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Effect of bovine colostrum on the serum insulin-like growth factor-I (IGF-I), the IGF binding proteins-2 and -3 and the thyroid hormones in weaning piglets

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Abstract

This study examined the effect of a bovine colostrum supplementation on growth performance, feed intake and the hormonal response of piglets at weaning. Ninety-six newly-weaned piglets were assigned for four weeks to one of the two treatments: Control (diet with bovine milk whey) and Colostrum (diet with bovine colostrum whey) treatments. The supplements were incorporated in a commercial diet at 20 g/kg during the first 2 weeks after weaning and lowered to 10 g/kg for the next 2 weeks. Body weight and feed intake were measured weekly. Blood samples were taken weekly for determination of circulating IGF-I, its binding proteins and the thyroid hormones (T_3 and T_4). During the first week of the trial, the Colostrum-fed piglets presented improved growth performance, feed intake and feed efficiency and a higher concentration in circulating IGF-I (+15 %) compared to the Control piglets. In both treatments, the circulating thyroid hormones were reduced by weaning and the levels measured at weaning were recovered earlier by the Colostrum-fed piglets compared to the Control group ($P<0.05$). It is concluded that hormonal response observed after the bovine colostrum supplementation is, at least in part, consequent of the positive action of bovine colostrum on the feed intake.

Keywords: bovine colostrum, pigs, weaning, IGF-I, IGFBP, thyroid hormones

Zusammenfassung

Die Wirkung von Rinderkolostrum auf den Serum IGF-I Faktor, die IGF Bindungsproteine -2 und -3 sowie die Thyroidhormone wachsender Schweine

Untersucht wird der Einfluss von Rinderkolostrumgaben auf Wachstumsleistungen, Futteraufnahme und Hormonantworten bei wachsenden Schweinen. Sechsundneunzig Absetzferkel wurden zwei Gruppen zugeordnet die während vier Wochen unterschiedlich gefüttert wurden. Eine Gruppe erhielt im Aufzuchtfutter Molkenmilchpuder, das Futter der zweiten Gruppe dagegen Kolostrummolke. In den ersten zwei Versuchswochen betrug dieser Zusatz 20 g/kg Futter und in den zwei Folgewochen 10 g/kg. Körpergewicht und Futterverbrauch wurde wöchentlich erfasst. Wöchentliche Blutproben wurden zur

Bestimmung von IGF-I, Bindungsproteinen und Thyroidhormonen entnommen. In der ersten Versuchswoche zeigte die Kolostrumgruppe gegenüber der Kontrollgruppe ein besseres Wachstum, bessere Futteraufnahme und -verwertung sowie eine höhere IGF Konzentration (+15 %). In beiden Versuchsgruppen war der Thyroxidhormonspiegel zum Absetzzeitpunkt reduziert erholte sich jedoch bei der Kolostrumgruppe signifikant schneller. Es wird geschlussfolgert, dass die beobachtete Hormonantwort nach einem Rinderkolostrumzusatz auf eine Verbesserung der Futteraufnahme hinweist.

Schlüsselwörter: Rinderkolostrum, Schwein, Absetzferkel, IGF-I, IGFBP, Thyroxidhormone

Introduction

Colostrum is the milk produced by a mammal for the first 24 to 96 h postpartum. More than a rich source of essential nutrients, colostrum is also bringing biologically active components to the new-born which are essential for specific functions. The most important bioactive components in colostrum include:

- growth factors (insulin-like growth factors, transforming growth factors and epidermal growth factors) which promote the growth and development of the new-born and
- antimicrobial factors (lactoferrin, lysozyme, lactoperoxidase and immunoglobulins) which provide passive immunity and protection against infections during the first weeks of life (BLUM and BAUMRUCKER 2008).

Several authors have shown that weanling pigs fed with a bovine colostrum supplemented diet presented better growth performance, feed intake and feed efficiency than piglets receiving the same diet without colostrum (see BOUDRY *et al*. 2008 for a review). However, mechanisms by which the bovine colostrum exerts its effects are currently unknown. Several studies investigated the effect of bovine colostrum on the gastro-intestinal tract (HUGUET *et al*. 2006 and 2007, KING *et al*. 2007 and 2008) and the immune system (BOUDRY *et al*. 2007) of the newly-weaned piglets but very few information was found about the effect on the endocrinal system (HUGUET *et al*. 2006 and LE HUEROU-LURON *et al*. 2003).

Insulin like growth factor-I (IGF-I) is a very potent mitogenic growth factor that has been shown to affect proliferation and differentiation of a wide variety of cell types (BEE *et al.* 2007). In vivo IGF-I is bound to one of six high affinity IGF binding proteins (IGFBPs). The IGFBPs prolong the circulating half-life of IGF, transport IGF from the extracellular space into tissues and localize IGF to specific cell types and tissues (COHICK 1998). IGFBP-2 and -3 account for the majority of circulating IGFBPs activity in growing pigs (COLEMAN and ETHERTON 1991). IGFBP-2 has a higher affinity for IGF-II and inhibits IGF action by preventing the binding of IGF to IGF receptors while IGFBP-3 has a similar affinity for IGF-I and –II and potentiates the action of IGF (RAJARAM *et al*. 1997). The thyroid hormones (3.5.3'-triiodothyronine, T_3; and thyroxine, T_4) are metabolic hormones which may modulate IGF-I levels (BUONOMO and BAILE 1991).

