

Prenatal Multivitamin-Mineral Supplementation: Minimizing Adverse Events

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Healthcare providers usually advise women to take a prenatal multivitamin-mineral supplement prior to, during, and after pregnancy (postpartum). However, upon taking that advice, many pregnant women struggle with taking the supplement and battle adverse effects such as nausea, vomiting, constipation, or other discomforts. Starting a prenatal multivitamin-mineral is one thing, but continuing with it is another. The following article sheds some light on prenatal multivitamin-mineral supplementation, explaining the importance of vitamins and minerals during pregnancy, identifying the difficulties of taking prenatal supplements, and highlighting ways to improve prenatal vitamin-mineral intake. Pregnant women and healthcare providers will also be introduced to a study currently being conducted by the Motherisk program which hopes to help pregnant women who are having difficulties with common multivitamin-mineral supplements.

Why is prenatal multivitamin-mineral supplementation recommended?

Vitamin and mineral supplementation is often recommended prior to and during pregnancy to ensure that the mother has an adequate supply of vitamins and minerals and to promote healthy development of the baby.

1. Maintaining an adequate supply of vitamins and minerals in the mother.

Even with the nutrition, health care, and resources available, some pregnant women may still lack the right amount of vitamins and minerals (vitamin or mineral deficiency) because of:

- insufficient dietary intake,
- nausea and vomiting in pregnancy (NVP),
- nutrients being poorly absorbed by the digestive system,
- gastrointestinal (GI) medical conditions such as Crohn’s disease, which can restrict dietary intake,
- lack of knowledge or misconceptions about vitamins and minerals, and
- smoking, which can lower the circulating levels of some vitamins.

Although diet is the preferred source of vitamins and minerals, supplementation can help pregnant women (or women planning pregnancies) to achieve the daily recommended dietary allowances (RDAs) for pregnancy (Table 1), particularly of those vitamins and minerals that are inadequately or not commonly consumed through diet.

Table 1. Daily Recommended Dietary Allowances (RDA) in Singleton Pregnancy †

Vitamin or Mineral	*RDA (per day)
Vitamin A	770 micrograms retinol equivalent
Vitamin E	15 milligrams α-Tocopherol equivalent
Vitamin K	90 micrograms
Vitamin C (ascorbic acid)	85 milligrams
Vitamin D (cholecalciferol)	5 micrograms
Vitamin B1 (thiamine)	1.4 milligrams
Vitamin B2 (riboflavin)	1.4 milligrams
Vitamin B6 (pyridoxine hydrochloride)	1.9 milligrams
Vitamin B12 (cyanocobalamin)	2.6 micrograms
Niacin	18 milligrams
Folic Acid	600 micrograms
Iron	27 milligrams
Calcium	1000-1300 milligrams
Zinc	11 milligrams

Iodine	220 micrograms
Phosphorous	700 milligrams
Selenium	60 micrograms
Magnesium	360 milligrams
Fluoride	3 milligrams
Copper	1.0 milligrams

† Food and Nutrition Board, Institute of Medicine, National Academies (2004). Dietary reference intakes (DRIs): For individuals, elements. Available: <http://www.iom.edu/Object.File/Master/21/372/0.pdf>

*Note: These are standard amounts, thus some women with certain medical conditions or circumstances may need more or less of the daily RDA.

Approximately 20 to 30% of pregnant women have a vitamin and mineral deficiency. Without prophylaxis (i.e. supplementation), roughly 75% of pregnant women would be deficient in at least one vitamin.(1) Vitamin and mineral deficiencies may have a negative effect on the mother's health. Table 2 outlines some common examples.

Table 2. Examples of the Potential Effects of Vitamin or Mineral Deficiencies on the Mother's Health and Pregnancy Outcome.

