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Anemia and Iron Deficiency according to Feeding Practices in Infants Aged 6 to 24 Months*

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ABSTRACT

The prevalence of iron deficiency in later infancy and the toddler years(25% to 40% at 1 year of age) has not decreased remarkably, except in Western countries. The purpose of this study was to 1) determine the relationship between current feeding practices and iron status, and 2) assess compliance to infant feeding instructions. Two groups of infants were examined. The first group of 302 infants aged 6 to 24 months was seen at a well baby clinic while the second group of 135 infants of the same age group was assessed by venipuncture. Cutoff values for laboratory tests were as follows : hemoglobin<11g/dL, mean corpuscular volume(MCV)<72 fl ; red cell distribution width(RDW)>15% ; serum ferritin level<10ng/ml ; and transferrin saturation(serum iron/TIBC)<10%. The diagnosis of iron deficiency anemia(IDA) was made when a low hemoglobin level was associated with either low ferritin or low transferrin saturation. Of the 302 children brought to the well baby clinic, 12.3%(n=37) were found to have anemia(hemoglobin<11.0g/dL). In terms of children grouped according to feeding practices, it was found that children with anemia comprised 32.0%(24/75) of the prolonged breast-fed group(Group A), significantly more than the 4.0%(7/176) of the artificial milk feeding group(Group B) and 3.9%(2/51) of the switched from breast milk to iron-fortified weaning foods group(Group C). Among the 107 children with IDA, iron deficiency in 105 children(98.1%) was suggested by their dietary histories : exclusive or prolonged breast-feeding for more than 6 months without iron fortification in 98 infants ; cow's milk consumption> 500ml/day without iron fortification during infancy(n=12), or>800ml without iron-fortified foods after infancy(n=15) ; and the use of unfortified formula or unbalanced diets, mainly limited to rice gruel. Despite the relatively high(79.6%) motivation on the part of the infants' mothers and supervision by professional personnel, the poor results in the infants receiving iron-fortified foods were due to poor compliance(85.7%). Among the mothers of 98 IDA patients who were contacted by telephone, it was revealed that 29% did not give the oral iron preparation for more than 2 months. Furthermore, negligence or disregard by the parents occurred in 14% of the cases, discontinuance of the oral iron preparation by the parents due to side effects occurred in 6%, and the children's refusal or poor oral intake and no further trial occurred in 6%. The dietary history of a large group of infants was highly predictive of their risk for anemia. Continued consumption of breast milk until the age of 1 year is not warranted unless iron-fortified foods are given concomitantly. Because there is a problem with compliance, more successful and safe strategies for preventing iron deficiency woold include dual coverage

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in the form of therapeutic iron supplementation as well as use of iron-fortified foods for toddlers who are at risk of iron deficiency. (*Korean J Nutrition* 31(1) : 96~101, 1998)

KEY WORDS : anemia · breast milk · formula · infant · iron deficiency · weaning.

Introduction

The prevalence of iron deficiency or iron deficiency anemia(IDA) in later infancy and the toddler years(30 to 35% at about 1 year of age) has not improved throughout the world, despite improvements in general health and nutrition[1-3]. From about 4 months of age, iron stores are insufficient to maintain the rapidly expanding blood volume associated with normal growth. If there is not a steady supply of dietary iron, stores become depleted and IDA develops. Due to the high iron requirements in infancy and the relative lack of variety in infants' diets, with milk being the main source of calories, iron deficiency tends to be prevalent even in developed countries, especially among those patients of lower socioeconomic class.

It is known that iron deficiency may impair not only physical activity but also mental functions such as learning[4][5]. Children with iron deficiency are found to have more psychomotor deficits and achieve lower scores in aptitude tests at the age of 12 months than those with normal iron status[6]. Therefore, preventing the development of iron deficiency is imperative during late infancy, when increased vulnerability to iron deficiency coincides with the rapid growth and differentiation of the brain[7][8]. Recent studies have reported that 15 to 40% of infants fed only human milk and/or non-fortified solid food developed iron deficiency during infancy and early childhood[9-11]. In addition, the introduction of solid foods has been implicated as a cause of a marked decrease in the bioavailability of iron from human milk[12].

