Effect of Oral Administration of Fe^{2+}-Fumarate on Erythrocyte Profile and Growth Rate of Suckling Piglets

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Abstract

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The aim of this study was to investigate efficiency of oral administration of Fe^{2+}-fumarate in form of paste in preventing iron deficiency anaemia of suckling piglets. Piglets in group 1 (n = 20) were given 200 mg Fe^{2+}-fumarate on days 6 and 11 after birth. Piglets in group 2 (n = 20) were given 200 mg Fe^{3+}-dextran i.m. on day 3. A group of piglets (group 3, n = 10) treated with Fe^{3+}-dextran on day 21 was included in the study. All piglets had free access to weaning pellets (124 mg Fe/kg). Haemoglobin concentration (Hb), packed cell volume (PCV), erythrocyte count (RBC), MCV, MCH and MCHC, body weight (BW) and daily weight gain (DWG) were determined. On day 6, haemoglobin concentration and packed cell volume were significantly lower in group 1 compared to group 2 ($P < 0.05$). On days 14, 21, 28, and 35 no significant differences in examined indices were found between group 1 and group 2 and all indices were comparable to physiological values. Haematological indices of group 3 were characteristic for hypochromic anaemia. Anaemia in group 3 had detrimental effect on growth rate of piglets. Supplementation of Fe to piglets with Fe^{2+}-fumarate under conditions of this trial was efficient in preventing anaemia and was comparable to i.m. administration of Fe^{3+}-dextran.

Anaemia, iron, haemoglobin, Fe^{3+}-dextran, Fe^{2+}-fumarate

The piglet is born with an iron reserve of approximately 50 mg (Venn et al. 1947). During the first week, the piglet doubles its body mass from 1.5 to 3 kg. At the same time the plasma volume expands by 30 % (Jain 1986). In order to synthetise haemoglobin sufficient for the piglet not to develop anaemia, 7–10 mg Fe per day is required (Venn 1947). The sow´s milk, however, provides the piglet with approximately 1 mg Fe per day only (Kleinbeck 1999). Suckling piglets with no extra iron supplementation develop iron deficiency after 14 days post partum (Zimmermann 1995). An early supply of iron is therefore essential for them. Parenteral or oral preparations for iron supply are available. Bivalent iron Fe^{2+} is up to 16 times better absorbed than trivalent iron Fe^{3+}. Only preparations with bivalent iron can be recommended for oral iron therapy (Dietzfelbinger 1987). According to Thoren-Tolling and Jonsson (1977) the distribution of stainable iron in lymph nodes, liver and spleen seven days after intramuscular injection of iron dextran in newborn piglets was comparable to that for oral administration (iron dextran) at that stage of the experiment. Oral Fe is available for haemoglobin synthesis sooner after administration than injected Fe^{3+}–dextran (Framstad et al. 1997). Oral administration of amino acid–chelated iron to pregnant sows in preventing piglet anaemia has not been successful (Egeli et al. 1998a). In herds where water-based iron is used, there is a large proportion of anaemic piglets. It seems that as long as the piglets get enough milk, they are less interested in drinking the iron solution (Jorgensen 2000). Individual administration of oral Fe preparations is thus recommended. Fe^{2+}-fumarate-based products

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for oral administration have been used successfully in human medicine (Davidsson et al. 2000; Lares-Assef et al. 1999). Effect of oral Fe^{2+}-fumarate administration on somatic growth and selected haematological indices in piglets under experimental conditions were evaluated by Kotrbáček (2001).

The aim of this study was to investigate the effect of oral administration of Fe^{2+}-fumarate in the form of paste on erythrocyte profile and growth intensity of suckling piglets as compared with intramuscular administration of Fe^{3+}–dextran under field conditions.

