

Effects of Iron Administration Method on Anemia Prevention and Production Performance of Piglets

Nenad Stojanac¹, Ognjen Stevančević¹, Marko Cincović¹, Branislava Belić¹, Nada Plavša¹ & Miroslav Urošević²

ABSTRACT

Background: Anemia caused by iron deficiency can lead to increased susceptibility to infection, lower production performance and higher mortality rates. Modern piglets grow rapidly, as within a few days of birth they double their body weight, thereby increasing blood volume. This increasing amount of blood naturally increases the requirement for hemoglobin (Hb) production, each molecule of which contains iron. This study examined the impact of different an iron application method on hematological values of iron (Fe), hemoglobin (Hb), hematocrit (Hct) and production performance of piglets in the suckling and nurturing stages.

Materials, Methods & Results: The study was performed on two farrow-to-finish farms (I and II) of capacities of 2500 and 900 sows, respectively. Piglets were divided into four experimental groups: the IM group was given iron intramuscularly on the third day of life; the SC group was given iron subcutaneously on the third day of life; the PO group was given iron perorally on the third day of life; and the control group C was not given any iron. On the third day of life and at weaning (day 28) piglets' body weights were measured and their blood was taken for analysis, while at the end of the nurturing stage (day 70), only body weights were measured. The influence of the farm was tested, as well as the impact of the day of blood sample collection and the impact of the method of iron administration on the Fe, Hb and Hct levels, using a combined model. These parameters were considered as fixed effects, whereas iron administration methods were considered as randomized effects. The effect of method of iron administration on the values of Fe, Hb and Hct in the blood of piglets was tested by ANOVA and Fisher's post-hoc test. Piglets treated with iron had significantly ($P < 0.01$) higher values of Fe, Hb and Hct, as well as improved average daily gain (ADG) and lower mortality rate than piglets which did not receive iron, in which anemia developed. At weaning, those piglets administered iron via SC injection had higher ($P < 0.01$) blood levels of Fe, Hb and Hct compared to the IM and PO groups. These piglets also produced the highest ADG, while in piglets with IM and PO administered iron, no significant differences were observed in ADG ($P > 0.05$).

Discussion: The piglets that did not receive iron had clinical signs of anemia (pallor of mucous membranes, pallor of the skin of the whole body), while these symptoms were not identified in piglets which received iron. Anemia in piglets which did not receive iron likely contributed to the higher mortality of piglets in both phases, suckling and nurturing, compared with piglets that received iron. Due to lower production performance, the growth rate of group C piglets lagged behind, resulting in twice the mortality rate in the nurturing stage compared to piglets with iron administered IM, SC or PO. In piglets, which were treated with iron there were no significant differences in mortality in the suckling and nurturing stages, which indicates that all three modes of administration of iron had the same effect on mortality. In this study, the subcutaneous method of iron administration proved to be the most effective on blood values and production performance of piglets. In this study, subcutaneous injection of iron was the most effective administration method and consequently the best production performances.

Keywords: anemia, iron, hematocrit, hemoglobin, pigs.

INTRODUCTION

Bearing in mind that during the gestation phase, only 35 to 50 mg of iron is transferred per piglet from the sow, newborn piglets have low iron reserves [21,22]. Sows' milk contains a limited level of iron [23], so piglets only receive 1-2 mg of iron per day through milk [3], while their daily requirements are actually 7-10 mg [11].

Due to the prevention of anemia caused by iron deficiency in newborn piglets, there is, worldwide, routine application of a single parenteral administration in the form of an iron dextran injection (200 mg Fe3+) when piglets are 2-4 days old [18]. This method of iron application produces good results in preventing iron deficiency [12], but also has a number of negative effects: acute toxicosis, risk of disease transmission, anaphylaxis, risk for iatrogenic disease transmission, local infection-abscess, damage to *nervus fibularis* and *nervus tibialis* [5]. Because of these negative side effects, iron is often administered into piglets orally, via feed, water, or oral emulsions [7]. Oral administration of iron also has negative effects, such as: inadequate feed and water intake by very young piglets, leading to insufficient iron intake, the impossibility of precise dosages (some piglets ingest more and others less feed and/or water), and inadequate oral administration of emulsions by people [19].

