Original Article

Oral administration of iron and toltrazuril in combination improves survival rate and growth rate and reduces anaemia in piglets

Pachara Pearodwong[1] Padet Tummaruk[2,3*]

Abstract

The present study was performed to determine the efficacy of an oral administration of iron and toltrazuril in combination on the growth rate, survival rate and the incidence of anaemia in suckling piglets. A total of 406 piglets were randomly allocated to one of three groups: *i.*) CONTROL (n = 161), the piglets were administered iron dextran 200 mg intramuscularly and toltrazuril (20 mg/kg) orally at 3 days of age; *ii.*) NEGATIVE (n = 84), the piglets were not treated with iron until 7 days of age, and toltrazuril was given at 5 days of age and *iii.*) TREATMENT (n = 161), the piglets were fed with an oral suspension of iron and toltrazuril combination at 3 days of age (iron 228 mg and toltrazuril 50 mg). Blood samples were obtained by randomly sampling piglets (n = 218) at 2 (n = 56), 7 (n = 80) and 21 days (n = 82) of age. Haemoglobin, haematocrit and completed blood count were evaluated. On average, the body weight of piglets at 0, 7 and 21 days of age did not differ among groups ($P > 0.05$). However, average daily weight gain (ADG) during 0–7 days of age in TREATMENT and NEGATIVE groups were higher than those in the CONTROL group (177.8, 177.7 and 160.3 g/d, respectively, $P < 0.05$). Piglet mortality during the first 7 days postpartum in the TREATMENT group was lower than in the CONTROL group (0.62 and 3.73%, respectively, $P < 0.05$). The incidences of severe diarrhoea were 5.0, 2.4 and 0% in groups *i*), *ii*) and *iii*), respectively ($P < 0.05$). The haemoglobin, haematocrit and red blood cell (RBC) counts of piglets in the CONTROL and TREATMENT groups were higher than those in the NEGATIVE group at 7 days postpartum ($P < 0.05$). However, at 21 days of age, piglets in the CONTROL group had a higher haemoglobin, haematocrit and RBC count than piglets in the TREATMENT group ($P < 0.05$). In conclusion, oral administration of iron and toltrazuril in combination is a novel technique for treatment of coccidiosis and prevent anaemia in piglets.

Keywords: anaemia, average daily gain, iron, mortality, piglet

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Introduction

Swine production in Thailand has become more industrialised, and litter size of sows has increased rapidly during the past decades due to an introduction of modern hyperprolific sow genetics from European countries (Thongkhuy *et al*., 2020). One of the most important strategies to obtain a high productivity (i.e. 30-40 pigs weaned per sow per year) in modern swine industry is to improve farrowing management (Vila and Tummaruk 2016; Kirkwood *et al*., 2021; Taechamaeteekul *et al*., 2022). The keys for successful farrowing management consist of effective farrowing supervision, care of newborn piglets and optimisation of cross-fostering management (Vila and Tummaruk, 2016; Kirkwood *et al*., 2021; Vongsariyavanich *et al*., 2021). These management practices are gaining increasing interest in the swine research field due to the increased litter size in modern hyperprolific sows (Muns *et al.,* 2016; Kemp *et al*., 2018).

Iron is an essential element for blood production, oxygen conveyance and energy generation. In piglets, the deficiency iron may result in anaemia, poor growth performance, poor reproductive performance, immune deficiency, reduced feed efficiency, diarrhoea and high mortality. Furthermore, iron deficiency can increase the severity of infectious diseases that cause blood loss, such as *Trichuris suis* in pigs (Pedersen *et al*., 2001). In general, supplementation of iron in the piglets is carried out within 3 to 5 days after birth by using intramuscular administration of iron dextran 200 mg per piglet (Jullapanont *et al*., 2012). In practice, it is rather common to use the same needle for iron administration in all piglets within the litter and sometime also between litters. This practical work can increase the risk of diseases transmission among piglets both within and between litters. For instance, viremia and microscopic lesion of porcine circovirus type 2 has been detected in a piglet injected using a contaminated needle (Patterson *et al.,* 2011). Thus, investigating a needleless method for iron administration may help to reduce the transmission of diseases in pigs. Recently, a combination product of toltrazuril and iron has been developed for oral application (Streyl *et al.,* 2015). In an experimentally induced *cystoisosporosis* in piglets, the combined oral application product of toltazuril and iron could cure piglets experimentally infected with *Cystoisospora suis* as well as an injectable product (Streyl *et al*., 2015). However, the efficacy of the combination product of toltrazuril and iron on piglet growth performance, survival rate and blood parameters has not been determined. The present study was performed to determine the efficacy of an oral suspension of iron and toltrazuril combination on growth rate, survival rate and anaemia problems in suckling piglets. Additionally, the possibility of implementing a novel post-farrowing care of piglets, using a needleless method for treatment of coccidiosis and preventing anaemia problems, was evaluated.

