Original Articles

An Intervention Study to Increase Knowledge and Use of Folic Acid among Relatives in Neural Tube Defect-Affected Families in Washington, D.C.

Julianne Byrne,[1,2] Susan Carolan,[2] Rashad Arcement,[3] Matthew Kozlowski,[3] Inna Taller,[3] Stephanie Ried,[4] and Robert Keating[4]

[1]Westat, Rockville, Maryland
[2]Boyne Research Institute, Drogheda, Ireland
[3]George Washington University School of Medicine and Health Sciences, Washington, D.C.
[4]Children's National Medical Center, Washington, D.C.

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BACKGROUND: Little is known about the level of knowledge and use of folic acid among near relatives in U.S. families of a child with spina bifida. We hypothesized that relatives would be more knowledgeable than the general population and more likely to take folic acid. Further, we hypothesized that relatives would be more motivated by an intervention to increase their use of folic acid. **METHODS:** We conducted an intervention study among females in families attending a hospital spina bifida clinic in Washington, DC. **RESULTS:** The 231 subjects consisted of the affected individuals, mothers, sisters, and aunts. The average age was 34 years. At baseline, most (87.4%) reported that they had heard of folic acid; 37.6% were currently taking multivitamins with folic acid and 6.9% were taking folic acid tablets. The intervention significantly increased both knowledge (to 99%) and intake of folic acid from 41.9 to 48.5%. Folic acid intake increased significantly among African-American women and women with less education, women who were older, married, with children, and nonsmokers. **CONCLUSIONS:** This intervention was successful in increasing folic acid intake among female relatives in spina bifida–affected families. By the end of the study, almost all women had heard of folic acid and folic acid use had increased by 16%. Among these women at higher than expected risk for having an affected child, this rate of intake, while more than the general population, still falls short of optimum. Fortification of food with folic acid may be the only way to ensure increased folic acid intake. *Birth Defects Research (Part A) 73:424–429, 2005.* © 2005 Wiley-Liss, Inc.

Key words: folic acid; NTD relatives; intervention; Washington, DC; spina bifida; families

INTRODUCTION

Congenital malformations are the leading cause of death in U.S. infants before their first birthday, and neural tube defects (NTDs) are among the most common birth defects (National Center for Health Statistics, 2004). Children with spina bifida, which comprises about one-half of all NTDs, often have impaired mobility, requiring use of wheelchairs, and have shortened life expectancies (Hunt, 1999). The burden of care falls on the families. In 1992, lifetime care for spina bifida was estimated to cost $300,000 per case (MMWR, 1995). However, folic acid, a B vitamin, was shown in clinical trials to prevent between 50 and 72% of new cases (MRC Vitamin Study Research Group, 1991; Czeizel and Dudas, 1992) if taken around the time of conception. In a community intervention in China, folic acid alone led to major reductions in the occurrence of NTDs (Berry et al., 1999). Thus, for the first time, a simple method of primary prevention of birth defects has been found. The U.S. govern-

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*Correspondence to: Julianne Byrne, PhD, Westat, 1650 Research Blvd, WB474, Rockville, MD 20850-3195. E-mail: juliannebyrne@westat.com
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ment recommends that every woman capable of becoming pregnant should take a 400 μg folic acid tablet daily (MMWR, 1992). The U.S. government has mandated that a number of foods, such as bread, pasta, rice, and cereals, be fortified with folic acid to a level of 140 μg per 100 gm of grain (FDA, 1996). Some breakfast cereals are fully fortified (100%), containing the full 400 μg that is recommended.

Public health campaigns to promote folic acid have been enthusiastically embraced worldwide. In the United States, the Centers for Disease Control and Prevention (CDC), the March of Dimes, and some states carry out surveys to monitor campaign results. In 2004, a March of Dimes survey reported that 77% of women surveyed had heard of folic acid and 40% said that they took a vitamin supplement including folic acid daily (CDC, 2004).

There have been no reports to date concerning folic acid use among women in NTD-affected families in the United States. Studies in Ireland suggest that family members are well informed about folic acid, but their usage of folic acid pills is low. However, an intervention study suggested that they could be prompted to increase their folic acid intake (Byrne, 2003).

The overall objective of increasing folic acid intake is to prevent NTDs. It has not been easy to evaluate that objective. One recent CDC report claimed that the observed 19% reduction in new cases might be attributable to food fortification, but recognized that a downward trend had been in place before food fortification (Honein et al., 2001; Williams et al., 2002). Wald et al. (2001), who conducted the first randomized clinical trial reported in 1991, recently made a persuasive case for increasing the recommended 400-μg level to 5 gm daily; their projections indicated that 5 gm would reduce risk by about 85%. Various forms of intervention have been implemented and shown to raise knowledge and use of folic acid. For instance, one study in Australia evaluating the impact of a leaflet campaign showed that it had enduring effects, even years afterward (Watson et al., 2001). No intervention study in NTD families has been reported from the United States.