The aim of this study was to investigate the effect of parenteral (intramuscular and subcutaneous) and peroral administration of iron in newborn piglets by measuring: a) levels of Fe, Hb and Hct, and; b) production performance of piglets.

MATERIALS AND METHODS

Animals and housing

The study was performed on two farrow-to-finish farms (I and II) of capacities of 2500 and 900 sows, respectively. On both farms, the production technology was based on a weekly rota management system. Every week, 110 (farm I) or 40 (farm II) sows gave birth to piglets. Sows, 3-7 days before their due date, were moved into the farrowing facility, at which time they were washed and bathed. Lactation on farm I lasted 28 ± 3 days, and on farm II, 26 ± 2 days, after which the piglets were transferred to nursery, and sows to mating facilities. Production data for both farms are shown in Table 1. Sows were Yorkshire, Landrace and

F1 (Yorkshire \times Landrace) while boars are of Duroc race. On farm I, vaccination of sows was implemented against classical swine fever, atrophic rhinitis [16], colibacillosis and clostridial necrotizing enteritis, and on farm II, sows were vaccinated against porcine parvovirus and classical swine fever. Piglets on farm I were vaccinated against enzootic pneumonia (7th day of life), porcine circovirus type 2 (21st day of life) and classical swine fever (45th and 90th day of life), and on farm II against enzootic pneumonia (7th day of life) and classical swine fever (45th and 90th day of life).

Sows were kept in individual compartments during farrowing and the same nutrition technology for both sows and piglets was implemented on both farms. Sows were fed twice per day, and in the last week of lactation before weaning, three times per day. Water was available to sows and piglets *ad libitum*. Sows drank water from mechanical nipples positioned at a height of 50 cm, while water nipples for piglets were at a height of 10 cm. Additional feed was introduced to the piglets on the 5th day of life; pre-starter feed was put on the floor and in small feeders. On farm I there were 22 compartments in a farrowing room, while on farm II, one farrowing room had 40 compartments.

Table 1. Production data for the farms.

Farm	I	II
Herd size (number of sows)	2500	900
Number of farrowings/sow/year	2.28	2.31
Number of live born pigs/litter	13.21	13.92
Number of stillborn pigs/litter	0.78	0.55
Lactation length (days)	28.72	26.34
Pig mortality during lactation (%)	9.87	10.06
Number of pigs weaned/sow/year	26.83	28.30
Weight of pigs weaned (kg)	7.87	7.43
Number of pigs in study	1200	420

Experimental design, piglet selection and sampling

During the formation of the experimental groups, piglets were selected randomly, but taking into account piglet weight, so that each group contained piglets of similar weight. All sows in the study were from the second to the fifth farrowing parity. At 3 days old, male piglets were surgically castrated. On farm I, 1200 piglets from 110 litters were included in the study, and on farm II 420 piglets or 40 litters. The piglets were

divided into 4 groups: in the first, the piglets received 200 mg of an iron dextran complex intramuscularly (IM) on the third day of life; in the second group, the piglets received 200 mg of iron *per os* (feed using the doser) in the form of a micro-emulsion on the third day of life (PO); the third group of piglets were given 200 mg of an iron dextran complex subcutaneously (SC); while the fourth group of piglets did not receive iron, so acted as the control group (C). Subsequently, piglets were labeled with tattoo numbers and ear color tags (4 colors), to enable easier tracking.

