

Periconceptional use of folic acid in Shanxi Province of northern China

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Abstract

Objective: To understand the periconceptional use of folic acid and its association with selected characteristics in northern China.

Design: As part of a population-based case–control study on external structural birth defects, we analysed periconceptional use of folic acid among control mothers.

Setting: The study was conducted in four counties (Pingding, Xiyang, Taigu and Zezhou) in Shanxi Province of northern China.

Subjects: The subjects in this study were the control mothers, who were interviewed between January 2003 and May 2005.

Results: Of the 480 respondent mothers, 49 women (10.2%) reported ever using folic acid supplements, and only 16 women (3.3%) used it periconceptionally. The rates of any use and periconceptional use did not change significantly with study year. Periconceptional use of folic acid was significantly increased among women with more than high school education (odds ratio (OR) = 4.57, $P < 0.10$), women who were not farmers (OR = 4.72, $P < 0.05$), women with a history of birth-defect-affected pregnancy (OR = 32.73, $P < 0.05$) and women who planned their pregnancy (OR = 7.88, $P < 0.10$).

Conclusion: The rate of periconceptional folic acid use was among the lowest of those reported from other countries. More work should be done to improve preconceptional use of folic acid with special attention on less educated women and women farmers.

Keywords

Folic acid
Periconceptional use
Neural tube defects

Neural tube defects (NTDs), being the most common congenital malformations, are a major cause of stillbirth and infant mortality, and account for up to a third of stillbirths and a quarter to a third of neonatal deaths in China. Within China, the prevalence rate of NTDs varies dramatically between the north, which has a very high rate, and the south, which has a much lower rate; as well as between urban and rural areas, with rural areas reporting higher rates^{1,2}. Shanxi Province, located in northern China, has one of the highest birth prevalences of NTDs in the world. The prevalence was reported as 10.55 per 1000 births in 1986/87 by a hospital-based surveillance system², and as 14.9 per 1000 births in 1997 from a local government retrospective investigation. These rates are over 10 times higher than those reported from southern China or the USA during the same period¹.

The relationship between folic acid supplementation during the periconceptional period and reduced incidence of NTDs is well established^{3–5}. In 1992, the US Public Health Service took the lead in recommending that all women capable of becoming pregnant should consume 400 µg of folic acid per day to prevent NTDs⁶. This recommendation was subsequently followed by agencies

and societies in many other countries. In China, the Ministry of Health recommended in 1992 that all women who are newly married or planning pregnancy should consume a daily supplement containing 0.4 mg of folic acid to prevent NTDs⁷.

Recently, an increasing number of studies have been conducted to assess the compliance of intake of folic acid supplements and to discuss the best method of administration of folic acid to women^{8–20}. However, few to date have reported on the actual use of folic acid supplements in the Chinese population. Therefore the main aim of the present study was to understand the actual use of folic acid supplements during the periconceptional period and its association with selected sociodemographic and obstetric characteristics in the high NTD prevalence area of Shanxi Province, China.

Materials and methods

Study setting

The study was conducted in four counties (Pingding, Xiyang, Taigu, and Zezhou) in Shanxi Province, China. In 2003, our population-based surveillance data showed

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the overall birth prevalence rate of NTDs (including terminations) to be 13.9 per 1000 births in the four-county area. The prevalence rate of each county was greater than 10 per 1000 births.

Data collection

Beginning in November 2002, a case-control study was conducted to probe the risk factors of external structural birth defects in the study area. When any external malformation was identified by the birth defects surveillance system, a newborn infant without identified congenital anomaly in the same county and of the same sex, maternal ethnic group and with the closest date of conception to the case was selected as a control. Trained health-care workers collected the data through face-to-face interviews with mothers of cases and controls in hospitals, private or community general practice clinics, or at home, within the first week after delivery. A structured questionnaire was used to collect the information on the women's sociodemographic characteristics, use of folic acid supplements as well as other potential risk factors. The study was approved by the institutional review boards of Peking University.

In the present analysis, data on the folic acid intake and sociodemographic and obstetric characteristics of control mothers between January 2003 and May 2005 were extracted to evaluate the periconceptional use of folic acid and its association with selected characteristics in the study population.

Definition of folic acid use

Two types of folic acid use were analysed in this study. 'Any use of folic acid' was defined as having ever used folic acid supplements related to the last pregnancy regardless of the duration and timing. 'Periconceptional use of folic acid' was defined as having used folic acid supplements between 2 months before and 1 month after the last menstrual period and continued for at least 1 month.

