutation are affected more in Asia than in countries that use grain fortification with folic acid – such as the US, Australia, and New Zealand. But more studies are needed to prove whether alterations in diet and use of folate supplements can be sufficient to overcome negative health effects caused by the MTHFR gene mutations.

Caution is also needed with high-dose supplementation of folic acid in pregnant women with different forms of the MTHFR gene as very high intake of folate may have unintended negative effects on their offspring – particularly on early brain development, as demonstrated by recent human and animal studies. But ultimately, future studies are critical to

determine a safe upper limit for all people – and pregnant women particularly – who have different genetic profiles.

This article was originally published on The Conversation. Read the original article.

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