Materials and Methods

Experimental designs: In total, 41 Landrace x Yorkshire crossbred sows (parity 1–5) and 406 piglets were randomly allocated to one of the following three groups: *i.*) CONTROL (20 sows and 161 piglets, 81 and 80 piglets from primiparous and multiparous sows, respectively), the piglets were administered iron dextran 200 mg intramuscularly and toltrazuril orally at 3 days of age (20 mg/kg, Coxzuril 5%® containing toltrazuril 50 mg/ml, BIC Chemical co. ltd., Nakhonpathom, Thailand); *ii.*) NEGATIVE (n = 84 piglets, 44 and 40 piglets from primiparous and multiparous sows, respectively), two piglets from each litter served as negative control. The negative control piglets were not treated with iron until 7 days of age, and toltrazuril was given at 5 days of age and *iii.*) TREATMENT (21 sows and 161 piglets, 81 and 80 piglets from primiparous and multiparous sows, respectively), the piglets were fed with an oral suspension of iron and toltrazuril combination at 3 days of age (Baycox® iron oral 1 ml containing toltrazuril 50 mg and iron 228 mg as iron dextran, Bayer Animal Health GmbH, Germany). In all litters, 10 piglets with individual body weight at birth above 1.0 kg were included in the experiment.

Animals: This experiment followed the guidelines of The Ethical Principles and Guidelines for the Use of Animals for Scientific Purposes by the National Research Council of Thailand and was approved by the Institutional Animal Care and Use Committee (IACUC) in accordance with the university regulations and policies governing the care and use of experimental animals (protocol ID. 1831089). The experiment was carried out in a commercial swine herd in Thailand and included 41 sows and 406 piglets. The numbers of primiparous (parity number 1) and multiparous sows (parity numbers 2–5) were 21 and 20, respectively. All sows in the experiment were kept in a close house equipped with an evaporative cooling system. During gestation, the sows were kept in individual stalls (1.2 m^2) and fed a commercial gestation diet twice a day. The gestating sows received the feed 2.5 kg of feed per sow per day following a standardised feeding pattern to meet the nutritional requirements (NRC, 2012).

General management: Sows were transferred from gestating house to the farrowing barn at about one week before parturition. In the farrowing barn, the sows were placed in individual crates (1.5 m^2) at the centre of the farrowing pens (4.2 m^2). The floor of the farrowing pens was fully slatted having a concrete base at the centre for sows and steel slats at both sides for piglets. A warm creep area equipped with a heating lamp was provided for piglets in all pens during the first week postpartum. Sows were fed a commercial lactation diet twice a day. Feed offered to sows was reduced to 2.0 kg for 2–3 days before farrowing. After farrowing, the amount of feed offered to sows was increased daily until *ad libitum* feed was reached at one week of lactation. Sows and piglets had *ad libitum* access to water by one nipple drinker for the sow and one nipple drinker for the piglets. The parturition process was carefully monitored by researcher and stock persons and the sows were interfered as little as possible. Birth intervention was performed only when dystocia was clearly identified. Dystocia was considered when an interval of > 30 min had elapsed from the birth of the previous piglet. The routine procedures performed on piglets included weighing, tail docking and teeth clipping on the first day of life. At 3 days of age, 200 mg (1 ml) of iron dextran was administered intramuscularly (Gleptosil®; Alstoe Ltd. Animal Health, Leicestershire, England) to all the piglets in the CONTROL group. For the TREATMENT group, the administration of iron dextran was omitted, and 1.0 ml of a combined product of toltrazuril and iron (Baycox® Iron, Bayer Animal Health GmbH, Germany) was provided orally to all piglets at 3 days of age. Creep feeding was routinely provided to the piglets from five days of age onwards.