Data analysis

Data were entered and checked using EpiData Software (version 2.0; EpiData Association). Statistical analysis was performed with SPSS for Windows (version 11.5; SPSS Inc.). The chi-square test or Fisher's exact test (two-tailed) was used to analyse differences in the rates or proportions among two or more groups in univariate analyses. In multivariate analyses, all variables significant in univariate analyses were added into the logistic regression models simultaneously to evaluate their independent effect, adjusting for each other. Risks were estimated by the odds ratio (OR), and the precision of the OR was assessed by its 95% confidence interval. $P < 0.05$ was the criterion for significance in univariate analyses. Considering the relatively small sample sizes for multivariate analyses, we used $P < 0.10$ as the criterion for significance in multivariate logistic regression models.

Results

General characteristics of the study population

From January 2003 to May 2005, 503 control mothers were interviewed. Of the 503 control mothers, 23 (4.6%) did not provide information on folic acid intake, leaving 480 (95.4%) in this analysis. The median age of the women was 25 years, ranging from 16 to 41 years. Most women (477, 99.4%) were Han nationality. The distribution for other demographic and obstetric characteristics is shown in Table 1.

Status of folic acid use

The status of folic acid use of the respondent women is shown in Table 2. Of the 480 respondents, 49 women (10.2%) reported ever using folic acid supplements related to their last pregnancy, and only 16 women (3.3%) took supplements during the periconceptional period according to our definition. Of the 49 folic acid users, 47 (95.9%) took supplements containing folic acid alone and only one woman used a multivitamin containing folic acid. The median cumulative duration of intake was 60 days, ranging from 3 to 212 days.

Distribution of folic acid use by selected characteristics

Table 3 presents the distribution of folic acid use by selected characteristics. The percentages of women who

Table 1 Demographic and obstetric characteristics of the 480 respondent women

Characteristic	<i>n</i>	%
Year		
2003	215	44.8
2004	210	43.8
2005	55	11.5
Age (years)		
< 20	15	3.1
20–25	188	39.2
25–30	154	32.1
> 30	117	24.4
Missing	6	1.2
Education		
Less than high school	410	85.4
High school	53	11.0
Junior college or higher	13	2.7
Missing	4	0.9
Occupation		
Farmer	326	67.9
Other	146	30.4
Missing	8	1.7
Parity		
Primiparous	305	63.5
Multiparous	174	36.3
Missing	1	0.2
History of birth defects		
Yes	12	2.5
No	467	97.3
Missing	1	0.2
Planned pregnancy		
No	136	28.3
Yes	335	69.8
Missing	9	1.9

Table 2 Status of folic acid use among the 480 women who responded

Status of folic acid use	<i>n</i>	Rate (%)
Ever used (any use)	49	10.2
Started before LMP	22	4.6
Used for at least 1 month	42	8.7
Started between 2 months before LMP and 1 month after LMP for at least 1 month (periconceptual use)	16	3.3

LMP – last menstrual period.

reported any use and periconceptual use of folic acid were not significantly different by study year. Both any use of folic acid and periconceptual use were significantly more frequent among women with higher levels of education ($P < 0.01$ for any use, $P < 0.05$ for periconceptual use) and among women with a history of birth-defect-affected pregnancy ($P < 0.001$ for both). Women farmers were less likely to use supplements during the periconceptual period than women with other occupation ($P < 0.01$). Women who planned their pregnancy more frequently used folic acid during the

Table 3 Distribution of folic acid use by demographic and obstetric characteristics

Characteristic	Any use		Periconceptual use	
	<i>n</i>	Rate (%)	<i>n</i>	Rate (%)
Year				
2003	18	8.4	4	1.9
2004	24	11.4	10	4.5
2005	7	12.7	2	3.0
	$\chi^2 = 1.43$	$P = 0.23$	$\chi^2 = 1.02$	$P = 0.31$
Age (years)				
< 20	2	13.3	0	0.0
20–25	21	11.2	6	3.2
25–30	12	7.8	5	3.2
> 30	13	11.1	5	4.3
	$\chi^2 = 1.44$	$P = 0.70$	$\chi^2 = 0.84$	$P = 0.84$
Education				
Less than high school	36	8.8	12	2.9
High school	9	17.0	2	3.8
Junior college or higher	4	30.8	2	15.4
	$\chi^2 = 9.49$	$P < 0.01$	$\chi^2 = 6.05$	$P < 0.05$
Occupation				
Farmer	28	8.6	5	1.5
Other	20	13.7	10	6.8
	$\chi^2 = 2.88$	$P = 0.09$	$\chi^2 = 9.26$	$P = 0.002$
Parity				
Primiparous	32	10.5	10	3.3
Multiparous	17	9.8	6	3.4
	$\chi^2 = 0.06$	$P = 0.80$	$\chi^2 = 0.01$	$P = 0.92$
History of birth defects				
Yes	7	58.3	4	33.3
No	42	9.0	12	2.6
	$\chi^2 = 31.0$	$P < 0.001$	$\chi^2 = 34.3$	$P < 0.001$
Planned pregnancy				
Yes	34	10.1	15	4.5
No	13	9.6	1	0.7
	$\chi^2 = 0.04$	$P = 0.85$	$\chi^2 = 4.12$	$P = 0.04$

periconceptual period ($P < 0.05$). The percentages of any use and periconceptual use did not differ between four age groups or between two parity groups.

