

ALBION®

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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PREGNANCY LACTATION AND CHANGE IN NUTRIENT NEEDS

The improvement of maternal and infant health is a primary goal of the United States, as well as much of the rest of the world. Reviewing public health nutrition programs and specific intervention trials has shown that maternal nutritional modifications can produce positive health benefits that are cost effective.

Pregnancy and lactation increase the nutritional requirements of women due to the demands of fetal and infant growth and development. The nutritional demands are further enhanced by the changes in maternal structure and metabolism that come with pregnancy and lactation. The total change in nutrient demand is not the simple sum of the nutrient needs to support the growth and development of the fetus, coupled with the normal needs of the non-reproducing women. [Picciano MF, pp. 394-395, Present Knowledge of Nutrition 7th Edition, ILSI Press 1996], Picciano states:

“Maternal metabolism is adjusted through the use of hormones as mediators, redirecting nutrients to highly specialized maternal tissues specific to reproduction (i.e., placenta and mammary gland), and transferring nutrients to the developing fetus or infant”.

These increased nutritional needs of pregnancy and lactation come about from:

PHYSIOLOGICAL ADJUSTMENTS OF PREGNANCY

- Hormonal changes
- Changes in blood volume and composition
- Adjustments in renal function
- Weight gain and its components

NUTRITION NEEDS TO SUPPORT THE PREGNANCY

- Basic increased energy needs
- Protein needs
- Vitamin and mineral demands

ENDOCRINE REGULATION OF LACTATION

NUTRITIONAL SUPPORT OF LACTATION

If the fetus does not receive adequate nutrition during the gestation period, all other things (i.e., genetics, etc.) being equal, at birth the mature size of each cell will be less than the cell size of an adequately nourished fetus. Furthermore, the total number of cells per tissue or organ will be less. This is an irreversible condition. There are other permanent physiological conditions, including neural transmitter damage within the brain that can result from improper fetal nutrition.

Pregnancy and lactation have been shown to increase the nutritional needs for energy, protein, Vitamin A, Vitamin D, Vitamin E, Vitamin C, thiamine, riboflavin, niacin, pyridoxine, Vitamin-B12, calcium, phosphorus, iron, zinc, iodine, and selenium. In Table 1, the relative changes in demands for the minerals mentioned are summarized.

Calcium and Pregnancy

Calcium metabolism in pregnancy is dramatically altered through a complex array of hormonal mechanisms, in addition to the needs of the fetus. Total circulating calcium in the pregnant female steadily decreases to values 5% below those of the nonpregnant female. The fetus' demand for calcium progressively increases during the course of the pregnancy from a start of 7 mg/day, to as high as 350 mg/day near term. This points to a need to increase the recommended daily intake of calcium during pregnancy. Below are a couple of interesting findings on the use of calcium supplementation in pregnancy.

CALCIUM SUPPLEMENTATION IN NULLIPAROUS WOMEN FOR THE PREVENTION OF PREGNANCY-INDUCED HYPERTENSION, PREECLAMPSIA AND

PRETERM BIRTH: AUSTRALIAN RANDOMIZED TRIAL, FRACOG and the ACT Study Group, Crowther CA, Hiller JE, Pridmore B, Bryce R, Duggan P, Hague WM, Robinson JS, Aust NZ Obstet Gynecol 1999 Feb; 39(1):12-8.

A multi center, randomized controlled double-blind trial in five maternity hospitals in Australia assessed the effect of a daily supplement of calcium (1.8 g oral calcium or an oral placebo) taken daily until delivery, from less than 24 weeks gestation on the frequency of pregnancy-induced hypertension, preeclampsia and preterm birth (<37 weeks gestation) in 456 nulliparous women with singleton pregnancy. Treatment with calcium reduced the risk of preeclampsia and the risk of preterm birth significantly. No significant differences were seen between the two groups in the frequency of pregnancy-induced hypertension, although the study only had statistical power to detect large differences in this outcome. An updated systematic review of the nine randomized trials of calcium supplementation in pregnancy showed a significant reduction in the risk of hypertension and preeclampsia although no effect on preterm birth. In summary, calcium supplementation during pregnancy was

shown to reduce the risk of preeclampsia and preterm births in this nulliparous population. The available evidence for systematic review of all the randomized trials of calcium supplementation showed benefit in reducing the risk of hypertension and preeclampsia.