Prior to the application of iron in each litter, four piglets were randomly selected from each group (IM, PO, SC and C) and blood samples were taken from them by puncture of brachiocephalic plexus. These piglets were additionally marked with a stamp on the other ear, and at weaning on 28th day of life, blood samples were again taken from them. Approximately 2 mL of blood was collected into tubes containing heparin (the anticoagulant for determination of iron concentration in blood plasma) or ethylenediaminetetraacetic acid (the anticoagulant for determination of Hb and Hct). Blood samples were sent to the laboratory for analysis within 30 min of collection. On farm I, blood samples were taken from 440 piglets (110 from each group), and on farm II from 160 piglets (40 from each group).

Blood analyses and production performance monitoring

Blood was sampled and after 4 h centrifuged for 10 min at speed of 6000 revolutions per min. The iron analysis was done using the Ferrozine method. The readout was performed on an automated analyzer Biosystems Model A15, at the wavelength of 560 nm. The control sera produced by Biosystems were used in two levels (normal and pathogen) and in duplicates. Hb concentration and Hct values in donor blood were analyzed using a Siemens ADVIA 120 analyzer. The controls were performed at three levels with the control blood.

The following indicators of production performance were monitored in all piglets in the study: weight of piglets, average daily gain (ADG) and mortality of piglets. Piglet weight and ADG were measured for each litter separately and in total for each experimental group. All piglets were measured on the third day of life, at weaning (28th day of life) and at the end of the nurturing stage (70th day of life). The mortality rate of piglets was calculated for each experimental group.

Statistical analysis of hematological values

The influence of the farm was tested, as well as the impact of the day of blood sample collection and the impact of the method of iron administration on the Fe, Hb and Hct levels, using a combined model. These parameters were considered as fixed effects, whereas iron administration methods were considered as randomized effects. The effect of method of iron administration on the values of Fe, Hb and Hct in the blood of piglets was tested by ANOVA and Fisher's post-hoc test.

In order to examine whether the method of iron administration was associated with an increase of the proportion of piglets with Fe, Hb and Hct levels in the higher quartiles of known reference values, Cochran-Armitage's test for trend was used. The following reference values were used: Fe 94.9-201.1 µg/dL, Hb 10-16 g/dL, Hct 32-50%. Statistical analysis was conducted using the statistical packages Statistica and Statgraphic Centurion.

Statistical analysis of productivity performance

Data were entered into an Excel spreadsheet (Microsoft Excel 2010) and imported into Stata (Stata 8 Intercooled for Windows 9x) in which data were analyzed. Descriptive analysis was completed using Minitab version 14 (MiniTabR14b) and Excel (Microsoft Excel 2010). For ADG, the differences among the methods of iron administration were statistically analyzed with a one-way ANOVA test in a completely randomized design using Statistical Packages for the Social Sciences [15]. The significant differences among means were compared using Post Hoc Test. Mortality rates were analyzed in a logistic regression using the procedure GENMOD in SAS (chisquared (χ^2) values were generated as the test statistic) and the results are expressed in percentages.

RESULTS

Iron, hemoglobin and hematocrit concentration

The impact of piglets' farm of origin proved to not be a significant factor, as there were no significant differences in the values of Fe, Hb and Hct between piglets in the same iron-administration groups but originating from the two farms. On the other hand, significant changes occurred in piglets' blood values (Fe, Hb and Hct) over time. Within group C, a significant increase in the concentration of Fe was observed

on the 28th day compared with the 3rd day, as well as a significant decrease in Hb, and Hct values. In piglets after IM, PO or SC administration of iron supplements, a significant increase in the concentration of Fe and Hb was observed, while no significant differences were observed in Hct values (Table 2). Prior to the application of iron (on the 3rd day), there was no significant difference in the values of Fe, Hb and Hct in the four groups of piglets. By the 28th day, though, the method of Fe administration on day 3 produced a significant impact on examined hematological parameters (Table 2).

