Folate and vitamin B_{12} status of women in Newfoundland at their first prenatal visit

Research

Recherche

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Abstract

Background: Newfoundland has one of the highest rates of neural tube defects in North America. Given the association between low maternal folic acid levels and neural tube defects, a cross-sectional study was conducted to obtain baseline data on the folate and vitamin B_{12} status of a sample of women in Newfoundland who were pregnant.

Methods: Blood samples were collected between August 1996 and July 1997 from 1424 pregnant women in Newfoundland during the first prenatal visit (at approximately 16 weeks' gestation); this represented approximately 25% of the women in Newfoundland who were pregnant during this period. The samples were analysed for serum folate, vitamin B_{12}, red blood cell folate and homocysteine.

Results: Median values for serum folate, red blood cell folate and serum vitamin B_{12} were 25 nmol/L, 650 nmol/L and 180 pmol/L, respectively. On the basis of the interpretive criteria used for red blood cell folate status, 157 (11.0%) of the 1424 women were deficient (< 340 nmol/L) and a further 180 (12.6%) were classified as indeterminate (340–420 nmol/L). Serum homocysteine levels, measured in subsets of the red blood cell folate status groups, supported the inadequate folate status. Serum vitamin B_{12} levels of 621 (43.6%) women were classified as deficient or marginal; however, the validity of the interpretive criteria for pregnant women is questionable.

Interpretation: A large proportion of pregnant women surveyed in Newfoundland in 1997 had low red blood cell folate levels.

In Newfoundland the incidence of neural tube defects, including anencephaly and spina bifida cystica, is one of the highest in North America, with 3.2 neural tube defects per 1000 births documented between 1976 and 1991.[1]

Maternal folate status and folic acid intake at the time of conception are strongly implicated in the etiology of neural tube defects. Several case-control studies documented significantly decreased relative risks of occurrence[2,3] and recurrence[4] of neural tube defect births for women who consumed folic acid supplements during the periconceptional period. Kirke and colleagues[5] showed that plasma and red blood cell folate levels were significantly lower in women who gave birth to a child with a neural tube defect. In Newfoundland 64% of a sample of mothers who gave birth to children with neural tube defects had folate intakes below the national recommended levels (168 μg/d),[6] compared with 27% of mothers who gave birth to healthy babies.[7] These findings suggest that poor maternal folate status may be associated with the high incidence of neural tube defects in Newfoundland.

We assessed the folate levels of women in Newfoundland at their first prenatal visit to establish baseline data prior to the implementation of cereal grain fortification with folic acid. In addition, given the association between low serum vitamin B_{12} and increased risk for neural tube defects,[5] we also assessed serum B_{12} concentrations.

Methods

An anonymous cross-sectional survey of patients was conducted from August 1996 to July 1997, and blood samples were collected from 1424 women in Newfoundland (25% of all pregnancies) at their first prenatal visit. For each subject blood was collected and frozen, and samples (linked by identification numbers) were shipped to the Public Health Laboratory in St. John's, Nfld., for the preparation of sera and red blood cell lysates. Folate concentrations in sera and red blood cell lysates were determined using the IMx Folate System (Abbott Laboratories, Abbott Park, Ill.), and vitamin B_{12} concentrations in sera were determined using the IMx B12 System (Abbott Laboratories). Samples were classified with respect to folate and vitamin B_{12} status as deficient (serum folate < 6 nmol/L, red blood cell folate < 340 nmol/L, serum vitamin B_{12} < 130 pmol/L); indeterminate (6–7 nmol/L, 340–420 nmol/L, 130–160 pmol/L, respectively); or normal (> 7 nmol/L, > 420 nmol/L, > 160 pmol/L, respectively) based on criteria established by the manufacturer. Serum homocysteine concentrations, a further biochemical indicator of cellular folate status, were evaluated for a subset of 370 samples, comprising equal numbers of samples from the red blood cell folate status groups, using reverse-phase high-performance liquid chromatography with fluorescence detection.[8] Significant differences ($p < 0.05$) between log-transformed variables were determined by 1-way ANOVA, and differences between groups were assessed by the Neuman–Keuls procedure.[9,10]

Ethics approval for the study was obtained from the Human Investigation Committee, Memorial University of Newfoundland.

