# Combined treatment with vitamin A and iron to prevent piglet anemia

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## Summary

**Objective:** To determine if vitamin A enhances the effect of iron in preventing piglet anemia.

**Materials and methods:** Neonatal pigs (n = 96) from crossbred sows were assigned to three treatments, with four replicates per treatment. Treatments consisted of control (no iron), 200 mg injectable iron (iron dextran) at 2 days of age (Day 2), and 200 mg injectable iron (iron dextran) with 2000 IU oral vitamin A (vitamin A palmitate) on Day 2. The study was continued until Day 21. Blood samples were collected on Days 1, 7, 14, and 21, and liver and spleen samples were collected on Day 21. Hemoglobin concentration, hematocrit, total iron-binding capacity, and iron concentration were measured in plasma, liver, and spleen samples. Body weight was recorded on Days 0 and 21. Deaths were recorded through the study.

**Results:** Weight gain and mortality did not differ significantly between pigs treated with iron alone and pigs treated with both iron and vitamin A ($P > .05$). Hemoglobin concentration, hematocrit, and iron concentration in plasma, liver, and spleen samples in pigs treated with both iron and vitamin A were higher, and total iron-binding capacity was lower, than in pigs treated with iron alone ($P < .05$).

**Implications:** Iron nutrition status is better in piglets provided with both iron and vitamin A than in piglets treated with iron alone. The combination of vitamin A and iron is more effective than iron alone in preventing piglet anemia.

**Keywords:** swine, piglet anemia, vitamin A, iron

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**Resumen - Tratamiento combinado de vitamina A y hierro para prevenir la anemia de lechón**

**Objetivo:** Determinar si la vitamina A mejora el efecto del hierro en la prevención de la anemia de lechón.

**Materiales y métodos:** Se asignaron cerdos recién nacidos (n = 96) de hembras híbridas a tres tratamientos, con cuatro repeticiones por tratamiento. Los tratamientos fueron control (sin hierro), 200 mg de hierro inyectable (hierro dextrán) a los 2 días de edad (Día 2), y 200 mg de hierro inyectable (hierro dextrán) con 2000 IU de vitamina A oral (palmitato de vitamina A) en el Día 2. El estudio se continuó hasta el Día 21. Se recolectaron muestras de sangre en los Días 1, 7, 14, y 21, y se recolectaron muestras de hígado y bazo en el Día 21. Se midió la concentración de hemoglobina, hematocrito, capacidad total de fijación de hierro, y la concentración de hierro en muestras de plasma, hígado, y bazo. El peso corporal se registró los Días 0 y 21. La mortalidad se registró durante del estudio.

**Resultados:** La ganancia de peso y la mortalidad no difirieron significativamente entre cerdos tratados solamente con hierro y cerdos tratados con hierro y vitamina A ($P > .05$). La concentración de hemoglobina, hematocrito, y la concentración de hierro en muestras de plasma, hígado, y bazo de cerdos tratados con hierro y vitamina A fueron más altos, y la capacidad total de fijación de hierro fue más baja, que en cerdos tratados solamente con hierro ($P < .05$).

**Implicaciones:** El estatus de nutrición de hierro es mejor en los lechones a lo que se les trató con hierro y vitamina A que en los lechones tratados solamente con hierro. La combinación de vitamina A y hierro es más efectiva que el hierro solo en la prevención de anemia de lechón.

**Résumé - Traitement combiné de vitamine A et de fer afin de prévenir l'anémie chez les porcelets**

**Objectif:** Déterminer si la vitamine A augmente l'effet du fer pour prévenir l'anémie chez les porcelets.

**Matériels et méthodes:** Des porcelets nouveau-nés (n = 96) issus de truies croisées ont été assignés à trois groupes de traitement, avec quatre réplications par traitement. Les groupes étaient: témoin (aucun fer), 200 mg de fer injectable (fer dextran) à 2 jours d'âge (Jour 2), et 200 mg de fer injectable (fer dextran) avec 2000 UI de vitamine A (palmitate de vitamine A) au Jour 2. L'étude s'est poursuivie jusqu'au Jour 21. Des échantillons sanguins ont été prélevés aux Jours 1, 7, 14, et 21, et des échantillons de foie et de rate obtenus au Jour 21. La concentration d'hémoglobine, l'hématocrite, la capacité totale de liaison

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du fer, et la concentration de fer ont été mesurés dans le plasma, le foie, et la rate. Le poids corporel a été enregistré aux Jours 0 et 21. Les mortalités ont été notées tout au long de l'étude.