EFFECT OF CALCIUM SUPPLEMENTATION ON PREGNANCY-INDUCED HYPERTENSION AND PREECLAMPSIA: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS, Bucher HC, Guyatt, Cook RJ, Hatala R, Cook DJ, Lang JD, Hunt D, JAMA 1996 Apr 10;275(14):1113-7.

The researchers analyzed 14 randomized trials that involved 2459 women, in an attempt to evaluate the effect of calcium supplementation during pregnancy on blood pressure, preeclampsia, and adverse outcomes of pregnancy. Each trial yielded differences in blood pressure change between calcium supplementation and control groups. The pooled analysis showed a 5.4mm Hg reduction in systolic and a 3.44mm Hg reduction in diastolic pressures for the calcium supplemented pregnant women. The odds for preeclampsia in women with calcium supplementa-

tion compared to placebo was 0.38 (substantially less). The conclusion of the researchers was that calcium supplementation during pregnancy leads to an important reduction in systolic and diastolic blood pressure and preeclampsia. While pregnant women at risk of preeclampsia should consider taking calcium, more research needs to be done to determine calcium's impact on maternal and fetal morbidity.

Zinc and Pregnancy

A review of the human studies on the role of maternal zinc status as a mediator of pregnancy outcome showed mixed results. The reasons for this may revolve around the use of small sample sizes, condition variations of the studies and lack of sensitive and specific laboratory measures to assess zinc status. Animal studies, on the other hand, have provided a large base of information that supports the need for adequate maternal zinc intake to achieve normal fetal growth and the prevention of malformations.

Plasma zinc starts to decrease in early pregnancy and continues to decline until term, at which time it is at a level that is 35% below those seen in

Table 1

MINERAL RECOMMENDED DIETARY ALLOWANCES OF ADULT WOMEN, PREGNANT WOMEN, AND LACTATION WOMEN: PERCENTAGE INCREASE OVER ALLOWANCES OF NON REPRODUCING ADULT WOMEN.

	Adult women (25-49 years)	Pregnant women (Third trimester)	Lactating Women	Percentage increase over non reproducing adult women	
				Pregnancy (%)	Lactation (%)
Calcium (mg)	800	1200	1200	50	50
Phosphorus (mg)	800	1200	1200	50	50
Iron (mg)	15	30	15	100	0
Zinc (mg)	12	15	19	25	58
Iodine (µg)	150	175	200	16	33
Selenium (µg)	55	65	75	20	36

nonpregnant females. The typical diet of US pregnant women contains 9-11 mg/day of zinc, which is not sufficient to maintain adequate zinc levels throughout pregnancy.

PRENATAL IRON SUPPLEMENTS IMPAIR ZINC ABSORPTION IN PREGNANT PERUVIAN WOMEN, O'Brien KO, Zavaleta N, Caulfield LE, Wen J, Abrams SA, *J Nutr* 2000 Sep;130(9):2251-5.

Prenatal inorganic iron supplements may adversely influence zinc absorption during pregnancy. To examine the impact of prenatal iron supplements on supplemental zinc absorption, fractional zinc absorption was measured in 47 pregnant Peruvian women during the third trimester of pregnancy (33 +/- one week gestation). Of these 47 women, 30 received daily prenatal supplements from week 10-24 of pregnancy until delivery. Supplements contained 60 mg of Fe from iron sulfate and 250 mcg of folate without zinc, or the same formulation with 15 mg zinc from zinc sulfate [16 women received supplements without zinc, 14 women received supplements with zinc, 17 women received no supplement]. Zinc concentrations were measured in plasma, urine and cord blood. The percentage zinc absorption and plasma zinc were significantly different in all three groups, with the women receiving the prenatal iron, but no zinc having the poorest values. Cord zinc was also measured, and it was directly proportional to the maternal plasma zinc levels. The researchers concluded that the use of the prenatal supplement without zinc leads to a poorer zinc status in the pregnant women and their offspring. In addition, they felt that the inclusion of zinc in prenatal supplements may

reduce the potential for inorganic iron supplements to adversely influence zinc status in populations at risk for deficiency of both these nutrients.