Data: The sow parameters recorded during the experiment were body condition score, backfat thickness (measured the day before parturition at the last rib and 6–8 cm from the midline using A-mode ultrasonography; Renco-Lean meter®; Minneapolis, MN, USA), gestation length (calculated from the date of first insemination to the date of farrowing), farrowing duration (defined as the time interval between the expulsion of the first and last piglets), total number of piglets born per litter (TB), number of piglets born alive per litter (BA), number of stillborn piglets per litter and mummified foetuses per litter. The occurrence of dystocia was also recorded.

Piglet parameters recorded during the experiment consisted of birth order and rectal temperature 24 h after birth, measured using a digital thermometer (Verridian Dual Scale 9-Second Digital Thermometer Model 08-357; Verridian Healthcare Co. Ltd., IL, USA; display resolution of 0.01 ± 0.1 °C accuracy). All piglets were dried immediately after birth with drying powder, weighed and then weighted again at 7 and 21 days of age. Average daily weight gain (ADG) from birth to 7 days (ADG7) and from birth to 21 days (ADG21) of age was calculated. Mortality of piglets was recorded at 7 and 21 days of age to calculate piglet pre-weaning mortality at 7 and 21 days, respectively. The occurrence of diarrhoea was also observed and recorded, and diarrhoea severity was defined as normal, mild, moderate and severe: "normal" referred to piglets without signs of diarrhoea, "mild" referred to piglets with a mild degree of diarrhoea, having pasty to semi-liquid faeces, "moderate" referred to piglets with some moderate degree of diarrhoea, having semi-liquid to liquid faeces without any signs of dehydration, and "severe" referred to piglets with severe degree of diarrhoea, having liquid faeces and apparent dehydration. The evidence of diarrhoea problems in piglets was determined in all litters 4 – 6 times daily from birth until weaning.

Blood collection: Blood samples were obtained from randomly sampling piglets (77, 67 and 74 samples in CONTROL, NEGATIVE and TREATMENT groups, respectively). The blood samples were collected from the jugular vein of the piglets at 2 (n = 56), 7 (n = 80) and 21 days (n = 82) of age. The piglets in each group were randomly chosen for blood collection, and the blood samples were kept in EDTA tubes. In total, 218 blood samples were collected. Haemoglobin, haematocrit and red blood cells (RBC) were evaluated by an Auto Hematology Analyzer (Mindray BC-5150, Shenzhen Mindray Bio-Medical Electronics Co., Ltd., ShenZhen, P.R. China). Anaemia was defined as a haemoglobin level below 8.0 g/dl (Svoboda et al. 2017).

Statistical analysis: The statistical analyses were carried out using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Descriptive statistics of sow performance and piglet characteristics, including non-missing values, mean values and range, were generated using the MEANS procedure of SAS. The distribution of the data was determined using the UNIVARIATE procedure of SAS. Piglet was defined as an experimental unit. Continuous traits (i.e. ADG, body weight, haemoglobin, haematocrit, RBC and other blood parameters) were analysed by using multiple ANOVA, applying the GLM procedure of SAS. The statistical models included treatment group (CONTROL, NEGATIVE and TREATMENT) as the main effect and parity number of sows (primiparous and multiparous) as a fixed effect, as well as the interaction between parity and treatment group. Differences of least square means were compared using the least significant difference (LSD) test. Categorical data (i.e. piglet mortality at 7 and 21 days postpartum and piglets with anaemia) were analysed by using logistic regression, applying the GENMOD procedure of SAS. The statistical models included the effect of treatment group (CONTROL, NEGATIVE and TREATMENT), parity number of sows (primiparous and multiparous) and the interaction between parity and treatment groups. Least square means were obtained from the statistical models and compared by using the LSD test. In addition, ADG from birth to 21 days of age was compared among groups of diarrhoea scores (i.e., normal, mild, moderate and severe) by using one-way ANOVA. A P value < 0.05 was considered statistically significant.

Results

Sow reproductive performances: On average, TB, BA, stillborn piglets and mummified foetuses were 16.3 ± 3.5, 14.2 ± 2.8, 1.3 ± 1.7 and 0.9 ± 1.2 piglets per litter, respectively. Average gestation length of sows was 115.6 ± 1.5 days (range: 112–119), and farrowing duration was 404.8 ± 312.1 min (range: 113–1440). The average backfat thickness of sows at farrowing and at weaning was 17.3 ± 2.6 and 15.4 ± 3.2 mm, respectively. The average backfat loss during lactation was 11.5% and varied among sows from lost 29.4% to gained 8.3%. The average backfat loss was 10.8% and 12.1% in primiparous and multiparous sows, respectively (P = 0.663).