At weaning, on the 28th day of life, piglets that received iron subcutaneously had the highest average values ($P < 0.01$) of Fe, Hb and Hct. The IM group had a slightly lower average value of Fe than the SC group, but it was higher than the average Fe level of the PO group. The average level of Hb in group C piglets was around half that of piglets which were injected with Fe, and was below the threshold value defining anemia (8 g/dL). By day 28, the average Hct value in piglets which received iron was slightly increased or remained the same as on the third day, while in piglets from group C, a significant decrease of Hct was observed on the day of weaning compared with on day 3 (Table 2). The iron administration method significantly affected values of iron ($F = 48.97$, $P < 0.001$), hemoglobin ($F = 32.2$, $P < 0.001$) and hematocrit ($F = 5.79$, $P < 0.01$) measured in the piglets' blood. Fisher's tests showed that piglets with SC administered iron had significantly higher values of these parameters compared to the piglets which received Fe via IM or PO administration (Figures 1-3). Analysis of trends showed, overall, a strictly positive association between iron administration and Fe, Hb and Hct values. However, on comparing the method of iron administration, we found that there was a significant positive trend only

for SC iron administration, but not for the other types of iron administration. In practice, this means that the proportion of piglets whose values of Fe, Hb and Hct were in the higher quartiles did increase, but that these increasing trends were significant only for SC administration of Fe. The trend of changes in the concentration of Fe for the different iron administration methods is shown in Figures 4 and 5.

Production performance parameters

The weight of piglets on the 3rd day of life was very similar in all four groups, and there was no statistically significant difference between average piglet weights from the two investigated farms ($P > 0.05$). At weaning (on the 28th day), group C piglets had significantly the lowest weight ($P < 0.01$), while group SC piglets had the highest weight ($P < 0.01$). The same weight ratios with even more pronounced differences were observed at the end of the nurturing stage (Table 3). Regarding the same time period, ADG is a consequence of the differences in weight at the beginning and end of the study, and consequently, the ADG was significantly lowest ($P < 0.01$) in group C, and the highest ($P < 0.01$) in group SC piglets. For piglets which received iron (IM, PO and SC groups), the highest weight, and therefore the greatest ADG, was observed in the group with SC administered Fe, while the difference in ADG between groups IM and PO was very small, with no statistical significance ($P > 0.05$) [Table 3]. The mortality rate of piglets in the farrowing and during the nurturing phase on both farms was significantly higher in group C piglets. On both farms, there were no statistically significant differences ($P > 0.05$) in mortality rates of piglets in the farrowing and during the nurturing stage between IM, PO and SC groups of piglets (Table 3).

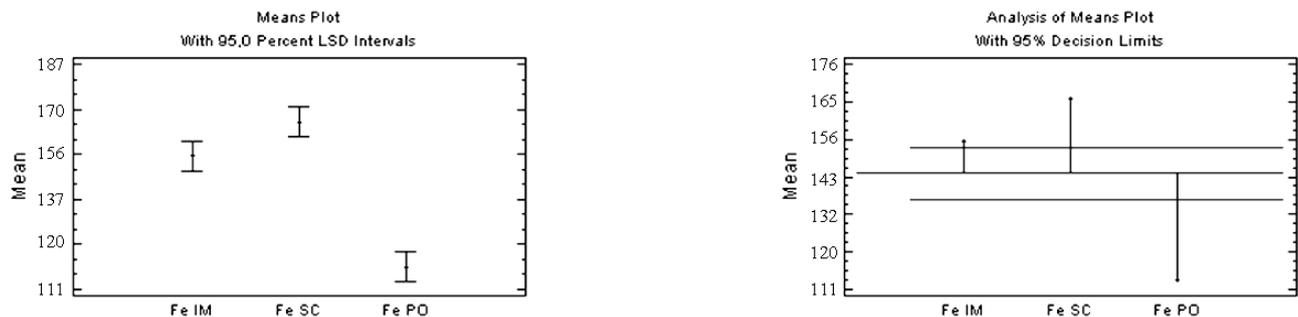


Figure 1. Effect of iron administration method on Fe value in piglets blood and its change relative to the overall average.

