November 2004

Preventing neural tube defects by folic acid fortification of flour

Rashid Jooma
Aga Khan University, rashid.jooma@aku.edu

Editorial

Preventing Neural Tube Defects by Folic Acid fortification of Flour

R. Jooma

Department of Neurosurgery, Jinnah Postgraduate Medical Centre, Karachi.

Neural tube defects (NTDS) are a group of seriously disabling birth malformations of which spina bifida and anencephaly are most frequent. No data is available for the incidence of NTDS in Pakistan but anecdotal testimony from health professionals suggest that it is not inconsequential and is probably at the higher end of the world range (0.5 to 12 per 1000 live births).

JPMC Study

A year-long prospective study conducted in the obstetrical service of Jinnah Postgraduate Medical Centre (JPMC), Karachi for the year 2002, observed 9892 deliveries (312 still-born). Amongst these, there were 34 births with various NTDs of whom there were 16 live births. Anencephaly was the commonest of the neural abnormalities (19 cases with only 3 live births) followed by 11 myelomeningocoeles with 7 live births. There were 3 babies with encephalocoeles and 4 cases of spina bifida aperta.

Folic Acid Consumption and NTDS

Over the past two decades a strong link has been established between the occurrence of NTDs and a deficiency of folate in the diet of the mother at the time of conception.[1] The initial observations came from the findings that these defects were prevalent in the low socio-economic groups and the high incidence of NTDs during periods of nutritional deprivation such as famines.

Since these initial observations, it has been clearly shown by various scientific studies that increasing the dietary intake of folate in women of childbearing age and supplementations with 0.4 to 4 mg folic acid a day, 4 weeks prior and 8 weeks after conception significantly reduces the birth of babies with NTDs.[2] Thus NTDs may be viewed as a folate deficiency disorder preventable by augmentation of folic acid intake. A recent study of women bearing NTD babies revealed a high level of autoantibodies to folate receptors[3] and this could explain the mechanism whereby a relative folic acid deficiency may occur resulting in failure of neural tube closure and the rationale of augmenting folic acid in young women to levels that would overcome the receptor block.

Increasing Folate intake

Folate is largely found in fruits (especially citrus), leafy green vegetables, animal liver and to a lesser extent in beans and lentils. The non-pregnant adult's daily requirement of 100 micrograms is usually met but the 400 micrograms a day required by the mother to afford protection from NTDs affecting the foetus may not be available in the average Pakistani diet.

The 3 strategies of nutritional interventions that may be used are:

1. To encourage consumption of a folate rich diet through process of public education. However, this would require that the target audience be accessible through the mass media and have the economic resources for provision of the appropriate foodstuff in the requisite quantities.

2. Provision of supplements of folic acid to women of childbearing age using the national Lady Health Workers network. However, because many pregnancies are unplanned and NTDs arise in the foetus between days 15 and 28 post-conception when most women are unaware that they are pregnant and by the time she comes to a health care worker for antenatal care, it is too late to prevent the malformations by supplementation.

3. Universal folic acid fortification of a basic food ingredient is the most effective strategy to ensure adequate blood levels in the mother in the critical peri-conceptional period as the embryonic closure of the neural tube is taking place.

Recommendation for Folic Acid Fortification

To ensure that all women in Pakistan of childbearing age increase their intake by 400 micrograms per day, enrichment of flour would be that most efficient vehicle of fortification. The current recommendation is for the fortification of folic acid to the level of 240 micrograms per 100 gram of flour (240ppm).[4] That such an intervention does work in reducing devastating birth defects has now been well established from studies of other countries.[5]

Fortification in other Countries

A number of countries have adopted a range of folic acid fortification approaches. In the U.K. the Committee on Medical Aspects of Food and Nutrition Policy[4] recommended voluntary fortification at 240ug/100g white flour. The United States of America and Canada adopted mandatory fortification (140ur/100 gm of cereal grain and 150ug/100 gm of white flour respectively) and the early reports show a decline in NTD births of 1991 to 70%.[6,7] In Costa Rica, where mandatory fortification was introduced in 1999 at a level of 180ug folic acid/100gm of wheat and maize flour, a

maize flour, a reduction of NTD births at the National Children's Hospital in San Jose has been reported from 106 cases in 1995 to 26 cases in 2001.[8] Chile introduced mandatory fortification at a level of 220ug/100gm of white flour in 2000 and has reported a 31% decrease in NTD cases within the first two years.[9] The cost of fortification in the USA is about 1 cent per person per year and the expenditure on each NTD prevented in estimated at less than $1000.[10]

Studies confirm that the greater the background rate of NTDs, the greater the beneficial effect of folic acid and thus in countries such as Pakistan the benefit should be at the very least be as much as that reported in Nova Scotia, Canada, where a reduction in the absolute numbers of open NTDsfrom 30 in 1991 to 9 in 2000 i.e., a 70% decline has been documented.[7]

Study of Technical Issues required

In the context of other public health measures, folic acid fortification of flour would not be overly expensive with the cost of the folic acid itself being about $0.15 per metric ton of flour. Data from the local flour milling industry would allow the final determination of the increment to the cost of a maund of ata. Studies are required of the best methods to be employed in our flour mills and chakkies to ensure even distribution of the nutrient mix between batches of flour. Technically it is easy to add folic acid to the "pre-mix" in an on-going fortification programme such as iron, zinc and some B vitamins as has been done in Chile.