Blood concentrations of IGF-I, T_3 and T_4 are reported to respond proportionally to feeding level (CARROLL *et al*. 1998, HATHAWAY *et al*. 2003, SAGGAU *et al*. 2000).

Considering the effect of bovine colostrum on feed intake and growth performance and the implication of IGF-I in growth and the influence of nutritional status on IGF-I, IGFBP-2 and -3 and the thyroid hormones, was investigated in the present study the effects of bovine colostrum supplementation on these hormones in newly-weaned piglets.

Materials and methods

The experimental protocol used in this study has been reviewed and approved by the Animal Care and Use Committee (protocol No. 02/05) of Gembloux Agro-Bio Tech (University of Liège) in accordance with the EC Directive 86/609/ECC for Animal Experiments.

Animals

Ninety-six Belgian Piétrain × (Large White × Landrace) piglets weaned at 26 ± 2 days of age with an average BW of 8.3 ± 0.8 kg were selected from 15 litters (Animal Breeding, Quality Production and Welfare Unit, Walloon Agricultural Research Centre, Gembloux, Belgium).

Treatments

Two treatments were compared:
- a control diet (commercial diet with bovine milk whey powder) and
- a colostrum diet (commercial diet with bovine colostrum whey powder).

The commercial diet (SCAR, Herve, Belgium) was a starter diet free of any growth promoters. This commercial diet was distributed the week before weaning to the 15 litters from which the piglets were selected for the trial. The two supplements were mixed with the commercial diet at a rate of 20 g/kg for the first 2 weeks of the trial and 10 g/kg for the next 2 weeks. Compositions of the experimental diets are given in Table 1. The bovine colostrum whey used in this study was prepared from bovine colostrum standardised at 75 g of Ig per litre (Centre d'Economie Rurale, Marloie, Belgium). This colostrum was defatted by centrifugation. Whey was obtained after rennet coagulation at 37 °C for 24 h and separation from curds by a mechanical press. The whey was then freeze-dried. The milk whey used was a commercial spray-dried powder (Euroserum, Port-sur-Soane, France). All pigs had *ad libitum* access to a four-hole feeding through and a nipple drinker.

Experimental design

The animals were blocked according to BW and gender and assigned to one of the two treatments. For each treatment, the piglets were housed in four pens of 12 piglets (6 males, 6 females). Piglets from the same litters were distributed between the two treatments.

BW and feed consumption were evaluated weekly to determine the average daily gain (ADG), the average daily feed intake (ADFI) and the feed efficiency (G/F) which is obtained by the ratio: BW gain/feed intake. Piglets were weighed in the early morning without feed or water restriction.

Table 1
Centesimal and chemical compositions of the Control and Colostrum diets
Futtermittel und chemische Zusammensetzung für die Kontroll- und Kolostrumgruppen

	Control diets		Colostrum diets	
	20 g/kg	10 g/kg	20 g/kg	10 g/kg
Ingredients, g/kg feed				
Barley	247	249.5	247	249.5
Wheat	189	191	189	191
Soybean meal, 49 % CP	175.5	177	175.5	177
Nutribig premix[a]	147	148.5	147	148.5
Maize	98	99	98	99
Heat treated maize	49	49.5	49	49.5
Toasted Soybeans	41.5	42	41.5	42
Chicory pulp	24.5	24.2	24.5	24.2
Soybean oil	5	5	5	5
Synthetic amino acids and minerals[b]	4.5	4.5	4.5	4.5
Milk whey powder	20	10	0	0
Colostrum whey powder	0	0	20	10
Chemical composition, g/kg dry matter				
Dry matter, g/kg feed	869	871	867	870
Crude protein	182	183	194	189
Ether extract	35	34	34	34
Crude fiber	36	36	36	36
Starch	365	385	377	381
Ash	60	60	60	60
Lysine	9.7	9.3	10.1	9.3

[a]The premix (Roche Vitamins, Deinze, Belgium) is composed by 60 % of milk products, 12 % of oleaginous seeds, 10 % of cereal seeds by-products, 5 % of tuber and roots by-products and 12 % of minerals and vitamins (vitamins, minerals and amino acids supplied per kilogram of premix: vitamin A, 100 000 IU; vitamin D3, 13 000 IU; vitamin E, 335 mg; vitamin K3, 9 mg; vitamin B1, 13 mg; vitamin B2, 34 mg; vitamin B3, 100 mg; vitamin B6, 20 mg; vitamin C, 302 mg, vitamin PP, 200 mg; folic acid, 2 mg; choline, 2 163 mg; iron (as $FeSO_4$), 1,332 mg; copper (as $CuSO_4$), 1 100 mg; manganese (as $MnSO_4$), 400 mg; cobalt (as $CoSO_4$), 7 mg; zinc (as $ZnSO_4$), 1 583 mg; iodine (as CaI_20_6), 14 mg; selenium (as Na_2SeO_4), 3 mg; Ca, 39 586 mg; P, 8 584 mg; Na, 8 100 mg; L-lysine HCl, 16 240 mg; DL-methionine, 6 630 mg; L-threonine, 2 990 mg; L-tryptophan, 260 mg; lysine, 22 740 mg; methionine, 8 994 mg; threonine, 10 217 mg; tryptophan, 2 352 mg).
[b]Providing the following per kilogram of the complete diet (g): methionine, 0.25; lysine, 0.5; threonine, 0.5; tryptophan, 0.25; monocalcique phosphate, 3