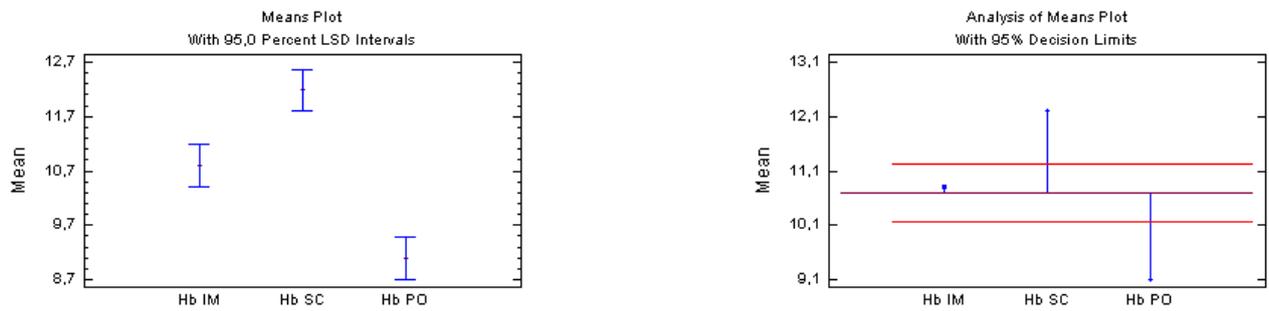


Figure 2. Effect of iron administration method on Hb value in piglets blood and its change relative to the overall average.

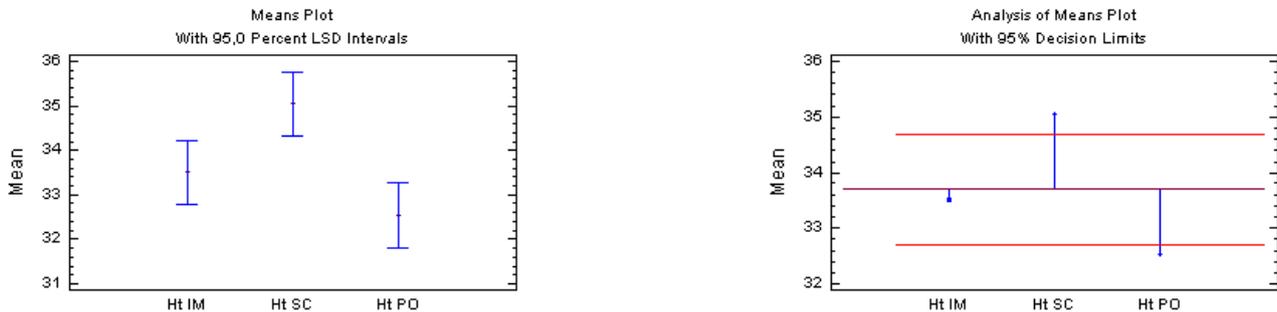


Figure 3. Effect of iron administration method on Hct value in piglets blood and its change relative to the overall average.

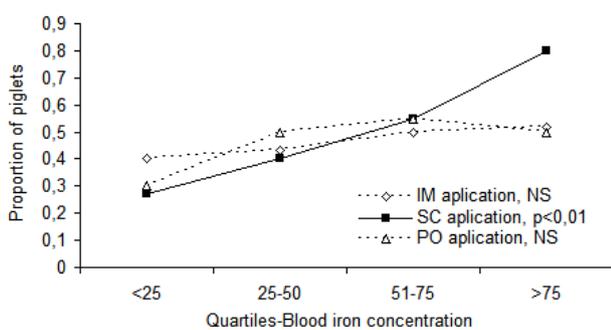


Figure 4. Trend of changes of concentration of Fe in the blood of piglets which had iron administered compared to control piglets with no iron.

