

Awareness of Neural Tube Defects in Family Physicians

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ABSTRACT

Objective: The aim of this study was to measure the knowledge level of physicians working in family health centers about the conditions leading to neural tube defect (NTD) and preventive measures.

Material and Methods: In this cross-sectional study, 406 general practitioners and family medicine specialists made a survey consisted of 13 questions. Chi-square, Fisher's Exact test and Pearson chi-square analysis were applied as statistical methods.

Results: A total of 406 physicians (family medicine specialists: 110, general practitioners: 296) participated in the study. 81.53% of the participants were working in a city and 18.47% were working in the countryside. The number of referral to general practitioners before pregnancy was significantly higher than that of family medicine specialists. ($p < 0.05$). 36.95% of the respondents knew that the neural tube was closed in the first month of embryological life. Folic acid initiation rate was 99.26% for patients planning pregnancy. Initiation of vit B12 with folic acid was 28.33% in patients planning pregnancy. The rate of knowing that vitamin B12 deficiency causes NTD was 39.41% (family medicine specialists: 50%, general practitioners: 35.47%), and FMSs were statistically significant ($p < 0.05$).

Discussion: While the number of pregnant women who received folic acid only was sufficient, the number of pregnant women who took vitamin B12 with folic acid was very low. Family medicine specialists and general practitioners had insufficient knowledge that using vitamin B12 in combination with folic acid prevented NTD development. By preparing and implementing algorithms that can prevent NTDs, many life-long complications can be prevented.

Keywords: family medicine, folic acid, neural tube defect, vitamin B12

INTRODUCTION

Neural tube defects (NTD) develop on the first 28th day of embryological life when the neural tube that needs to be closed remains open [1]. Genetic and environmental factors are considered responsible in the etiology [2]. Although there are various mutations among genetic factors, it is not clearly proven; however, maternal age lower than 19 years and older than 40 years considered as a risk factor [3,4]. Among environmental factors; low folic acid, vitamin B 2-6-12, choline, betaine, n-3 polyunsaturated fatty acids, zinc and vitamin D levels and high homocysteine levels are seen in neural tube defects [2,5,6]. Although the frequency of NTD is 1/1000, its frequency may vary between 0.2-10% in various regions of the world [7]. It is very

important to take necessary precautions before and during pregnancy in order to prevent NTDs due to mortality and serious morbidities. Because of this serious effects, Republic of Turkey Ministry of Health started a support program for folic acid intake during pregnancy, since 1999 [8].

To prevent NTD, it is necessary encourage to intake B2-6-12 vitamins, choline, betaine and n-3 polyunsaturated fatty acids which are using folic acid together with single carbon metabolism. Genetic screening is recommended because of the possibility that the polymorphism in a single carbon mechanism may lead to the development of NTD. Other conditions that may contribute to the development of NTD include the consumption of alcohol, tea and coffee in women of childbearing age and the low consumption of fruits and vegetables

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[9,10,11,12]. The risk of NTD may increase due to folic acid and vitamin B12 deficiency in women who have undergone bariatric surgery [13]. Peker E et al. showed that, NTD folic acid and vitamin B12 with low levels of homocysteine was found to be accompanied with elevated levels [14]. At the 28th day of gestation, 6 NTD children can be born in every 10000 live births with the values of the erythrocyte folate level above 1000 nmol / L, and when this value drops to 500 nmol / L, an average of 25.4 NTD children is born [15]. NTD is a serious health problem and brings moral and material burden for family and society. Pregnancy tracking is done by family physicians in Turkey is a sharp maintained [16].

The aim of this study is to determine the levels of knowledge all doctors (general practitioner / family medicine specialist) working as a family doctor about folic acid and vit B12, which should be given during the first trimester of pregnancy and in the periconceptional period for prevention of NTDs.

MATERIALS AND METHODS

The cross-sectional study was carried out according to the permission of İzmir Katip Çelebi University Non-invasive Clinical Research Ethics Committee dated 10.10.2018 and numbered 323 decision. The criteria for inclusion in the study were to be an active family physician in primary care, and the maximum number of clinicians was tried to be reached by performing snowball sampling between 1 November 2018 and 1 December 2018. The study was initiated by two authors working as family physicians in primary care and reached a total of 406 clinicians (family medicine specialists: 110, general practitioners: 296).