The dose of folic acid required to be taken by women peri-conceptionally to prevent NTDs has been addressed in a meta-analysis by Wald et al.[11] and their dose-response model predicts an escalating reduction of risk from 23% with an intake of 0.2 mg/day of folic acid, 36% from an intake of 0.4 mg/day and as much as 85% by taking 5 mg of folic acid daily. We do not at present have data of folic acid levels in the young women of Pakistan. However, both the high incidence of maternal anaemia documented in the National Health Survey[12] and the high incidence of NTDs that we have observed in our institutional setting are surely veritable markers of folate impoverishment in the diet of our women and make a cogent argument for the level of fortification chosen to achieve the desired daily intake of at least 450 micrograms a day to be best equated to the highest levels recommended by health authorities round the world.

Folic acid is stable in stored flour but is sensitive to light and heat. Study of the losses that occur in the distribution and storage conditions existing in Pakistan and during the shelf life would also be required. Further study to quantify the degradation of folic acid during preparation of nans and chappatis is also essential to allow determination of the "overage" needed to achieve a level of 250 microgram of folic acid in the final product for every 100 gram of flour used in the making of local breads.

Conclusion

Spina bifida and anencephaly are two of the most common and severe birth defects. One causes permanent paralysis and the other foetal or infant death. There is now excellent evidence that increased consumption of supplemental folic acid can prevent many of these defects and the effect is more pronounced where the background rate of NTDs is in the higher range.[13] Folic acid-preventable birth defects are as preventable as polio and as a public health measure, equally urgent. The technology to fortify is simple, inexpensive and almost immediately implemented for large population groups.

Folic acid enrichment of flour should be considered as a priority public health measure by the State. Opportunities to implement a sustainable, inexpensive public health intervention to prevent major human disease come rarely. Folic acid fortification of flour is one of the rare opportunities. Governments of nations with a high background incidence of NTDs who ignore folic acid fortification "are committing public health malpractices".[14]

References

1. Centres for Disease Control and Prevention. Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. MMWR Morbid Mortal Wkly Rep 1992;41:1-7.
2. Wald N, Sneddon J, Densem J, et al. Prevention of neural tube defects: results of the MRC Vitamin Study. Lancet 1991;338:132-7.
3. Rothenberg SPn, da Costa MP, Sequeira JM, et al. Autoantibodies against folate receptors in women with a pregnancy complicated by a neural-tube defect. N Engl J Med 2004;350:134-42.
4. Committee on Medical Aspects of Food and Nutritional Policy. Folic acid and the prevention of disease. Report of the committee on medical aspects of food and nutrition policy. London: The HMSO, 2000, PP. 1-101.
5. Ray JG, Meier C, Vermeulen MJ, et al. Association of neural tube defects and folic acid food fortification in Canada. Lancet 2002;360:2047-8.
6. Honein MA, Paulozzi LJ, Mathews TJ, et al. Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects. JAMA 2001;285:2981-6.
7. Persad VL, Van den Hof MC, Dube JM, et al. Incidence of open neural tube defect in Nova Scotia after folic acid fortification. CMAJ 2002;167:241-5.
8. Chen LT, Rivera MA. The Costa Rican experience: reduction of neural tube defects following food fortification programs. Nutr Rev 2004;62:S40-3.
9. Castilla EE, Orioli IM, Lopez-Camelo JS, et al. Preliminary data on changes in neural tube defect prevalence rates after folic acid fortification in South America. Latin American Collaborative Study of Congenital Malformations (ECLAMC). Am J Med Genet 2003;123A:123-8.
10. Wald NJ. Folic acid and the prevention of neural tube defects. N Engl J Med 2004;350:101-3.
11. Wald NJ, Law MR, Morris JK, et al. Quantifying the effect of folic acid. Lancet 2001;358:2069-73.
12. National Survey of Pakistan 1990-94. Islamabad: PMRC, 1998.
13. Berry RJ, Zhu LI, Ericson DJ, et al. Prevention of neural tube defects with folic acid in China. N Engl J Med 1999;341:1485-90.
14. Oakley GP. Folic acid fortification: time for a concerted effort. CMAJ 2002;167:848.