Piglet performances: Across parity groups, the numbers of piglets included in the experiment and the body weights of the piglets at 0, 7 and 21 days of age are presented in Table 1. On average, the body weight of piglets at 0, 7 and 21 days of age did not differ significantly among groups (P > 0.05). However, ADG levels during 0–7 days of age in TREATMENT and NEGATIVE groups were higher than the CONTROL group (P < 0.05). The ADG from 0 to 21 days of age did not differ among groups (P > 0.05). Piglet mortality during the first 7 days of life in the TREATMENT group was lower than that in the CONTROL group ($P < 0.001$). However, piglet mortality from 0 to 21 days of age did not differ among groups ($P > 0.05$) (Table 1).

Table 2 demonstrates body weight, ADG and piglet mortality in CONTROL, NEGATIVE and TREATMENT groups by parity groups of sows. In primiparous sows, piglet mortality from 0 to 21 days of age tended to be lower in the TREATMENT group compared with the CONTROL group (2.47 and 9.88%, respectively, $P = 0.069$). However, no difference in piglet mortality between CONTROL and TREATMENT was observed in multiparous sows (Table 2). Furthermore, in primiparous sows, the ADG of piglets during the first 7 days postpartum in the TREATMENT group was higher than that in the CONTROL group ($P < 0.05$).

Table 1 Body weight at 0, 7 and 21 days of age, average daily gain (ADG) from 0–7 and 0–21 days of age and pre-weaning mortality from 0–7 days and from 0–21 days of age in piglets treated with an oral suspension of iron and toltrazuril in combination (TREATMENT) compared with CONTROL and NEGATIVE groups (least square mean ± SEM).

Variables	CONTROL	NEGATIVE	TREATMENT	*P* value [c]
Number of piglets	161	84	161	-
Body weight at birth (gram)	1,446 ± 20.3	1,400 ± 28.0	1,425 ± 19.9	0.399
Body weight at 7 days of age (gram)	2,573 ± 42.1	2,646 ± 57.5	2,671 ± 41.0	0.236
Body weight at 21 days of age (gram)	5,335 ± 102.0	5,107 ± 138.4	5,104 ± 100.0	0.261
ADG from 0–7 days (gram/day)	160.3 ± 4.55[a]	177.7 ± 6.22[b]	177.8 ± 4.48[b]	0.011
ADG from 0–21 days (gram/day)	185.2 ± 4.41	179.6 ± 5.99	174.9 ± 4.37	0.252
Number of piglets at 7 days	155	83	160	
Piglet mortality from 0–7 days (%)	3.73[a]	1.19[ab]	0.62[b]	0.113
Number of piglets at 21 days	149	81	152	
Piglet mortality from 0–21 days (%)	7.45	3.57	5.59	0.461

[a,b] different superscript letters within rows indicate significant differences ($P < 0.05$), [c] *P* value was obtained from the *F* test from multiple ANOVA models.

Table 2 Body weight at 0, 7 and 21 days of age, average daily gain (ADG) from 0–7, 0–21 and 7–21 days of age and pre-weaning mortality from 0–7 days and from 0–21 days of age in piglets treated with an oral suspension of iron and toltrazuril in combination (TREATMENT) compared with CONTROL and NEGATIVE groups in primiparous and multiparous sows (least square mean ± SEM).

