Neural tube defects and periconceptional folic acid in England and Wales: retrospective study

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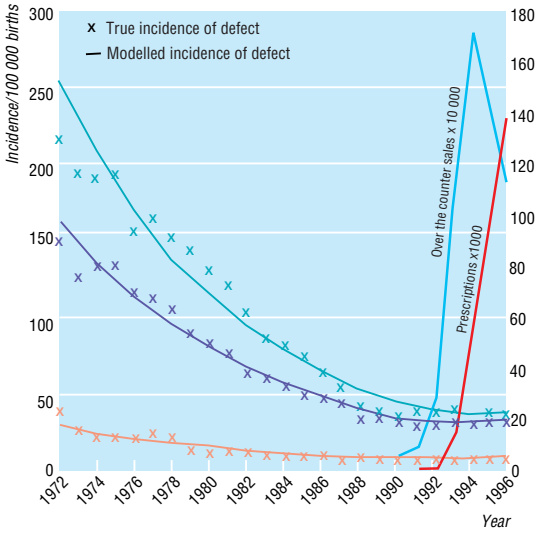
The risks of a first occurrence and a recurrence of neural tube defects have been shown to be reduced by periconceptional folic acid supplementation—that is by taking folic acid from 3 months before conception to 3 months after conception.[1 2] The Expert Advisory Group in the United Kingdom recommended in 1992 that women who were trying to conceive should take 0.4 mg folic acid per day.[3] We assessed whether there had been any change in the incidence of neural tube defects since this recommendation was made.

Methods and results

The number of live births, stillbirths, and pregnancies terminated because the fetus had a neural tube defect (spina bifida, anencephaly, or encephalocele) as well as the total number of live births, stillbirths, and abortions among residents of England and Wales from 1972 to 1996 were obtained from the Office for National Statistics. The true incidence of these abnormalities was defined as the number of affected infants (born alive or dead) plus the number of pregnancies terminated after prenatal diagnosis of a neural tube defect and expressed as a proportion of 100 000 live births, stillbirths, and terminations for neural tube defects. The number of prescriptions dispensed and the number of preparations sold over the counter containing 400 μg to 500 μg folic acid were provided by the Department of Health and Self Medication UK, a department of Intercontinental Medications Statistics-Health, (Pinner, Middlesex), respectively. The total number of prescriptions dispensed was available but data for over the counter sales do not include information from Boots pharmaceutical stores because they do not provide this information.

The incidence of each defect was modelled against the calendar year using a logarithmic transformation of the incidence. To assess whether rates of decline have been more rapid since 1992, a term was added to the model to reflect the number of years since 1992. Further analyses in which a square root was used instead of logarithmic transformation gave similar results. All models were fitted using the SAS statistical package.

Before 1992 there was a significant drop in the incidence of each of the defects ($P=0.0001$ for each abnormality) (figure). The incidence of spina bifida fell from 215/100 000 in 1972 to 38/100 000 in 1991; the incidence of anencephaly fell from 149/100 000 to 29/100 000; and the incidence of encephalocele fell from 39/100 000 to 9/100 000. Since 1992 the rates of decline have stabilised and the decline was significantly less rapid than before 1992 ($P=0.002$ for spina bifida, $P=0.0001$ for anencephaly, and $P=0.03$ for encephalocele). The number of prescriptions of folic acid dispensed increased between 1992 and 1996, and over the counter sales increased between 1990 and 1994 and declined in 1995-6.



True incidence and modelled incidence of spina bifida (blue), anencephaly (purple), and encephalocele (orange) per 100 000 births in England and Wales, 1972-96, and number of prescriptions dispensed and preparations sold over the counter containing 400μg to 500 μg of folic acid, 1992-6

Comment

The incidence of neural tube defects has been decreasing since the early 1970s. Our study shows that although there has been a large increase in the number of prescriptions dispensed and preparations sold over the counter of folic acid since 1992 in England and Wales, the rate of decline in the true incidence of neural tube defects has slowed. Although periconceptional supplementation with folic acid has been shown to be effective in randomised controlled trials, no reduction in the incidence of neural tube defects has yet occurred. Supplementation may not be taken at the right time,[4] or may not be taken by those women who are at the highest risk, or the recommended dose may be too low. It is also possible that the incidence of these defects has reached such a low level that it is not possible to achieve further reduction through supplementation or that a longer interval is required to show the true effect of supplementation on the incidence. Our study is observational, and we do not know what the incidence would have been in the absence of folic acid supplementation. Additionally, sales and prescriptions may not represent the actual use of folic acid. There is a need for continued health education on the use of folic acid before pregnancy or immediately after conception in unplanned pregnancies.

