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Awareness of Folic Acid for Neural Tube Defect Prevention Among Israeli Women

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ABSTRACT The failure of neural tube closure during early embryogenesis results in a range of neural tube defects (NTD), the most common of which is spina bifida. The role of folic acid in reducing the rate of NTD has been well-established. Three recent cases of infants with NTD inspired this investigative study into the level of awareness and knowledge of folic acid and its function in the prevention of NTD among Israeli women. Of 920 women interviewed, only 51 (5.5%) had heard of folic acid, and 27 (2.8%) were reported to have taken it. The source of information and the motivation for self-medication were also explored with regard to socioeconomic and health profile. Awareness of folic acid was significant among women aged 17–29 years ($P = 0.005$) and those aged 30–39 years ($P = 0.009$), and among semireligious and nonreligious women ($P = 0.008$ and 0.01, respectively). Among women who were aware of folic acid, only nonreligious women tended to take it. No correlation was found between folic acid intake and age, religiosity, nationality, number of pregnancies, and health status among women who were aware of folic acid intake. The poor level of awareness, evident in our study, demands that the medical community broadcast the benefit of folic acid. Furthermore, government health initiatives, such as the addition of folic acid to flour preparations, may effectively ensure its appropriate daily intake. These improved education and prevention programs may forcibly reduce the rate of NTD-affected pregnancies. *Teratology 60:29–32, 1999.* © 1999 Wiley-Liss, Inc.

The failure of neural tube closure during early embryogenesis results in a spectrum of neural tube defects (NTD). They are one of the most common malformations, responsible for causing severe handicaps and debilitation. NTD can usually be diagnosed prenatally by means of fetus ultrasonography and maternal αfetoprotein measurement. NTD include spina bifida, accounting for 50% of NTD, anencephaly (40%), and meningocele and meningomyelocele. Ninety percent are classified as "open" malformations. A multifactorial theory has been proposed, suggesting genetic and environmental influences (Spina Bifida Association of Canada, '94a). A woman with prior history of an NTD-affected pregnancy is at a high risk of recurrence. Nevertheless, 95% of affected infants do not have siblings with NTD. There is a geographical variation in the incidence of NTD, ranging from 1.1/1,000 live births in Denmark and France (Brock, '82), to 12/1,000 live births in South Wales (Carter, '69). The incidence of NTD in Israel is 0.74/1,000 life births (Merlob et al., '89). It has been estimated that one out of four affected fetuses will be stillborn, one of two will result in spontaneous abortion, and the remaining one of four will survive (Creasy and Alberman, '76).

Folic acid is a water-soluble B-complex vitamin, essential for nucleoprotein synthesis and the maintenance of erythropoiesis (American Hospital Formulary Service, '93). The benefit of folic acid in reducing the prevalence of NTD is well-established (Czeizel and Dudas, '92; Medical Research Council (MRC) Vitamin Study Research Group, '91; Morbidity and Mortality Weekly Report (MMWR), '92). It was demonstrated by the Center for Disease Control that the daily intake of 0.4 mg of folic acid, if commenced 1–3 months prior to conception until 3 months postconception, reduces by 50% the incidence of NTD in the general population (U.S. Center for Disease Control, '92). Among women who had a previous history of an NTD-affected pregnancy, folic acid reduced the incidence by 72% (MRC Vitamin Study Research Group, '91). The Spina Bifida Association of Canada ('94b) published a policy statement urging that "all women of childbearing age supplement their daily diet with 0.4 mg folic acid to reduce the risk of first occurrence of spina bifida and other NTD," and that "those women with a previous NTD affected pregnancy or a close family history of NTD supplement their daily diet with 4 mg folic acid." Considering the fact that many pregnancies are unplanned, there is a

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current trend to recommend folic acid as a food additive in an effort to ensure an adequate daily intake. In Canada and the United Kingdom, several brands of flour are fortified with folic acid (National Academy of Sciences, '94), while in the US, cereal and grain fortification with folic acid began in 1998.

In Israel, no such supplementation program exists. Furthermore, there is no official governmental program aimed at promoting the intake of folic acid as a means to prevent the occurrence of NTD.

During a 6-month period, 3 children were born at the Assaf Harofeh Medical Center with NTD. These cases were the inspiration for our study, which explored Israeli women's awareness of the role of folic acid in the prevention of NTD.

MATERIALS AND METHODS

Case reports

Case 1 was the eighth child of a Moslem family with no history of NTD. Fetal ultrasonography (US) was first performed during gestational week 28, at which time NTD was evident. The newborn male (birth weight, 2,630 g) suffered from spinal meningocele and hydrocephalus. Case 2 was the ninth child of a Jewish orthodox family. There was a positive family history of meningomyelocele. Fetal US was also first performed during gestational week 28; however, NTD was not revealed. The newborn female (birth weight, 3,270 g) suffered from sacral meningocele. Case 3 was the first twin of a young Jewish couple. Level 2 fetal US, performed during gestational weeks 14 and 21, failed to reveal the existence of an NTD. The newborn female (birth weight, 2,445 g) suffered from sacral meningomyelocele.

