

Maternal Nutrition & Supplementation - Effects on Pregnancy Outcome

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INTRODUCTION

- Review increased micronutrient needs in pregnancy
- Highlight health risks of micronutrient deficiency in pregnancy
- Review the rationale for the new SOGC / Motherisk Folic Acid Clinical Practice Guideline



Vitamin A

- Essential for normal reproduction, embryonic development and growth
- Pregnancy RDI: 0.4 - 0.8 mg/day
- 57% of Native Canadian women have low daily vitamin A intake
- Mega dose of Vitamin A (> 10,000 IU): association with NTD
- SOGC: beta-carotene as source; **not** retinol since potentially teratogenic



Calcium & Vitamin D

- Critical for bone development and integrity
- In Canadian climate: lack of vitamin D production
- Native Canadians: 46% have low vitamin D and calcium intake
- Calcium inhibits iron absorption



Iron

- In 1st - 2nd trimesters: placenta accumulates iron to release to fetus later
- Between 28-38 wks - fetus grows from 1 to 3.4 kg
- Iron requirement throughout pregnancy: 27 mg/day
- Average iron intake by Canadian women: 12 mg/day
- CDC: start iron supplementation in 1st prenatal visit
- Calcium inhibits iron absorption



Maternal Iron Status

- Strong emerging evidence: neonatal hemoglobin linked to child development
- Evidence that maternal anemia linked to neonatal anemia
- Severe maternal anemia may be a *human teratogen*



Iodine

- Critical for fetal brain development
- Endemic low iodine - low IQ in babies
- Maternal hypothyroidism - even sub clinical (high TSH) - lower IQ
- Till 8 weeks - fetus has no thyroid function
- Till 16 weeks - fetus still dependent on mother's thyroid hormone
- Pregnancy RDI: 160 IU/day
- 15% of US women of childbearing age have low urine iodine
- RDI should probably be increased to 240 IU/day



Folic acid

Numerous observational studies since 1966 – showed increase NTD with low folate:

- **Wald**: RCT of 5 mg folate vs. placebo in mothers with previous NTD: 85% protection
- **Czeizel**: RCT of 0.4 mg folate in women with no previous NTD: potential eradication of 75% of NTD (ie folate-dependent)
- **Dublin**: case control study: 900 nM RBC folate - needed for optimal protection against NTD



Folic Acid

Wald (Lancet 2001;358:2071):

Using the Dublin study (protective levels against NTD):

- 0.4 mg/day: risk reduction of only 36%
- **5 mg/day: risk reduction of 85%**



Prenatal Multivitamins Containing Folic Acid

Recently:

- Associated with decreased risk of neural tube defects and other malformations





Meta-analysis: Prenatal vitamins containing folic acid and prevention of other malformations

***Cardiac**: > 20,000 patients

OR: 0.72 (0.62-0.84); protective effect: 28%

***Limb**: 15,000 patients

OR: 0.23 (0.06-0.79); protective effect: 77%

***Cleft palate**: > 22,000 patients

OR: 0.68 (0.45-0.96); protective effect: 32%



Prenatal Multivitamins Containing Folic Acid

- Associated with decreased risk of neonatal cancers
- For neuroblastoma: fortification studies have strengthened causation



Meta-analysis: prenatal vitamins containing folic acid and neonatal cancers

- **Neuroblastoma**: 585 patients
OR: 0.53 (0.42-0.68); protective effect: 47%
- **Leukemia**: 1995 patients
OR: 0.60 (0.50-0.74); protective effect: 40%
- **Brain**: 931 patients
OR: 0.73 (0.60-0.88); protective effect: 27%



JOINT SOGC - MOTHERISK CLINICAL PRACTICE GUIDELINE

PRE-CONCEPTIONAL VITAMIN/FOLIC
ACID SUPPLEMENTATION
JOGC DECEMBER 2007



Recommendations

- Use of MV containing FA for all women of childbearing age
- Use of MV containing FA as opposed to FA alone
- Diet alone is unlikely to provide adequate RBC folate levels
- 80 to 85% of women should take 5 mg FA
- Women should not take more than 1 dose/day of MV
- 5 mg FA supplementation will not mask B12 deficiency
- Preconception use (2-3 months) of MV containing folic acid and throughout pregnancy and postpartum (4-6 weeks)



FA dose for women at low risks of NTD

Good diet & good MV compliance (15-20%)

Use MV containing 0.4 - 1.0 mg FA

Poor lifestyle or poor MV compliance (80-85%)

Use MV containing 5 mg FA



FA dose for women at increased risks of NTD

- Use MV containing 5 mg FA - 3 months preconception until 10-12 week post conception
- Then switch to a MV containing 0.4 – 1.0 mg FA for remaining of pregnancy and postpartum period



Who is at increased NTD risk?

