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HUMAN NUTRITION

RESEARCH NOTES

A COMPILATION OF VITAL RESEARCH UPDATES ON HUMAN NUTRITION

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THE IRON CONUNDRUM

For sometime now, it seems that every time there is a report on iron and health that gets the attention of the media, it is for negative reasons. It has gotten to the point that many supplement companies are no longer formulating their multiple vitamin/mineral formulations to contain iron. Yet, when one actually scrutinizes the reports there is always a qualifier that goes along with the negative finding. It seems that there may be other factors that could have accounted for the connection between iron levels and whatever the health problem in question might be. However, fear has been put in place for not just the victims of hemachromatosis, but for those who may be heterozygous for this trait. How many people know if they are or not? Right or wrong, that is the way things are today. With all the work that has been done to demonstrate the way our body is designed to regulate iron transfer and protect against too much iron gaining access to our internal workings, we still feel threatened by overexposure to the ingestion of iron, an essential nutrient, in our diets. The World Health Report for 2002 states that iron deficiency is one of the 10 top health risks in the world along with HIV, tobacco, etc. It affects over 2 billion people and causes over 1 million deaths per year – some of them in North America.

In the publication put out by the Centers for Disease Control (CDC) called Morbidity and Mortality Weekly Review [51(40):897-899, 2002], it is stated that although iron deficiency is more common in developing countries, a significant prevalence was observed in the USA, among certain populations, such as toddlers and females of childbearing age. In fact, this report from the CDC shows that in the USA iron deficiency anemia remains 2-5 percentage points above our country's 2010 health objectives. The estimated prevalence of iron deficiency is greatest among toddlers aged 1-2 years (7%) and adolescents and adult females ages 12-49 years (9%-16%)(Table 1) The prevalence of iron deficiency was approximately two times higher among non-Hispanic black and Mexican-American females (19%-22%) than among non-Hispanic white females (10%). Note the data in Table 1 shows the prevalence of iron deficiency to be similar in the two study periods reported (NHANES III 1988-94) and (NHANES 1999-2000) for most age and sex groups. The main exceptions being found in males aged 12-69 years and women aged 50-69 years, where we see a significant increase in iron deficiency in the more recent findings. So, iron deficiency anemia may actually be rising in the USA. Maybe all of that negative publicity on iron intake is working after all. In almost every group listed

Table 1: Prevalence of iron deficiency – United States, National Health and Nutrition Examination surveys, 1988-1994 and 1999-2000*

Sex/Age Group (years)	1988 – 1994			1999 – 2000		
	Number	Percent %	(95% CI†)	Number	Percent %	(95% CI)
Both sexes						
1 - 2	1,339	9	(6 - 11)	319	7	(3 – 11)
3 – 5	2,334	3	(2 – 4)	363	5	(2 – 7)
6 - 11	2,813	2	(1 – 3)	882	4	(1 – 7)
Males						
12 – 15	691	1§‡	(0.1 – 2)	547	5‡	(2 – 8)
16 – 69	6,635	1‡	(0.6 – 1)	2,084	2‡	(1 – 3)
≥ 70	1,437	4	(2 – 3)	381	3§	2 – 7)
Females**						
12 – 49	5,982	11	(10 – 12)	1,950	12	(10 – 14)
12 – 15	786	9	(6 – 12)	535	9	(5 – 12)
16 – 19	700	11	(7 – 14)	466	16	(10 – 22)
20 – 49	4,495	11	(10 – 13)	949	12	(10 – 16)
White, non-Hispanic	1,827	8	(7 – 9)	573	10	(7 – 13)
Black, non-Hispanic	2,021	15	(13 – 17)	498	19	(14 – 24)
Mexican American	1,845	19	(17 – 21)	709	22	(17 – 27)
50 – 69	2,034	5‡	(4 – 7)	611	9‡	(5 – 12)
≥ 70	1,630	7	(5 – 8)	394	6	(4 – 9)

* All racial/ethnic groups except where noted.
† Confidence interval.
§ Unreliable; relative standard error (i.e., standard error/prevalence estimate) is >30%.
‡ p<0.05 for comparison between surveys within age and sex category.
** Nonpregnant only.