The purpose of this study was to 1) determine the relationship between current feeding practices and iron status, and 2) assess compliance to infant feeding instructions.

Subjects and Methods

Two groups of infants were examined. The first group of 302 infants aged 6 to 24 months was seen at a well baby clinic in Seoul, Korea, while the second group of 135 infants of the same age group with IDA was seen at Inha General and University Hospital in Inchon, Korea. Blood samples were obtained by venipuncture after parental consent for recruitment to the study had been given. Children with dehydration, chronic illness, and previous transfusion history or major congenital anomalies were excluded from the study.

The children were divided into the following three groups according to their feeding practices : 1) Group A, comprising 75 children fed with breast milk up to 10 months of age, regardless of iron fortification ; 2) Group B, comprising 176 children artificially fed with iron-fortified formulas and/or cereals since birth ; and 3) Group C, comprising 51 children breast-fed up to 5 to 6 months of age, and then switched to iron-fortified formulas and/or cereals at 5 to 6 months of age. The iron-fortified milk formulas and cereals commercially available in Korea contain 6~9mg of ferrous sulfate per 100g(1.16~1.74mg per 100kcal). Home-made weaning foods or foods without specific indications of iron fortification were considered as non-iron fortified foods. Zen macrobiotic diets consisting mainly of glutinous rice, brown rice, adlay rice, barley, ground sesame seeds, beans, wheat, oats and soybeans, were also considered non-iron fortified foods. Main weaning foods were defined arbitrarily as foods given almost daily.

Hemoglobin, hematocrit, mean corpuscular volume(MCV), and red cell distribution width(RDW) were determined with the use of a Coulter S-Plus IV (Coulter Corp., Fl, USA). Children with a hemoglobin count $<$11g/dL were classified as having anemia because the lower limit of the 95% range for hemoglobin is estimated to be 11 g/dL[13][14]. Cutoff values for other laboratory tests were as follows : MCV $<$72 fl ; RDW$>$15% ; serum ferritin level$<$10ug/L ; and transferrin saturation(serum iron/TIBC)$<$10%. The diagnosis of IDA was made when a low hem-

oglobin level was associated with either low ferritin or low transferrin saturation. Serum ferritin levels were measured by an enzyme immunoassay(Abbott laboratories, USA). Serum iron and total iron binding capacity were measured by spectrophotometry(Latron, Japan).

Mean, standard deviation, and the Student's t-test were used in the statistical analysis. Out of 302 children brought to the well baby clinic, 267 children were regarded as a comparison group while 35 of these children were excluded due to the presence of IDA. Differences in proportions were tested for statistical significance by the chi-square test with Yates correction.

Results

1. Results from the well baby clinic

As shown in Table 1, 12.3%(n=37) of 302 children brought to the well baby clinic were found to have anemia(hemoglobin<11.0g/dL). Children with anemia comprised 32.0%(24/75) of the prolonged breast-fed group(Group A), significantly more than the 4.0%(7/176) of the iron-fortified feeding from birth group(Group B) and 3.9%(2/51) of the switched from breast milk to iron-fortified formulas and/or cereals group(Group C)($p<0.001$, respectively). Children with MCV<75 fl comprised 28.0%(21/75) of Group A, significantly more than the 4.5%(8/176) of Group B and 9.8%(5/51) of Group C. Children who had RDW>15% comprised 26.7%(20/75) of Group A, compared with 5.1%(9/176) of Group B and 9.8% of Group C(5/51). Of the 75 children breast-fed for a prolonged period(Group A), 42 children were found to have been given iron-fortified formulas or cereals, among whom 9.5%(n=4) had anemia, compared with 60.6%(20/33) in those who had been given non-iron fortified foods or had not been given weaning foods(Table 2).

2. Infants and young children with IDA versus the comparison group

There were significantly higher proportions of home-made porridge, Zen macrobiotic food, yogurt and cow's milk in the diets of the IDA group than in the diets of the comparison group. On the other hand, there were lower proportions of iron-fortified formulas or cereals, eggs, meat, fish, and bread in the diets of the IDA group(Table 3). Boiled rice and rice gruel were the most common first-weaning foods in both groups. Zen macrobiotic diets in Korea consist mainly of ground brown rice and sesame seeds, beans, wheat, oats, soybeans, and water. Vegetables include potato, beetroot, pumpkin, tomato, broccoli, cauliflower, cabbage, and turnip.