None of the aforementioned women took folic acid prior to, or during, the first trimester of pregnancy; nor were they aware of its potential role in the prevention of NTD. A dietitian calculated their daily folic acid and dietary intake using a food frequency questionnaire (Gibson, '90). We preferred this method for calculating food requirements during the long period of pregnancy over the other method of a 24-hr interview. The average daily dietary intake of folic acid was 236 µg, 168 µg, and 132 µg for cases 1, 2, and 3, respectively. In all three cases, the daily amount achieved was well below that of the recommended daily amount (RDA) of 400 µg.

Patients

Nine hundred and twenty women participated in the study, performed during 1997. They were recruited from two sources: 1) family health clinics in two large cities in Israel; and 2) the maternity unit at the Assaf Harofeh Medical Center.

Each woman was personally interviewed according to a specific questionnaire. They were asked if they had heard about folic acid supplements before pregnancy, what the source of their information was, and whether they indeed took folic acid supplements. They were also asked if they know the reason for the recommendation. In addition, we asked several demographic questions: marital status, nationality, origin, religiosity, health status, and number of children.

Religious women were those who subjectively considered themselves as bound to the rules of faith, while nonreligious women were not bound to these rules. Semi-religious women considered themselves only partially committed to the rules. We compared those women who were aware of folic acid supplements with those who were not, as well as those who used folic acid supplements and those who did not.

Continuous data such as age and number of pregnancies is presented as mean ± SD. The chi-square test was used for comparisons between various groups.

RESULTS

Nine hundred and twenty women were interviewed. Their age was 30 ± 5 (17–47) years (mean± SD (range)). Four hundred and twenty-six women (46.3%) were interviewed in the maternity department and 494 women (53.7%) were interviewed in family health clinics. Patient characteristics are described in Table 1. Forty-one women (4.5%) reported chronic problems such as hypertension, diabetes, asthma, peptic ulcer, or anemia. The average number of pregnancies was 2 ±1. Fifty-one women (5.5%) had heard about folic acid supplementation prior to their pregnancy. Out of these 51 women (Table 2), 27 had taken folic acid supplements, representing 52.9% of those aware of folic acid, and 2.93% of the study population. The source of knowledge, the reasons for having taken folic acid (according to these women), and their ethnic origin are presented in Table 2.

The 920 women were compared according to their awareness of folic acid supplementation (Table 3). Awareness of folic acid was significant among women aged 30–39 years ($P = 0.009$) and 17–29 years ($P = 0.005$). Awareness was also significant among nonreligious ($P = 0.01$) and semireligious ($P = 0.008$) but not among religious women (Table 3).

Among women who were aware of folic acid supplement, nonreligious women took it more as compared to semireligious or religious women ($P = 0.01$) (Table 4). No significant difference was found with regard to age, nationality, number of pregnancies, and health status (Table 4).

No case of NTD was diagnosed among the 920 children born to these women.

DISCUSSION

Despite the well-established benefit of folic acid in reducing the risk of NTD, the majority of women in our study (94.5%) were unaware of its existence. Only 53% of those who had heard of folic acid followed the recommendation regarding intake before and during pregnancy. Furthermore, among the women who had taken folic acid, only 4 (out of 27) were aware of the purpose of its intake.

TABLE 1. Patient characteristics (total of 920)

Factor	No. (%)
Place of interview	
Maternity department	426 (46.3)
Family health clinic	494 (53.7)
Marital status	
Married	910 (98.9)
Widow/divorced/single	10 (1.1)
No. of pregnancies	
First	330 (35.9)
Second	281 (30.5)
Third	204 (22.2)
Fourth or fifth	105 (11.4)
Nationality	
Jewish	879 (95.5)
Christian	34 (3.7)
Moslem	7 (0.8)
Place of origin*	
Eastern Europe	300 (33.1)
North Africa	365 (40.3)
Asia	102 (11.3)
Mixed origin	42 (4.6)
Israeli Arabic	37 (4.1)
Western Europe	24 (2.7)
Ethiopia	16 (1.8)
South Africa	19 (2.1)
Health status	
Healthy	879 (95.5)
Not healthy	41 (4.5)

*Total = 905 women, missing data in 15 for this specific question.

TABLE 2. Characteristics of women who had heard of folic acid

Factor	No. (%) (total = 51)
Took folic acid	27 (53.94)
Source of knowledge	
Article reading	14 (27.5)
Gynecologist	7 (13.7)
Friend	4 (7.8)
Professional*	3 (5.9)
Family physician	1 (2)
Unknown source	22 (43.1)
Reasons for taking folic acid**	
Prevent general malformations	7 (25.92)
Prevent neurologic malformations	4 (14.81)
Healthy	4 (14.81)
Prevent abortions	1 (3.7)
Unknown	11 (40.76)
Origin	
Eastern Europe	28 (54.9)
Europe and USA	5 (9.8)
North Africa	10 (19.6)
Asia	8 (15.7)

*One nurse, two pharmacists.
**Total = 27.

