

Folic Acid Fortification: Evidence and Global Progress

Two page summary

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Efficacy of supplementation with folic acid for the prevention of NTDs

Numerous clinical trials and cohort studies have conclusively shown that folic acid supplementation prevents neural tube defects (NTDs). A Cochrane review in 2012 confirmed that folic acid supplementation prevents first and second time occurrence of NTDs. Overall existing data suggests that folic acid supplementation or fortification reduces NTD prevalence by 60-85%.

Effectiveness of supplementation with folic acid for the prevention of NTDs.

While supplementation has proven highly effective in trials, the effectiveness of folic acid supplementation has not been realized in practice. This relates to the fact that folic acid supplements need to be started **before** pregnancy, in order to prevent NTDs, and global evidence indicates that health education to encourage women planning or able to get pregnant has not achieved sufficient behavior change in the form of sustained folic acid supplement use. Existing data suggests folic acid supplementation coverage infrequently exceeds 50%, with younger women and the most disadvantaged the least like to take the supplements. As a result, reductions in NTD prevalence have not been recorded as a result of folic acid supplementation.

Effectiveness of fortification in prevention of NTDs (including cost-effectiveness)

Folic acid fortification, on the other hand has proven highly effective at preventing NTDs. A meta-analysis of 8 studies, published in 2010, recorded an average reduction of 46%. A review of 17 studies in 2012 that compared NTD prevalence before and after fortification of flour recorded reductions of 15.5% to 58%. A review by the Food Fortification Initiative (FFI) undertaken in 2013 and updated in 2015, found that all studies have recorded reductions in NTDs, with the exception of one study from Peru that appears to have classified NTDs incorrectly. Because of the low cost of fortification and the high cost of treating and caring for patients with NTDs, folic acid fortification has a cost-benefit ratio of 1:12 in Chile to 1:48 in USA

Evidence for other benefits of fortification with folic acid

Fortification with folic acid has also been found to reduce folate deficiency and folate deficiency anemia in older adults. It could also potentially prevent 13% of neonatal deaths; those attributable to congenital birth defects. There is also evidence developing that folic acid fortification may prevent strokes and ischemic heart disease.

Evidence for other benefits of flour fortification

The majority of evidence for the impact of fortification with folic acid is from the fortification of wheat and maize flour. As wheat and maize flour are frequently

fortified with additional nutrients, in particular iron, zinc and B vitamins, wheat and maize flour fortification has also been shown to reduce iron deficiency, anemia and, to a lesser extent zinc and vitamin A deficiency.

Safety of folic acid fortification

A number of concerns have been raised about the safety of folic acid. Overall however, no clear evidence exists that folic acid causes cancer, asthma, twinning or cognitive impairment. Where the evidence is equivocal, it should be noted that potential risks have been attributed to folic acid supplementation, rather than fortification. Mandatory fortification provides 40% and 59% of the recommended daily intake of folic acid in Australia and the US respectively; levels highly unlikely to cause any negative impacts.

Current global status of folic acid fortification

81 countries currently have mandatory legislation for the fortification of wheat flour; all but 5 of these require fortification with folic acid. The Philippines is one of the 5 countries with mandatory fortification of wheat flour that does not include folic acid. A number of countries in the region have mandatory legislation for folic acid fortification of wheat flour and two others are planning such legislation.

Although the number of countries with mandatory fortification of wheat flour with folic acid is growing, an estimation by Oakley and colleagues suggests that only 15% of folic-acid preventable spina bifida and anencephaly is currently prevented. This estimate assumes that 75% of spina bifida and anencephaly cases can be prevented if reproductive age women can receive 400ug of folic acid from wheat flour fortification. The calculation takes into account the amount of folic acid provided, the wheat flour consumption and the compliance with mandatory legislation.

Lessons learnt in achieving optimal impact of fortification with folic acid

Global experience has shown that it is necessary to have mandatory legislation in order to achieve a public health impact. Equally important, mandatory legislation needs to be enforced by national food control systems. WHO recommends wheat and maize flour fortification as an effective intervention and has made recommendations on the amount of folic acid that needs to be added to wheat and maize flour in order to be optimally effective. WHO has also recently released recommendations for assessing population risk of NTDs based on red blood cell folate levels. It is important to be aware that the risk of having an NTD-affected pregnancy occurs at higher folate levels than folate deficiency. Ie folate deficiency underestimates the risk of NTDs.

Conclusions

Fortification with folic acid for the prevention of NTDs is a proven intervention. Numerous countries have demonstrated the feasibility of fortification of wheat flour with folic acid and substantial reductions in NTDs. Fortification with folic acid highly cost-effective and requires no behavior change. There are also other potential benefits of increased folic acid intake and fortified flour can also reduce other nutrient deficiencies. Using Oakley's methodology, fortification of wheat flour with folic acid in the Philippines could provide 288ug of folic acid per day to reproductive age women and prevent about 2,565 NTDs per year.