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1 MRC Vitamin Study Research Group. Prevention of neural tube defects: results of the Medical Research Council vitamin study. *Lancet* 1991;338:131-7.
2 Czeizel AE. Prevention of congenital abnormalities by periconceptional multivitamin supplementation. *BMJ* 1993;306:1645-9.
3 *Report from an Expert Advisory Group (1992) on folic acid and the prevention of neural tube defects.* London: Department of Health; Scottish Office Home and Health Department; Welsh Office; Department of Health and Social Services, Northern Ireland, 1992.
4 McGovern E, Moss H, Grewal G, Taylor A, Bjornsson S, Pell J. Factors affecting the use of folic acid supplements in pregnant women in Glasgow. *Br J Gen Pract* 1997;47:635-7.

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Commentary: Food should be fortified with folic acid

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Kadir and colleagues set out to evaluate the effect of government recommendations made in 1992 on the use of periconceptional supplementation with folic acid to prevent neural tube defects. They identified a marked increase of over 100-fold in the number of prescriptions dispensed and preparations sold that contained 400 μg to 500 μg of folic acid between 1991 and 1996. This evidence of increased consumption was not, however, accompanied by an accelerated fall in the notification of neural tube defects, either among births or therapeutic terminations of affected pregnancies.

This finding is not totally surprising. Between 1993 and 1996 surveys showed that folic acid was being taken by 2% to 3% of women before pregnancy and that this figure then rose to over 30% of women.[1 2] The risk of neural tube defects has been associated with maternal red cell folate concentrations in a dose-response relation; this in turn is related to consumption of folic acid.[3] The average daily intake of folates is about 200 μg. Wald and colleagues have estimated that an increase of an additional 400 μg daily should lead to a 53% reduction in the risk of neural tube defects occurring.[4]

The analysis by Kadir et al covers the time from before 1992 until 1996 when the proportion of women taking periconceptional supplements of folic acid ranged from 2% to about 30%, so the average proportion would probably have been around 15%. If this were correct, the expected reduction in the incidence of neural tube defects would be about 8%—that is, 15% of 53%. Such a small change would hardly be discernible in national notifications given the known underreporting of cases of neural tube defects.[5] Moreover, Mathews and colleagues showed that women who were taking supplements before conception were women with pregnancies that were likely to be at a lower risk of the defects than those who were not taking supplements.[2]

An expensive and large scale campaign of health education has increased the proportion of prospective mothers who take folic acid before conception to not much more than 30%. Since about 40% of pregnancies are unplanned, this is likely to reflect the best effect that can be expected through encouraging individual women to buy and take supplements of folic acid. Full coverage of the population can only be achieved by implementing a policy to fortify a staple food with folic acid; this is being considered by the UK government and has already been implemented in the United States, although at a comparatively low 100 μg/day. The only way of solving this problem is to implement a policy of fortification that is designed to increase the average daily folic acid intake of every woman by 400 μg. Evidence suggests that this would about halve the prevalence of neural tube defects without causing any associated adverse effects. Indeed, evidence exists that it would bring about other health benefits across the population including a modest reduction in ischaemic heart disease.[6]

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1 Wild J, Sutcliffe M, Schorah CJ, Levene MI. Prevention of neural-tube defects. *Lancet* 1997;350:30-1.
2 Mathews F, Yudkin P, Neil A. Folates in the periconceptional period: are women getting enough? *Br J Obstet Gynaecol* 1998;105:954-959.
3 Daly LE, Kirke PN, Molloy A, Weir DG, Scott JM. Folate levels and neural tube defects: implications for prevention. *JAMA* 1995;274:1698-1702.
4 Wald NJ, Law M, Jordan R. Folic acid food fortification to prevent neural tube defects. *Lancet* 1998;351:834.
5 Murphy M, Seagrott S, Hey K, O'Donnell M, Godden M, Jones N, et al. Neural tube defects 1974-94: down but not out. *Arch Dis Child* 1996;75:F133-4.
6 Wald NJ, Watt HC, Law MR, Weir DG, McPartlin J, Scott JM. Homocysteine and ischemic heart disease: results of a prospective study with implications regarding prevention. *Arch Intern Med* 1958;158:862-7.

A typical hazard

Wallabies on the runway

North Queensland, the size of France, is lucky to enjoy the service of the Royal Flying Doctor Service. Recently, we flew a seven seater plane to retrieve a neonate of 28 weeks' gestation at Ingham, a kangaroo hop away at 120 km north of Townsville. As the plane descended and approached I saw two sets of flashing lights resembling fireflies going up and down the runway. When we got out of the plane I was surprised to see two police cars with their flashing lights of red, yellow, and blue. "That was a clean landing," said one burlesque officer to our pilot. The pilot sighed, "There was one which came into view just as I landed; otherwise it was pretty good." It transpired that the two police cars were dashing up and down the runway to clear it of the many kangaroos and wallabies. When we had got the baby and his mother back on the plane the police officers repeated the same fumigating act. A kangaroo, with a baby in its pouch, hopped past my window as the plane took off.

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