- Previous NTD or family history of NTD
- Use of anti-epileptic drugs
- Use of folate antagonists (ex. MTX, sulfas)
- Malabsorption disorders (ex. IBD)
- Obese (BMI > 35)
- Smokers
- Ethnicity (ex: Sikh, Celtic, Northern China)
- Diabetic
- Compliance and Lifestyle issues



Commonly Asked Questions:

If 40% of Ontario women did not attain the recommended 900 nM RBC folate level due to poor compliance with their MV containing 1 mg of FA - why assume they would use 5 mg?

Nguyen 2007:

- Mean compliance in taking prenatal vitamins: 54 – 59% (range 0 - 100%)
- Partial compliance with 5 mg/day will increase levels to the protective range in many more women



Commonly Asked Questions: (2)

Would high dose of folic acid mask B12 deficiency?

- Not according to existing studies
- Prenatal vitamins contain B12
- Measurement of B12 levels are not required prior to initiating supplementation



Commonly Asked Questions: (3)

FA and Cancer ?

Several suggestions of high folate associated with “increased risk of cancer “

- Kim (2006): 13 published case control studies
- Overall: a 30-35% reduction in the risk of breast cancer

Theoretical increased risk of worsening pre-cancerous progress: the “dual effect theory”



Commonly Asked Questions: (4)

FA & Cancer ?

Decrease in breast cancer incidence in USA despite doubling of folate levels

- Ovarian cancer:

Prospective cohort study: "... suggests that relatively high dietary folate intake may be associated with reduction of ovarian cancer....."

* Reduction in cancers of: head & neck, pancreas, esophageal, gastric



Commonly Asked Questions: (5)

FA and Twinning ?

Association between folate status and risk of twinning:

- Systematic review: « possible », but no-significant evidence of periconceptional folate intake and twinning



Commonly Asked Questions: (6)

What about the long term use of FA ?

- Guideline recommends the use of FA in the perinatal period
- Use of FA is therefore limited to usually recurrent 6- to -12-month time periods
- Other long-term uses (non perinatal context) of FA in the clinical context (alcoholism, anemia, liver and kidney diseases...) are not discussed



TAKE HOME

- Use of MV containing FA for all women of childbearing age
- Use of MV containing FA as opposed to FA alone
- Diet alone is unlikely to provide adequate folate levels
- 80 to 85% of women should take 5 mg FA within a multivitamin
- Women should not take more than 1 dose/d of MV
- 5 mg FA supplementation will not mask B12 deficiency
- Preconception use (2-3 months) of MV containing folic acid and throughout pregnancy and postpartum (4-6 weeks)



Case 1

- A 24 y.o. woman with celiac disease comes for first visit due to unplanned pregnancy which she wants to keep
- She is now 8 weeks pregnant (10 weeks gestation)
- She did not supplement with prenatal vitamins
- ***Issues to discuss?***



Case 1 (cont'd)

- She has not supplemented with folic acid, thus not preventing NTD
- Having celiac, she is not eating cereals, hence not benefiting from flour fortification if folate
- ***How should you manage her?***



Case 1 (cont'd)

- AFP in serum: 4SD higher than the mean
- Detailed Level 2 ultrasound: Lumbo- sacral Spina Bifida





Case 2

- A 32 y.o. woman is coming to see you planning pregnancy.
- Her nutrition is based mostly on meat and cereals. She hardly touches green vegetables and she tries to avoid bread due to overweight.



Case 2 (con'd)

- She is not very keen of medication. In the past, she became pregnant failing her oral contraceptives.
- How much folic acid would you recommend she take ?
- Consider 5 mg folic acid, as the typical 1 mg in most prenatal vitamins may not be sufficient to prevent neural tube defects in this non compliant patient.