THE EFFECT OF ZINC SUPPLEMENTATION ON PREGNANCY OUTCOME, Goldenberg RL, Tamura T, Neggers Y, Copper RL, Johnston KE, DuBard MB, Haulth JC, *JAMA* 1995 Aug 9;274(6):463-8.

To evaluate whether zinc supplementation during pregnancy is associated with an increase in birth weight, the researchers conducted a randomized double-blind placebo-controlled trial. The trial was conducted at the University of Alabama (Birmingham) outpatient clinic and delivery service. The trial included 580 medically indigent, but otherwise healthy African-American pregnant women with plasma zinc levels below median values when they were enrolled in the prenatal care program. The randomization took place at 19 weeks gestation. The women were subdivided via the population median body mass index of 26 kg/m² into two groups for additional analyses. Women who were taking a non zinc-containing prenatal multivitamin/mineral were randomized to receive either a daily dose of 25 mg of zinc or a placebo until delivery. Birth weight, gestational age at birth, and head circumference were measured at birth. All infants from women in the zinc-supplemented group had a significantly greater birth weight and head circumference at birth. In women with a body mass index less than 26 kg/m², zinc supplementation was associated with a 248 gram higher infant birth weight and a 0.7 cm larger infant head circumference. The researchers concluded that daily zinc supplementation in women with relatively low plasma

zinc concentrations in early pregnancy is associated with greater infant birth weights and head circumferences, with the effects occurring predominately in women with a body mass index less than 26 kg/m².

PHYSIOLOGICAL SIGNIFICANCE OF ZINC: PERINATAL APPROXIMATION, Luna C, Villanueva LA, *Gynecol Obstet Mex* 2001 Feb;69:77-81.

The authors state that zinc is a very important micronutrient in several biological functions. During pregnancy, zinc deficiency causes fetal-growth retardation, malformations and other poor pregnancy outcomes. The additional need for zinc during pregnancy can be met by increases in zinc intake, bioavailability or by physiologic adjustments in zinc homeostasis. However, there are factors associated with low intestinal zinc absorption such as diets high in phytate, and inorganic iron or inorganic calcium supplementation. Further studies of maternal zinc status are necessary to define a prophylactic supplementation to prevent zinc deficiency during pregnancy.

Iron and Pregnancy

The iron expense of pregnancy is estimated to be about 1040 mg of iron. Of that total, 200 mg is retained by the mother when the blood volume decreases after delivery and 840 mg are permanently lost. Iron is transferred to the fetus (about 300 mg) and used for the formation of the placenta (50-75 mg), expansion of red cell mass (about 450 mg), and blood loss during delivery (about 200 mg). Hemoglobin, serum iron, transferrin saturation, and serum ferritin all decline during preg-

nancy. There is now a large volume of evidence linking iron deficiency anemia in early pregnancy to prematurity and low birth weight, which are the most common causes of infant morbidity and mortality.

IRON SUPPLEMENTATION IN PREGNANCY - EVIDENCE AND CONTROVERSIES, Haram K; Nisen ST, Ulvik RJ, Acta Obstet Gynecol Scand 2001 Aug;80(8):683-8.

Approximately 20% of women in industrialized countries have iron deficiency during pregnancy. This article focuses on the diagnostic problem of anemia and iron deficiency and discusses different strategies for iron supplementation in pregnancy. S-ferritin is commonly used to diagnose empty iron stores and is considered useful in early pregnancy as a diagnostic tool. Mean Cellular Volume (MCV), s-Fe and erythrocyte distribution width are too specific. Serum Transferrin Receptor (sTfR) is a relatively novel promising indicator of iron deficiency. Iron demands of the pregnant women are discussed as well as the dietary content of iron. Both beneficial and adverse effects of iron supplementation are outlined. It is not documented in humans that iron supplementation has any substantial effect on birth weight or various complications of pregnancy. However, supplementation does correct iron store and biochemical parameters of iron deficiency, including hemoglobin concentration and maintains the maternal iron stores in the puerperium. Recent literature also suggests that iron supply to the pregnant women may have beneficial effects on the iron content of the neonates the first year of life.