**Résultats:** Le gain de poids et les mortalités n'étaient pas significativement différents entre les porcs traités avec le fer seul et ceux traités avec le fer et la vitamine A ($P > .05$). La concentration d'hémoglobine, l'hématocrite, et la concentration de fer dans le plasma et les échantillons de foie et de rate étaient plus élevés chez les porcs traités avec le fer et la vitamine A, et la capacité totale de liaison du fer était plus basse, que celle notée chez les porcs traités avec le fer seul ($P < .05$).

**Implications:** Le statut nutritionnel du fer est meilleur chez les porcelets ayant reçu du fer et de la vitamine A que chez les porcelets n'ayant reçu que seulement du fer. La combinaison de vitamine A et de fer est plus efficace que le fer seul pour prévenir l'anémie chez les porcelets.

Anemia is the most prevalent nutritional deficiency in the world.[1] Both iron and vitamin A deficiencies were independent risk factors for anemia among Marshall Islands preschool children.[2] Attempts to improve iron status have been thwarted by deficiency of and adverse interaction with other micronutrients.[1] Confinement-reared pigs develop iron deficiency anemia (hypochromic, microcytic anemia) early in life. Anemia occurs because piglets are born with unusually small iron stores, milk contains low levels of iron, and pigs have a very rapid growth rate.[3] Anemia interferes with growth, and affected pigs are listless and more susceptible to infectious diseases than are normal pigs.

Supplemental vitamin A increased hemoglobin levels and packed cell volume (PCV) in pregnant women with deficient iron status or marginally deficient or deficient vitamin A status.[4] Vitamin A supplementation thereby contributed to control of nutritional anemia, and there was a synergistic interaction between vitamin A and iron in combined therapy. Vitamin A supplementation of pregnant women was associated with higher birth weight and lower prevalence of anemia among their infants.[5] Vitamin A deficiency appears to be related to the pathogenesis of anemia by several biological mechanisms, eg, improvement of growth and differentiation of erythrocyte progenitor cells, promotion of immunity to infection, less severe anemia of infection, and mobilization of iron stores from tissues.[6,7]

Concomitant supplemental vitamin A and ferrous sulfate promoted the hematopoietic effect of iron supplementation in young male rats.[8] Concomitant supplementation of vitamin A enhanced the response to weekly supplementation of iron and folic acid in anemic teenagers in urban Bangladesh.[9] A relationship between vitamin A and iron may have relevance in the treatment of nutritional anemia, and some studies suggest that supplementation with both vitamin A and iron is superior to iron alone in treating nutritional anemia in humans and rats.[10] The aim of this study was to evaluate combined treatment with iron and vitamin A in preventing piglet anemia.

## Materials and methods

### Study animals

Ninety-six piglets (Duroc × Large White × Landrace), born to eight crossbred multiparous sows (third or fourth parturition; Large White × Landrace) inseminated with semen from the same boar, were used in this study. All experimental procedures, care, and handling of animals were conducted according to guidelines on the care and use of animals for scientific purposes.[11] All animal experiments were approved by the Local Ethics Committee of Animal Research (permit no. C 16/6).

### Experimental design

Piglets were assigned to eight blocks (12 piglets per block) on Day 0 (the day of birth) according to the following criteria: litter, gender, and weight. Each animal in a block was randomly allotted to one of 12 groups which comprised three treatments (four replicates per treatment). Treatments consisted of the control (no supplemental iron; n = 32); intramuscular (IM) injection of 200 mg iron as iron dextran (Bestar Laboratories Ltd, Shanghai, China) on Day 2 (n = 32); and IM injection of 200 mg iron as iron dextran plus oral administration of 2000 IU vitamin A as vitamin A palmitate (Beijing Zhongnongjianuo Technology Co Ltd, Beijing, China) on Day 2 (n = 32).

Immediately after birth, all piglets were encouraged to suckle to ensure ingestion of colostrum, then litter size was equalized to 12 by cross-fostering. Within 12 hours after birth, piglets in each litter were stratified according to weight and randomly assigned by weight to treatment groups. Piglets within each litter were equally allotted to the 12 groups; thus, each sow nursed piglets belonging to each of the 12 groups. Piglets were individually identified with ear tags.