Vitamin or Mineral	Reason for vitamin or mineral requirement	Potential effects of vitamin or mineral deficiency
Iron	The iron supply may be depleted during the 1st trimester. Iron requirements increase significantly in the 2nd and 3rd trimesters, especially since the growing baby takes a lot more of this mineral from the mother during the later half of the pregnancy.	Iron deficiency paired with any significant blood loss (i.e. medical condition, surgery) may result in iron deficiency anemia – a condition in which certain components of blood (i.e. red blood cells, hemoglobin) are low in the blood supply.
Zinc	Development of the baby.	Possible health concerns due to zinc deficiency: - Complicate or prolong labour. - Increase risk for pre-term delivery. - Increase risk of damage to tissues surrounding the baby (also known as premature rupture of membranes). - Possible risk of birth defects. - Maternal depression.
Iodine	Iodine requirements increase during pregnancy because of changes in hormone levels and thyroid gland activity. About 65% of thyroxine, a hormone secreted by the thyroid gland, is comprised of iodine.	Iodine deficiency can put a pregnant woman at risk for hypothyroidism (ie. underproduction of thyroxine).
Vitamin B6	Fetal development.	Vitamin B6 deficiency during pregnancy has been associated with worsening nausea and vomiting in pregnancy. Vitamin B6 deficiency can impair pancreatic insulin production, thus increasing the risk for gestational diabetes (diabetes that can appear during pregnancy).
Folic Acid	Proper development of brain, spinal cord, and nerves in baby.	Increase risk of neural tube defects such as spina bifida.

Vitamin and mineral deficiencies, in general, may worsen the overall fatigue, lack of energy, and physical weakness experienced by many pregnant women. Therefore, vitamin and mineral supplementation can help to prevent or alleviate such deficiencies and associated health problems in the mother.

2. Promoting healthy development of the baby.

Vitamins and minerals play a major role in the development of a baby; hence it is important that the mother supplies an adequate amount of these nutrients to her unborn baby/babies. Many studies stress the importance of taking folic acid prior to and early in pregnancy, as it can reduce the risk of neural tube defects such as spina bifida by about 70%. The neural tube is a structure in the baby that develops into the brain, spinal cord, and other parts of the nervous system. Evidence also shows that periconceptional (before becoming pregnant) multivitamin-mineral intake reduces the overall occurrence of birth defects, in addition to neural tube defects. Zinc also plays a significant role in the development of various tissues (ie. muscle, nerves, bone) and organs (ie. heart, lungs, kidneys), thus there is great need for it in the first trimester when these tissues and organs begin their development. An adequate supply of iron, together with zinc and folic acid, in the 2nd and 3rd trimesters can improve the baby's growth and reduce the risk of low birth weight,

or a baby weighing less than 2500 grams at birth. Therefore, vitamin and mineral supplementation helps to supply nutrients to the growing baby, thus promoting healthy development.

3. Nutritional requirements in multifetal (more than one baby) pregnancies.

Diet should be the primary source of vitamins and minerals, and women with multifetal pregnancies should consult with their health care providers about the special diets recommended for multifetal pregnancies. Several studies have shown that incorporating multivitamin-mineral supplementation into the care of women expecting twins and higher-order multiples can have a positive impact on the woman's health and the pregnancy outcome. To date, there have been no vitamin-mineral supplementation studies with twin or higher-order multiple pregnancies.

It is known that women with multifetal pregnancies are at greater risk for vitamin and mineral deficiency, particularly of folic acid and iron. Deficiencies may occur because of the large and early increase in tissue mass—for example, in blood volume, uterus, placenta(s), total fetal weight—which usually occurs sooner than in a singleton pregnancy.(2) A prenatal multivitamin-mineral supplement will likely help women expecting twins and higher-order multiples achieve sufficient amounts of vital nutrients.

Currently, it is believed that the amount of supplemental folic acid recommended in multifetal pregnancies is the same as that for singleton pregnancies – 600 µg daily. There is conflicting literature regarding whether or not folic acid taken periconceptionally (before becoming pregnant) is associated with increasing the chance of a multifetal pregnancy. Due to the limited research about supplementation during multifetal pregnancies, the amount and timing of supplementation should be discussed fully by the woman with her health care providers such as perinatologist, obstetrician, registered dietitian-nutritionist, and/or medical internist.