The study was conducted by using the survey application on the internet. The survey was conducted on general practitioners and family medicine specialists who performed family medicine in a period of 1 month between 1 November 2018 and 1 December 2018. In this study, which was determined as cross-sectional type, a questionnaire consisting of 13 questions was applied by the family physicians in order to evaluate the neural tube defect awareness after the informed consent form was obtained. The first 5 questions are about socio-demographic data and the remaining 8 questions are related to the level of knowledge of neural tube defects. Persons with known psychiatric illnesses, those with deficiencies in the questionnaire and non-volunteers were excluded from the study. The data obtained in this study were analyzed with IBM SPSS Statistics Version 22 package program.

The chi-square analysis was applied to examine the relationships between the groups of nominal variables. Fisher's Exact Test was used in cases where the expected values in the eyes were not sufficient in 2x2 cross tables and in the RxC tables Pearson chi-square analysis was applied with the help of Monte Carlo Simulation. When interpreting the results, 0.05 was used as the level of significance.

Neural Tube Defect Awareness Form

1. What is your age?
2. What is your gender? male or female
3. The area where you work? City / Rural
4. How many years have you been working as a doctor? year
5. What is your education status?
 - a. Family medicine specialist
 - b. General practitioner
6. What percentage of your pregnant patients apply to you before pregnancy?
 - a. 0-24.9 %
 - b. 25-49.9 %
 - c. 50-74.9 %
 - d. 75-100 %
7. When does the neural tube close in embryological life?
 - a. At the end of 1st month
 - b. At the end of the 2nd month
 - c. At the end of the 3rd month
8. Do you look at the folic acid levels of your patients planning pregnancy? Yes / No
9. Do you start folic acid for your patients planning pregnancy? Yes / No
10. When do you start folic acid?
 - a. I start if the folate level is low
 - b. I start if the folate level is normal
 - c. I want her to see an obstetrician.
 - d. I start regardless of the folate level
11. Do you look at the vitamin B12 levels of your patients planning pregnancy? Yes / No
12. When do you start vitamin B12?
 - a. I start if the vitamin B12 level is low
 - b. I start if the vitamin B12 level is normal
 - c. I want her to see an obstetrician.
 - d. I start regardless of the vitamin B12 level
13. Do you know that vitamin B12 deficiency can cause neural tube defects? Yes / No

FINDINGS

The age of the 406 physicians who were included in the study and the number of years they worked and the sociodemographic characteristics of these physicians were determined in the following tables (**Tables 1 and 2**).

Age and working years are seen to be significantly higher in general practitioners ($p < 0.05$). In order to be able to practice family medicine under contract in Turkey, family medicine specialists are given some priorities according to general practitioners. General practitioners, on the other hand, are placed in suitable positions according to the score they get according to their working period. As a result, the age and working time of general practitioners working as family physicians are higher than family medicine specialists.

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Table 1. Distribution of physicians according to age and number of years of work

	n	Mean	Median	Min	Max	ss
Age	406	39.65	40	25	65	8.4
How many years have you been working as a physician?	406	14.79	15	0.25	40	8.96

Table 2. Frequency distribution table for demographic information

		n	%
Gender	Male	219	53.94
	Female	187	46.06
	Total	406	100
Your region	City	331	81.53
	Rural	75	18.47
	Total	406	100
Education status	Family medicine specialist	110	27.09
	General practitioner	296	72.91
	Total	406	100
What% of your patients who are planning pregnancy apply to you before pregnancy?	0-25	312	76.85
	25-50	56	13.79
	50-75	21	5.17
	75-100	17	4.19
	Total	406	100
The neural tube closes in which month of embryological life?	1. month	150	36.95
	2. month	57	14.04
	3. month	199	49.01
	Total	406	100
Do you start giving folic acid on your patients planning pregnancy?	Yes	403	99.26
	No	3	0.74
	Total	406	100
When do you start giving folic acid?	I'm starting if the folate level is missing	32	7.94
	I'm starting if the folate level is normal	55	13.65
	I want him to apply to another center	1	0.25
	Regardless of the folate level	315	78.16
	Total	403	100
Do you start giving vitamin B12 when you start giving folic acid to your patients who are planning pregnancy?	Yes	115	28.33
	No	291	71.67
	Total	406	100
When do you start giving Vitamin B12?	I'm starting if the Vit B12 level is missing	309	76.11
	I'm starting if the Vit B12 level is normal	19	4.68
	I want him to apply to another center	14	3.45
	I start prophylactically regardless of Vit B12	64	15.76
	Total	406	100
Do you know that vitamin B12 deficiency can make neural tube defects (NTD)?	Yes	160	39.41
	No	246	60.59
	Total	406	100