Variables	CONTROL	NEGATIVE	TREATMENT
Primiparous sows			
Number of piglets	81	44	81
Body weight at birth (gram)	1,432 ± 27.1[a]	1,343 ± 37.7[a]	1,398 ± 26.1[a]
Body weight at 7 days of age (gram)	2,563 ± 56.9[a]	2,574 ± 77.8[a]	2,643 ± 53.5[a]
Body weight at 21 days of age (gram)	5,215 ± 145.7[a]	5,086 ± 192.1[a]	4,990 ± 140.0[a]
ADG from 0–7 days (gram/day)	161.2 ± 6.5[a]	176.5 ± 8.6[ab]	183.7 ± 6.3[b]
ADG from 0–21 days (gram/day)	179.0 ± 6.3[a]	177.8 ± 8.3[a]	171.2 ± 6.1[a]
Piglet mortality from 0–7 days (%)	5/81 (6.2%)[a]	1/44 (2.3%)[a]	1/81 (1.2%)[a]
Piglet mortality from 0–21 days (%)	8/81 (9.9%)[a]	2/44 (4.6%)[a]	2/81 (2.5%)[a]
Multiparous sows			
Number of piglets	80	40	80
Body weight at birth (gram)	1459 ± 30.2[a]	1457 ± 41.5[a]	1455 ± 28.6[a]
Body weight at 7 days of age (gram)	2584 ± 61.9[a]	2717 ± 84.7[a]	2659 ± 58.3[a]
Body weight at 21 days of age (gram)	5456 ± 142.8[a]	5254 ± 199.3[a]	5218 ± 145.7[a]
ADG from 0–7 days (gram/day)	159.3 ± 6.4[a]	178.8 ± 8.9[a]	171.9 ± 6.3[a]
ADG from 0–21 days (gram/day)	191.4 ± 6.2[a]	181.3 ± 8.6[a]	178.5 ± 6.3[a]
Piglet mortality from 0–7 days (%)	1/80 (1.3%)[a]	0/40 (0%)[ab]	0/80 (0%)[b]
Piglet mortality from 0–21 days (%)	4/80 (5.0%)[a]	1/40 (2.5%)[a]	7/80 (8.8%)[a]

[a,b] different superscript letters within rows indicate significant differences ($P < 0.05$).

Across groups, severe diarrhoea was detected in 2.5% of the piglets. The evidence of severe diarrhoea problems was 5.0, 2.4 and 0% in CONTROL, NEGATIVE and TREATMENT groups, respectively ($P < 0.001$). However, mild to moderate degrees of diarrhoea were also detected in all groups. No laboratory diagnosis was confirmed for the cause of diarrhoea. The frequency distribution of piglets with different degrees of diarrhoea is shown in Figure 1. Average daily weight gain from birth to 21 days of age in piglets with severe diarrhoea was lower than in piglets with normal, mild and moderate diarrhoea scores (67.7 ± 19.2 versus 206.2 ± 5.8, 177.8 ± 3.2 and 155.9 ± 4.7 g/d, respectively, $P < 0.001$).

Blood parameters: Table 3 demonstrates haemoglobin, haematocrit, RBC count and other blood parameters in piglets in the TREATMENT group compared with the CONTROL and NEGATIVE groups. On average, haemoglobin, haematocrit and RBC count in piglets did not differ significantly among groups at day 2 postpartum. Haemoglobin, haematocrit and RBC count of piglets in the CONTROL and TREATMENT group were higher than those in the NEGATIVE group at day 7 postpartum (Table 3). However, other blood parameters did not differ significantly between CONTROL and TREATMENT groups at day 7 postpartum. At day 21 of age, piglets in the CONTROL group had a higher haemoglobin, haematocrit and RBC count than piglets in the TREATMENT group.

However, no difference in the proportion of anaemia piglets was found among groups ($P > 0.05$). In the CONTROL group, the proportion of anaemia piglets was 5.0%, 0% and 3.5% at 2, 7 and 21 days of postnatal life, respectively (Table 3). Similarly, in the TREATMENT group, the proportion of anaemia piglets was 10.5%, 0% and 7.1% at 2, 7 and 21 days of postnatal life, respectively (Table 3). On the other hand, the proportion of anaemia piglets in the NEGATIVE group was 40.0%, higher than both CONTROL and TREAMENT groups ($P < 0.001$) (Table 3). The levels of haemoglobin in piglets in CONTROL, NEGATIVE and TREATMENT at days 7 postpartum in primiparous and multiparous sows are presented in Figure 2. The levels of haemoglobin at day 7 postpartum did not differ significantly between CONTROL and TREATMENT groups in both primiparous and multiparous sows. However, both CONTROL and TREATMENT groups had higher haemoglobin levels at day 7 postpartum than the NEGATIVE group ($P < 0.001$).