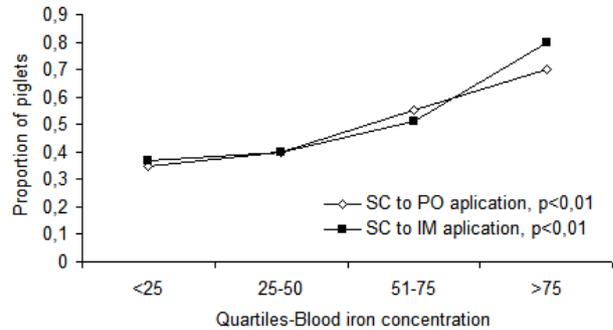


Figure 5. Trend of changes in concentrations of Fe in blood of piglets with iron administered via SC injection compared to IM and PO administration of iron.

Table 2. Effect of application of iron on hematological values in piglets.

	Group				SEM	Influence of	
	IM	PO	SC	C		day*	application
						P-value	P-value
Iron (µg/dL)							
3 d	34.86	35.59	34.53	34.95	0.41	<0.01	<0.01
28 d	155.63	114.75	168.43	72.25	0.73		
Hemoglobin (g/dL)							
3 d	8.95	9.03	8.93	8.95	0.13	<0.05	<0.05
28 d	10.78	9.13	12.21	6.33	0.14		
Hematocrit (%)							
3 d	32.79	32.80	32.99	33.07	0.15	<0.01	<0.05
28 d	33.49	32.55	35.05	24.91	0.20		

IM: intramuscularly; PO: peroral; SC: subcutaneously; C: control. *Influence of day was examined only for the control group-C.

Table 3. Production performance of piglets after using different iron administration methods.

	Group				P-value
	IM	PO	SC	C	
Weight (kg)					
3 d	1.93	1.95	1.98	1.96	>0.05
28 d	7.41	7.49	7.99	6.87	<0.01
70 d	20.98	20.45	21.96	17.25	<0.01
Average daily gain (kg/day)					
3-28 d	0.22	0.21	0.24	0.19	<0.01
29-70 d	0.32	0.30	0.33	0.24	<0.01
Pig mortality (%)					
3-28 d	8.90	8.46	8.55	9.26	<0.01
29-70 d	3.22	3.42	3.07	5.16	<0.01

IM: intramuscularly; PO: peroral; SC: subcutaneously; C: control.

DISCUSSION

This study shows the importance of iron administration for piglets and influence of the iron administration method on hematologic values and thus on prevention of anemia in piglets, all with the aim of achieving the best production results. Piglet anemia as a result of iron deficiency was described many years ago [22], and for that reason, today all over the world, iron is preventively administered to piglets at birth. In this study, the piglets that did not receive iron had clinical signs of anemia (pallor of mucous membranes, pallor of the skin of the whole body), while these symptoms were not identified in piglets which received iron. Anaemia was confirmed in control piglets (no iron administered), as the average Hb value on the 28th day of life was 6.33 g/dL in piglets from farm I and farm II. Many authors suggest that the Hb threshold for Hb is 8.0 g/dL; levels below this indicate anemia [4,6,10]. Piglets which did not receive iron also had significantly lower blood values of Fe and Hct than piglets treated with iron preparations, which has also been confirmed in other studies [8,20,24]. In the current study, the clear development of anemia in piglets which were not treated with iron confirms both the benefit of iron administration and the fact that piglets, during pre-weaning, intake only small amounts of solid feed which can be a source of iron [19].

The method of iron administration has an impact on the level of iron in the blood of piglets, and therefore on the blood levels of Hb and Hct [2], which was confirmed in this study. Intramuscular administra-

tion of iron prevails worldwide; subcutaneous application is less common, while oral application is rarely used in modern intensive pig production.