Materials and Methods

Experimental design

The study took place in a commercial herd. The litters were kept with the sows in farrowing crates on plastic slatted floor until weaning. The piglets were given no medical treatment, and no death loss was recorded. All piglets were individually tattooed a number in the ear. Altogether 50 piglets (6 litters) were divided randomly into 3 groups (split litters). Group 1 had 20 piglets, group 2 had 20 piglets and group 3 had 10 piglets. The feeding frequency and nutrient concentration of the milk are the major factors underlying the rate of gain during the suckling period (Holub 1982). The design involving split litters minimised the effect of the sow. On day 6 of life, the piglets in group 1 were given each 200 mg of Fe^{2+}-fumarate orally. The same dose was repeated on day 11. Fe^{2+}-fumarate was administered in the form of paste. The paste contained Fe^{2+}-fumarate 13.2 g in 40 g, *Enteroccocus faecium* 80. 10^9 CFU, Retinoli acetas 80 000 IU, Colecalciferolum 8000 IU, Tocoferoli alfa acetas 400 mg. The piglets in group 2 were injected with 200 mg Fe^{3+}–dextran (i.m.) on day 3 of life. Piglets in group 3 were given 200 mg Fe^{3+}–dextran (i.m.) on day 21 of life. Group 3 served as negative control. Weaning pellets (Fe 124 $mg \cdot kg^{-1}$) were offered to all litters *ad libitum* (from day 7-35). Piglets in all litters were weaned on day 28.

Sampling

Blood (1.5 ml) was collected from the piglets on days 6, 14, 21, 28 and 35 by puncture of the cranial vena cava, using ethylenediaminetetraacetic acid (EDTA) as anticoagulant.

Haematological examination

On the day of sampling, blood was analysed for the following indices: haemoglobin concentration (Hb), packed cell volume (PVC), erythrocyte count (RBC), mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), mean corpuscular haemoglobin (MCH). Haemoglobin concentration was measured spectrophotometrically using cyanomethaemoglobin method. Packed cell volume was measured using standard capillary tubes and centrifugation in a microhematocrit Janetzki TH12 centrifuge. Erythrocytes were counted in Bürker´s chamber using Haym´s solution. MCV, MCH and MCHC were calculated.

Body weight and weight gain

The piglets were weighed (BW) at birth (day 1) and on days 6, 14, 21, 28, and 35. Mean daily weight gain (DWG) of piglets in each group after one week was calculated.

Statistical evaluation

The results were statistically evaluated by analysis of variance (ANOVA). All results are presented as mean values and standard deviations of each index.

Results

Haemoglobin concentration (Hb, Fig. 1)

Hb in group 2 on day 6 was higher ($P < 0.05$) compared to groups 1 and 3. Between days 6 and 14, Hb in groups 1 a 2 increased ($P < 0.01$). Hb in group 3 decreased between days 6 and 21 ($P < 0.05$). Hb in group 3 on days 14 and 21 was lower ($P < 0.01$) than in groups 1 and 2. After administration of Fe-dextran in group 3 on day 21, an increase was observed on day 28 ($P < 0.01$) reaching values of groups 1 and 2. In group 1, Hb decreased between days 21 and 28 ($P < 0.05$). Differences in Hb between groups 1 and 2 on days 14, 21, 28 and 35 were not significant.

Packed cell volume (PCV, Fig. 2)

On day 6, PCV in group 2 was higher ($P < 0.05$) compared to groups 1 and 3. Between days 6 and 14, PCV in groups 1 and 2 increased ($P < 0.01$). PCV in groups 1 and 2 on days 14 and 21 was higher than in group 3 ($P < 0.01$). PCV in group 1 decreased between days

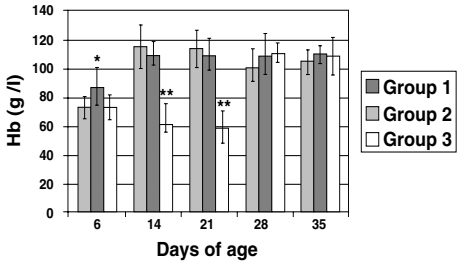

Fig. 1. Haemoglobin concentration during the trial (Hb) * $p < 0.05$, ** $p < 0.01$

