

Trends in periconceptional folic acid use by relatives in Irish families with neural tube defects

J BYRNE, C BYRNE, D COLLINS

Boyne Research Institute, Duke House, Duke Street, Drogheda, Ireland and
Children's National Medical Center, Washington, DC, USA

Abstract

Close relatives in families who have a child with a neural tube defect (NTD) are at greatly increased risk of having an affected child. Periconceptional folic acid reduces the risk of both occurrence and recurrence of NTDs substantially. Public health authorities currently recommend that the diets of all women between the ages of 15 and 44 who are capable of becoming pregnant be supplemented with folic acid tablets daily. We wondered if relatives in NTD families were more likely to use folic acid. From data obtained by interview with uncles and aunts in Irish NTD families we evaluated folic acid use in 144 of their pregnancies occurring between 1990 and 2000.

There was a significant trend towards increasing use of folic acid both before and during pregnancy over the 10 years covered by the study. During the most recent years, 1998-2000, 57.9% of pregnancies reported by aunts were supplemented beforehand and 89.5% during the pregnancy. Pregnancies to smokers were significantly less likely to be supplemented with folic acid.

In this study close relatives of an NTD child were more likely to report periconceptional folic acid use than the general public. While these results are encouraging, more remains to be done to ensure in this high risk group to ensure that the full prevention potential of folic acid is realised.

Introduction

Folic acid taken daily before and during early pregnancy has been shown to prevent between 50% and 70% of new cases and recurrent cases of neural tube defects (NTDs)^{1,2}. Results of these clinical trials have been confirmed in other studies^{3,4} and have resulted in the recommendation from the Irish Department of Health and the US government, among others, that all women who are between the ages of 15 and 44 and who are capable of becoming pregnant should take a 400µg tablet of folic acid daily^{5,6}. However, it has proved difficult in practice to achieve general compliance with this recommendation. In a report published in 1997 only 2.7% of Dublin women were taking folic acid.⁷ In the United States uptake of folic acid increased from 28% in 1995 to only 32% in 1998.⁸ More recently,

an all-Ireland dietary survey estimated that only 2% of Irish women aged 18-35 years achieved the recommended folate intake.⁹ While both Irish and US public health authorities recommend a higher folic acid dose for women who have already had an affected pregnancy, there are no special recommendations for relatives who may be at higher risk of having an affected child.

The recurrence risk for NTDs in family members is approximately 10-15 times greater than the population risk. In Ireland currently the average recurrence risk (risk to mothers who have already had an affected child) is estimated at about 15 per 1000 births¹⁰. Only 5% of NTD births are to women who have had a previously affected pregnancy. The risk faced by uncles and aunts of the proband of having a child with an NTD has not been well established. These first

cousins, or third-degree relatives, are generally considered least at risk, since their genetic relationship is less than proband's siblings or than uncles and aunts. However, although in the aggregate the risk to first cousins may be no greater than the population risk, there is some evidence that the risk to first cousins may be greater for children of mothers' siblings than for other types of first cousins.^{11,12} It might be expected that publicity concerning the benefits of folic acid would have a greater impact among close relatives of an affected person, and their use of folic acid would be correspondingly greater than the population in general. There is little information on this point so far.

This paper describes use of folic acid before and during the first trimester of pregnancy (periconceptional use) to both uncles and aunts in Irish families where a child has been born with an NTD.

Methods

As part of a retrospective interview study of extended families with an NTD, we interviewed uncles and aunts in 74 families of a child with a neural tube defect (NTD) in the North East region of Ireland, including both Northern Ireland and the Republic of Ireland. The overall objective of this study was to discover patterns in families suggestive of an underlying genetic influence on etiology.

Between April and November 2000, staff of the Boyne Research Institute interviewed 260 uncles and aunts in families where the parents and/or proband had previously been interviewed. The interview covered the health of the relative (birth defects, medical conditions and cancer), their reproductive history and the health of offspring, medications and diet during the three months before and during the first trimester of each pregnancy. Questions concerning vitamins sought information about multivitamins with and without folic acid, folic acid pills and iron pills on their own. Lifestyle questions sought information on heavy alcohol intake (more than 2 glasses daily on average), smoking more than 5 cigarettes daily, and use of drugs such as marijuana, cocaine or heroin. The same set of questions was asked separately for the three months before each pregnancy and for the first three months of each pregnancy.

From the pregnancies of the 260 relatives interviewed we extracted information for this report on only those pregnancies that ended between January 1 1990 and January 4 2000. Over the ten years covered by this report, 74 uncles and aunts in 24 NTD families reported 144 pregnancies. All pregnancies occurred after the birth of the proband with NTD. Sixty-nine pregnancies were related to the proband via the father and 75 via the mother. Pregnancies reported by uncles alone comprised 58, by aunts alone comprised 55 pregnancies, 17 pregnancies were reported by uncles and their wives together, for 13 pregnancies the wife provided a proxy interview for her husband, and for one pregnancy a sister provided a proxy interview for her brother.

