



# ARTIGO ORIGINAL

# CLOSURE OF THE NEURAL TUBE DEFECT: CURRENT STATUS OF PREVENTION

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### **ABSTRACT**

Objective. This is a study about the prevention of neural tube defect, the most frequent malformation involving the embryo nervous system. The recommended method of prevention is to take folic acid (0.4 mg/day) three months before conception and during the first three months of pregnancy because the closure of the neural tube occurs between 24 to 28 weeks of pregnancy.

Method. Physicians, gynecologists and primary doctors, women in reproductive age from the general population and female college students of health science were asked regarding their knowledge about prevention of neural tube defect. Three hundred and eighteen questionnaires were applied to 56 doctors, and 262 women of reproductive age.

Results. Among the doctors interviewed about their knowledge of the prevention of neural tube defect, 28 (50%) responded that they give emphatic guidance on its prevention, 44 (79%) prescribe folic acid to their patients, but only 16 (28.6%) do so in the correct period and only 3 (5.4%) answered that they do not prescribe any form of prevention. In the group of women of reproductive age, only 29 (11.1%) were correctly oriented, while 185 (70.6%) reported they did not take any prevention for neural tube defect.

Conclusion. Data from this work showed that prevention of the neural defect is not performed satisfactorily by doctors or by women of reproductive age.

**Key words**. Neural tube defects; myelomeningocele; prevention; folic acid.

## **RESUMO**

### DEFEITO DE FECHAMENTO DO TUBO NEURAL: ESTADO ATUAL DA PREVENÇÃO

Objetivo. Foi realizado um estudo sobre o conhecimento da prevenção do defeito do fechamento do tubo neural, que é uma das malformações mais frequentes que envolvem o sistema nervoso do embrião. A prevenção recomendada é feita com ácido fólico (0,4 mg/dia) administrado três meses antes da concepção e no primeiro trimestre da gestação, pois o fechamento do tubo neural ocorre de 24 a 28 semanas de gestação.

Método. Foi investigado o conhecimento sobre a prevenção do defeito do fechamento do tubo neural em médicos ginecologistas e do programa de saúde publica, mulheres em idade reprodutiva incluindo acadêmicas da área de saúde e da comunidade em geral. Foram aplicados 318 questionários, sendo 56 para os médicos e 262 para as mulheres em idade reprodutiva.

Resultados. Entre os médicos entrevistados sobre o conhecimento da prevenção de defeito do fechamento do tubo neural, 28 (50%) responderam que fazem uma orientação enfática quanto a sua prevenção, 44 (79%) indicam às suas pacientes o ácido fólico, mas apenas 16 (28,6%) o fazem no período correto, e apenas 3 (5,4%) responderam que não indicam nenhuma forma de prevenção. No grupo de mulheres em idade reprodutiva, apenas 29 (11,1%) tinham sido orientadas corretamente, enquanto 185 (70,6%) referiram não fazer qualquer prevenção de defeito do fechamento do tubo neural.

Conclusão. Os dados deste trabalho mostraram que a prevenção do defeito em análise não está sendo realizada de forma satisfatória pelos médicos ou pelas mulheres em idade reprodutiva na população estudada.

Palavras-chave. Defeito de fechamento do tubo neural; mielomeningocele; prevenção; ácido fólico.

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### Introduction

The closing of the neural tube occurs in the embryonic period from 24 to 28 weeks of pregnancy. If there is some disorder in this period some defects can occur like myelomeningocele, spina bifida occulta, meningocele, encephalocele and anencephaly, among others.<sup>1,2</sup>

Myelomeningocele usually cause serious problems in children, such as motor and sensory deficit of the inferior limbs, neurogenic bladder and bowel, hidrocefalus, among others.<sup>2</sup>

Prevention of the neural tube defect with folic acid was initially demonstrated in the work of Smithells et al,<sup>3</sup> and confirmed in other studies. This prevention can mainly be carried out with a diet rich in folic acid and prophylactic supplementation of folic acid for women in reproductive age period before conception.<sup>3-11</sup>

The simple supplementation of folic acid three months before conception and during the first three months of pregnancy is enough to reduce about 70% though 80% in the incidence of closure of the neural tube.<sup>6</sup>

The aim of this study was to evaluate the current knowledge of health's professionals and women in reproductive age regarding of neural tube defects prevention.