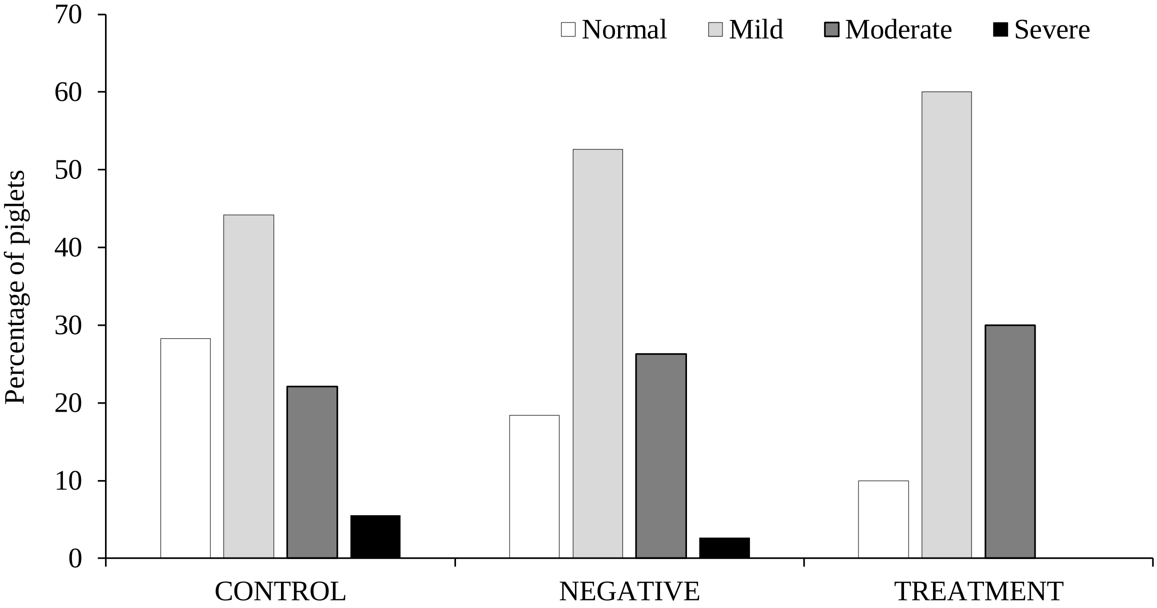

Figure 1 Frequency distribution on the proportion of piglets with different diarrhoea scores (i.e. normal, mild, moderate and severe diarrhoea) in CONTROL, NEGATIVE and TREATMENT groups.

Table 3 Haemoglobin, haematocrit and red blood cell (RBC) counts in piglets treated with an oral suspension of iron and toltrazuril in combination (TREATMENT) compared with CONTROL and NEGATIVE groups in primiparous and multiparous sows (least square mean ± SEM).

Variables	CONTROL	NEGATIVE	TREATMENT	*P* value
Day 2				
Number of piglets	20	17	19	-
Haemoglobin (g/dl)	10.1 ± 0.4	10.1 ± 0.4	10.1 ± 0.5	1.000
Haematocrit (%)	31.2 ± 1.2	31.8 ± 1.2	31.3 ± 1.4	0.935
RBC count (x 10^6 cells)	4.8 ± 0.2	5.0 ± 0.2	4.9 ± 0.2	0.889
MCV (fl)	64.6 ± 1.0	63.9 ± 1.0	64.2 ± 1.2	0.896
MCHC (g/dl)	32.2 ± 0.3	31.6 ± 0.3	32.2 ± 0.4	0.334
Piglets with anaemia (%)	1/20 (5.0%)^a	1/17 (5.9%)^a	2/19 (10.5%)^a	0.776
Day 7				
Number of piglets	28	25	27	-
Haemoglobin (g/dl)	10.7 ± 0.2^a	8.1 ± 0.2^b	10.4 ± 0.2^a	<0.001
Haematocrit (%)	34.7 ± 0.7^a	27.6 ± 0.8^b	34.6 ± 0.8^a	<0.001
RBC count (x 10^6 cells)	4.8 ± 0.1^{ab}	4.5 ± 0.1^b	4.9 ± 0.1^a	0.062
MCV (fl)	72.9 ± 1.0^a	61.2 ± 1.1^b	70.9 ± 1.1^a	<0.001
MCHC (g/dl)	30.9 ± 0.2^a	29.4 ± 0.2^b	30.1 ± 0.2^c	<0.001
Piglets with anaemia (%)	0/28 (0.0%)^a	10/25 (40.0%)^b	0/27 (0.0%)^a	<0.001
Day 21				
Number of piglets	29	25*	28	-
Haemoglobin (g/dl)	13.0 ± 0.3^a	12.9 ± 0.3^a	10.4 ± 0.3^b	<0.001
Haematocrit (%)	41.7 ± 1.0^a	43.1 ± 1.1^a	34.5 ± 1.0^b	<0.001
RBC count (x 10^6 cells)	6.0 ± 0.2^{ab}	6.4 ± 0.2^a	5.8 ± 0.2^b	0.060
MCV (fl)	69.9 ± 1.0^a	67.3 ± 1.1^a	60.3 ± 1.0^b	<0.001
MCHC (g/dl)	31.2 ± 0.3^a	30.0 ± 0.3^b	30.1 ± 0.3^b	0.006
Piglets with anaemia (%)	1/29 (3.5%)^a	0/25 (0%)^a	2/28 (7.1%)^a	0.383