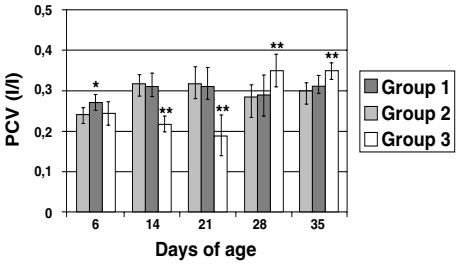

Fig. 2. Packed cell volume during the trial (PCV) * $p < 0.05$, ** $p < 0.01$

21 and 28 ($P < 0.05$). PCV in group 3 increased between days 21 and 28 ($P < 0.01$) and on days 28 and 35 was higher ($P < 0.01$) than in groups 1 and 2. Differences in PCV between groups 1 and 2 on days 14, 21, 28 and 35 were not significant.

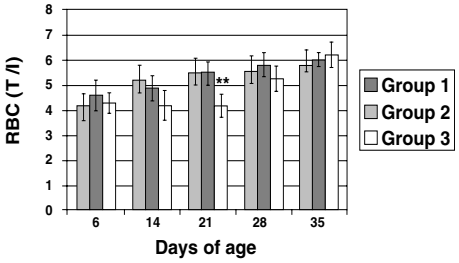

Fig. 3. Red blood cell count during the trial (RBC) * $p < 0.05$, ** $p < 0.01$

Red blood cell count (RBC, Fig. 3)

RBC in group 3 on day 21 was lower compared to groups 1 and 2 ($P > 0.01$). RBC increased between days 21 and 28 in group 3 ($P > 0.01$). Differences in RBC between groups 1 and 2 were not significant.

MCV, MCH (Table 1)

On days 14 ($P < 0.01$) and 21 ($P < 0.01$), MCV and MCH in group 3 were lower than in groups 1 and 2. Between days 21 and 28, MCV ($P < 0.05$) and MCH ($P < 0.05$) in group 1 decreased. In group 2, MCV decreased

Table 1
Values of MCV, MCH and MCHC during the trial. Groups with different alphabetic superscripts differ significantly at $P < 0.01$

Day of age	Indices	Group 1 mean ± SD	Group 2 mean ± SD	Group 3 mean ± SD
6	MCV (fl)	59.0 ± 6.0	58.6 ± 6.5	59.5 ± 6.0
	MCH (pg)	17.8 ± 2.6	19.1 ± 3	18.1 ± 2.5
	MCHC (g/l)	0.30 ± 0.02	0.33 ± 0.05	0.30 ± 0.03
14	MCV (fl)	62.4 ± 8.3^a	64.6 ± 8.0^a	52.6 ± 6.3^a
	MCH (pg)	22.4 ± 4.6^a	22.4 ± 2.2^a	15.9 ± 1.3^b
	MCHC (g/l)	0.36 ± 0.05^a	0.35 ± 0.04^a	0.30 ± 0.03^b
21	MCV (fl)	59.6 ± 8.0^a	57.4 ± 8.0^a	45.8 ± 11.0^b
	MCH (pg)	20.8 ± 2.1^a	19.4 ± 2.0^a	14.0 ± 1.6^b
	MCHC (g/l)	59.0 ± 6.0	58.6 ± 6.5	59.5 ± 6.0
28	MCV (fl)	51.7 ± 7.0^a	49.3 ± 10.0^a	67.9 ± 10.0^b
	MCH (pg)	18.3 ± 2.5^a	18.2 ± 2.9^a	21.3 ± 2.2^b
	MCHC (g/l)	0.36 ± 0.03^a	0.37 ± 0.05^a	0.32 ± 0.04^b
35	MCV (fl)	53.6 ± 6.5	54.0 ± 5.0	57.7 ± 6.8
	MCH (pg)	18.2 ± 2.3	19.1 ± 1.4	18.4 ± 2.3
	MCHC (g/l)	0.34 ± 0.03^a	0.35 ± 0.02^a	0.30 ± 0.03^b

between days 21 and 28 ($P < 0.05$). MCV and MCH in group 3 increased between days 21 and 28 ($P > 0.01$). MCV and MCH in group 3 on day 28 were even higher than in groups 1 and 2 (MCV, $P < 0.01$; MCH, $P < 0.05$). Differences in MCV and MCH between groups 1 and 2 were were not significant.