This article reports knowledge and use of folic acid among relatives in spina bifida–affected families in which the affected individual was attending a spina bifida clinic in Washington, DC. We also report on the results of an intervention study intended to increase knowledge and use of folic acid among relatives.

MATERIALS AND METHODS

Registry of Cases

Each family was identified from the records of the Spina Bifida Clinic of Children's National Medical Center (Washington, DC). Initial contact was either when the family attended the weekly clinic or by telephone after review of medical records. The Institutional Review Board of Children's National Medical Center reviewed and approved this study.

Eligibility Criteria

In each family attending the Clinic, the following persons were eligible for the study: probands (the person with spina bifida), mothers, sisters, and aunts. Potential subjects were female, between the ages of 18 and 44, mentally competent, capable of becoming pregnant (not sterilized), English-speaker, and resident of the United States. Further, probands with a syndrome of which spina bifida was a part (i.e., Rubenstein-Taybi syndrome) were ineligible, since it is not clear that folic acid is effective in this context, or that relatives are at increased risk. We originally intended to enroll Spanish-speaking families but found that study resources made that impossible. Relatives did not need to be blood relatives; adoptive families, foster mothers, and half-siblings were included.

Interview: The Spina Bifida Family History Questionnaire

At the time the family was identified for the study, study personnel first administered the standard family history interview that identified each relative in the family (siblings, uncles, and aunts of both parents of the proband). The interview included basic demographic information on the parents, the outcome of the parents' pregnancies, and the numbers of siblings of the mother and father. At that time contact information (telephone number) was requested for each relative. Then, for eligible family members, the preintervention questionnaire was administered.

Preintervention interview: The Folic Acid Preintervention Questionnaire

The purpose of the folic acid preintervention questionnaire was to determine the respondent's level of knowledge about folic acid and its usefulness, as well as usage of folic acid, at baseline, before the intervention was carried out. The questionnaire included three questions (nos. 3, 4, and 5) from the Behavioral Risk Factor Surveillance System (BRFSS) of CDC, an ongoing, state-based telephone survey of the U.S. population, including the District of Columbia. Although not a primary hypothesis of this project, this information permits comparisons with nationally collected data.

Intervention

The intervention consisted of a mailed-out package of information about folic acid. Each package contained a letter repeating the recommendations for folic acid use and dietary suggestions, as well as brochures about folic acid from the March of Dimes and the CDC, and a coupon from a cereal manufacturer, General Mills. The material was packaged in a brightly-colored envelope with a white label and a commemorative stamp, in order to increase the chances of the subject opening and reading the material. The preintervention questionnaire was done between June 3, 2003 and September 3, 2003. The postintervention questionnaire was done between June 22, 2003 and October 2, 2003. The length of time elapsed between both questionnaires averaged 25 days and ranged from 2 to 86 days. The goal was to have posttests done within 28 days of the pretests.

Some preintervention questionnaires were done in the Clinic; most were done over the telephone; all postintervention questionnaires were conducted over the telephone.

Numbers of Participants

From families attending the clinic and from the clinic records, families that could not be reached and those with no eligible members were eliminated; 193 families were asked to participate. Of these families 11 (6%) had no English-speaking ability and were excluded, 18 refused (9%), 3 families (2%) did not live in the U.S., and the balance, 161 (83%) families agreed to participate. From the 161 participating families, 145 had one or more eligible relatives, for a total of 300 eligible relatives.

Of the 300, 231 eligible relatives (hereinafter called "subjects") agreed to participate and completed the preintervention questionnaire and 3 refused (1.3%). The remaining 66 either could not be located or reached or were not reached by the time the study closed, despite multiple efforts.

Of the 231 subjects who completed the preintervention questionnaire, 203 completed the study by doing the postintervention questionnaire. Of the 28 who did not complete the study, the telephone had been disconnected for 10 and the remaining 18 could not be reached despite multiple attempts. Thus, 87.9% of those subjects who completed the preintervention interview also completed the postintervention interview. The number of relatives per family who participated in both phases ranged from one to five, with an average of 1.5. Nearly two-thirds (62.6%) of subjects were the only ones in their families to participate. Only one non-blood relative participated; she was a foster mother.