Source: MMWR © 2002 Centers for Disease Control and Prevention (CDC)

in Table 1, we are seeing higher levels of people with iron deficiency in more recent accumulated data than in the older data.

Of course iron is an important nutrient, and it plays a wide range of vital roles in the body, including its most essential role in the transport and storage of oxygen from the lungs to muscle and other cells for oxidative energy. No one has questioned the essentiality of maintaining a good iron level in the body. Iron deficiency has many negative effects, and these negative effects are critical. The literature is full of well documented research pointing to a real concern about iron nutriture in the perinatal women, infants, children, and adolescents. In fact, mounting evidence is indicating that maternal iron deficiency during pregnancy has more negative impact than previously thought.

Problems When Iron Deficiency Is Not Prevented Through Proper Perinatal Nutrition

It has often been argued that the use of iron in prenatal supplement formulas is not really necessary. Some have gone so far as to recommend against it. Here are some findings that should give the opponents of prenatal iron second thoughts.

Poorer behavioral and developmental outcome more than 10 years after treatment for iron deficiency in infancy, Lozoff B, Jimenez E, Hagen J, Mollen E, Wolf A.W, Center for Human Growth and Development, University of Michigan, Ann Arbor, Michigan 48109-0406, Pediatrics 2000 Apr;105(4):E51

This study was done to determine the long term effects of iron deficiency in infancy. This was a longitudinal follow up study of children who had been treated for iron deficiency as infants. Participants were in periurban San Jose, Costa Rica. The researchers reevaluated 87% of the original 191 children, now ages 11 to 14 (average 12.3years). The children were free of iron deficiency and growing normally by USA standards. Those who had chronic, severe iron deficiency in infancy (n=48) were compared with those who had good iron status before and/or after iron therapy in infancy (n=114). A comprehensive set of tests were run on these children. The children who had severe, chronic iron deficiency in infancy scored lower on measures of mental and motor functioning. After control for background factors, differences remained statistically significant in arithmetic achievement and written expression, motor functioning, and some other specific cognitive processes. More of the iron deficient children had repeated a grade and/or been referred for special services or tutoring. Parents and teachers rated their behavior as more problematic in several areas – anxiety/depression, social problems and attention problems were seen. The researchers concluded that severe chronic iron deficiency in infancy identifies children who continue at developmental and behavioral risk >10 years after treatment. In other words iron deficiency in infancy may result in permanent and irreversible damage to motor skill and proper cognitive functioning.

Infancy: Mental and Motor Development, Walter, Tomas, Institute de Nutricion y Tecnologia de los Alimentos, Universidad de Chile, Santiago, Am J Clin Nutr 1989 Sep;(3 Suppl):655-61

In a prospective cohort study of 196 infants from birth to age 15 months, the relationship of iron status to psychomotor development, the effect of a short term trial of oral iron or placebo, and the effect of longer term oral iron therapy was assessed. Development was assessed with the Bayley Scale of Infant Development in anemic, nonanemic, iron deficient, and control children. The anemic infants had significantly lower indices than did control or nonanemic iron deficient infants. No difference between the effect of oral administration of iron or placebo was noted after 10 days or 3 months of iron therapy. A hemoglobin concentration of less then 105 g/L and anemia duration of greater than 3 months were correlated with significantly lower motor and mental scores, suggesting that when iron deficiency progresses to anemia, adverse influences in the performance of developmental tests appear and persist, despite iron therapy. Correcting the iron deficiency anemia state in infants at a later date does not seem to reverse the damage already done by the iron deficiency.