MCHC (Table 1)

On days 14, 21, 28 and 35, MCHC in group 3 was lower compared to groups 1 and 2 ($P > 0.05$). No significant differences in MCHC between group 1 and 2 were found.

Daily weight gain (DWG, Fig. 4)

Between days 28 and 35, DWG in groups 1 ($P < 0.01$) and 2 ($P < 0.01$) increased. DWG in group 3 on days 14, 21 and 28 was lower compared to groups 1 and 2 (all, $P > 0.01$). DWG in group 3 increased between days 21 and 35 ($P > 0.01$), but body weight remained to be lower than in groups 1 and 2 ($P > 0.01$). No significant differences in DWG between groups 1 and 2 were found.

Body weight (BW, Fig. 5)

With exception of days 1 and 6, BW in group 3 was lower than in groups 1 and 2 in all periods of the trial (all, $P > 0.01$). No significant differences in BW between groups 1 and 2 were found.

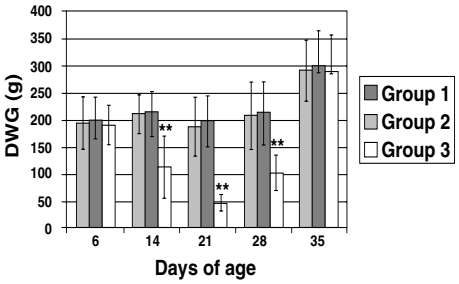

Fig. 4. Daily weight gain during the trial (DWG) * $p < 0.05$, ** $p < 0.01$

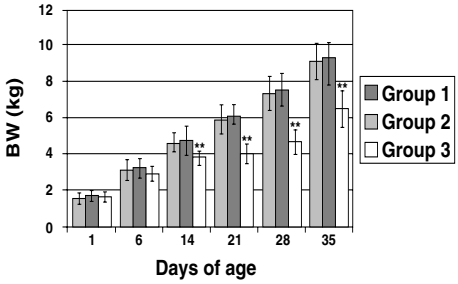

Fig. 5. Body weight during the trial (BW) * $p < 0.05$, ** $p < 0.01$

Discussion

Lower values of Hb and PCV in group 1 (Fe^{2+}-fumarate) on day 6 did not result in a lower body weight and weight gain compared to group 2 (Fe^{3+}–dextran). Although there was a significant decrease of Hb, PCV, MCV and MCH in group 1 from day 21-28, those indices remained comparable with group 2. Neither in group 1, nor in group 2 any piglet become anaemic (i.e. no piglet had Hb less than 80g/l). After weaning at 35 days of age no further decrease of Hb, PCV, MCV and MCH in group 1 was found. We suggest that this was due to the fact that piglets started to feed on weaning pellets (Fe^{3+} 124 mg/kg) intensively. Reference ranges in haematology for healthy piglets were investigated by Egeli et al. (1998b). Reference ranges for 35-day-old piglets are as follows: Hb – 101 ± 10; PCV – 0.32 ± 0.03; RBC – 5.79 ± 0.68; MCV- 56.5 ± 6.6; MCH – 17.6 ± 2.1; MCHC – 311 ± 10. In our trial, haematological indices of piglets obtained on day 35 in groups 1 and 2 were found to be within normal physiological range. Since there was a significant decrease of Hb, PCV, MCV and MCH in group 1 on day 28, we consider the double dose of iron as high as 200 mg to be appropriate and we recommend to let piglets free access to feed with Fe to prevent further decline.

