Meta-analysis confirms folic acid supplementation unlikely to increase cancer risk

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Researchers have established that short-term use of folic acid supplements is unlikely to substantially increase or decrease overall cancer risk and has little effect on the risk of developing any specific cancer including cancer of the colon, prostate, lung, and breast, according to a meta-analysis involving almost 50,000 individuals published Online First in the *Lancet*.

"The study provides reassurance about the safety of folic acid intake, either from supplements or through fortification, when taken for up to 5 years", explains Robert Clarke from the University of Oxford, UK, one of the lead authors.

"The nationwide fortification of foods involves much lower doses of folic acid than studied in these trials, which is reassuring not only for the USA who have been enriching flour with folic acid to prevent neural tube birth defects (such as spins bifida) since 1998, but also for over 50 other countries where fortification is mandatory (eg, Australia, South Africa, Chile, Argentina, and Brazil)."

Clarke and colleagues from the B-Vitamin Treatment Trialists' Collaboration conducted a meta-analysis of all large randomised trials of folic acid supplementation (alone or in combination with other B vitamins) up to the end of 2010.

They found that those who took daily folic acid for 5 years or less were not significantly more likely to develop cancer than those who took placebo, with 1904 (7.7%) new cases of cancer reported in the folic acid groups and 1809 (7.3%) in the placebo groups.

Even among those with the highest average intake of folic acid (40 mg per day) no significant increase in overall cancer incidence was noted.

What is more, there was no significant difference between folic acid and placebo groups in the number of participants experiencing colorectal, lung, breast, prostate, or any other type of cancer.

Importantly, there was also no evidence that the risk of developing cancer increased with longer folic acid treatment.

"Both the hopes for rapid cancer prevention and the fears about rapidly increased cancer risk from folic acid supplementation were not confirmed by this meta-analysis", says Clarke.

But he cautions, "It remains to be seen whether any beneficial or harmful effects on cancer incidence will eventually emerge with even longer treatment or follow up."

Writing in a linked Comment, Cornelia M Ulrich, Director of the National Center for Tumor Diseases and German Cancer Research Center and Joshua W Miller from Rutgers University in the USA discuss the importance of taking into account the dual relationship of folate with cancer—how it may cause existing cancer cells to grow, but protects against initiation—when interpreting the results. They note that this relationship has potentially significant ramifications for "those who consume excess folic acid from fortification and supplements combined. Notably, 1% of the US population, depending on age, sex, and ethnic origin, exceed the tolerable upper limit (1 mg/day) for total consumption

of folic acid."

More information: www.thelancet.com/journals/lan … (12)62001-7/abstract

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