The potential benefits of multivitamin-mineral supplementation in multifetal pregnancies include:

- preventing iron deficiency anemia,
- reducing the risk or severity of preeclampsia, a medical condition that usually occurs in late pregnancy and is characterized by hypertension (i.e. high blood pressure), albuminuria (loss of a certain blood protein in urine), and edema (buildup of fluid in tissues),
- reducing the chances of preterm labour,
- prolonging gestation to prevent premature delivery of the babies,
- reducing the risk of low birth weight.

Although the effects of multivitamin-mineral supplementation on multifetal pregnancies require further study, supplementation appears to be an important element in the prenatal care of women having multiple-birth children.

What makes multivitamin-mineral supplementation difficult during pregnancy?

Although vitamin and mineral supplementation is beneficial and recommended during pregnancy, many pregnant women struggle with taking common prenatal multivitamin-mineral supplements. Common problems associated with vitamin and mineral supplementation include:

1. aggravated nausea and vomiting in pregnancy;
2. gastrointestinal (GI) symptoms such as constipation, diarrhea, heartburn, acid reflux, or abdominal discomfort;
3. aggravated GI medical conditions such as irritable bowel syndrome (IBS), Crohn's disease, or ulcerative colitis; or
4. supplement properties such as tablet size, iron dose, taste, or odour.

1. Nausea and Vomiting in Pregnancy (NVP)

Nearly 80% of pregnant women experience some degree of NVP; up to 20% will suffer for more than 3 months, and for some women, NVP can last the entire pregnancy. Approximately 1% of pregnant women experience hyperemesis gravidarum (HG), the most severe form of NVP which can require hospitalization. Evidence shows that multifetal pregnancies are twice as likely to be linked with severe NVP(3). Symptoms include nausea, vomiting, gagging, and dry heaving, all of which can occur at any time throughout the day, can last for various lengths of time, and can occur at different intensities. NVP may make pregnant women very sensitive to what and how much they eat and drink. The large tablet size and high iron dose of common prenatal supplements may cause or aggravate NVP.

2. Gastrointestinal (GI) Symptoms

Many pregnant women experience an increasing sensitivity in their digestive and GI systems. Constipation, which is not unusual during pregnancy, may be caused or aggravated by the high iron dose found in common prenatal multivitamins-minerals. Other

symptoms such as heartburn, acid reflux, diarrhea, and indigestion also do not make it comfortable to take common prenatal supplements.

3. Gastrointestinal (GI) Medical Conditions

Some pregnant women are dealing with or develop a GI medical condition such as IBS, Crohn's disease, ulcerative colitis, peptic or duodenal ulcer, or an *H. pylori* bacterial infection. Any of these medical conditions can make the woman's GI system sensitive to high iron doses, which may cause or aggravate adverse events (i.e. nausea, vomiting, constipation, diarrhea, heartburn).

4. Prenatal Multivitamin-mineral Supplement Properties

Many pregnant women describe common prenatal supplements as large, bulky horsepills with chalky, bitter textures that leave a bad aftertaste. Attempting to swallow a large tablet amidst NVP may worsen the NVP. Common prenatal supplements may also contain an aggravating iron dose. The daily recommended intake of iron is 27-30 mg; yet most common prenatal supplements contain about 60 mg of elemental iron, combining iron and calcium into a single tablet. Calcium has been found to inhibit iron absorption in the body, thus a large iron dose is needed to compensate for some of the iron not absorbed due to calcium interference. High iron doses may cause or aggravate GI symptoms such as nausea, vomiting, constipation, and heartburn.

Some suggestions to increase tolerance of prenatal multivitamin-mineral supplements.