After sociodemographic features; The chi-square test results of the relationship between the study area and the variables were examined and no statistical significance was found with any parameter (**Table 3**).

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Table 3. Chi-square test result of the relationship between the study area and variables

		Your region						Chi Square Test	
		City		Rural		Total		Chi Square	p
		n	%	n	%	n	%		
Do you start giving folic acid on your patients planning pregnancy?	Yes	328	99.09	75	100	403	99.26	Fisher's exact	1
	No	3	0.91	0	0	3	0.74		
	Total	331	100	75	100	406	100		
When do you start giving folic acid?	I'm starting if the folate level is missing	30	9.15	2	2.67	32	7.94	*	0.144
	I'm starting if the folate level is normal	48	14.63	7	9.33	55	13.65		
	I want him to apply to another center	1	0.3	0	0	1	0.25		
	Regardless of the folate level	249	75.91	66	88	315	78.16		
	Total	328	100	75	100	403	100		
Do you start giving vitamin B12 when you start giving folic acid to your patients who are planning pregnancy?	Yes	97	29.31	18	24	115	28.33	0.606	0.436
	No	234	70.69	57	76	291	71.67		
	Total	331	100	75	100	406	100		
When do you start giving Vitamin B12?	I'm starting if the Vit B12 level is missing	254	76.74	55	73.33	309	76.11	*	0.403
	I'm starting if the Vit B12 level is normal	16	4.83	3	4	19	4.68		
	I want him to apply to another center	9	2.72	5	6.67	14	3.45		
	I start prophylactically regardless of Vit B12	52	15.71	12	16	64	15.76		
	Total	331	100	75	100	406	100		
Do you know that vitamin B12 deficiency can make neural tube defects (NTD)?	Yes	131	39.58	29	38.67	160	39.41	0.021	0.884
	No	200	60.42	46	61.33	246	60.59		
	Total	331	100	75	100	406	100		

The statistical relationship between the same variables and the educational status was also investigated (Table 4). There was a statistically significant relationship between the educational status and the rate of referral to the family physician before the pregnancy ($p < 0.05$). There was a statistically significant relationship between the educational status and the knowledge that vitamin B12 deficiency could perform neural tube defect (NTD) ($p < 0.05$). No statistically significant relationship was found between the educational status of the physician and other parameters.

There is a statistically significant relationship between the educational status and the pre-pregnancy admission rates of patients planning pregnancy ($p < 0.05$). According to their educational level, 73.64% and 78.04% of the patients of family medicine specialists and general practitioners, respectively, and 0-24.9% of the patients admitted before pregnancy gave the answer.

Although not statistically significant, 74.31% of family medicine specialists and 79.59% of general practitioners start folic acid regardless of folate level.

Although not statistically significant, 27.27% of family medicine specialists and 28.72% of general practitioners start folic acid while their patients are planning pregnancy, along with vitamin B12.

There is a statistically significant relationship between educational status and knowing that Vitamin B12 deficiency

can cause neural tube defect (NTD) ($p < 0.05$). 50% of family medicine specialists and 35.37% of general practitioners know that vitamin B12 deficiency can cause neural tube defect (NTD).

DISCUSSION

Approximately 2/3 of the participants in the study had a lack of knowledge about neural tube embryology. General practitioners, in particular, lacked more information about the relationship between vitamin B12 and neural tube defects than family medicine specialists. Almost all participants had sufficient knowledge about the relationship between folic acid and neural tube defects.

Patients who are planning pregnancy should apply to the family doctor before delivery for healthy pregnancy and after performing the necessary tests, various treatments should be applied accordingly. As in all over the world, in our country, the number of applications to family physicians before pregnancy is low. The most common reason for this is the unintended pregnancies. Unwanted pregnancy rates were 34% in Western Europe, 54% in Eastern Europe and 45% in the United States in 2011 [17,18]. Similarly, 76.85% of Family Physicians (family medicine specialists and general practitioners) stated that only 0-24, 9% of their patients planning pregnancy had referred to the family physician before pregnancy.