Twelve pigs (four randomly selected pigs from each treatment) were euthanized by electrocution on Day 21. Applying the electrodes to the head of pigs for a minimum of 5 seconds resulted in instantaneous loss of consciousness (collapse, immediate mydriasis, no vocalization), and subsequently applying the electrodes to the thorax of pigs for a minimum of 15 seconds caused cardiac arrest within 1 minute. Death was confirmed and electrodes were removed from the thorax. The liver and spleen were removed as soon as possible after euthanasia and stored at -20°C until iron analysis 10 days later.

### Housing and feeding

The farrowing barn housed piglets and their sows in farrowing crates with thermostatically controlled creep boxes and plastic-coated slatted floors. Air temperature of the farrowing pens was maintained at approximately 18°C through the experiment. Temperature in the creep boxes was maintained at approximately 32°C using a 250-watt electric heat lamp from Day 0 to Day 6. Temperature in the creep area was reduced to 30.5°C, 29°C, 27°C, and 25°C on Days 7, 11, 15, and 19 by changing to bulbs of 240, 225, 210, and 195 watts, respectively. On Day 1, all piglets were processed according to standard commercial practices, including teeth clipping, tail docking, and ear notching. During the previous gestation and lactation, the dams of the experimental pigs were fed a corn-soybean meal-based diet formulated to meet National Research Council[12] nutrient requirement estimates (Table 1). During the study, sows and piglets had ad libitum access to feed and water.

### Parameters measured

Piglets were individually weighed on an electronic scale accurate to 0.1 kg within 12 hours after birth and on Day 21. Blood samples collected in EDTA tubes were obtained via vena cava puncture on Days 1, 7, 14, and 21. One portion of the blood from each pig was immediately prepared for hemoglobin and hematocrit determination. The second EDTA tube of blood from each pig was chilled to 4°C and centrifuged at 2000*g*. Plasma was harvested and stored at -20°C until iron and total iron-binding capacity were determined 2 days later.

**Table 1:** Composition of diets for gestating and lactating sows in a study on the effects of supplementing piglets with both iron and vitamin A to prevent anemia

| Ingredient | Basal diet | |
|---|---|---|
| | Gestating sows | Lactating sows |
| Corn (%) | 61 | 57 |
| Wheat bran (%) | 15 | 12 |
| Barley (%) | 9 | 0 |
| Soybean meal (%) | 11 | 22.5 |
| Soybean oil (%) | 0 | 2 |
| Fish meal (%) | 0 | 3 |
| Limestone (%) | 0.95 | 1.2 |
| Dicalcium phosphate (%) | 1.8 | 0.9 |
| Salt (%) | 0.25 | 0.25 |
| L-lysine HCl (%) | 0 | 0.15 |
| Trace and vitamin premix (%)* | 1.0 | 1.0 |
| Total (%) | 100 | 100 |
| **Calculated composition** | | |
| Digestible energy (MJ/kg) | 12.75 | 13.26 |
| Crude protein (%) | 13.23 | 18.22 |
| Lysine (%) | 0.55 | 1.08 |
| Methionine + Cystine (%) | 0.46 | 0.61 |
| Calcium (%) | 0.83 | 0.81 |
| Available phosphorus (%) | 0.5 | 0.4 |

* Premix for gestating sows provided, for each kg of complete diet, vitamin A, 8000 IU; vitamin $D_3$, 1200 IU; vitamin E, 44.7 IU; vitamin $K_3$, 1.5 mg; vitamin $B_{12}$, 15 μg; thiamine, 1 mg; riboflavin, 3.8 mg; pantothenic acid, 12 mg; niacin, 10 mg; pyridoxine, 1 mg; biotin, 0.2 mg; folic acid, 1.1 mg; choline, 1 g; copper, 8 mg; iodine, 0.13 mg; iron, 80 mg; manganese, 30 mg; selenium, 0.15 mg; and zinc, 70 mg. For lactating sows, the premix provided, for each kg of complete diet, vitamin A, 6000 IU; vitamin $D_3$, 1200 IU; vitamin E, 44.7 IU; vitamin $K_3$, 1.5 mg; vitamin $B_{12}$, 15 μg; thiamine, 1 mg; riboflavin, 3.8 mg; pantothenic acid, 12 mg; niacin, 10 mg; pyridoxine, 1 mg; biotin, 0.2 mg; folic acid, 1.3 mg; choline, 1 g; copper, 8 mg; iodine, 0.15 mg; iron, 90 mg; manganese, 35 mg; selenium, 0.15 mg; and zinc, 70 mg.