TABLE 3. Comparison of women according to their awareness of folic acid

Factor	Were aware of folic acid (%)	Were not aware of folic acid (%)	*P* value
Age			
40–47 years	7 (0.76)	75 (8.15)	NS
30–39 years	38 (4.13)	486 (52.82)	0.009
17–29 years	6 (0.65)	308 (33.49)	0.005
No. of pregnancies			
1	17 (1.84)	313 (34)	NS
2	15 (1.63)	265 (28.8)	NS
3	14 (1.82)	190 (20.5)	NS
4 and more	5 (0.54)	100 (10.87)	NS
Nationality			
Jewish	50 (5.45)	829 (90.1)	NS
Non-Jewish	1 (0.1)	40 (4.35)	
Religiosity*			
Religious	4 (0.43)	55 (5.98)	NS
Semireligious	8 (0.87)	249 (27)	0.008
Nonreligious	32 (3.48)	349 (38)	0.01
Did not answer**	7 (0.76)	216 (23.48)	

*The definition of religiosity was a subjective parameter according to the women asked. The difference lay in the proportion of observing religious rules. Religious women were those who followed the rules of faith. Semireligious were those who partially followed the rules of faith, while the nonreligious ignored these rules.
**Was not calculated by chi-square test.

In 1994, in a similar study performed in the United Kingdom, out of 109 pregnant women attending a clinic at which a notice on folic acid intake during pregnancy was posted, only 20 (18%) actually followed the recommendations (Metson, '95).

In a Canadian survey on folic acid performed during 1994, 18% of 123 women attending a Montreal genetic clinic were aware of the benefit of folic acid. It was noteworthy that only 37% of women with a positive family history of NTD were aware of the importance of folic acid, and that only 18% of them adhered to a regular folic acid supplementation regime (Fraser, '95).

Awareness of folic acid was significant among women under 39 years of age. Younger women are probably more exposed to information on prenatal care. Nevertheless, being aware of folic acid was not reflected by higher intake rates. Previous experience with other pregnancies was not examined. Emphasis should be stressed on giving explanations to older women, and it is crucial to explain the importance not only of awareness but of compliance with folic acid supplementation.

Two out of the three women who prompted us to perform the study were religious. Indeed, religious women in our study were less aware of folic acid. Furthermore, religious women who were aware did not take folic acid. Taking into consideration the fact that religious women in Israel usually conceive more frequently and until an older age, as compared to nonreligious women, we should focus on this population with aggressive educational programs.

Healthcare workers were not themselves interviewed. It would be of special interest to determine the level of commitment among medical professionals in their promotion of the intake of folic acid prior to and during pregnancy. The information from such a survey may shed light on whether the inadequate level of awareness among women is a reflection of a lack of knowledge among medical professionals themselves, of

TABLE 4. Women who were aware of folic acid: comparison between those who used it and those who did not

Factor	Took folic acid (%)	Did not take folic acid (%)	*P* value
Total	27	24	
Age			
40–47 years	1 (1.96)	2 (3.92)	NS
30–39 years	19 (37.25)	15 (29.41)	NS
17–29 years	7 (13.73)	7 (13.73)	NS
Religiosity			
Religious	2 (3.92)	2 (3.92)	NS
Semireligious	14 (27.47)	18 (35.3)	NS
Nonreligious	9 (17.65)	1 (1.96)	0.01
Did not answer*	2 (3.9)	5 (9.8)	
Nationality			
America and Europe	3 (5.88)	2 (3.92)	NS
Eastern Europe	12 (23.5)	15 (29.4)	NS
North Africa	7 (13.72)	4 (7.84)	NS
Asia	5 (9.8)	3 (5.88)	NS
No. of pregnancies			
1	6 (11.76)	9 (17.64)	NS
2	9 (17.6)	4 (7.84)	NS
3	6 (11.76)	4 (7.84)	NS
4 and more	6 (11.76)	7 (13.72)	NS
Health status			
Healthy	23 (45.1)	22 (43.13)	NS
Not healthy	4 (7.84)	2 (3.92)	NS

*Was not calculated by chi-square test.

poor attempts to disseminate correct information, or in fact a reflection of poor assimilation of information among the women themselves.

The high financial and emotional strain of NTD necessitates a concerted effort to minimize the risk of NTD-affected pregnancies.

Our data suggest that an increased awareness of the benefits of folic acid significantly affects behavior. The lack of awareness, among Israeli women studied, was irrespective of origin, number of pregnancies, nationality, or health profile. This finding would suggest the need for multifaceted, i.e., community-, government-, and hospital-based education programs, that address all women of childbearing age, belonging to all sectors of society.

An alternative option is to follow the Canadian and US example and fortify flour and bread with folic acid. The extensive education and prevention programs which promote the use of folic acid prior to and during pregnancy will reduce the morbidity and mortality caused by NTD-affected pregnancies.

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