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Table 4. Chi-square test result of relationship between educational status and variables

		Education status						Chi Square Test	
		Family medicine specialist		General practitioner		Total		Chi Square	p
		n	%	N	%	n	%		
What% of your patients who are planning pregnancy apply to you before pregnancy?	0-25	81	73.64	231	78.04	312	76.85	9.276	0.026
	25-50	18	16.36	38	12.84	56	13.79		
	50-75	10	9.09	11	3.72	21	5.17		
	75-100	1	0.91	16	5.41	17	4.19		
	Total	110	100	296	100	406	100		
The neural tube closes in which month of embryological life?	1. month	42	38.18	108	36.49	150	36.95	0.101	0.951
	2. month	15	13.64	42	14.19	57	14.04		
	3. month	53	48.18	146	49.32	199	49.01		
	Total	110	100	296	100	406	100		
Do you start giving folic acid on your patients planning pregnancy?	Yes	109	99.09	294	99.32	403	99.26	Fisher's exact	1
	No	1	0.91	2	0.68	3	0.74		
	Total	110	100	296	100	406	100		
When do you start giving folic acid?	I'm starting if the folate level is missing	10	9.17	22	7.48	32	7.94	*	0.632
	I'm starting if the folate level is normal	18	16.51	37	12.59	55	13.65		
	I want him to apply to another center	0	0	1	0.34	1	0.25		
	Regardless of the folate level	81	74.31	234	79.59	315	78.16		
	Total	109	100	294	100	403	100		
Do you start giving vitamin B12 when you start giving folic acid to your patients who are planning pregnancy?	Yes	30	27.27	85	28.72	115	28.33	0.082	0.774
	No	80	72.73	211	71.28	291	71.67		
	Total	110	100	296	100	406	100		
When do you start giving Vitamin B12?	I'm starting if the Vit B12 level is missing	86	78.18	223	75.34	309	76.11	0.673	0.88
	I'm starting if the Vit B12 level is normal	4	3.64	15	5.07	19	4.68		
	I want him to apply to another center	3	2.73	11	3.72	14	3.45		
	I start prophylactically regardless of Vit B12	17	15.45	47	15.88	64	15.76		
	Total	110	100	296	100	406	100		
Do you know that vitamin B12 deficiency can make neural tube defects (NTD)?	Yes	55	50	105	35.47	160	39.41	7.088	0.008
	No	55	50	191	64.53	246	60.59		
	Total	110	100	296	100	406	100		

Neural tube closure is a procedure involving highly complex mechanisms [19]. Closure of the neural tube depends on the embryological events occurring during central nervous system formation [20,21]. In the study, 36,95% of the total participants (38,18% of the FMSs, 36,49% of the general practitioners) answered the closing time of the neural tube correctly. There was no statistically significant difference between the two groups.

The low number of pre-pregnancy visits to family medicine causes lack folic acid and vitamin B12 prophylaxis for preventing the development of NTD. In a study conducted in Germany, only 37.8% were found to use prenatal folic acid to prevent NTD development [22]. In the study, the majority of patients do not apply to the health institution before pregnancy and do not take folic acid and vitamin B12. In a study published in 1964, it was first reported that NTD, megaloblastic anemia and ablatio