Statistical Methods

We tested differences in the proportions of women who had heard of folic acid, and the proportions of women who are taking folic acid, between pre- and postinterviews, using McNemar's test for correlated proportions in a 2×2 table with a correction for continuity, and alpha set at 0.05 (Fleiss, 1981). McNemar's test assesses change from a pretest to a posttest in the same (correlated) individuals. The data were analyzed in both EpiInfo 6.04 and EpiInfo 2002, which are statistical data analysis programs available at no cost from the CDC (http://www.cdc.gov).

RESULTS

Aunts (38.6%) and mothers (37.6%) comprised most of the subjects, with 10.4% of subjects consisting of sisters and 11.7% being the probands themselves (Table 1). The average age of subjects was 34.0 years; 62% had at least some college education. Slightly under one-half (45.5%) were in managerial/professional occupations; slightly under one-half were white (46.8%), 33% were African-American, and 12% were Hispanic. Most subjects were married and most had children. Fewer than one in five was a current smoker. The majority (87.4%) had heard of folic acid. Of those who had heard, less than one-half were currently taking multivitamins, 37.6% were taking multivitamins with folic acid, and 6.9% were currently taking folic acid on its own. At baseline, nearly three-quarters knew that folic acid prevented spina bifida, although 21.3% said that folic acid prevented Down syndrome (an incorrect answer), and 12.9% did not know what folic acid did. Most knew that the best time to take folic acid was before and during early pregnancy (81.7%) and most knew of other ways to get folic acid; some, 5.4%, were unsure (Table 2). A doctor or a nurse was the most frequently acknowledged source of folic acid information.

We compared relatives who answered both interviews on different factors. At baseline, relatives who had more education were more likely to have heard of folic acid. White women were more likely than others to have heard of folic acid. Otherwise, there were only slight differences in knowledge of folic acid according to age, marital status, having children, or smoking status (Table 3).

At baseline, before the intervention (Table 4), relatives who were more educated, older, married, with children, and nonsmokers were more likely to take multivitamins or folic acid.

Table 1
Characteristics of the Study Sample at Baseline, $n = 231$

	n	(%)
Relationship of respondents		
Proband	27	11.7
Mother	87	37.6
Sister	24	10.4
Paternal aunt	60	26.0
Maternal aunt	29	12.6
Information missing	4	1.7
Age		
18–24	40	17.8
25–29	26	11.6
30–34	28	12.4
35–39	60	26.7
40–44	71	31.6
Education		
Grade school only	13	5.8
Completed high school	73	32.3
Some college	50	22.1
College graduate	72	31.9
Post graduate	18	8.0
Occupation of respondent		
Working class/student/unemployed	122	54.5
Other—managerial/professional	102	45.5
Ethnicity		
White	108	46.8
African-American	77	33.3
Hispanic	27	11.7
Other and unknown	19	8.2
Married		
Yes	148	65.8
Have children:		
Yes	157	70.1
Currently smoke?		
Yes	41	18.3
Ever heard of folic acid?		
Yes	202	87.4
Currently take multivitamin pills or supplements, including liquid supplements	92	45.8
Currently taking multivitamins	86	42.6
Currently taking multivitamins with folic acid	76	37.6
Currently taking folic acid pills	14	6.9

The intervention increased knowledge of folic acid from 88.7 to 99.0% ($p < 0.001$; Table 3). When the data were stratified by the major demographic factors, individuals in all strata showed an increase in knowledge. Intake of folic acid also increased significantly over baseline, reaching 48.5% after the intervention ($p = 0.02$; Table 4). Statistically significant increases were noted for all demographic factors. Relatives who were less well educated, who were older, married, with children, nonsmokers, and African-American women were more likely to take folic acid or a multivitamin after the intervention. Whereas probands and mothers increased their intake, the largest increase in folic acid intake occurred among aunts.

We wondered if women not located for the postintervention questionnaire were, in detectable ways, different from women who did both questionnaires. We compared both groups on the demographic variables in Table 1 and