1. Take supplements at night or prior to sleeping. Pregnant women can then relax and sleep, as opposed to being awake and dealing with any aggravated symptoms.
2. Take supplements with a bit of food. Taking supplements on an empty stomach may aggravate symptoms. Having a bit of food prior to taking the supplement prepares the stomach to digest the solid tablet.
3. Treat all other symptoms or medical conditions as much as possible to ease taking prenatal supplements.
 - a. Managing nausea and vomiting symptoms may require changes in eating habits as well as medications.
 - b. Treat heartburn and acid reflux with antacids upon consultation with a doctor.
 - c. Minimize indigestion by chewing food more thoroughly and eating slowly.
 - d. Treat constipation by increasing intake of fibre and liquids or use a stool softener for severe constipation, upon consultation with a doctor.
4. Pregnant women who have major difficulty with swallowing tablets should consider a chewable multivitamin-mineral (often these are children's vitamins) or liquid vitamins. These options enable short-term supplementation, and pregnant women may need to consider switching to the right type of multivitamin-mineral once symptoms improve.
5. Consider enrolling in the Motherisk study.



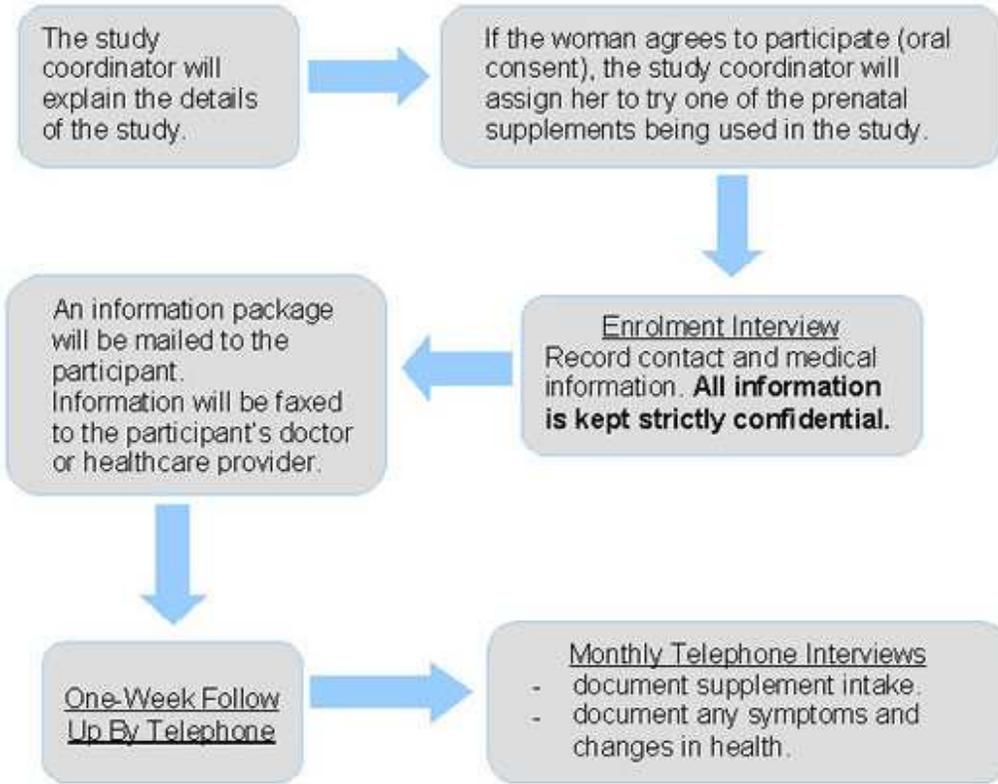
Motherisk® Study: Assessing the Tolerability of Alternative Prenatal Multivitamins

Currently, the Motherisk program at the Hospital for Sick Children (Toronto, Canada) is conducting a study to assess the tolerability of two alternative prenatal multivitamins-minerals, other than Materna® or similar prenatal supplements. The study is still enrolling pregnant women who are interested in trying a potentially more tolerable prenatal supplement.

Who can participate in the study?

Any pregnant woman who either did not start or discontinued her multivitamins-minerals (prenatal or regular) due to NVP, GI symptoms (i.e. nausea, vomiting, constipation, diarrhea, heartburn), GI medical conditions (i.e. IBS, Crohn's disease, ulcerative colitis, peptic/duodenal ulcer, etc.), or difficulties with the supplement itself (i.e. large tablet size, bitter taste, chalky texture).