#### **M**ETHOD

This research was carried out during the period of 2006 to 2008, by the main author in Cuiabá (MT) and Cacoal (RO), and in hospitals of Cuiabá (MT), Brazil, and the respondents were allocated into several groups.

Questionnaires were applied to two groups of gynecologists and primary doctors (table 1), and to a group of women in reproductive age (table 2).

This study was approved by the Ethics Committee from the Federal University of Mato Grosso, Cuiabá, Brazil.

### **R**ESULTS

From women of reproductive age, only 14.5% took folic acid and followed a diet with folic acid, and 10.7% took only folic acid. Only 26.8% of doctors prescribed folic acid and diet with folic

Table 1. Questionnaires applied to the gynecologists and doctors of public health how much knowledge of the defects of closing of the neural tube.

Question	Answer				
Knowledge of malformation?	Detailed	Moderate	Superficial	Not known	
Guides to their patients about the prevention of malformation?	Ever	Often	Sporadically	Never	
What kind of prevention, typically prescribe to their patients?	Folic acid + diet	Folic acid	Diet	None	
What is the period that usually start the folic acid?	≥ 1 month before pregnancy or in all women of reproductive age	At the first trimester of pregnancy	In any period of pre-natal	Unknown or not use	
What dosage of folic acid which is usually recommend to their patients?	≥ 4 mg/day	≥ 1 mg/day	≥ 400 mg (0,4 mg)/day	Unknown or not use	
Would like to receive guidance about the disease and its prevention through	Printed material	Lecture or seminar	Others forms	Has no interest	

Table 2. Questionnaire applied to women in reproductive age about how much knowledge their have on defects of closing of the neural tube (spina bifida).

Detailed	Moderate	Superficial	Not known
Regularly	Much time	Once	Never
Strongly	Good orientation	Superficial	Never
Folic acid + diet	Folic acid	Diet	None
≥ 1 month before pregnancy or in all women of reproductive age	At the first trimester of pregnancy	In any period of pre-natal	Unknown or not use
≥ 4mg/day	≥ 1mg/day	≥ 400 mg (0.4 mg)/day	Unknown or not use
Printed material	Lecture or seminar	Others forms	Has no interest
	Regularly  Strongly  Folic acid + diet  ≥ 1 month before pregnancy or in all women of reproductive age  ≥ 4mg/day	Regularly Much time  Strongly Good orientation  Folic acid + diet Folic acid  ≥ 1 month before pregnancy or in all women of reproductive age  ≥ 4mg/day ≥ 1mg/day  Printed material Lecture or	Regularly Much time Once  Strongly Good orientation Superficial  Folic acid + diet Folic acid Diet  ≥ 1 month before pregnancy or in all women of reproductive age  ≥ 4mg/day  ≥ 1mg/day  ≥ 400 mg (0.4 mg)/day  Printed material Lecture or Others forms

acid, and 51.8% prescribed only folic acid. In the general population, only 16.7% took preventive measures that prescribed folic acid and diet (table 3).

The majority of the population prefers to receive information through printed material (figure 1).

It was also observed that 29 (11.1%) women in reproductive age and 16 (28.6%) of physicians interviewed had correct knowledge about the timing to initiate the prevention of neural tube defect.

## DISCUSSION

Folic acid is a water soluble vitamin found in 90% of green vegetables such as spinach, cauliflower, broccoli, and others.<sup>12</sup> A daily ingestion of 180 µg is necessary for non-pregnant women and 400 µg for pregnant women.13 The lack of this vitamin causes malformations<sup>14</sup> with poor association of genetic factor.11 It occurs mainly in Caucasians, with family history of the disease and of low socio-economic class.15 Some teratogenicites have been found in neural tube defect

Table 3. The type of prevention indicated according to group, doctors and population.

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		Prevention						
Sample	Total	Folic acid plus diet	Folic acid	Diet	None			
	n (%)	n (%)	n (%)	n (%)	n (%)			
Women*								
Group 1	51 (19.5)	9 (17.6)	11 (21.6)	1 (2)	30 (58.8)			
Group 2	75 (28.6)	5 (6.7)	6 (8)	4 (5.3)	60 (80)			
Group 3	36 (13.7)	12 (33.3)	7 (19.4)	2 (5.6)	15 (41.7)			
Group 4	100 (38.2)	12 (12)	4 (4)	4 (4)	80 (80)			
Total	262 (100)	38 (14.5)	28 (10.7)	11 (4.2)	185 (70.6)			
Physicians	56 (100)	15 (26.8)	29 (51.8)	9 (16.1)	3 (5.4)			
Total (sample)	318 (100)	53 (16.7)	57 (17.9)	20 (6.3)	188 (59.1)			

<sup>\*</sup>Women in reproductive age pregnant or not with: high school completed (group 1), college uncompleted – health science (group 2), college completed, schooling (group 3), and incomplete superior college uncompleted - medicine student (group 4).