Iron was measured in plasma, liver, and spleen using atomic absorption spectrophotometry. Liver and spleen samples were prepared for iron analysis by blotting dry, drying in a forced-air oven at 100°C, then wet-ashing with nitric acid in a microwave oven as described by Kegley et al.[3] Hemoglobin and total iron-binding capacity were measured by using commercially available test kits (Sigma Chemical Co, St Louis, Missouri). Hematocrit was measured using microcapillary tubes as described by Kegley et al.[3]

Deaths were recorded in each group. Mortality for each group was calculated as the total number of pigs at the beginning of the experiment minus the number of dead piglets at the end of the experiment, expressed as a percentage of the total number of pigs.

## Data analysis

Data were analyzed by analysis of variance (ANOVA) using PROC MIXED of SAS (SAS 9.0, SAS Institute Inc, Cary, North Carolina). Variables included weight gain, mortality, iron concentrations in the liver and spleen, hematocrit, hemoglobin concentration, plasma iron concentration, and total iron-binding capacity. The model for weight gain, mortality, and iron concentrations in the liver and spleen included treatment and litter as fixed effects. The model for hematocrit, hemoglobin concentration, plasma iron concentration, and total iron-binding capacity included treatment, litter, day, and the interaction of treatment and day as fixed effects. When treatment effect was a significant source of variation, differences were determined using the DIFF option of SAS. Least squares means were calculated for each independent variable. Statistical significance was set at $P < .05$ for all statistical tests.

## Results

Weight gains during the study were greater ($P < .05$) for pigs treated either with iron alone or with iron and vitamin A than for the controls (Table 2). Weight gains did not differ significantly between pigs treated with iron alone and pigs treated with both iron and vitamin A ($P > .05$).

Mortality during the study was higher in the control group ($P < .05$) than in the treated groups (Table 2). Mortality did not differ significantly between pigs treated with iron alone and pigs treated with both iron and vitamin A ($P > .05$).

On Day 21, iron concentrations in liver and spleen samples from pigs that received no iron were lower ($P < .05$) than concentrations in pigs treated with iron (Table 2). Concentration of iron in the liver was 10% higher in pigs treated with both iron and vitamin A than in pigs treated with iron alone ($P < .05$; Table 2). Concentration of iron in the spleen did not differ significantly between pigs that were treated with iron alone and pigs treated with both iron and vitamin A ($P > .05$; Table 2).

Hematocrits did not differ significantly on Day 1 (Table 3). On Days 7, 14, and 21, hematocrits were lower in control pigs than in either group of pigs treated with iron ($P < .05$). On Day 7, hematocrits were 10.3% higher ($P < .05$) in pigs treated with both iron and vitamin A than in pigs treated with iron alone. On Days 14 and 21, hematocrits did not differ significantly between pigs treated with iron alone and pigs treated with both iron and vitamin A ($P > .05$).

Hemoglobin concentrations did not differ significantly on Day 1 (Table 4). On Days 7, 14, and 21, hemoglobin concentrations were lower in control pigs ($P < .05$) than in either group of pigs treated with iron. On Days 7, 14, and 21, hemoglobin concentrations were 11.2%, 10.6%, and 10.7% higher, respectively, in pigs treated with both iron and vitamin A than in pigs treated with iron alone ($P < .05$).

Plasma iron concentrations did not differ significantly on Day 1 (Table 5). Plasma iron concentrations were lower in controls than in pigs treated with iron on Days 7, 14 and 21 ($P < .05$). On Days 7 and 14,

**Table 2:** Effects of treatments with iron and iron plus vitamin A* on least squares means for growth, mortality, and iron concentrations in the liver and spleen in 21-day-old pigs†

| Treatment | Body weight (kg) | | | Mortality (%) | Iron (mg/kg)‡ | |
|---|---|---|---|---|---|---|
| | Day 0 | Day 21 | Gain | | Liver | Spleen |
| Control | 1.32 | 5.04 | 3.72[a] | 12.5[a] | 97[c] | 375[c] |
| Iron | 1.34 | 5.73 | 4.39[b] | 3.13[b] | 594[d] | 903[d] |
| Iron with vitamin A | 1.30 | 5.82 | 4.52[b] | 3.13[b] | 652[e] | 974[d] |
| SE | 0.04 | 0.25 | 0.06 | 0.59 | 10.37 | 13.18 |

* Pigs born Day 0 were treated on Day 2 with iron dextran (200 mg intramuscularly) or with the same dose of iron dextran plus oral vitamin A (2000 IU), or no treatment (control).

