Clinical

Preventing neural tube defects in Ireland

Prof Michael Turner of the UCD Centre for Human Reproduction, Coombe Women and Infants University Hospital, wants the Government to concentrate on the cost implications of not bringing in mandatory folic acid food fortification for maternity, neonatal and rehabilitation services — rather than the implications the policy might have for food prices

Neural tube defects (NTDs) are a group of serious congenital neurodevelopmental malformations, where there is incomplete closure of the neural tube during the first month after conception. In a national audit of 2009-11, the incidence was 1.04/1,000 births: 45 per cent had anencephaly, 49 per cent had spina bifida and 6 per cent had an encephalocoele (McDonnell et al, 2015). Anencephaly is incompatible with survival beyond the first week of life. In contrast, a recent comprehensive report from Temple St Hospital estimated that 500 patients in the country and their families face the lifelong consequences of coping with spina bifida.

Some NTDs are genetic in origin and, at present, are not preventable. However, since the early 1990s there is evidence from two European randomised controlled trials that oral folic acid (FA) supplementation started before pregnancy can prevent both the occurrence and recurrence of more than half of NTDs. This led to recommendations internationally that periconceptually, women at low risk should take 400 micrograms oral FA supplementation daily, and that women at high risk of a NTD should take 4mg daily on prescription from their doctor.

In 1993, the Health Promotion Unit of the Department of Health advised that "women likely to become pregnant should take an extra 400µg of folic acid prior to conception and during the first 12 weeks of pregnancy". While all women should also follow the recently launched National Healthy Eating Guidelines, there is strong evidence that natural folate intake alone is completely inadequate for the prevention of NTDs, and to meet the WHO daily requirements for pregnancy.

Strategy ineffective

However, the supplementation strategy had little impact worldwide on decreasing the prevalence of NTDs, because half of clinical pregnancies are unplanned — and women often did not initiate supplementation until they were aware of their pregnancy.

As a result, many countries decided subsequently to also implement a strategy of mandatory folate food fortification. In 1998, it was decided in the United States, for example, to fortify flour for the making of bread.

Food fortification

More than 70 countries to date have implemented mandatory FA food fortification, which, in a 2010 meta-analysis, was shown to halve the number of NTDs. However, to date, mandatory fortification has not been implemented in the European Union (EU).

In 2005 in Ireland, the Minister for Health commissioned a report to find the best solution to reduce the prevalence of NTDs nationally. The report, published in 2006, "revised current recommendations to women regarding folic acid supplements, to specifically advise all women of childbearing age to take 400µg daily". The report also recommended, similar to the US, mandatory fortification in this country of all bread at a level of 120µg per 100g of bread.

In 2008, a report from the implementation group on folic acid fortification by the Food Safety Authority of Ireland (FSAI) recommended that mandatory fortification should be put on hold because a survey of foetal medicine units had reported a reduction in NTDs, which was attributed to an increase in RBC folate levels in women associated with a 30 per cent increase in dietary folate in the Irish population following voluntary food fortification.

Voluntary fortification

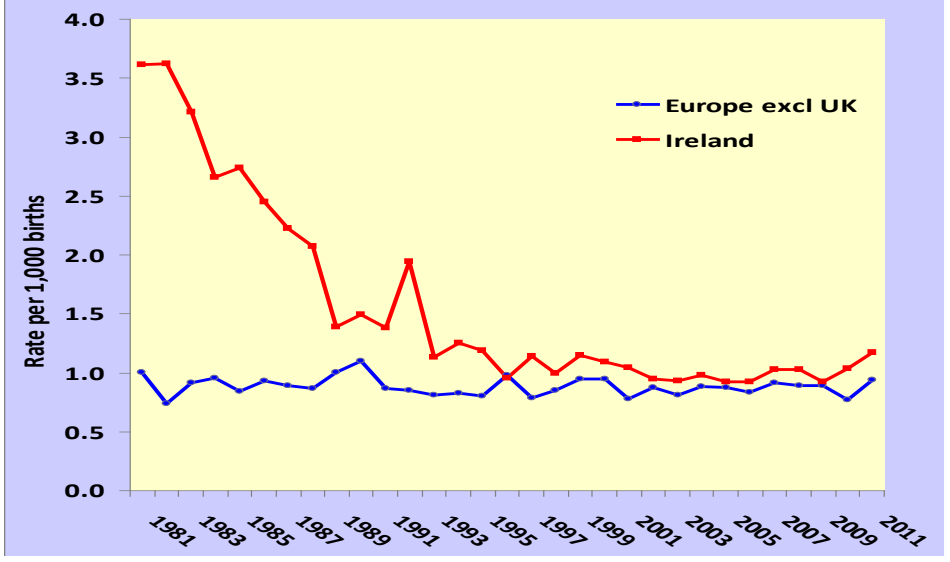
In an influential paper presented to the Nutrition Society meeting in June 2008, a survey of major supermarkets in Dublin by the FSAI identified 211 foods that were fortified voluntarily (Flynn et al, 2008). The range of food fortified was extensive, although there was variability within brands.

Compared with a 1999 national survey, the FSAI estimated that FA fortification had increased from 67µg to 90µg per day. The principal food categories for the increased dietary fortification were fat spreads and bread products. An analysis of all bread products marketed in Ireland found that about one-fifth of breads were fortified, but there was wide variation in the level of fortification. The paper highlighted that a major disadvantage of voluntary fortification is that it may be unevenly distributed across populations.

In a study conducted in 2013-4, the level and ranges of foods fortified with FA were compared with previous levels in 2004 and 2008 (Kelly et al, 2015). Over time, the levels of FA added to breads, fruit juices, milks and yoghurts increased, but the levels added to dairy and fat spreads halved. However, in 2013-4, only 2 per cent of breads were fortified compared with 60 per cent of cereals.