^{a,b} different superscript letters within rows indicate significant differences ($P < 0.05$); * piglets (n = 25) in the negative group were administered iron dextran 200 mg intramuscularly at day 7 of age.

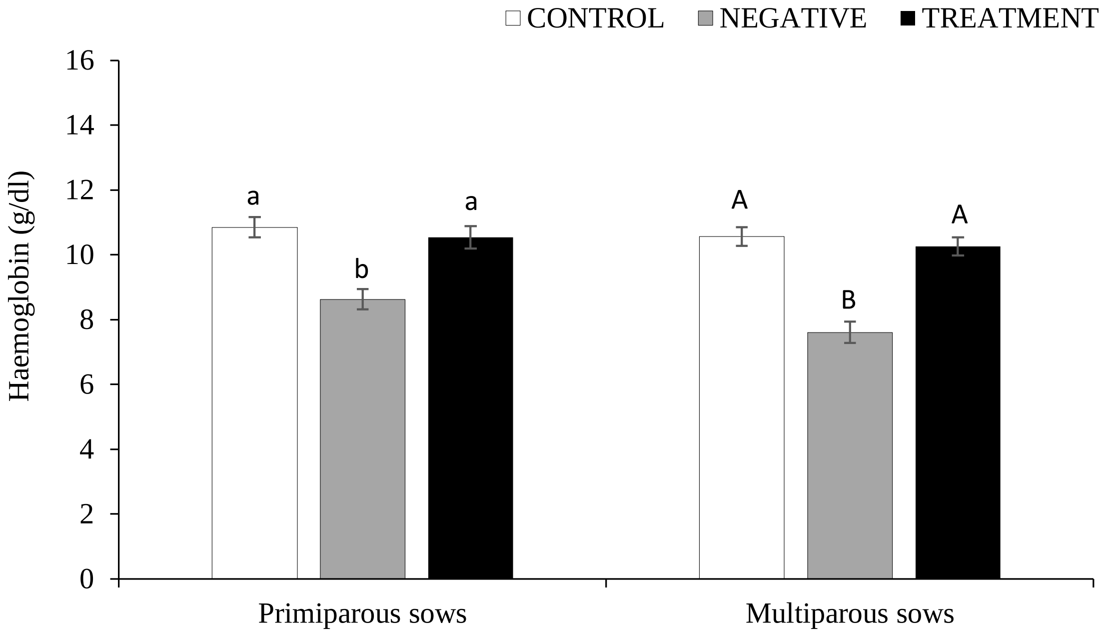

Figure 2 Levels of haemoglobin (g/dl) in piglets in CONTROL, NEGATIVE and TREATMENT groups at 7 days postpartum in primiparous and multiparous sows. a, b A, B different letters differ significantly ($P < 0.05$).