Multivariate analyses

According to the results of univariate analyses, we employed two logistic regression models in multivariate analyses. In one model, any use of folic acid served as dependent variable, and the variables of education and history of birth defects, which were significant characteristics in univariate analyses, were added into the model as independent variables. In the second model with periconceptual use of folic acid as the dependent variable, education, occupation, history of birth defects and planned pregnancy were added into the model simultaneously as independent variables. The results of multivariate analyses are presented in Table 4. Any use of folic acid was significantly increased among women with high school education (OR = 2.37, $P < 0.05$) and with junior college or higher education (OR = 4.25, $P < 0.05$) compared with those having less than high school education, and among women with a history of birth-defect-affected pregnancy (OR = 17.85, $P < 0.05$). Higher periconceptual use of folic acid was significantly related to junior college or higher education (relative to less than high school; OR = 4.57, $P < 0.10$), non-farmer occupation (OR = 4.72, $P < 0.05$), history of birth-defect-affected pregnancy (OR = 32.73, $P < 0.05$) and planned pregnancy (OR = 7.88, $P < 0.10$).

Discussion

In recent years, a number of studies from different countries have reported the status of folic acid use during the periconceptual period. The rate of periconceptual

Table 4 Results of multivariate logistic regression analyses ($\alpha = 0.10$)

Characteristic	Any use		Periconceptual use	
	OR	95% CI	OR	95% CI
Education				
Less than high school	1.00		1.00	
High school	2.37**	1.02–5.53	1.01	0.19–5.52
Junior college or higher	4.25**	1.09–16.59	4.57*	0.73–28.72
Occupation				
Farmer			1.00	
Other			4.72**	1.29–17.24
History of birth defects				
No	1.00		1.00	
Yes	17.85**	5.32–59.88	32.73**	6.68–160.43
Planned pregnancy				
No			1.00	
Yes			7.88*	0.93–66.68

OR – odds ratio; CI – confidence interval.

* $P < 0.10$; ** $P < 0.05$.

use of folic acid in different regions varied dramatically, from 0.5% to 52%⁸. According to results from the March of Dimes surveys, 31% of women of childbearing age in the USA reported daily folic acid supplementation in 2002⁹. In Canada, current periconceptional use was reported to be 28% among Toronto women¹⁰. In Israel, the figure was 30.5% in 2002¹¹. In the northern Netherlands, a study performed at the end of 2000 revealed that 61% of women used folic acid in some part of the advised period and 36% used it in the entire advised period¹³. In a Mediterranean area, although 68% of women had taken folic acid at some time during pregnancy, only 6.9% of the women had taken folic acid during the effective period from 4 weeks before conception to 4 weeks after conception in 2000¹⁴. In the United Arab Emirates in 1999, 67.9% of women reported intake of supplementary folic acid any time, and 45.5% used it periconceptionally¹⁵. Our study determined that only 10.2% of women reported having ever used folic acid, and very few women (3.3%) used folic acid supplements periconceptionally. The figures did not change markedly from 2003 to 2005. Thus the rates of periconceptional folic acid use among this Chinese population were among the lowest of those reported from other countries.

Although two other approaches can also be used to increase the consumption of folic acid (increasing dietary consumption and fortification of food with folic acid), daily use of supplements is still currently the preferred method in our country. Increased dietary folic acid consumption is not easy to achieve for rural populations owing to poor economic conditions and great difficulty in modifying individual dietary habits. Furthermore, evidence suggests that it is hard to achieve adequate intake of folic acid by diet alone for NTD prevention¹⁶. Fortification of food with folic acid was considered the most cost-effective method in other countries¹⁷. But it seems not to be effective in our setting, since most residents in rural areas consume self-planted and self-processed food supplies. In China, tablets containing 0.4 mg folic acid alone were the most common supplements used. A cohort study with very large sample size conducted in our country has indicated that periconceptional intake of supplements containing 0.4 mg folic acid alone can reduce the risk for NTDs by 85% in northern areas of China⁵. In addition, the tablets are easy to transport, distribute and store, and the cost of folic acid alone is relatively lower than the other two approaches.