Reliability Study

In order to establish the reliability of reporting of parents of folic acid use, we re-interviewed 20 respondents. Respondents were chosen for the reliability study by selecting every 10th respondent who said that they had a pregnancy or fathered a pregnancy, yielding approximately a one in four sample. Respondents were not eligible for the reliability study if they lived overseas, or if there was a proxy respondent for the first interview. Selection of respondents with replacement from the next eligible relative was carried out. The entire interview was repeated with the same respondent, and from the re-interview, two variables were selected for this comparison. The first variable was use of folic acid tablets on their own during the three months before pregnancy and the second was use of folic acid tablets on their own during the first three months of each pregnancy.

Statistical Methods

Comparisons were tested with the chi-square test for proportions, with alpha set at 0.05 and a two-tailed test. Mantel-Haenszel procedures were used to compare odds ratios. The dataset was created in EPI-

INFO (ver 6.04). Statistical analyses were done using SABER and EPI-INFO.

Results

The 144 pregnancy outcomes consisted of 110 full term pregnancies and 25 miscarriages; there were 4 premature children and 3 stillbirths, 1 ectopic pregnancy and one child who died shortly after birth. Overall, 25.7% of pregnancies were supplemented beforehand, and 44.4% were supplementing during pregnancy (Table 1). There were no significant differences in rates of folic acid supplementation before pregnancy by use of any other vitamin product, or by iron use or by smoking or drinking or according to maternal or paternal relative or by the type of NTD. During pregnancy also, with a single exception, there were no differences in these variables according to whether the pregnancy was supplemented with folic acid or not. However, women who smoked were much less likely to take folic acid. Only 20% of pregnancies to smokers were supplemented during the first trimester compared to nearly 50% of pregnancies to non-smokers ($p=0.008$). A number of respondents lived overseas and their folic acid use might differ from relatives living in Ireland. We found that folic acid use both before and during pregnancy was less likely among relatives living overseas than those on the island of Ireland.

To evaluate possible biased information depending on who was the respondent, we looked at folic acid use by uncles interviewed alone ($N=27$) and compared it to that reported by aunts. For folic acid use

Table 1 Folic Acid intake before and during 144 pregnancies to Irish families with a relative with an NTD

	Folic acid supplementation before pregnancy			Folic acid supplementation during pregnancy		
	Yes			Yes		
	N	%	p	N	%	p
Overall	37/144	25.7		64/144	44.4	
Respondent						
Aunts & wives	26/88	29.6		48/88	54.6	
Uncles alone	11/56	19.6	NS	16/56	28.6	0.01
Lived on the island of Ireland						
Yes	37/121	30.6		62/121	51.2	
No	0/25	0	0.01	2/25	8.0	0.01
Smoked more than 5 cigarettes daily						
Yes	7/38	18.4		5/25	20.0	
No	30/106	28.3	NS	59/119	49.6	0.01
Drank more than 2 glasses daily						
Yes	1/4	25.0		2/4	50.0	
No	36/140	25.7	NS	62/140	44.3	NS

Table 2 Time trends in folic acid use before and during 88 pregnancies reported by aunts in Irish NTD families

	Folic acid supplementation before pregnancy		Folic acid supplementation during pregnancy	
	Yes		Yes	
	N	%	N	%
1990-1991	3/19	15.8	5/19	26.3
1992-1993	2/17	11.8	7/17	41.2
1994-1995	4/17	23.5	8/17	47.1
1996-1997	6/16	37.5	11/16	69.8
1998-2000	11/19	57.9	17/19	89.5

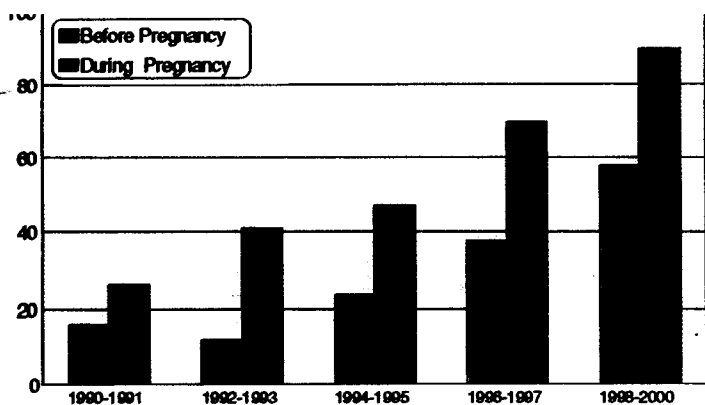


Figure 1

Periconceptional use of folic acid by aunts in Irish NTD families by year of pregnancy

before and during pregnancy, uncles reported about 40% less use than did aunts. This difference reached statistical significance for folic acid use during pregnancy only ($p < .01$; Table 1).

Among the 24 families included in this report, the type of NTD varied: three families had a child with anencephaly, five had spina bifida occulta, one had an encephalocele and 15 had spina bifida. There were no statistically significant differences in usage of folic acid either before or during pregnancy by any of the four NTD types.