Table 2
Level of Knowledge About Folic Acid at Baseline (n = 202, Includes Only Those Who Had Heard of Folic Acid)

	n	(%)
Benefits of folic acid (Choose all that apply)		
Helps prevent birth defects	162	80.2
Helps prevent spina bifida	146	72.3
Helps prevent Down syndrome	43	21.3
Don't know, not sure	27	12.9
Single best time to take folic acid (Choose only one)		
Before you become pregnant	25	12.4
During pregnancy	2	1.0
Before and during early pregnancy	165	81.7
Don't know, not sure	11	5.0
Other ways to take folic acid (Choose all that apply)		
Eat more foods, such as broccoli, cereals, and orange juice	142	70.3
Take a daily multivitamin with folic acid	142	70.3
Take both folate rich foods and multivitamins	178	88.1
Don't know, not sure	11	5.4
Where did you first hear about folic acid?		
TV or radio	27	13.4
Doctor or nurse	89	44.1
Magazine, newspaper	23	11.4
Relative	38	18.8

found that only one was statistically significant. There were no significant differences on age, education, occupation, marital status or children, smoking, ever heard of folic acid, or currently taking a multivitamin supplement or folic acid tablets on their own between women who did the postintervention interview and those who did not. The single variable that was significantly different was relationship to proband. Probands and first-degree relatives (mothers and sisters) were more likely to complete the second interview than aunts (95.6 vs. 69.4%; p = 0.0001). Thus, it seemed that closeness of relationship to the proband was a primary motivator to completing the study.

DISCUSSION

This survey of female relatives in NTD-affected families from Washington, DC showed that levels of knowledge about the benefits of folic acid were high, but use was low. Compared to the general public, reported by the March of Dimes (2002), rates of intake of a multivitamin containing folic acid were somewhat higher among these relatives at baseline (33 vs. 37.%, respectively). Knowledge of folic acid benefits was considerably higher among relatives than among the general public, 80.2% of relatives knew that folic acid prevented birth defects compared to 20% of the general public (March of Dimes, 2002). As with the March of Dimes survey, this group of relatives was more likely to take folic acid if they were older and had more years of education. The Folic Acid Surveillance Survey of Maryland, carried out in May 1999 using the BRFSS survey, showed that 29% of women specifically not planning a pregnancy knew that folic acid prevented birth defects, and 17% took a multivitamin daily (National Birth Defects Prevention Network).

Results from the short-term intervention reported here showed that it was successful in increasing both knowledge and use of folic acid among relatives. The intervention increased awareness of folic acid and significantly increased the percentage of women taking folic acid. How-

Table 3
Knowledge of Folic Acid Before and After the Intervention Stratified According to Sample Characteristics (n = 203, Includes Only Respondents Who Completed Both Questionnaires)

	Ever heard of folic acid?				
	Before intervention		After intervention		
Characteristic	n	%	n	%	p^a
Overall	180	88.7	201	99.0	<0.001
Education					
High school or less, n = 73	57	78.1	71	97.3	<0.001
More than high school, n = 127	120	94.5	127	100.0	0.04
Age					
18–35, n = 95	83	87.4	95	100.0	0.003
36–44, n = 104	93	89.4	102	98.1	0.008
Ethnicity					
White	93	96.9	96	100.0	0.3
African-American	54	78.3	69	100.0	0.3
Hispanic	17	77.3	20	90.9	<0.001
Other/unknown	16	100.0	16	100.0	—
Marital status					
Married, n = 129	114	88.4	127	98.4	<0.001
Not married, n = 70	62	88.6	70	100.0	0.02
Have children					
Yes, n = 139	123	88.5	137	98.6	<0.001
No, n = 59	52	88.1	59	100.0	0.02
Current smoker					
Yes, n = 36	30	88.3	35	97.2	0.13
No, n = 162	145	89.5	161	99.4	<0.001

[a]Before and after intervention values for each stratum compared using McNemar's test.

Table 4
Intake of Multivitamins or Folic Acid Supplements Before and After the Intervention Stratified According to Sample Characteristics (n = 203, Includes Only Respondents Who Completed Both Questionnaires)

	Intake of multivitamins or folic acid				
	Before intervention		After intervention		
Characteristic	n	%	n	%	p^a
Overall	85	41.9	98	48.5	0.02
Education					
High school or less, n = 73	20	27.4	29	39.7	0.02
More than high school, n = 127	63	49.6	67	58.2	0.5
Age					
18–35, n = 95	36	37.9	40	42.1	0.4
36–44, n = 104	47	45.2	56	53.8	0.04
Ethnicity					
White	43	44.8	45	46.9	0.8
African-American	30	43.5	40	58.0	0.02
Hispanic	6	27.3	7	33.3	1.0
Other/unknown	6	37.5	6	37.5	0.5
Marital status					
Married, n = 129	59	45.7	72	55.8	0.006
Not married, n = 70	23	32.9	23	32.9	0.7
Have children					
Yes, n = 139	68	48.9	80	57.6	0.02
No, n = 59	13	22.0	14	23.7	1.0
Current smoker					
Yes, n = 36	13	36.1	15	41.7	0.7
No, n = 162	68	42.0	79	48.8	0.03
Relative Type					
Proband, n = 27	8	29.6	10	37.0	0.48
Mother, n = 82	40	48.8	42	51.2	0.75
Sister, n = 23	6	26.1	6	26.1	0.48
Aunt, n = 67	28	41.8	37	55.2	0.03