† Ninety-six piglets from eight litters were used in the study, with four replicates per treatment for a total of 12 treatment groups. Litters were adjusted at birth on Day 0 by cross-fostering to 12 pigs per litter, with each pig in a litter randomly assigned to one of the 12 treatment groups. Means for Days 1, 7, and 14 represent eight pigs per treatment. Liver and spleen samples were collected from only four pigs per treatment on Day 21; thus, means for iron concentration in liver and spleen represent four pigs per treatment.

‡ Dry matter basis.

[ab] Means within a column with no common superscript are significantly different (ANOVA; $P < .05$).

[cde] Means within a column with no common superscript are significantly different (ANOVA; $P < .01$).

**Table 3**: Effects of treatments with iron, iron plus vitamin A, or no treatment* on Day 2 on mean hematocrit in pigs on Days 7,14, and 21

| Treatment | Hematocrit (L/L)† | | | |
|---|---|---|---|---|
| | Day 1 | Day 7 | Day 14 | Day 21 |
| Control | 31.2 | 23.8[a] | 21.3[a] | 20.4[a] |
| Iron | 30.7 | 31.1[b] | 35.7[b] | 37.6[b] |
| Iron with Vitamin A | 30.3 | 35.4[c] | 38.5[b] | 39.1[b] |

* Ninety-six piglets from eight litters were used in the study, with four replicates per treatment (litters adjusted by cross-fostering to 12 pigs per litter at birth on Day 0). Means for Days 1, 7, and 14 represent eight pigs per treatment. Blood samples for hematocrit were collected from only four pigs per treatment group on Day 21; thus, means represent four pigs per treatment.

† Least squares means. In the ANOVA model, there were significant effects of treatment (SE, 0.41; $P < .001$) and day (SE 0.39; $P < .01$), and the treatment × day interaction was significant (SE, 0.67; $P < .01$).

[abc] Means within a column with no common superscript are significantly different (ANOVA; $P < .05$).

plasma iron concentrations in pigs treated with both iron and vitamin A were higher ($P < .05$) than those in pigs treated with iron alone. On Day 21, plasma iron concentrations did not differ significantly between pigs treated with iron alone and pigs treated with both iron and vitamin A ($P > .05$).

Total iron-binding capacity was higher ($P < .05$) in control pigs than in pigs treated with iron on Days 7, 14, and 21 (Table 6).

On Day 7, total iron-binding capacity did not differ significantly between pigs treated with iron alone and pigs treated with both iron and vitamin A. On Days 14 and 21, total iron-binding capacity was lower in pigs treated with both iron and vitamin A than in pigs treated with iron alone ($P < .05$).

The effect of day on hematocrit, hemoglobin concentration, plasma iron concentration, and total iron-binding capacity was significant ($P < .05$). The treatment × day interaction was significant for hematocrit and plasma iron concentration ($P < .05$), but not for hemoglobin concentration and total iron-binding capacity ($P > .05$).

## Discussion

Iron deficiency is the main cause of piglet anemia.[13] Many researchers have proved that newborn pigs need supplemental iron, and administration of iron to the neonatal pig has been a standard practice in many parts of the world for many years. In the present study, weight gains between Day 0 and Day 21 were higher in pigs that were treated with iron on Day 2 than in pigs not treated with iron. Measures of iron nutrition, including hemoglobin concentration, hematocrit, plasma iron concentration, total iron-binding capacity, and concentrations of iron in liver and spleen were all significantly better in pigs that were treated with iron than in pigs not treated with iron, in agreement with other studies.[3,14,15]

Intramuscular injection of iron in newborn pigs is effective in preventing piglet anemia in practice. In this study, intramuscular injection of iron combined with oral vitamin A was more effective than treatment with iron alone. Hemoglobin and hematocrits levels are sensitive criteria for evaluating body biological response to iron. Plasma iron concentration is the indicator of iron deficiency, and total iron-binding capacity is the important index in iron metabolism, representing the ability of transferrin to carry iron in the blood.[16] In this study, hemoglobin concentration, hematocrit, plasma iron concentration, and iron concentrations in liver and spleen were higher and total iron-binding capacity was lower in pigs treated with both iron and vitamin A than in pigs treated with iron alone, showing that body iron status was better when piglets were treated with both iron and vitamin A. These data suggest that a combination of iron and vitamin A is more effective than iron alone in preventing piglet anemia. To the authors' knowledge, there are no previously published reports concerning the combination of iron and vitamin A in preventing anemia in pigs.