There were significant differences in hemoglobin, hematocrit, MCV, MCH, RDW, and platelet counts between the IDA group and comparison group, as seen in Table 4.

3. Dietary history and adjustments to diet in children with iron deficiency anemia

Among 107 children with IDA whose mothers answered the questionnaire, iron deficiency in 105 children(98.1%) was suggested by their dietary histories : exclusive or prolonged breast-feeding for more than 6 months without iron fortification in 98 infants among whom 20 were also given cow's milk> 500ml/day during infancy ; mainly cow's milk consumption>500ml/day without iron fortification during infancy(n=12) or >800ml/day without iron-fortified foods after infancy(n=15) ; and the use of unfortified formula or unbalanced diets mainly limited to rice gruel. Two children(1.4%) took oral iron, which was inadequate in duration and amount. Another infant who was given oral iron for 2 months received more than 700ml of cow's milk/day during the breast-feeding period. An infant, who was allegedly given iron-fortified foods, was found to have IDA.

As shown in Table 5, mothers tried to adjust foods, according to the recommendation of medical staff, to give iron-fortified foods to their IDA-afflicted infants. Despite the relatively high(80%) motivation on the part of the mothers, most mothers declared that their children showed poor appetites or refused the prepared foods after the change of foods. This was the main cause of poor compliance. That is, 86% of infants showed little change.

4. Compliance with oral iron medication in children with IDA(Table 6)

Telephone calls to the mothers of 98 patients with

IDA revealed the following : 71% had good compliance(iron medication for 3 months or more) ; 29% did not give the medicine for more than 2 months ; negligence or disregard by the parents occurred in 14% of the cases ; discontinuance by the parents due to side effects occurred in 6% ; the children's refusal or poor oral intake and no further trial occurred in 6% ; economic difficulty occurred in 2%.

Discussion

Although IDA has decreased during the past two decades with the improvement of infant nutrition, the prevalence of iron deficiency in infants has not decreased remarkably, except in Western countries[3)15)16)]. For example, IDA and iron deficiency were found in 25 and 37%, respectively, of children aged about 1 year from disadvantaged families in Montreal[17)]. The prevalence of anemia and iron deficiency(ferritin <12ug/l) was 46 and 60%, respectively, in children aged 9 to 24 months from a large urban area of Argentina[18)]. In Taiwan, the prevalence of iron deficiency and IDA was 34 and 15%, respectively, in children aged 6 to 24 months[19)]. Anemia(Hb<11g/dL) was detected in 25 to 39% of children, respectively, aged 6 to 22 months from the United Arab Emirates, and iron depletion was shown to be present in half of these children[20)].

Little change in the prevalence of iron deficiency may mean that infantile feeding practices have changed little in some areas. In our study, the prevalence of anemia in an apparently healthy population aged 6 to 24 months was 12%. However, an even greater percentage of individuals will show the biochemical changes of iron deficiency that precede the development of anemia, because anemia is a late manifestation of iron deficiency. Indeed, the prevalence of a ferritin level<10ng/ml was 30% in another of our studies(in press).

Late weaning causes deleterious effects on nutrition because infants, unaccustomed to variety in their diets, have a tendency to continue eating the same foods. While many commercial weaning foods are fortified with iron and ascorbic acid, there are household foods that do not always provide enough iron. In practice, boiled rice or cow's milk is the preferred weaning food or alternative to formula and breast milk partly because of convenience, economy, and misinformation. After the first year of life, a child begins to consume regular household food and, at this time, marked differences in iron content and iron availability between different diets become apparent.