THE ROLE OF PROPHYLACTIC

IRON SUPPLEMENTATION IN PREGNANCY, Singh K, Fong YF, Arulkumaran S, Int J Food Sci Nutr 1998 Sep;49(5):393-9.

The prevalence, causes and role of iron prophylaxis in pregnant women was studied. All women delivered at the National University Hospital, Singapore in 1993 had their hemoglobin estimated. If it was less than 11 g/dl, blood was taken for serum iron, ferritin, transferrin, red cell zinc porphyrin, serum folate, serum B-12 and thalassemia screen to establish cause of anemia. Data was also collected with regard to their antenatal progress and iron prophylaxis. Logistic regression, Chi-square test, Fisher's exact test, and the Mantel-Haenszel tests were also used to assess the relationships between categorical variables. The prevalence of anemia in first antenatal visit was 20.6%, while the prevalence of anemia at delivery was 15.3%. The commonest cause of anemia in pregnancy was due to iron deficiency (81.3%). In the non-anemia group, 90.7% were taking prophylactic iron supplements compared to 50.6% in the anemic group. Of the 752 women found to be anemic at booking, 591 received prophylactic iron supplements, while 161 women did not. A total of 166 (28.1%) of those with prophylactic iron remained anemic at delivery, whereas 140 (87%) of those who did not receive iron supplementation remained anemic at delivery. Of the 2516 non anemic women who received prophylactic iron, 118 (4.7%) developed anemia at delivery, while 133 (34.1%) of the 390 women who did not receive iron prophylaxis were anemic at delivery. Multivariate logistic regression analysis revealed the odds of anemia for a woman not on iron therapy was about eleven times that of her counterpart

on prophylactic iron therapy. A 55% reduction in odds of anemia was estimated per 1 g% increase in hemoglobin at booking. Prophylactic antenatal iron supplements not only prevent a fall, but also improved the hemoglobin levels during pregnancy. Those who were not on any iron supplements were eleven (11) times more likely to develop anemia in the present pregnancy.

Ferrochel® During Pregnancy

RELATIVE EFFECTIVENESS OF IRON BIS-GLYCINATE CHELATE (FERROCHEL®) AND FERROUS SULFATE IN THE CONTROL OF IRON DEFICIENCY IN PREGNANT WOMEN, Szarfarc SC, Nunez de Casana LM, Fujimori E, Guerr-Shinohara EM, Vianna de Oliveira IM, Archivos Latinoamericanos de Nutricion S 51 (1) 2001: 42-47.

AA - The relative effectiveness of daily supplementation of iron deficiency during pregnancy using 15 mg/day of iron from iron bis-glycinate chelate (Ferrochel) (71 pregnant women), or 40 mg of iron from ferrous sulfate (74 pregnant women) was evaluated by measuring hemoglobin, transferrin saturation and serum ferritin at the beginning of the study (<20 weeks pregnancy) and at 20-30 weeks and 30-40 weeks thereafter. Ingestion for 13 weeks or more was considered adequate. Seventy three percent of the Ferrochel consuming group and 35% of the ferrous sulfate consuming group were considered to have taken the treatment adequately. The decrease in levels of all the measure parameters was significantly less pronounced in the group that consumed Ferrochel in spite of the lower treatment dose. Iron deple-

tion was found in 30.8% of the women treated with Ferrochel and 54.5% of the women that consumed ferrous sulfate. Of the factors responsible for non compliance, taste was reported in 29% of the ferrous sulfate consumers, with no complaints from the Ferrochel group. It was concluded that the daily supplementation with Ferrochel was significantly more effective, in spite the lower dose for Ferrochel as compared to ferrous sulfate.