In a study in humans with low vitamin A status or deficient iron status, supplemental vitamin A was associated with higher hemoglobin level and hematocrit, thereby contributing to control of nutritional anemia, and there was a synergistic interaction between vitamin A and iron in combined

**Table 4**: Effects of treatments with iron, iron plus vitamin A, or no treatment* on Day 2 on mean hemoglobin in pigs on Days 7, 14, and 21

| Treatment | Hemoglobin (g/L)† | | | |
|---|---|---|---|---|
| | Day 1 | Day 7 | Day 14 | Day 21 |
| Control | 97.5 | 71.4[a] | 57.5[a] | 1.1[a] |
| Iron | 96.6 | 103.3[b] | 110.8[b] | 21.6[b] |
| Iron with Vitamin A | 96.5 | 114.9[c] | 122.6[c] | 29.9[c] |

* Ninety-six piglets from eight litters were used in the study, with four replicates per treatment (litters adjusted by cross-fostering to 12 pigs per litter at birth on Day 0). Means for Days 1, 7, and 14 represent eight pigs per treatment. Blood samples for hemoglobin were collected from only four pigs per treatment group on Day 21; thus, means represent four pigs per treatment.

† Least squares means. In the ANOVA model, there were significant effects of treatment (SE, 4.77; $P < .05$) and day (SE 3.87; $P < .001$), but the treatment × day interaction was not significant (SE, 0.20; $P = 6.69$).

[abc] Means within a column with no common superscript are significantly different (ANOVA; $P < .05$).

**Table 5**: Effects of treatments with iron, iron plus vitamin A, or no treatment* on Day 2 on mean plasma iron concentrations in pigs on Days 7, 14, and 21

| Treatment | Plasma iron (μmol/L)† | | | |
|---|---|---|---|---|
| | Day 1 | Day 7 | Day 14 | Day 21 |
| Control | 12.31 | 11.66[a] | 11.57[a] | 11.14[a] |
| Iron | 12.47 | 13.12[b] | 13.43[b] | 13.62[b] |
| Iron with Vitamin A | 12.11 | 13.69[c] | 14.37[c] | 14.17[b] |

* Ninety-six piglets from eight litters were used in the study, with four replicates per treatment (litters adjusted by cross-fostering to 12 pigs per litter at birth on Day 0). Means for Days 1, 7, and 14 represent eight pigs per treatment. Blood samples for plasma iron were collected from only four pigs per treatment group on Day 21; thus, means represent four pigs per treatment.

† Least squares means. In the ANOVA model, there were significant effects of treatment (SE, 0.15; $P < .001$) and day (SE 0.14; $P < .01$), and the treatment × day interaction was significant (SE, 0.25; $P < .001$).

[abc] Means within a column with no common superscript are significantly different (ANOVA; $P < .05$).

**Table 6**: Effects of treatments with iron, iron plus vitamin A, or no treatment* on Day 2 on mean total iron-binding capacity in pigs on Days 7, 14, and 21

| Treatment | Total iron-binding capacity (μmol/L)† | | | |
|---|---|---|---|---|
| | Day 1 | Day 7 | Day 14 | Day 21 |
| Control | 126 | 125[a] | 123[a] | 124[a] |
| Iron | 123 | 120[b] | 118[b] | 117[b] |
| Iron with vitamin A | 125 | 117[b] | 113[c] | 112[c] |

* Ninety-six piglets from eight litters were used in the study, with four replicates per treatment (litters adjusted by cross-fostering to 12 pigs per litter at birth on Day 0). Means for Days 1, 7, and 14 represent eight pigs per treatment. Blood samples for total iron-binding capacity were collected from only four pigs per treatment group on Day 21; thus, means represent four pigs per treatment.

† Least squares means. In the ANOVA model, there were significant effects of treatment (SE, 1.15; $P < .001$) and day (SE 0.79; $P < .001$), but the treatment × day interaction was not significant (SE, 0.36; $P = 1.37$).