Iron Deficiency anemia and infant development: effects of extended oral iron therapy, Lozoff, B, Wolf, A.W., Jimenez, E.: Center for Human Growth and Development, University of Michigan, Ann Arbor, Michigan 48109-0406, J Pediatr 1996 Sep;129(3):382-9

A double blinded, controlled trial was done in Costa Rica involving 32 (12 to 23 month old) infants with iron deficiency anemia and 54 nonanemic control subjects. The study was done to determine whether extended

oral iron therapy corrects lower developmental test scores in infants with iron deficiency anemia. In the study, anemic infants were treated with orally administered iron for 6 months; half the nonanemic children were treated with iron and half with placebo. Developmental test scores and hematologic status were evaluated before treatment, after 3 months, and after 6 months. The iron deficient anemic infants received lower mental test scores than the nonanemic infants at all three time test points. More of the anemic children were rated as unusually tearful and unhappy. The anemic infants tended to come from families with lower maternal education and less support for child development. The researchers concluded that lower mental test scores persisted in infants with iron-deficiency anemia despite extended oral iron therapy and an excellent hematologic response. Iron deficiency anemia may serve as a marker of a variety of nutritional and family disadvantages that may adversely affect infant development.

Commentary

To further state the importance of being aware of the need to guard against poor iron status in the fetus, we offer this from Dr. Betsy Lozoff:

Perinatal Iron Deficiency and the Developing Brain, Commentary: Dr. Betsy Lozoff, Center for Human Growth and Development, University of Michigan, Ann Arbor, Michigan 48109-0406, Pediatric Research 48:137-139 (2000)

"....studies also demand that we rethink the traditional dogma that the human fetus suffers few ill effects of maternal iron deficiency, unless severe. Infants born to mothers with nutritional iron deficiency in pregnancy are rarely anemic, but they may have lower iron stores and/or develop iron deficiency sooner postnatally. There is now solid evidence that brain iron deficiency can occur even with a normal Hb level. In young animals of every species tested to date, iron is prioritized to the red cells over all other organs, including brain. If the developing human hippocampus and other CNS functions are vulnerable to perinatal iron deficiency, as the de Ungria study shows in the rat, there are major public health implications. WHO estimates that more than 30% of pregnant women in developing countries have iron deficiency anemia, and one in four to five babies develops iron deficiency anemia. Anemia is a late manifestation of iron deficiency, and iron deficiency without anemia is even more widespread. If subtle effects of iron deficiency in infancy lay the ground for later problems in cognitive and behavioral functioning, then a large unrecognized population of children could be at risk due to perinatal iron deficiency, a nutritional problem that can be prevented or treated."

Research from Albion on Using Ferrochel® In a Prenatal Program

Relative effectiveness of iron bis-glycinate chelate (Ferrochel®) and ferrous sulfate in the control of iron deficiency in pregnant women, Cornbluth Szarfarc S, Núnez de Cassana LM, Fujimori E, Guerra-Shinohara EM, Vianna de'Oliveira MV, Sao Paulo University, Sao Paulo, Brazil, National University of Cajamarca, Peru, Archivos Latinoamericanos de Nutricion, Supplement Vol, 51, No. 1, 2001.

The relative effectiveness of daily supplementation of iron deficiency during pregnancy using 15mg/day of iron from iron bis-glycinate chelate 71 pregnant women), or 40 mg iron from ferrous sulfate (74 pregnant women) was evaluated by measuring hemoglobin, transferring saturation and serum ferritin, at the beginning of the study (<20 weeks of 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 measured parameters was significantly less pronounced in the group that consumed Ferrochel in spite of the lower treatment dose. Iron depletion was found in 30.8% of the women treated with Ferrochel and in 54.5% of the women that consumed ferrous sulfate. Of the factors responsible for non compliance, taste was reported in 29.8% of the ferrous sulfate consumers and none in the groups that consumed Ferrochel. It was concluded that daily supplementation with Ferrochel was significantly more effective in providing iron to pregnant women, in spite of the lower dose, than supplementation with ferrous sulfate.