Discussion

The present study revealed that an oral administration of iron and toltrazuril combination is a possible tool for implementing a novel postpartum care of piglets, using a needleless method for treatment of coccidiosis and preventing anaemia. Furthermore, the growth rate and survival rate of piglets in the TREATMENT group (i.e. needleless method) during the first 7 days of life were better than those in the CONTROL group. Anaemia was clearly observed in the piglets that did not receive iron treatment (40% of piglets in the NEGATIVE group), but evidence of anaemia was not found in the CONTROL (0%) and TREATMENT (0%) groups at 7 days of age. Moreover, the percentage of piglets with anaemia did not differ significantly between the TREATMENT and CONTROL groups at weaning. A clinical trial on the oral supplementation of iron in piglets indicated that an oral supplementation of liquid organic iron (100 mg/ml) for 400 mg per piglets at 24 and 72 h postpartum could effectively prevent anaemia and normalised the growth performance of the piglets as compared with a conventional intramuscular iron injection (Jullapanont *et al*., 2012). However, the oral administration of 4 ml of iron twice, at 24 and 72 h postpartum, is not practical and increase the workload of the farmer (Jullapanont *et al*., 2012). Therefore, both the efficacy of the iron suspension and the concentration need further improvement. A previous study in Belgium has demonstrated that the supplementation of iron in creep feed from 7 to 21 days of life could also be used in practice (Maes *et al*., 2011). Nevertheless, the lack of iron supplementation during 1–7 days of age and the amount of creep feed consumed by the piglets is difficult to control. In the present study, creep feeding was routinely provided to the piglets from 5 days of age onwards. However, this may have led to the risk of anaemia in suckling piglets. Alternatively, the supplementation of iron glycine chelate in lactating sow feed has also been shown to improve haemoglobin, haematocrit and the reproductive performance of sows (Tummaruk *et al*., 2003). However, a high incidence of anaemia was still observed in suckling piglets without iron injection (Tummaruk *et al*., 2003). These studies indicate the possibility of administrating iron to suckling piglets via the oral route instead of the intramuscular route. Under field conditions, the 3-day-old piglets commonly receive 200 mg of iron via intramuscular injection; however, the same needle is commonly used to inject several piglets. This practice increases the risk of disease transmission among the piglets and should therefore be avoided. The present study demonstrated that only 1 ml of the medical treatment containing toltrazuril 50 mg and iron 228 mg could effectively reduce the incidence of anaemia in 7-day-old piglets, similar to the use of 1 ml iron dextran (200 mg) injection. Therefore, this could be recommended to be used as a novel technique for postpartum care of piglets with a needleless method for the treatment of coccidiosis and the prevention of anaemia.

Interestingly, although piglet diarrhoea was observed in all groups, the incidence of severe diarrhoea in the TREATMENT and NEGATIVE groups was lower than that in the CONTROL group. Likewise, piglet pre-weaning mortality tended to be lower in the TREATMENT group than in the CONTROL group. Moreover, ADG levels during 0–7 days of age in the TREATMENT and NEGATIVE groups were higher than in the CONTROL group. The severity of diarrhoea in piglets influenced their ADG levels. In the present study, the ADG values varied considerably from 67.7 to 206.2 g/d, and this variation was associated with the severity of diarrhoea. Therefore, the strict control of diarrhoea in suckling piglets is crucial to optimise their ADG. In the present study, diarrhoea was most prevalent in the second to third weeks of age. In previous studies, diarrhoea caused by coccidiosis typically occurred in suckling piglets at 5–14 days of age (Streyl *et al*., 2015; Joachim *et al*., 2018). Once diarrhoea occurs, a large number of oocytes can be shed through faeces for 5–16 days. Coccidiosis in piglets, caused by *Cystoisospora suis*, has been identified as the most common cause of diarrhoea in suckling piglets (Driesen *et al*., 1993; Streyl *et al*., 2015). A previous filed study has demonstrated that a combination of oral toltrazuril and iron could effectively control coccidiosis and maintain body weight at weaning compared to conventional treatment (Streyl *et al*., 2015). Therefore, to limit or eliminate coccidiosis from suckling piglets, an optimal toltrazuril treatment protocol should be implemented. In some litters, repeated treatment with toltrazuril is recommended. These data indicate that oral administration of an iron and toltrazuril combination can effectively control the incidence of diarrhoea in suckling piglets. The low incidence of diarrhoea in the TREATMENT group led to a lower piglet pre-weaning mortality and a higher growth rate.

Our study shows that oral administration of iron and toltrazuril in combination is a possible novel technique for postpartum care of piglets, representing a needleless method for the treatment of coccidiosis and the prevention of anaemia. Furthermore, the growth and survival rates of the piglets in the needleless group were better than those in the control group. The level of haemoglobin of the piglets treated with the iron and toltrazuril combination were still above the anaemia threshold, and the proportion of piglets with anaemia did not differ significantly compared to the control group.

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