What is involved in participating in the study?



What are the alternative prenatal multivitamins-minerals?
Women are randomly assigned to try either PregVit® or Orifer F®.

Common vs. New Generation Prenatal Multivitamin-mineral Supplements

Recently, there have been attempts to improve prenatal multivitamin-mineral supplements, particularly in terms of the iron dose and the overall tolerability of these supplements. The most common prenatal multivitamin-mineral supplement on the market is Materna® which is used by about 70% of pregnant women. Taken as a single daily tablet, Materna® initially contained 60 mg of elemental iron. In 2004, Materna® lowered the iron dose to 27 mg. Orifer F® and PregVit® are two prenatal multivitamins that differ from each other, but they are also potentially more tolerable compared to Materna®. Table 3 displays some of the properties of the two alternative prenatal multivitamins.

Table 3. Differing properties in PregVit® and Orifer F®.

Properties	PregVit®	Orifer F®	Daily Recommended Dietary Amount (RDA)
# daily oral tablets	<p style="text-align: center;">2</p>  <p style="text-align: center;">pink, morning tablet blue, evening tablet</p>	<p style="text-align: center;">1</p> 	
Iron	35 mg elemental iron (pink tablet)*	60 mg elemental iron	27 mg elemental iron
Folic Acid	1.1 mg (blue tablet)	0.8 mg	0.4 – 1.0 mg
Calcium	300 mg (blue tablet)*	125 mg	1000-1300 mg
Vitamin C	120 mg (pink tablet)	50 mg	80-85 mg
Zinc	15 mg (pink tablet)	20 mg	15 mg
Vitamin B6	10 mg (pink tablet)	9 mg	1.9 mg
Distribution	Doctor's prescription**	Over the counter	

*Separating iron from calcium minimizes calcium interference, optimizes iron absorption, and allows for a lower iron dose. A lower iron dose may minimize the common iron adverse events of nausea, vomiting, constipation, and other GI upset.

**Use of doctor's prescription enables PregVit® to be covered by insurance.

Summary

- Multivitamin-mineral supplementation is recommended prior to, during, and after pregnancy.
- Multivitamin-mineral supplementation helps to prevent vitamin and mineral deficiencies in the mother and to promote healthy development of the baby.
- Incorporating prenatal multivitamin-mineral supplements into the care of women expecting twins or more benefits the mother's health and improves pregnancy outcome.
- Many pregnant women struggle with common prenatal supplements due to NVP, GI symptoms (i.e. constipation), GI medical conditions (i.e. IBS), or supplement properties (i.e. tablet size).
- Pregnant women who can tolerate common prenatal supplements should continue their regimen. However, for those who find them intolerable, it is important to consider alternative multivitamin-mineral supplements to ensure adequate nutrient intake.
- The Motherisk program is currently inviting women to enroll in a study where pregnant women are introduced to alternative prenatal multivitamin-mineral supplements that may be better tolerated.

Contact information to join the study or obtain more information:

Patricia Nguyen, Study Coordinator
Telephone: 416-813-7283 (voicemail #2)

Email: patricia.nguyen@utoronto.ca

Attention Physicians, obstetricians, midwives, or other healthcare providers:

If you have a patient who is interested in participating in the study, please contact the study coordinator and leave the patient's name and telephone number. The study coordinator will contact the patient.

Website Links:

www.duchesnay.com

www.pregvit.com

www.motherisk.org

References:

1. Baker, H., DeAngelis, B., Holland, B., Gittens-Williams, L., & Barrett, T. (2002). Vitamin profile of 563 gravidas during trimesters of pregnancy. Journal of American College of Nutrition 21(1), 33-37.
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3. Kallen, B. (1987). Hyperemesis during pregnancy and delivery outcome: a registry study. European Journal of Obstetrics, Gynecology, and Reproductive Biology 26 (4), 291-302.