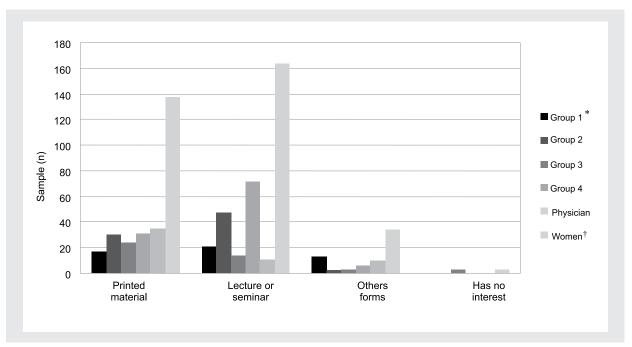


Figure 1. Preferred source of information of physician and women

\*Women in reproductive age pregnant or not with: high school completed (group 1), college uncompleted – health science (group 2), college completed, schooling (group 3), and incomplete superior college uncompleted – medicine student (group 4). †Total of women who participated of the study (n = 262).

occurrence, such as valproate, carbamazepine, alcoholism, among others.<sup>16</sup>

The occurrence of folic acid deficiency in the diet was determined by the Food and Drug Administration (FDA) and standardized in 1998 for supplementation of folic acid in foods in the United States, <sup>17</sup> resulting in the decrease incidence of neural tube defect in USA. In 2004, the *Agência Nacional de Vigilância Sanitária* (Anvisa) also start to request the supplementation of folic acid in Brazil. <sup>18</sup>

Smithells et al. were the first to demonstrate that folic acid deficiency was involved in the occurrence of the neural defect in humans. They studied the dose of serum folic acid in pregnancy in the first trimester comparing it with the occurrence of the neural tube closure when they had low serum level of folic acid, <sup>19</sup> however, there were various criticisms of the methodology of this study. <sup>3,4</sup>

The controversy was solved in the study Medical Research Council Vitamin Study in 1991, when they demonstrated a reduction of 72% in the occurrence of that congenital disease with the use of 4mg of folic acid in 1,817 pregnancies of women who had a previous child with

the malformation and those without any case in previous pregnancy or family history.<sup>6</sup>

According to the study of the American Collaborative Study of Congenital Malformations (ECLANC), Brazil had the highest rate of the disease with 3,3 newborn infants with malformation for 1,000 live births, followed by Argentina (2,6:1,000), and Uruguay (1,7:1,000).<sup>20</sup>

In the Hospital de Base do Distrito Federal, Brasília, 303 newborn infants with neural tube defect were studied from 1993 to 2003. Myelomeningocele was the prevalent defect, being located in 91.4% in the lombossacral region and only 38.3% of the mothers had received adequate prenatal assistance.<sup>21</sup>

Sens et al. studied the knowledge of the gynecologists of the University Hospital of the Universidade Federal de Santa Catarina, in Florianópolis, about existence of neural tube defect, the dosage of folic acid and recomendations about folic acid. Only 33.3% of the doctors had informed the correct dosage and period for the use of folic acid. Seventy eight point two percent of women who had given birth were unaware of the importance of folic acid in the prevention of congenital malformations.<sup>22</sup>



Gaiva and Anjos, from the Faculty of Nursing, Universidade Federal de Mato Grosso, Cuiabá, studied the epidemiological profile of the patients with myelomeningocele and prepared a manual for parents and children.<sup>23</sup>

Therefore, the lack of information about the period, use and correct dosage of folic acid (0.4 mg per day) of the population, including the health professionals, is probably related to the high rates of this malformation in this country. There should be more guidance by health professionals on the use of folic acid in the prevention of neural tube defect in women of reproductive age, in order to reduce these rates and improve the lives of many children in the country.

### **CONFLICTS OF INTERESTS**

The authors declare not to have conflicts of interests in this article.