[a]Before and after intervention comparisons for each stratum tested with McNemar's test.

ever, this intervention did not work for every woman. There were specific groups of women whose behavior was not significantly affected. Folic acid intake increased among African-American women, women with a high school education or less, women who were older than 35 years, and who were married and who had children, and among nonsmokers. Among relatives, aunts had the largest increase in folic acid intake. Other studies have shown that women who are white, older, college-educated, married, and who have children are more likely to take folic acid (MMWR, 1999; Byrne, 2003). In our study, women who had only a high school education and women who had more than a high school education both increased their intake of folic acid, but only the increase among women with less education reached statistical significance.

In line with other studies (Byrne, 2003) this study showed that female relatives who are also smokers were less likely than those who were nonsmokers to change their behavior as a result of the intervention. Health behaviors among smokers are quite different from nonsmokers; for instance, their diets are markedly deficient in other nutrients, such as vitamins A and C and fiber, compared to nonsmokers (Subar et al., 1990; CDC, 2004).

Other intervention studies have had mixed results. A similar intervention study conducted in Ireland doubled the use of folic acid pills to 19% among female relatives in Irish families with NTDs (Byrne, 2003). Another project in Southern Virginia running from 1997 to 1999, including a sustainability assessment, increased the proportion of women correctly responding that folic acid prevented certain birth defects to 88%. Intake of folic acid was not measured in this survey (MMWR, 1999). However, supplying free folic acid through family planning clinics in Georgia increased knowledge but did not increase either self-reported folic acid intake or serum folate levels (Watkins et al., 2004).

There are limitations to this study. We did not set out to measure the sustainability of the intervention, but only the immediate effects; thus, we cannot comment on the long-term effects. It is not clear how generalizable these results are. Non-English-speaking women were not enrolled due to limited resources. We contacted families of children attending the spina bifida clinic in Washington, DC. Although some relatives lived at a distance, the sample is not population-based. However, since the results are similar to those obtained from other surveys of NTD-affected families (Byrne, 2003), these results may be close to that expected from a larger, more representative sample of relatives. Women planning a pregnancy are more likely to be taking folic acid; we did not ask about pregnancy plans, so we cannot evaluate this aspect. We also did not ask if mothers were taking the higher folic acid dose (4.0 mg) recommended to prevent recurrences. Nearly two-thirds (62.6%) of women who completed both parts of the study were the only ones in their families to participate; in another one-quarter of participants (26.7%), two members

from the same family participated. It is possible that nutrition habits were correlated within families. We did not evaluate the data by family, so we cannot evaluate this idea. Such an analysis would have been beyond the scope of the study.

Surveys have indicated that there is significant heterogeneity among women in their levels of folic acid use: pregnancy contemplators, women of higher socioeconomic status, and married women are more likely to be taking folic acid (Sen et al., 2001). Conversely, there are significant groups of women who are unlikely to comply with the recommendations: smokers, younger women, and women with little education or income and who were low on fruit intake have been identified repeatedly as not being reached by health messages (MMWR, 1999). Language can also be a barrier: Spanish-speaking women in Arizona were only one-half as likely as English speakers to be aware of the benefits of vitamins (Perlow, 2001). Of more concern are reports from sites as far apart as Colorado and Sicily that some women who have already had an NTD-affected pregnancy or who have a family history are not following guidelines (Pepe et al., 1999; Callendar et al., 2001; Rinsky-Eng and Miller, 2002).

Relatives in NTD-affected families are at higher risk of having an NTD-affected pregnancy. Recurrence risks in excess of 10- to 15-fold have been reported in sibships (Byrne et al., 1997). There is also evidence for excess risks of NTDs among mothers' relatives, whether full-blood relatives or half-siblings (Carter and Evans, 1973; Nevin and Johnston, 1980; McManus, 1987; Chatkupt et al., 1992). In addition, among families with distant NTD-affected relatives the linking parent is more often female than male (Mariman and Hamel, 1992; Chatkupt et al., 1994).

Our study, and others, highlight the difficulties inherent in increasing intake among women who are possibly at increased risk for having an NTD-affected pregnancy and who have more knowledge of the condition than the general public. Fortification of food with folic acid has been associated with declines in NTD occurrence (Persad et al., 2002; Chen and Rivera, 2004) and may be the only way to bring about measurable declines in NTD incidence.

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