[Note: In animal studies, a single oral dose of 4.4 uc of ^{59}Fe as the amino acid chelate in Ferrochel administered to pregnant rats resulted in a 188% increase in iron deposits per fetus compared to FeCl (Subramanian KS, et. al., eds., Biological Trace Element

Research, Washington DC, ACS, 318, 1991). Researchers at Michigan State University administered this iron amino acid chelate to pregnant pigs beginning 4 weeks before expected parturition. At birth, the baby pigs had 35% more iron in the liver, 8% more iron in the spleen, and 3% more iron in their skeletal muscle than the control piglets. Their hemoglobin was 11% higher at birth and 127% higher at 3 weeks (Brady PS, Evaluation of an amino acid iron chelate hematinic, Report of Swine Research 1975, p.4). The studies clearly suggest greater placental transfer of iron to the unborn baby when the pregnant mother ingested Albion's amino acid chelated iron.]

Table 2

Clinical Features of Iron Deficiency*
• Symptoms of anemia**
• Pasophagia (heavy ice consumption)
• Koilonychia (brittle spoon nails)
• Blue sclera
• Glossitis
• Angular stomatitis
• Postcricoid esophageal web/ stricture
• Gastric atrophy
• Impaired immunity
• Decreased exercise tolerance
• Neuropsychological abnormalities
** Children may demonstrate irritability, memory loss, and learning difficulties. Adults show symptoms slowly, but They include fatigue and shortness of breath.

Iron Deficiency: Brief Review

Given the current trend of de-emphasis of iron in supplementation, and in light of the fact that iron deficiency has actually started a possibly insidious rise in the USA, and that iron deficiency is still the deficiency of highest proportion in the world, a review of some salient information on iron deficiency is offered here.

See Tables 2-4 below.

Parting Comments

Iron deficiency and iron deficiency anemia are still the most commonly encountered nutritional deficiencies in the world. Continued vigilance against this health hazard is warranted. Research is continuing to show that there is mounting evidence pointing to the long term dangers of iron deficiency in the fetus that predispose the child for long term problems that do not seem to be correctible after the fact. Leading researchers state that although the advisability of routine iron supplementation during pregnancy has been heavily debated, the mass evidence supports the practice of routine iron supplementation during pregnancy, although iron supplementation is certainly most important for those pregnant women who develop anemia.

Table 3

Laboratory Features of Iron Deficiency*
⊙ Hematologic • Microcytic Anemia • Thrombocytosis
⊙ Bone Marrow • Normal nuclear maturation • Cytoplasmic abnormalities • Absent iron stores on iron stain
⊙ Biochemical • Ferritin level is decreased • Total iron binding capacity is elevated • Iron saturation and serum iron are decreased

The possible side effects of oral iron therapy include:

- Constipation
- Diarrhea
- Nausea
- Epigastric discomfort
- Vomiting

These side effects are often the biggest reason for individuals not taking iron supplements, especially during pregnancy. Ferrochel, ferrous bisglycinate chelate, from Albion has

Table 4

Causes of Iron Deficiency Anemia*
• Gastrointestinal bleeding
• Genitourinary bleeding
• Menses
• Repeated blood donation
• Growth
• Pregnancy and lactation
• Poor diets
• Intestinal malabsorption
• Hookworm/intestinal parasites
• Gastric surgery
Handbook of Nutrition and Food, edited by Carolyn D. Berdanier, CRC Press LLC 2002

been shown to be one of the gentlest forms of iron. Published studies have shown that people taking Ferrochel have a much lower incidence in these side effects. In addition, Ferrochel has been shown to be superior to other commonly used iron forms in combating iron deficiency.

Ferrochel is CAS Registered, GRAS for food fortification, and Kosher Parvé. It is backed by a growing war chest of clinical evidence attesting to its superior performance. It is used worldwide in the efforts of many countries to fight the number one nutritional deficiency – iron deficiency.

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