[abc] Means within a column with no common superscripts are significantly different (ANOVA; $P < .05$).

therapy.[4] Iron in combination with vitamin A was more effective than iron alone in treating low iron status in rats that had lower blood hemoglobin concentration, hematocrit, and erythrocyte count after being fed a diet deficient in both iron and retinol.[8] Mwanri et al[17] conducted a randomized controlled trial to study the effects of dietary supplements on anemic children, using vitamin A alone, iron and vitamin A, iron alone, or placebo, administered in a double-blind design for 3 months. All supplements were administered in corn-based gruel. Results showed that after 3 months, mean hemoglobin concentration was higher by 13.5 g per L in children receiving vitamin A alone, compared with 3.5 g per L in the placebo treatment group ($P < .0001$). In addition, after 3 months, the mean body weight of children receiving vitamin A alone was higher by 0.6 kg, compared with 0.2 kg for the placebo treatment ($P < .0001$), and mean height for children receiving vitamin A alone was higher by 0.4 cm compared with 0.1 cm for the placebo treatment ($P = .0009$). However, in the group of children who received both vitamin A and iron supplementation, mean change from baseline was better in all indicators compared with the placebo treatment (mean change in hemoglobin 18.5 g per L, $P < .0001$; mean change in body weight 0.7 kg, $P < .0001$; and mean change in height 0.4 cm, $P < .0001$). The authors concluded that, in developing countries, vitamin A supplementation may have a useful role in combating anemia, as well as in improving children's growth.

Zhang et al[18] found that in broiler chickens, iron concentration in liver decreased and iron concentration in serum increased with an increase in dietary supplemental vitamin A. Duodenum iron concentration, tibia iron concentration, and erythrocyte count increased significantly with higher dietary supplemental vitamin A ($P < .01$), indicating that vitamin A can enhance iron metabolism.

The mechanism by which vitamin A alleviates iron deficiency anemia is not clear. There are several hypotheses. Vitamin A may form a complex with iron, maintaining its solubility in the intestinal lumen and preventing the inhibitory effects of phytates and polyphenols on iron absorption,[19,20] but Sajedianfard et al[21] concluded that the therapeutic effect of vitamin A in iron-deficiency anemia is probably not associated with its influence on iron absorption from the

gastrointestinal tract. The study of Amine et al[22] showed that vitamin A deficiency impairs erythropoiesis, but Roodenburg et al[23] found no evidence that vitamin A deficiency affected erythropoiesis and erythrocyte turnover. Transcription of the transferrin gene in vitro is stimulated by vitamin A,[24,25] suggesting that vitamin A is involved in synthesis of the glycosyl moieties of the transferrin molecule.

Vitamin A seems to be related to the pathogenesis of anemia by various biological mechanisms, such as enhancing the growth and differentiation of erythrocyte progenitor cells, potentiating immunity to infection and reducing the anemia of infection, and mobilizing iron stores from tissues.[7]

There was a significant positive correlation between plasma retinol and plasma iron in pregnant women.[26] By measuring plasma retinol concentrations of piglets before and after suckling, Hakansson et al[27] established that piglets were born with low levels of retinol (0.07 mg per L), that transfer of vitamin A via the placenta appeared to be limited, and that colostrum was a major means of retinol transfer to the young piglet. Davila et al[28] reported that, in rats, vitamin A concentration in colostrum on day 1 of lactation did not vary with maternal vitamin A intake during pregnancy; however, the concentration of vitamin A in milk increased with increasing maternal vitamin A intake during lactation. In swine, the highest mean concentrations of retinol were found in colostrum, while retinol concentration in sow milk decreased by 71% during the first week postpartum and remained relatively stable thereafter.[27] These results[17,27,28] indicate that transfer of vitamin A via the placenta is limited, that piglets are born with small vitamin A stores, that colostrum is the main source of vitamin A for newborn piglets, that colostrum vitamin A concentration is not affected by maternal vitamin A intake during pregnancy, and that the vitamin A status of piglets is influenced by maternal vitamin A intake during lactation.

## Implications

- Piglets have better iron nutrition status when provided with both iron and vitamin A than when treated with iron alone.
- Vitamin A may promote the role of iron in preventing piglet anemia.
- Under the conditions of this study, a combination of vitamin A and iron is more effective than iron alone in preventing piglet anemia.


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