In study conducted by Kotrbáček (2001) under experimental conditions, Fe^{2+}-fumarate paste was administered to day-old piglets that had been let to suck colostrum several times. Haematological values were measured till 21 days of age. The effect of oral administration of 100 mg fumarate-bound iron on haematological indexes in examined period was equal to that of parenteral administration of 200 mg $Fe^{3+}$and even stronger on some indexes in the 2nd week of life. In our study, when Fe^{2+}-fumarate was administered later, repeated and higher dose of Fe^{2+}-fumarate was necessary to achieve comparable haematological values to those obtained by i.m. administration of Fe^{3+}-dextran. This difference could be explained by lower intestinal absorption of iron in 6- and 11-day-old piglets. Lower intestinal absorption of iron in 10-day-old piglets is described by Iben (1998).

The differences between anaemic (group 3) and healthy piglets (groups 1 and 2) were as expected. Iron deficiency anaemia is generally accepted to be hypochromic (Egeli 1998b). This was also confirmed in our study. The lower Hb, PCV, RBC, MCV, MCH and MCHC showed to have detrimental effect on body weight and weight gain. The anaemic limit, i.e. the point when the anaemia begins to exert a detrimental effect on weight gain or gives rise to clinical symptoms of anaemia is set by most authors at a haemoglobin concentration of 80 g/l (Furugouri 1975; van Kempen 1987). One week after administration of Fe^{3+}-dextran, Hb, PCV, RBC, MCV and MCH increased significantly and reached values of groups 1 and 2. MCV and MCH in group 3 on day 28 were found to be significantly higher compared to groups 1 and 2. In study conducted by Holter et al. (1991), injection with iron on day 13 led to a rapid increase in the indices, with statistically significant increase for Hb, PCV, and MCV four days after treatment. A rise in MCV indicates production of new erythrocytes with greater number of large immature cells released into the circulation (Holter et al. 1991). This seemed also to be the case in this study. Although weight gain increased significantly after administration of Fe^{3+}–dextran in the anaemic group, the body weight remained to be significantly lower compared to groups 1 and 2.

We conclude that oral administration of Fe^{2+}-fumarate to suckling piglets was efficient in preventing anaemia under conditions of this trial and it resulted in good growth rate of the piglets, which was comparable to piglets that were given Fe^{3+}–dextran.

Účinek perorální aplikace fumarátu železa na erytrocytární profil a intenzitu růstu sajících selat ve srovnání s parenterální aplikací dextranu železa

Cílem práce bylo zjistit účinnost perorální aplikace fumarátu Fe^{2+} ve formě pasty pro prevenci anémie z nedostatku železa u sajících selat. Selatům ve skupině 1 (n = 20) byl aplikován fumarát železa (200 mg Fe^{2+}) 6. a 11. den života. Selatům ve skupině 2 (n = 20) byl 3. den aplikován dextran železa (200 mg Fe^{3+}) i.m. Součástí studie byla kontrolní skupina selat - skupina 3 (n = 10), kde byl aplikován dextran Fe^{3+} 21. den i.m. Všechna selata měla volný přístup k odstavovým peletám (124 mg Fe/kg). Stanovovány byly tyto parametry: koncentrace hemoglobinu (Hb), hematokrit (PCV), počet erytrocytů (RBC), MCV, MCH, MCHC, tělesná hmotnost a denní přírůstek. 6. den byla koncentrace hemoglobinu a hodnota hematokritu ve skupině 1 signifikantně nižší ve srovnání se skupinou 2 ($P < 0,05$). 14., 21., 28., a 35. den nebyly ve vyšetřovaných parametrech nalezeny žádné signifikantní rozdíly mezi skupinami 1 a 2 a tyto parametry byly srovnatelné s fyziologickými hodnotami. Hematologické parametry ve skupině 3 byly charakteristické pro hypochromní anémii. Anémie ve skupině 3 měla negativní vliv na intenzitu růstu. Suplementace železa selatům fumarátem Fe^{2+} za podmínek této studie byla efektivní a srovnatelná s i m. aplikací dextranu Fe^{3+}.

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