Although it is generally asserted that prolonged breast-feeding offers substantial protection against the development of IDA[21)22)], several recent studies have reported that 15 to 40% of infants who were fed only human milk with or without unfortified solid foods developed iron deficiency at infancy and early childhood[9-11)23)24)]. Pizarro et al[10)] showed that the prevalence of anemia at 9 months of age was 23% in breast-fed infants, 4% in infants fed iron-fortified formula, and 29% in those fed cow's milk without an iron supplement. According to Calvo, et al.[11)], at the ninth month the prevalence of anemia was 28% in the breast-fed group and 7% in the formula-fed group, without mention of iron fortification. In our study, those who had been given non-iron fortified foods or had been given little weaning food had a much higher prevalence(60%) of anemia compared with the previous reports. This supports the opinion that the total iron potentially absorbed by an exclusively breast-fed infant during the first year of life may be calculated to be 57.3mg/year[11)], as compared to the calculated 250mg of absorbed iron required during the first year of life[25)]. In the present study, many mothers complained that infants who had not started to take food from a spoon by 6 months later had difficulty adapting from the milking action of the suckling infant to the chewing action of the weanling infant. Many infants who are accustomed to breast-feeding have difficulty in managing diarrhea or febrile illness because of their refusal to suckle. The use of an unfortified formula or the early use of cow's milk in infants is likely to lead to iron deficiency.

Excessive whole-milk ingestion may lead to imbalances in the diet and iron deficiency, even after 12 months of age. In early infancy, as breast-feeding declines, vegan diets consisting of plant foods that are low in caloric density and high in bulk may be difficult for the weanling to consume in sufficient quantity to meet energy needs as stomach capacity is lim-

ited. There are also sociocultural practices that affect dietary intake[26]. In Korea, Zen macrobiotics are relatively prevalent as weaning foods, and are considered non-iron fortified. One reason we believe they are not iron-fortified is that ferrous sulfate is not suitable for commercial use because of its tendency to cause rancidity in cereals after prolonged storage. Unfortunately, vegan mothers who adhere to macrobiotics are especially likely to use disproportionate mixtures during weaning, a practice that we believe is usually inadequate to meet the energy requirements of young infants, as well as their requirements for other nutrients. The mixtures that have been found to cause problems include a cereal pap of rice, barley, and beans, which is frequently fed to macrobiotic infants, honey water with ground sesame seeds, and yogurt and diluted non-dairy creamer.

Our results can be applied to the selection of an appropriate approach to detect iron deficiency in individual infants on the basis of their nutritional history. The dietary history of a large group of infants in our study was highly predictive of their risk for anemia, as asserted in Pizarro, et al.[10]. Even in the group who when questioned stated that iron-fortified foods were given, the prevalence of anemia was 9.5%. The iron fortification of infant foods is appealing because it is easily targeted to the age group at greatest risk, and is less costly and more effective than the detection and treatment of anemia by use of iron batteries in individual infants[27]. However, reality is different from previous expectations that iron deficiency and IDA will be reduced. The main obstacle in achieving effective treatment with oral iron prescription in the present study was poor compliance. In fact, giving daily iron to an apparently healthy infant for several months may be difficult.

What is a more effective strategy for preventing iron deficiency? If the protective rate is 96% and iron fortification is given to 70% of infants, the rate of iron deficiency will be 33%. If therapeutic iron is added with a compliance rate of 70%, 10% will still show iron deficiency. If iron fortification is simultaneously given with therapeutic iron to 80%, the rate of iron deficiency will be reduced to 5% or less. When adequately fortified foods are not available, as is the case in many parts of the developing world, iron requirements in infants should be met by supplementation of the diet with medicinal iron. As the iron is supplied, the infant's appetite recovers. It is then easier to give the infant iron-fortified foods. Oral iron prophylaxis has been was successfully delivered to multigravid women during pregnancy with significant beneficial effects on the health of the mother, without the induction of increased susceptibility to malaria[28]. Oral iron given by mothers has been used to treat IDA in Gambian children who would otherwise have become more anemic. Other studies have shown good or excellent therapeutic effects without serious side effects[29][30].

In summary, the dietary history of a large group of infants was highly predictive of their risk for anemia. Continued consumption of breast milk until the age of 1 year is not warranted unless iron-fortified foods are given concomitantly. If the major impediment to iron deficiency elimination is low compliance, dual coverage by using iron-fortified foods and therapeutic iron supplementation is desirable for preventing iron deficiency in toddlers who are at risk for iron deficiency.

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