placenta could develop with a low folic acid level [23]. Low levels of plasma folate and vitamin B12 levels were correlated with cognitive decline, non-comorbid anxiety disorder, depression and neuropathy, preterm delivery and low birth weight [24,25,26]. On the other hand, increased intake of folic acid was also associated with some diseases; among them colorectal cancer, hypersensitivity reactions, masking of vitamin B12 deficiency, diabetes and thyroid diseases were seen [27]. The American Medical Association has determined that the maximum daily use of folic acid in non-pregnant adults is 1000 mcg/day [28]. In order to prevent neural tube defects, 400 mcg folic acid supplement should be recommended daily until 12 weeks of gestation [29,30]. According to the Canadian task force report on preventive health services, women with low-risk NTD have a daily dose of 0.4 mg of folic acid daily for women with moderate risk, starting 2-3 months before pregnancy and going through 12 weeks of gestation. In women with high risk, 4 mg folic acid should be supplemented daily [31]. In a study conducted on clinicians working in primary care in Puerto Rico, only 12.1% of the participants had sufficient knowledge that folic acid use prevented the development of neural tube defects [32]. In a study conducted in Southern Israel, it was seen that 94% of clinicians working in primary care routinely prescribed folic acid to women of childbearing age, but only 2% correctly knew that folic acid reduces the risk of developing neural tube defects [33]. In a study conducted on obstetricians, pediatricians and general practitioners in India, only 47.52% of the participants were aware that folic acid should be used before pregnancy and 11.88% were aware of the recurrence rate of neural tube defects [34]. In our study, it is seen that almost all of the primary care physicians 99.26% (99.09% of family medicine specialists, 99.32% of general practitioners) gave folic acid to their patients planning pregnancy to prevent the risk of developing neural tube defects.

In the study by Kerr SM et al., It was seen that daily intake of 400 mcg folic acid 28 days before conception and during a subsequent menstruation period decreased the NTD development in fetuses by 4.2 times [35]. In the study conducted by Van Gool JD et al., The folate level in erythrocytes increased to 1050 to 1340 nmol / L, which would provide an optimal decrease in NTD risk in approximately 20 weeks by taking 4 mg folic acid daily. Therefore, they recommended folic acid support to be started 5-6 months before conception [1]. In our study, 78.16% of the participants (74.31% of FMSs, 79.59% of general practitioners) started to give folic acid supplementation to pregnant patients regardless of blood folate level.

Enrichment of nutrients in folic acid and vit B12 (eg flour) and intake of folate-rich foods (eg green leafy vegetables) may prevent the development of NTD [36,37,38,39]. The risk of developing NTD increases with folic acid and vit B12 deficiency due to vegetarian diet [20].

In the study of Li K et al., It was found that, taking vitamin B complex, choline, betaine and n-3 polyunsaturated fatty acids together were more effective instead of folic acid alone to prevent the development of NTD [9]. In the present study, only 28.33% (27.27% of FMSs, 28.72% of GPs) of pregnant women planning pregnancy were started with folic acid and vitamin B12 together. On the other hand, 76,11% of the pregnant women with vitamin B12 deficiency (FMSs 78.18%, 75.34% of the general practitioners) were given vit B12. In contrast to the literature, 50% of the FMSs and 35.47% of the general practitioners knew that vitamin B12 deficiency could cause NTD. There was a statistically significant relationship between the two groups ($p < 0.05$). There was a statistically significant relationship between the two groups ($p < 0.05$).

If we look at the strengths of this study; there were no previous studies showing and comparing the level of knowledge of doctors on NTD prevention. It sufficiently represents FMSs who work actively in the health system and GPs who practice family medicine. Among other positive aspects, the knowledge levels of FMSs and GPs in family medicine were determined. The results obtained here can be used in pre-pregnancy counseling services in family medicine, in pregnant follow-ups, in family medicine specialty training and in-service training of family practitioners.

The low number of pre-pregnancy counseling services caused low rates of folic acid and vit B12 intake. According to the regions where some of the physicians participated, blood folate and vit B12 levels were not available. Afterwards, it is necessary to pay attention to the points mentioned in the planning of the studies to be carried out and to be carried out on larger groups.

CONCLUSION

While the clinicians participating in the study, start prescribing folic acid to almost all of the women who are planning pregnancy, only 28.33% of clinicians prescribe vitamin B12. Half of the family medicine specialists and about 2/3 of the general practitioners do not know that vitamin B12 deficiency can cause neural tube defects. We think that this issue should be emphasized during the obstetrics and gynecology rotation of family medicine specialization curricula. General practitioners had more insufficient knowledge of the relationship between vitamin B12 and neural tube defects, compared to family medicine specialists. In order to eliminate these deficiencies, this issue should be included in the regular in-service trainings of the Ministry of Health. During the regular supervision of family physicians conducted by the ministry of health, we think that the prescribing vitamin B12 and monitoring the B12 levels must be among the mandatory criteria for pregnancy monitoring which is included in the performance reviews of family physicians.

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