There was also wide variation in fortification practices between supermarket chains.

NTD rate per 1,000 births in Europe-Ireland 1981-2011



This key public health challenge needs to be addressed ... and should also be part of any Brexit discussions

In general, there has been a reduction in fortified folate food fortification, which means that total dietary folate has also been reduced since mandatory fortification was deferred. Similar downward trends have been identified in other European countries where fortification remained voluntary.

The reduction in total dietary folate has been compounded by a trend towards a reduction in women starting FA before pregnancy.

In an observational study of women delivering at the Coombe Women and Infants University Hospital, the number starting FA before pregnancy decreased from 45.1 per cent in 2009 to 43.1 per cent in 2013 ($p < 0.02$) (McKeating et al, 2015). The decrease occurred particularly in women who were multiparous, between 30 and 39 years of age, obese and Irish-born.

Following reports of an increase in the number of babies requiring surgery in the country for spina bifida, a comprehensive national audit for the years 2009-11 of 236 cases found that the rate of NTDs was 1.04/1000 births and that rates had not improved since the 1990s, despite the twin strategies of supplementation and voluntary food fortification. Similar audits were subsequently published using the EUROCAT registers, and showed little or no improvement in NTD rates since 1993 in either the UK or the rest of Europe (Khoshnnod et al, 2015).

Spina bifida

However, as termination for congenital malformations is not permitted in the Republic of Ireland, the prevalence of live births with spina bifida is twice as high as in the rest of Europe. In view of the heavy burden of illness for individuals, as well as the financial costs, the responsibility for prevention is arguably higher in Ireland.

Following publication of the updated national audit, the FSAI in 2016 produced an Update Report on Folic Acid and the Prevention of Birth Defects in Ireland. It recommended implementation of one of two options on fortification:

1. Mandatory fortification of bread or flour, together with voluntary fortification and advice on supplementation; or
2. Voluntary fortification together with advice on supplementation. Comparing option 2 with option 1, the report concluded that the evidence to support 2 in reducing NTD rates was weaker.

An observational study of 587 women, presenting for antenatal care in Dublin, found that 35 per cent did not know that they had to take FA before becoming pregnant, and only half of the women knew that the purpose of the FA was to prevent NTDs (Cawley et al, 2015). The women who were the least knowledgeable were those who were socially disadvantaged or who had recently arrived to live in Ireland.

Public campaigns

As there had been no recent public health campaigns about periconceptual FA, the all-island body Safefood has undertaken successful campaigns over the past three years to build awareness about the benefits of FA supplementation among women who may become pregnant, using social media communication channels.

Furthermore, the Department of Health has established a multidisciplinary folic acid policy group to advise the Minister on future policies on supplementation and fortification. The first report is due to be completed in Q4 this year.

A recent study, supported by Safefood at the UCD Centre for Human Reproduction in the Coombe Women and Infants University Hospital, of 502 women presenting for antenatal care found that while 98 per cent were taking FA, only 44 per cent started before pregnancy (Cawley et al, Journal of Public Health).

If women taking the recommended 400µg daily over-the-counter supplement were to achieve the optimum red blood cell folate of >906nmol/L associated with the prevention of NTDs, they needed to start supplementation at least six weeks before conception (or four weeks before the first day of their last menstrual period). Women who initiated FA during pregnancy often did so only when their pregnancy test was positive and after the neural tube had closed.

Thus, a supplementation strategy will only work if all women who could become pregnant in the near future, whether intentionally or not, are taking FA supplementation. Women who intend to become pregnant in the near future should also start FA at least a month before trying to conceive.

EU guidelines

A recent review compared the guidelines on FA supplementation in 20 European countries (Cawley et al, 2015).

Over half recommended that FA should be taken by women planning a pregnancy, and three recommended that FA should be taken by all women of childbearing age. The wording of the guidelines varied even within countries. There was also wide variation in the recommendations for high dose FA in women at increased risk of NTDs.

Four guidelines recommended starting FA at least four weeks before conception, but no guideline recommended starting at least 12 weeks before pregnancy as suggested by recent pharmokinetic studies.

As half of the guidelines were published before 2000, it is evident they need to be updated. Also, with the increasing mobility of young women between countries, public health communications need to be consistent and standardised across Europe.

Implementing mandatory food fortification in Ireland will be challenging. Fortifying bread is problematic because most flour used in Ireland is milled in the UK. Fortification of food is also difficult to mandate because food and food ingredients increasingly cross international borders with globalisation of markets.

Mandatory fortification will probably require EU legislation. It will require monitoring of folate levels in pregnant women, as well as vulnerable groups such as the elderly.

The optimum level of fortification needs to be agreed. It will require ongoing monitoring of NTD rates, as well as other clinical outcomes, to assess the impact of both supplementation and fortification policies across the island.

Changes in current fortification policies does have practical and cost implications that may conflict with governments' wishes to keep food prices low.

However, failure to act also has cost implications for maternity, neonatal and rehabilitation services, as well as heavy human costs.

There are growing public health concerns at the lack of progress in reducing the prevalence of NTDs across Europe since the early 1990s (Morris et al, 2015). In the UK, for example, the chief medical officers have endorsed mandatory FA food fortification. On the island of Ireland we need, as a priority, to update our current FA supplementation and fortification policies.

While revising the supplementation policy and its subsequent communication is in our own hands, reviewing the fortification policy probably requires close governmental collaboration with other European countries, whether they are in the EU or not.

This key public health challenge needs to be addressed sooner rather than later and should also be part of any Brexit discussions.

References on request