High dose folic acid does not prevent pre-eclampsia in high risk women

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Taking high dose folic acid supplements in later pregnancy (beyond the first trimester) does not prevent pre-eclampsia in women at high risk for this condition, finds a randomised controlled trial published by The BMJ today.

However, taking low dose folic acid supplements before and during early pregnancy to prevent birth defects, such as spina bifida, is still strongly recommended for all women, say the researchers.

Pre-eclampsia is a serious condition where abnormally high blood pressure and other complications develop during pregnancy. It affects about 3-5% of pregnancies and is dangerous for both mother and child.

Previous observational studies have shown a potential protective effect, but findings have been inconsistent, and there is currently no clear guidance for the use of high dose folic acid to prevent pre-eclampsia in women with risk factors for the condition.

So an international research team decided to conduct a randomised trial—the Folic Acid Clinical Trial (FACT) - to evaluate the effect of high dose folic acid supplementation beyond the first trimester of pregnancy on the risk of developing pre-eclampsia among pregnant women already at high risk for this condition.

They included 2,301 pregnant women who were between 8 and 16 weeks' pregnant at the start of the study and had at least one risk factor for pre-eclampsia (existing high blood pressure, pre-pregnancy diabetes, twin pregnancy, pre-eclampsia in a previous pregnancy, or a body mass index of 35 or more).

Women were randomised to receive either daily high dose (4 mg) folic acid or placebo in addition to up to 1.1mg of folic acid throughout pregnancy.

Information on personal characteristics and medical history was recorded and participants had a total of four follow-up visits during the study period.

After taking account of factors that could have affected the results, they found that pre-eclampsia occurred in 169 out of 1,144 (14.8%) women in the folic acid group and 156 out of 1,157 (13.5%) in the placebo group. There was no evidence of differences between the groups for any other adverse outcomes.

The researchers therefore conclude that high dose folic acid supplementation beyond the first trimester has no benefit for preventing pre-eclampsia. And they suggest that "high dose recommendation should now cease, and the search for an effective and acceptable strategy to prevent pre-eclampsia must continue."
In a linked editorial, Professor Lucy Chappell and colleagues stress that the lack of benefit reported in this trial "must not detract in any way from the importance of folic acid supplements for the prevention of neural tube defects."

However, they say these findings "are another disappointment in the long search for a more effective measure to prevent pre-eclampsia" and they call for continued efforts towards a global reduction in pre-eclampsia related deaths.

**More information:** Effect of high dose folic acid supplementation in pregnancy on pre-eclampsia (FACT): double blind, phase III, randomised controlled, international, multicentre trial
http://www.bmj.com/content/362/bmj.k3478

Editorial: Why is the search for pre-eclampsia prevention so elusive?
http://www.bmj.com/content/362/bmj.k3536

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