To evaluate trends in usage, we limited the analysis to responses from aunts or from aunts and uncles interviewed together, or to spouses of uncles. Usage of folic acid by aunts increased significantly both before ($p < .01$) and during ($p < .001$) pregnancy (Figure 1). The rate went from 15.8% of pregnancies supplemented beforehand in 1990-1 to 57.9% in 1998-2000. Supplementation rates during pregnancy went from 26.3% in 1990-1 to 89.5% in 1998-2000.

Results of the reliability study indicated that respondents were quite reliable in their reporting of folic acid use. The 20 respondents who were re-interviewed reported on 47 pregnancies. The reliability of reporting of folic acid use during the three months before pregnancy was very good; 91.6%, or 43 of 47, pregnancies had the same information. In only 4 pregnancies was the information different, supplied by 2 aunts and 2 uncles. Reliability was somewhat less for folic acid use during the first three months of pregnancy: 78.7%, or 37 of 47 pregnancies, had the same information. In the 10 pregnancies where information differed the uncle was the respondent in 8 instances. When we compared the reliability on both variables, only one respondent (an aunt) gave different answers to both questions. We evaluated the discordant answers for other factors. Outcome of pregnancy was not strongly related to reliability: of the 10 unreliable answers three pregnancies ended in miscarriage, and 7 in full-term deliveries. However, passage of time seemed to have an impact. Of the 10 unreliable answers, 8 referred to pregnancies ending between 1990 and 1995 and only two to pregnancies ending between 1996 and 2000. In summary, reliability of reporting of folic acid use in this study was excellent for use before pregnancy and good for use during pregnancy.

Discussion

This limited survey of uncles and aunts of Irish families with a child with a neural tube defect suggested that use of folic acid is significantly higher in these families than in the general population. Over the last decade of the twentieth century, reported usage in this group of relatives increased greatly. However, even in the most recent three years covered by the survey (1998-2000) only slightly more than half of aunts had supplemented their pregnancies beforehand, indicating considerable room for improvement in these vulnerable

smokers were significantly less likely to be supplemented with folic acid than pregnancies to non-smokers.

Available surveys of the Irish population suggest that folic acid recommendations are not being widely followed. One survey carried out in March 1995, in obstetric and fertility settings in Dublin, indicated that 5% of public and 20% of private patients had taken folic acid before pregnancy.¹³ In a regional survey reported in 1997, Howell et al indicated that 26.5% of women interviewed after delivery reported folic acid use before pregnancy.¹⁴ Lower rates were reported in a survey carried out among women in Dublin. There, only 2.7% of Dublin women were taking folic acid.⁷ An All-Ireland survey carried out between 1997 and 1999 indicated that only 2% of women aged 18-35 achieved the recommended folate intake.⁹ Compliance with folic acid recommendations in other jurisdictions may be better. Rates of around 30% are reported from surveys in the UK and the US.^{8,15}

There is little information on folic acid intake among relatives in NTD families. One survey carried out in Sicily found that among 18 pregnant women at risk for a recurrent NTD none had taken periconceptional folic acid.¹⁶

Our study found that pregnancies to smokers were less likely to be supplemented with folic acid. This is in line with other folic acid surveys which reported that smokers and women of lower income and education were less likely to take folic acid.^{17,18} In addition, the diets of smokers are markedly deficient in other nutrients, such as vitamin C, fibre and Vitamin A compared to non-smokers.¹⁹ Thus, raising folic acid intake among women who may have multiple unhealthy behaviours will present a significant challenge to the public health authorities.

Our results are subject to a number of limitations. First, in a historic survey, accuracy of recall can be problematic. In addition, male respondents may underreport their wives' intake; for this reason we limit the analysis of time trends to aunts' reports. However, the number of statistically significant associations in directions expected from other surveys suggests that the results are valid overall and may be generalisable. Other studies of the reliability of self-reported behaviour health risk factors suggest that agreement on repeat interview is high, which supports the generally good reliability found here.²⁰

The results of this study have implications for the Irish population in general. First, it seems that these aunts are strongly motivated to take folic acid since they have seen the effects of neural tube defects up close in their own families. Second, even with this strong motivation, smokers are still less likely to heed the recommendations. Thus, public health campaigns to increase usage of folic acid should target smokers and low income women more intensively in order to increase their knowledge and improve their diets. While many of these families are following recommendations, much remains to be done to increase pre-conceptional intake. Improved diet during the pre-pregnancy period to cover the vulnerable first six weeks of pregnancy remains the challenge for public health authorities everywhere.

In conclusion, there is much room for improvement in folic acid use by these families at highest risk of having a child with an NTD. Relatively passive public health messages, such as leaflets, posters and radio and TV spots, may not be enough. More aggressive publicity campaigns and personal contacts are needed to increase the use of this most effective preventive measure.

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CORRESPONDENCE:

Julianne Byrne,
 Boyne Research Institute, Duke House, Duke Street, Drogheda,
 Ireland. Telephone: 353-(0)41-983 6041. Fax: 353-(0)41-984 1339.
 Email: boyne@iol.ie.

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