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# REFERENCES

- 1. Lemire RJ, Shepard TH, Alvord EC Jr. Caudal myeloschisis (lumbo-sacral spina bifida cystica) in a five millimeter (horizon xiv) human embryo. Anat Rec. 1965;152:9-16.
- 2. McLone DG. Results of treatment of children born with myelomeningocele. Clin Neurosurg. 1983;30:407-12.
- 3. Smithells RW, Sheppard S, Schorah CJ, Seller MJ, Nevin NC, Harris R, et al. Apparent prevention of neural tube defects by periconceptional vitamin supplementation. Arch Dis Child. 1981;56:911-8.
- 4. Laurence KM, James N, Miller MH, Tennant GB, Campbell H. Double-blind randomised controlled trial of folate treatment before conception to prevent recurrence of neural-tube defects. Br Med J (Clin Res Ed). 1981;282:1509-11.
- 5. Milunsky A, Jick H, Jick SS, Bruell CL, MacLaughlin DS, Rothman KJ. Multivitamin/folic acid supplementation in early pregnancy reduces the prevalence of neural tube defects. JAMA. 1989;262:2847-52.
- 6. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. MRC Vitamin Study Research Group. Lancet. 1991;338:131-7.
- 7. Center for Disease Control and Prevention (CDC). Recommendations for the use of folic acid to reduce the number of cases of spina bifida and other neural tube defects. MMWR Recomm Rep. 1992;41(RR-14):1-7.

- 8. Lemire R, Loeser J, Leech R, Alvord E. In: Normal and abnormal development of the human nervous system. Hagerstown, Md: Harper and Row; 1975. p. 54-9.
- 9. Osaka K, Tanimura T, Hirayama A, Matsumoto S. Myelomeningocele before birth. J Neurosurg. 1978;49: 711-24.
- 10. McLone DG, Dias MS. Complications of myelomeningocele closure. Pediatr Neurosurg. 1992;17:267-73.
- 11. Schorah CJ, Smithells RW. Maternal vitamin nutrition and malformation of the neural tube. Nutr Res Rev. 1991:4:33-49.
- 12. Brody T. Vitamins. In: Brody T (ed). Nutritional biochemistry. San Diego: Academic Press; 1994. p. 355-484.
- 13. McNulty H. Folate requirements for health in different population groups. Br J Biomed Sci. 1995;52:110-9.
- 14. Hibbard ED, Smithells RW. Folic acid metabolism and human embryopathy. Lancet. 1965;1:1254.
- 15. Shurtleff DB, Lemire RJ. Epidemiology, etiologic factors, and prenatal diagnosis of open spinal dysraphism. Neurosurg Clin N Am. 1995;6:183-93.
- 16. Laurence KM, Carter CO, David PA. Major central nervous system malformations in South Wales. II. Pregnancy factors, seasonal variations, and social class effects. Br J Prev Soc Med. 1968;22:212-22.
- 17. Honein MA, Paulozzi LJ, Mathews TJ, Erickson JD, Wong LY. Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects. JAMA. 2001;285:2981-6.
- 18. Anvisa. Farinha terá ácido fólico para combater anencefalia em bebês [acesso em 27 jan 2009]. Disponível em: www. anvisa.gov.br/divulga/informes/2002120602.htm.
- 19. Smithells RW, Sheppard S, Schorah CJ. Vitamin deficiencies and neural tube defects. Arch Dis Child. 1976; 51:944-50.
- 20. Castilla EE, Oriloli IM, Lopez-Camelo JS, Dutra MG, Nazer-Herrera J; Latin American Collaborative Study of Congenital Malformations (ECLAMC). Preliminary data on changes in neural tube defect prevalence rates after folic acid fortification in South America. Am J Med Genet A. 2003;123A:123-8.
- 21. Filgueiras MG, Dytz JL. Avaliação do perfil de recémnascidos portadores de defeitos do tubo neural. Brasília Med. 2006;43:17-24.
- 22. Sens M, Nery L, Bernardi P, Nogueira Q, Pereira E. Avaliação do impacto da instituição do ácido fólico como medida de prevenção de malformações congênitas na cidade de Florianópolis. Anais da 6ª. Semana de Ensino, Pesquisa e Extensão, Universidade Federal de Santa Catarina; 2007.
- 23. Gaíva MAM, Anjos PSS. Ações de educação em saúde para os familiares de crianças e adolescentes portadores de espinha bífida. Manual: material educativo para ser utilizado junto a familiares de crianças e adolescentes portadoras de espinha bífida; impresso. Trabalho resultante de bolsa de iniciação científica; 2006.