Congenital Anomalies
Clinical and Laboratory Research
THE JAPANESE TERATOLOGY SOCIETY
doi: 10.1111/cga.12238

COMMENTARY

Preconceptional folic acid supplementation in Japan

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Although a recommendation for preconceptional folate supplementation was issued by the Japanese Ministry of Health and Welfare in 2000, and promotional efforts were made by various related academic societies, including the Japan Society of Obstetrics and Gynecology (JSOG) and the Japan Association of Obstetricians and Gynecologists (JAOG), uptake of folate supplementation has been insufficient. In the present report, we summarize the situation and present issues in Japan.

PROMOTION OF PRECONCEPTIONAL FOLATE SUPPLEMENTATION

In December 2000, the Japanese Ministry of Health and Welfare issued a statement announcing that "Healthcare workers should advise women who are planning a family, or whom are likely to become pregnant, that 400 μg/day folic acid (FA) should be taken as a nutritional supplement, in addition to that from regular dietary intake, at least one month prior to conception until 3 months after, in order to reduce the risk of neural tube defects (Hirahara 2002). In line with this statement, the JSOG provided information in 2008 on the association of neural tube defects with a deficit in FA intake in its guidelines for obstetric practice.

Further, The Ministry of Health, Labour and Welfare (2006) stated in guidelines on diet for pregnant women, the importance of ingesting a total of 480 μg/day FA and restated their recommended intake of 400 μg/day supplementary FA during periconceptional period. Other dietary guidelines during pregnancy from various experts have also been presented. Together, the importance of FA as a critical nutritional element has been increasingly promoted. It was also stated that intake of FA should not exceed 1000 μg/day and the importance of a balanced diet, with intake of other vitamins, as well as abstinence from smoking and alcohol, was also emphasized. Women with a history of neural tube defects affected pregnancy were recommended to take FA under the guidance of their general practitioner (as FA is often prescribed as Foliamine 5 mg/day).

COMMUNICATION OF FA INTAKE RECOMMENDATIONS

Since initial reports in the early 1980s on the association of congenital anomalies and reducing effects of FA intake, many researchers have suggested that preconceptional FA supplementation could reduce the incidence of neural tube defects (anencephaly, spina bifida, *etc.*) by 30–70% (Laurence et al. 1981; Smithells et al. 1983; Mulinare et al. 1988; Mills et al. 1989; Milunsky et al. 1989; MRC Vitamin Study Research Group 1991; Saitsu et al. 2003), leading to an international consensus on the importance of preconceptional FA supplementation. In Japan, despite the efforts of JSOG and JAOG, preconceptional FA supplementation was not universally accepted. This was partly due to the reluctance of the Ministry of Health, Labour and Welfare in the early 1990s, which considered that the Japanese diet traditionally included ample vegetables as compared to Western diets, but there also existed a lack of public understanding about the need for regular vegetable intake. In addition, there was a strong belief among the general population that the intake of any medication, including supplements, could do harm during pregnancy. Very few pregnant women are prescribed folate containing multivitamin-pills during their early stage of pregnancy in Japan. Finally, in 2000, the official recommendations described the benefits of preconception folic acid supplementation rather indirectly and stated that incidence of neural tube defects in the population was 'expected' to decrease.

Indeed, neural tube defects are not solely caused by a folic acid deficiency and scientific evidence to support the association remains sparse. This rather vague assertion was chosen so as not to cause concern to patients with neural tube defects and their parents. Also, at the time, government officials were promoting an increased vegetable intake of up to 350 g/day, which would provide the necessary levels of FA intake. Thus, the promotional message for preconception FA supplementation was rather muted compared to that in other countries.

The late campaign action of preconceptional FA supplementation and our efforts to improve the situation are not effectively provided to young women.

We recently conducted a survey that suggests approximately 80% of pregnant women are aware of the importance of FA supplementation during pregnancy, but the proportion of women who actually took FA before conception is limited to around 20% (unpublished data, Table 1). These data suggest that provision of information to young women regarding the importance of preconception FA supplementation is essential. Since most women see an obstetrician early on in their pregnancy, at which time neural tube closure is often complete, more effort aimed at spreading the information to young women, for example, school-aged girls, is necessary. However, there appears to be a reluctance in the educational arena to accept this recommendation. Promotion of healthier diets, not only for young women, but also in the general population, is critical for improving life-long health and welfare in Japan.

Absorption of FA from supplemental formulations is greater than that from food, and is therefore more efficient. Campaigns

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Received April 29, 2017; revised and accepted July 6, 2017.

Table 1 Folic acid (FA) intake in a survey of pregnant women, 2015

	Primipara	Multipara
Knowledge rate: awareness of the benefit of FA supplementation in the reduction of congenital anomalies	84.4 %	82.8 %
Intake rate**:** FA supplements during pregnancy	48.9 %	25.9 %

n = 103 (Japan Agency for Medical Research and Development grant programs survey, Grant No. 16gk0110023h0001).

emphasizing that FA is a supplement, and not a medication, might also help to promote intake of preconception FA.

In the Guidelines for Obstetric Practice (JAOG), first published by JSOG in 2008 (Minakami et al. 2014), preconceptional FA supplementation is a level B recommendation, a level that is classified as common sense. Thus, obstetricians are only required to provide appropriate general information when questioned by a patient. In the guidelines, an ideal response is provided to questions about the relationship between neural tube defects and FA intake: 'a FA intake of 400 μg/day would likely decrease the risk of developing disabilities caused by neural tube defects'. However, the guidelines provide no ideal answers regarding the nutritional elements that are necessary before conception. However, results from a meta-analysis show that 400 μg preconceptional FA supplementation suppresses the incidence of neural tube defects and preconceptional FA supplementation has been recommended by governments in various Western countries. This information is only provided as supporting evidence in the obstetric guidelines (JSOG).

POSSIBLE ADVERSE EFFECTS OF FA SUPPLEMENTATION

No reports to date have suggested that teratogenicity is associated with preconceptional FA supplementation. While there is good evidence that preconceptional FA supplementation suppresses the incidence of neural tube defects at a population level, there is an increased, though trivial, risk for pediatric respiratory disorders including asthma in certain individuals (Veeranki et al. 2015). Therefore, this information should be provided to women such that they can make informed decisions on whether to supplement their FA intake prior to conception.

CONCLUSION

Folic acid is an essential nutritional element, not only for women who plan to become pregnant, but also in the general population. It is important for the prevention of atherosclerosis and cerebrovascular disorders, to maintain cardiovascular health and in the prevention of cancer. However, the benefits of FA intake are not well publicized in Japan and further promotional efforts are thus warranted.

DISCLOSURE

None.

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