Attained education level has been reported in several studies to be positively related to the frequency of folic acid use^{11,15,18,19}. Our findings have confirmed this association again. Any use of folic acid was more frequent among women with high school education (OR = 2.37, $P < 0.05$) and with junior college or higher education (OR = 4.25, $P < 0.05$), compared with those with less than high school education. However, periconceptional use of folic acid was more frequent only among women with education more than high school (OR = 4.57, $P < 0.10$), and not with high

school education (OR = 1.01, $P > 0.10$). This result suggests that high school education increased the frequency of use, but not the frequency of correct use; while education more than high school increased not only the frequency of use, but also the frequency of correct use of folic acid. In our study population, 85.4% of women were educated to junior high school level or lower and only 2.7% of women had education level more than high school. Therefore, education characteristics should sufficiently be taken into account in developing measures of public education during the following campaign.

A Texas study indicated that women at high risk (i.e. those with a history of having an infant with an NTD) were more likely to recall and follow recommendations to use folic acid. Approximately 56.4% of mothers who had infants affected by an NTD recalled receiving postpartum advice to use folic acid, compared with 25.6% of control mothers ($P < 0.01$)²⁰. Our results agree with these findings. Of the 12 mothers with a history of birth-defect-affected pregnancy, seven (58.3%) reported any use of folic acid and four (33.3%) reported periconceptional use, compared with 9.0 and 2.6%, respectively, among the women without birth defects history. Dramatically increased rates of folic acid use were found among mothers with a history of birth-defect-affected pregnancy (OR = 17.85, $P < 0.05$ for any use; OR = 32.73, $P < 0.05$ for periconceptional use).

Planned pregnancy was markedly related to periconceptional use of folic acid in our study (OR = 7.88, $P < 0.10$). This finding is consistent with many other reports from different countries^{8,10,14,21,22}. In our population the percentage of unplanned pregnancy was 28.3%, similar to that in the Mediterranean area (30.1%)¹⁴ but markedly higher than that in the northern Netherlands (15%)¹³.

Another characteristic in our study associated with periconceptional folic acid use was occupation. Women farmers were more likely not to use the folic acid during the periconception period (OR = 4.72, $P < 0.05$). Noteworthy is that the majority (67.9%) of the women in our population were farmers, of whom 95.6% were less educated (with education less than high school). Therefore farmer women constitute an important population who should be the focus of future public education.

Some studies have revealed a significant association of folic acid intake with age. Hilton reported that inadequate folic acid intake was common in young women aged 18–24 years; the young women frequently had poor nutritional habits and were usually non-contemplators of pregnancy²³. Amitai *et al.* reported that 17–19-year-old women had a lower rate of folic acid utilisation than 25–29-year-old women in the Israeli population¹¹. However, we did not find any marked difference of folic acid use between age groups. In our study, only 15 (3.1%) women were younger than 20 years; therefore the rates of folic acid use may not stable in this age group owing to small sample size.

Our study also revealed that folic acid use was not different between primiparous and multiparous women (10.5 vs. 9.8% for any use, 3.3 vs. 3.4% for periconceptional use). This finding is consistent with results reported by Coll *et al.*; in their study, the percentage of correct folic acid use was 7.6 and 6.0% for primiparas and multiparas ($P = 0.208$), respectively¹⁴.

To our knowledge, this is the first report on the status of folic acid use in the population of northern China, where the NTD prevalence rate is among the highest in the world. However, our study has some limitations. The subjects of this study were the control mothers from a case-control study. Therefore, they may not represent a completely random sample of the whole population although the study was population-based. The interviews were conducted during the postpartum period and recall bias may have existed to a certain extent. Another limitation of our study could be that the sample size was not large enough. The overall rate of folic acid use in the study population was very low; therefore more subjects were needed to analyse the distribution of folic acid use by characteristics. In order to solve this limitation, we used $P < 0.10$ as the criterion of significance in multivariate analyses. In addition, items about awareness and knowledge of folic acid, and other important factors which impact on folic acid use, were not included in the questionnaire; therefore the reason for the lower rate of folic acid intake in this population could not be analysed in detail. Further studies should be performed in this population to probe the specific reasons for infrequent folic acid use, such as the cost of supplements, awareness and knowledge, belief, cultural barriers, approaches of public education and so on, so as to provide sufficient evidence for making an effective strategy for a folic acid campaign.

In conclusion, our study findings suggest that the rates of periconceptional folic acid use in our study population were much lower than those in most other countries. The use of folic acid is much more infrequent among less educated women, unexpectedly pregnant women or women who are farmers. Taking into consideration the fact that northern China has an extremely high prevalence rate of NTD, more work should be done in this region to improve preconceptional use of folic acid, with the next step focusing special attention on less educated women and women farmers in the rural area.

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