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Review article

Concentrations of blood folate in Brazilian studies prior to and after fortification of wheat and cornmeal (maize flour) with folic acid: a review

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ABSTRACT

Background: In July 2004, the Brazilian Ministry of Health through the National Health Surveillance Agency made the fortification of wheat flour and cornmeal (maize flour) with iron and folic acid mandatory, with the intention of reducing the rate of diseases such as neural tube defects.
Objective: The aim of the study was to investigate the impact of the folic acid fortified wheat flour and cornmeal on serum and red blood cell folate levels and on the reduction of neural tube defects in different Brazilian studies.
Methods: In order to compare folate concentrations in the Brazilian population prior to and following the implementation of mandatory fortification of wheat and cornmeal, studies that involved blood draws between January 1997 and May 2004 (pre-fortification period), and from June 2004 to the present (post-fortification period) were chosen. The data search included PubMed and Scopus databases as well as the Brazilian Digital Library of Theses and Dissertations. The following keywords were employed for the query: folate, folic acid, fortification, Brazil, healthy population, the elderly, children and pregnant women.
Results: A total of 47 Brazilian studies were selected; 26 from the pre-fortification period and 22 after the fortification implementation. The studies were classified according to the cohort investigated (pregnant women, children, adolescents, adults and the elderly). After the implementation of flour fortification with folic acid in Brazil, serum folate concentrations increased in healthy populations (57% in children and adolescents and 174% in adults), and the incidence of neural tube defects dropped.
Conclusion: Folic acid fortification of wheat flour and cornmeal increased the blood folate concentrations and reduced the incidence of neural tube defects.

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Introduction

Folic acid (FA) is a hydrosoluble vitamin essential for human health; its main roles in cell metabolism involve DNA synthesis and supplying methyl groups for homocysteine (Hcy), DNA, protein and lipid methylation reactions.[1]

The term folate is used to designate the polyglutamate form of water-soluble B vitamin present in edibles, while the term folic acid corresponds to the monoglutamate form used in supplements and in the fortification of food.[2] Folate rich foods include: green vegetables (broccolis, lettuce, spinach and asparagus), beans, fruit (lemons, bananas and melons), dry cereals, whole-grains, liver, kidney and mushrooms.[3] The physiological folate requirements increase when there is a corresponding increase in cell division such as during pregnancy, lactation and in early childhood; or whenever individuals are afflicted with certain diseases, such as hemolytic anemia, leukemia and other malignant diseases, as well as in alcoholism.[4]

It is believed to be difficult to obtain the required intake of this vitamin by means of a balanced diet alone (without fortified foods) when there is an increase in physiological necessities. A normal diet supplies around 0.25 mg of folate/day, considering a diet of 2200 calories per day. The difficulty in fulfilling the requirements may be explained by the low bioavailability of folate in foods and the low dietary intake of foods that are natural sources of this vitamin. Furthermore, high temperature processing of foods results in considerable loss of folate, reducing its content by 50%.[5]

The recommended dietary allowance (RDA), estimated average requirement (EAR) and the tolerable upper intake level (UL) reference values for folate differ according to age (children, adolescents and adults) remembering that intake requirements are higher for pregnant (RDA 600 µg/day and EAR 520 µg/day) and breast-feeding women (RDA 500 µg/day and EAR 450 µg/day).[6] During pregnancy, cells multiply intensively due to the widening of the uterus, placental development, increase in blood volume and fetal development, which increases folate and B12 vitamin necessities accordingly.[7]

Adequate intake of these vitamins is essential, since folate insufficiency has been identified as a risk factor for congenital disorders especially neural tube defects (NTDs). They result from neural tube closing failure during the early development of the embryo, typically between the 21st and 28th day after conception, most frequently resulting in anencephaly and spina bifida.

Since pregnancy is not always planned, it is important that women of child-bearing age have access to a suitable quantity of FA, at least one month prior to becoming pregnant. Accordingly, it is recommended that women of child-bearing age consume 400 µg of FA daily, via fortified foods, supplements or both, in addition to the quantity they acquire from their normal daily diet.[6] Considering the difficulties to obtain the folate requirements from a normal balanced diet, several countries decided to implement mandatory FA fortification of foods, starting with the United States in 1998, followed shortly by Canada, Chile and several others.

In Brazil, the Ministry of Health through the National Health Surveillance Agency (ANVISA) made the iron and FA fortification of wheat and cornmeal mandatory in July 2004, with the intention of reducing the rate of pathologies, like NTDs, nationally. When the RDC Resolution no. 344 was issued on December 13, 2002, ANVISA dictated that all wheat flour and cornmeal, whether sold directly to consumers or to the food industry for the manufacture of edibles, must be enriched with iron and FA. It was established that every 100 g of wheat flour and cornmeal must contain at least 4.2 mg of iron and 150 µg of FA.[8] However, no nationwide studies have been carried out to evaluate the concentrations of folate consumed by the Brazilian population prior to and following the mandatory implementation of fortified wheat flour and cornmeal. Accordingly, the purpose of this review is to investigate the impact of the FA fortification of wheat flour and cornmeal on serum and red blood cell folate levels, and to evaluate the reduction of NTDs in different strata of the Brazilian population.

Methods

In order to compare folate concentrations in the Brazilian population prior to and following the implementation of mandatory fortification of wheat flour and cornmeal, studies that involved blood draws between January 1997 and May 2004 (the pre-fortification period), and from June 2004 to the present (the post-fortification period) were chosen. Data reviewed included PubMed and Scopus databases as well as the Brazilian Digital Library of Theses and Dissertations. The following keywords were employed in the query: folate, folic acid, fortification, Brazil, healthy population, the elderly, children and pregnant women.

Studies in which the sample collection included both time periods were classified as “pre-fortification studies”, as long as the sample collection period prior to June 2004 was longer than the period after June 2004. Likewise, studies in which the collection period after June 2004 was greater than the period prior to mandatory fortification were classified as “post-fortification studies”. A number of studies did not specify the sample collection period; in these cases, emails were sent to the respective corresponding authors in order to determine this information.

Transversal and/or prospective studies were selected, without interventions, carried out on different cohorts of the Brazilian population, such as pregnant women, neonates, children and adolescents, adults and the elderly. The studies that evaluated the concentrations of folate in unhealthy populations were also selected and the data are presented in the Tables below but were not taken into consideration in the whole evaluation between the pre- and post-fortification periods. For consistency purposes , studies that presented folate concentrations expressed in ng/mL had their values converted into nmol/L using a conversion factor of 2.266[9] for this review.

In order to evaluate the concentrations of serum folate between the pre- and post-fortification periods, the increase of serum concentrations was estimated in children and adolescents and adults. Pregnant women were not considered for this evaluation, because the studies found presented great variations in the gestational age of the subjects within this cohort. Neonates and the elderly were not evaluated either, because few studies involving these cohorts were found for the two periods considered.