In this study, in piglets on the third day of life, no differences were observed in blood levels of Fe, Hb and Hct, which was to be expected given that piglets from all four experimental groups originated from the same sows. However, after applying the different iron administration methods, after a further 25 days (i.e. during the farrowing phase), there were significant differences in the blood levels of Fe, Hb and Hct in piglets given iron by different routes. On both studied farms, SC administration of iron induced the highest levels of Fe, Hb and Hct in the piglets, which was also found by Svoboda and Drábek in their study [18]. Also, SC iron administration produced the highest number of piglets with levels of iron in the higher quartiles, compared with other types of iron administration. Additionally, IM iron administration induced higher levels of Fe and Hb in piglets from both farms compared to PO iron administration. Significant increases in the Fe values in the blood of piglets on the 28th day of life compared to the third day, and reaching values within the physiological range in piglets with Fe administered via IM, SC and PO routes, shows that all three iron administration methods lead to normal values of Fe in piglets.

In group C piglets, we also observed an increase in the level of iron in the blood, but this value was below the physiological minimum, as found by Peters and Mahan [14] in their research. However, when we looked at the value of Fe in the blood only

of piglets which had iron administered, compared to the average of the three administration method groups, it was clear that the SC administration produced the highest level, while PO administration produced the lowest level. The values of Hb and Hct found in piglet blood followed a similar trend.

The reason for lower values of Fe in piglet blood after oral application of emulsion is likely due to lower intake, i.e. mistakes during the administration. In a previous study [13], no significant differences were found in the time required for administration of iron between the parenteral (injection) and peroral (in the form of emulsion) methods of administration (24 vs. 20 s per pig, respectively). Often, though, during peroral administration, piglets do not get the intended dose of iron [19], while this hardly ever occurs with parenteral administration. Maes *et al.* [12] reported no difference resulting between peroral and parenteral administration of iron in piglets. They administered iron via feed for several days after the birth of piglets, but it is obvious that in this kind of administration there is a high risk of low consumption of feed by piglets in this age group [19].

Peters and Mahan [14] reported that piglets which did not have iron administered at birth had a lower body weight and ADG at weaning compared to piglets which received iron injections, which was also confirmed in this study. At the end of the nurturing stage (70th day), piglets which did not receive iron had lower body weights, as a result of lower ADG during the nurturing period and less weight at weaning.

Piglets with SC administered Fe had the highest weight at weaning, and at the end of the nurturing phase, as a result of the highest ADG. These results are similar to those of Jolliff and Mahan [9], who reported that piglets with higher blood levels of Hb also had higher ADG. In the current study, piglets with IM

and PO administered Fe had very similar ADG, both during the suckling stage, and during the nurturing stage, indicating that there was no influence of these two methods of administration of iron on the ADG.

Anemia in piglets which did not receive iron likely contributed to the higher mortality of piglets in both phases, suckling and nurturing, compared with piglets that received iron. Due to lower production performance, the growth rate of group C piglets lagged behind, resulting in twice the mortality rate in the nurturing stage compared to piglets with iron administered IM, SC or PO. In piglets, which were treated with iron there were no significant differences in mortality in the suckling and nurturing stages, which indicates that all three modes of administration of iron had the same effect on mortality. As piglets grow, the amount of feed they eat increases, as does their iron intake from that feed. This, clearly, does not affect production performance or mortality in the suckling stage [1], while in the nurturing stage, consumption of feed rich with iron has a positive effect [9,17]. In the current study, all piglets consumed the same feed and thus, the effect of iron from feed on production performance and mortality was excluded.

CONCLUSIONS

In conclusion, piglets with iron administered at birth had significantly higher hematological values and better production performance than piglets which did not receive iron, and which subsequently developed anemia. In this study, subcutaneous injection of iron was the most effective administration method, resulting in highest levels of Fe, Hb and Hct in piglet blood, and consequently the best production performances.

Declaration of interest. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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