Results

Median values for serum folate, red blood cell folate and serum vitamin B_{12} were 25 nmol/L, 650 nmol/L and 180 pmol/L, respectively (Table 1). On the basis of the interpretive criteria, 157 (11.0%) of the 1424 women were deficient (< 340 nmol/L) in red blood cell folate, and a further 180 (12.6 %) were classified as indeterminate (340–420 nmol/L) (Table 2). Serum homocysteine levels measured in subsets of the red blood cell folate status groups supported the inadequate folate status; homocysteine levels for the red blood cell folate-deficient group were 11.9 ± 0.5 μM, the indeterminate group, 10.3 ± 0.7 μM, and for the normal group, 8.2 ± 0.6 μM.

Table 1: Characteristics of 1424 women in Newfoundland at their first prenatal visit

Characteristic	Median (and range)	Percentile			
		5th	25th	75th	95th
Age, yr	28 (15–47)	18	23	31	36
Hematocrit	0.35 (0.23–0.47)	0.30	0.33	0.37	0.40
Serum folate, nmol/L	25 (4–178*)	8	13	32	44
Red blood cell folate, nmol/L	650 (110–4050)	270	430	1050	1620
Serum vitamin B_{12}, pmol/L	180 (6–1000)	80	130	240	380

*Value represents maximum range value following a 1:4 dilution of serum.

Interpretation

On the basis of serum folate levels less than 4% of the women in our sample were deficient or at risk for becoming deficient in folate. Using the less conservative criteria of Bailey and colleagues[11] (i.e., < 7 nmol/L = deficient, 7–13 nmol/L = marginal), 2.4% and 23.3% of the women sampled would be categorized as deficient or of marginal status, respectively. Despite the lack of consensus concerning the limits for normal and deficient levels for serum folate during pregnancy,[12–15] it is generally agreed that serum folate is more reflective of recent folate intake and that levels normally decline with advancing pregnancy.[16,17] However, red blood cell folate concentration is independent of parity and plasma-volume expansion and is therefore more stable throughout pregnancy.[16] Given the long half-life of red blood cells, red blood cell folate concentration at the first prenatal clinic (16 weeks' gestation) should better reflect the folate status of pregnant women at the time of neural tube closure (21 days' gestation); using criteria similar to those used by other groups[11,13] 27% of the women in our sample had either deficient or marginal systemic folate stores. Serum homocysteine concentrations, which were inversely correlated with the folate concentrations, confirmed the depleted systemic folate stores.

According to category limits (i.e., deficient, indeterminate and normal) that were based on samples from women who were not pregnant, 43.6% of the women in our study were of deficient or indeterminate status for serum vitamin B_{12}. Although serum vitamin B_{12} levels are known to decline with advancing pregnancy,[18–20] there may not be any other reliable marker for B_{12} deficiency.[21] Benjamin and colleagues[22] set their limit for deficiency at 100 pg/mL (approx. 70 pmol/L), which would result in less than 5% of the women in our study classified as deficient in vitamin B_{12}. Clearly, further work is required to define appropriate interpretive criteria for serum vitamin B_{12} status in pregnant subjects, perhaps by linking serum B_{12} levels to other indices of B_{12} status, such as methylmalonic acid.[23] Although serum homocysteine concentration has also been used as an index of vitamin B_{12} status,[23,24] our regression analysis yielded no significant relationship between serum B_{12} status and serum homocysteine concentrations.

Table 2: Distribution of women with normal and abnormal folate and serum B_{12} levels in the study population

Component	Status; no. (and %) of women*		
	Deficient	Indeterminate	Normal
Serum folate†	27 (1.9)	20 (1.4)	1377 (96.7)
Red blood cell folate‡	157 (11.0)	180 (12.6)	1087 (76.3)
Serum vitamin B_{12}§	360 (25.3)	261 (18.3)	802 (56.4)

*Percentages based on 1424 women, except for serum vitamin B_{12} levels, which were based on 1423 women.
†Deficient, < 6 nmol/L; indeterminate, 6–7 nmol/L; normal, > 7 nmol/L.
‡Deficient, < 340 nmol/L; indeterminate, 340–420 nmol/L; normal, > 420 nmol/L.
§Deficient, ≤ 130 pmol/L; indeterminate, 130–160 pmol/L; normal, ≥ 160 pmol/L.

Unfortunately, we were unable to correlate the low folate levels with other relevant patient variables (e.g., dietary preferences, multivitamin usage, socioeconomic status or gravidity) because blood samples were given anonymously. Nevertheless, the fact that 27% of the pregnant women presented with deficient or indeterminate red blood cell folate levels is a serious public health concern that should be addressed.

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