*Calcium/Iron/Zinc -
Albion Advantage*

As noted in the author abstract on Ferrochel in pregnancy above, Ferrochel has been shown to be a very effective form of iron to use during pregnancy for the prevention of the development of iron deficiency. It compared in a very favorable fashion to ferrous sulfate for this indication. In radioactive isotope studies in pregnant animals, ⁵⁹Iron from Ferrochel was shown to cross the placenta and be deposited in the fetuses in significantly greater amounts compared to ⁵⁹Iron from ferrous sulfate. Ferrochel has been the subject of many clinical studies, and it has been shown

to be effective, safe, easy to tolerate, and less interactive with other dietary components than ionic forms of iron, like ferrous sulfate. It is important to note that studies have also clearly shown that Ferrochel is less constipating than ferrous sulfate, and this is a very important consideration during pregnancy. The many published clinical studies on Ferrochel that attest to Ferrochel's safety and effectiveness have lead to the GRAS status for food fortification that this patented form of iron has attained.

Albion's calcium amino acid chelate and zinc amino acid chelate have been shown to be superior in human and animal studies, as well. In a study [Heaney RP; Calcif Tiss Int (1990), 46: 300-4] that compared many forms of calcium (see Table 2 below), Albion's calcium amino acid chelate (bisglycino-calcium) was clearly the most bioavailable of all the calcium forms studied.

In a study [Schlomerich J, et al, Am J Clin Nutr (1987);45:1480-6] comparing the bioavailability of chelated zinc to zinc sulfate, the amino acid chelated zinc was seen to be absorbed at a rate that was 3 times that seen with the zinc

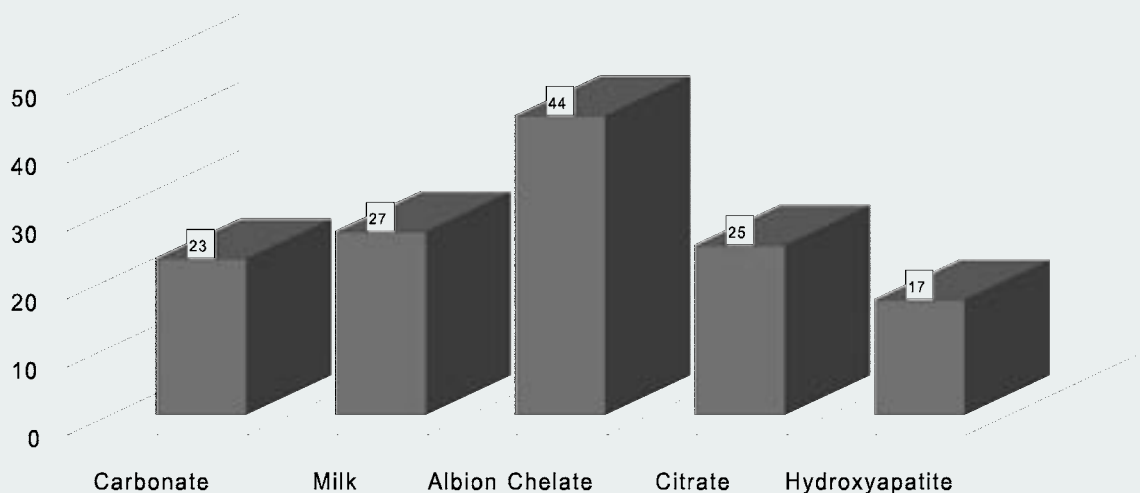
sulfate form. The authors concluded that 15 mg of elemental zinc from the amino acid chelate gave the same rise in serum zinc as did 45 mg of elemental zinc from zinc sulfate. The authors felt that this could allow a lower dose of zinc to be required, and vastly decrease the typical gastric erosive side effects seen with the higher dose of ionic zinc. This would lead to a greater compliance to supplementation with zinc, which is a very important consideration during pregnancy.

Summary

Pregnancy and lactation put high demands on the female body. Demands that lead to an increased requirement of many essential nutrients. Calcium, iron, and zinc are three of the mineral nutrients that are in extra demand during pregnancy and/or lactation. Albion's Calcium Chelazome[®], Ferrochel[®], and Zinc Chelazome[®] have been shown to be superior in bioavailability, safety and tolerance than other mineral forms. These characteristics make them desirable choices for the calcium, iron and zinc forms to place in prenatal or perinatal nutritional supplements.

Table 2

Calcium Absorption



ALBION[®]
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