Diet and whey analyses

The diets distributed during the trial were ground to pass a 1 mm screen (Cyclotec 1.093, Foss Tecator AB) before dry matter, ether extract, Kjeldahl N, crude fibre and ash analyses (AOAC 1990) were conducted. Samples from the 4 diets were also ground to pass a 0.5 mm screen for analyse of lysine (AccQ-Tag, Waters, Milford, MS, USA) and starch (adapted from FAISANT *et al.* 1995). The same analyses were performed on milk and bovine colostrum wheys. Additional analyses were conducted on both milk and colostrum wheys. IGF-I, IGF-II and insulin concentrations were determined with sandwich ELISA quantitation kits (Diagnostics Systems Laboratories, Assendelft, The Netherlands) according to the manufacturer's procedure. Total IgG and lactoferrin concentrations were measured by Sandwich ELISA (Bethyl laboratories, Montgomery, TX, USA) and reverse-phase HPLC (Shodex Asahipak C4P-50 4D column), respectively. The results of the analysis on the experimental diets and the wheys are presented in Tables 1 and 2, respectively.

Table 2
Chemical composition of the milk and colostrum wheys
Chemische Zusammensetzung der Milch- und Kolostrummolke

Composition, g/kg dry matter	Milk whey	Colostrum whey
Dry matter, g/kg powder	923	956
Crude protein	84	627
Ether extract	15	10
Ash	120	105
Lysine	4.9	43.4
IgG	2	496
Lactoferrin	<0.1	10.6
IGF-I	33 ng/g	2 500 ng/g
IGF-II	12 ng/g	25 ng/g
Insulin	<1 ng/g	<1 ng/g

Blood collection

Blood samples from the jugular vein were collected into dry tubes (Ref 368430, Becton Dickinson Benelux S.A., Erembodegem, Belgium). The day of weaning (day 0), blood was collected from one piglet of each litter. These animals were then excluded from the experiment. On days 7 and 21, half of the experimental piglets in each pen were blood sampled. The other half was sampled on the days 14 and 28. This method of sampling was used to minimise the effect of blood sampling on measured parameters.

Blood serum was separated by centrifugation at 1 000 × g for 15 min at 4 °C and then stored at –20 °C until analysis.

Hormone determination

T_3 and T_4 concentrations were determined in blood serum by RIA kits (DSL-3100 ACTIVE and DSL-3200 ACTIVE respectively, Diagnostic Systems Laboratories, Assendelft, The Netherlands) according to the manufacturer's procedure based on the presence of specific antibodies adhered to the internal surface of propylene tubes.

IGF-I was determined by RIA according to a method described by RENAVILLE *et al.* (1996). In this method, a cryoprecipitation step is used to eliminate aggregated proteins in the serum. Briefly, after acid-ethanol extraction (87.5 % ethanol and 12.5 % HCl mol l^{-1} v/v), an aliquot of the supernatant was neutralized with 0.855 mol Tris base l^{-1} at a ratio of 5:2. The samples were stored at –20 °C overnight and then centrifuged at 3 000 × g for 60 min at 4 °C. The supernatant was decanted into fresh test tubes and used in the RIA. The minimum detectable dose of IGF-I was 1 $ng.ml^{-1}$. Intra and inter-assay coefficients of variation were 12 % and 16 % respectively, for the low standard concentration (2.5 ng/mL) and 6.5 % and 9 %, respectively, for the high standard concentration (250 ng/mL).

Western ligand blotting was performed to evaluate serum IGFBP-2 and -3 concentrations according to a semi-quantitative method described in RENAVILLE *et al.* (1996). In short, 1 µl of SDS-denatured serum was applied to a 4 % stacking gel and electrophoresis was performed through a 12.5 % polyacrylamide gel. Prestained protein ladder (SM0671, Fermentas, Hanover, MD) was run in parallel lanes. The gels were then soaked in Towbin buffer (2.5

mmol Tris l^{-1}, 192 mmol glycine l^{-1}, 20 % (v/v) methanol, pH 8,3) and proteins were blotted onto nitrocellulose sheets (Hybond-C Extra, Amersham Biosciences, UK). Electrophoresis and electrotransfer were performed using the Mini-protean II system (Bio-Rad, Richmond, CA, USA). After saturation, membranes were incubated with ^{125}I-labelled rhIGF-I (see below iodination procedure; 4000 cpm cm^{-2} blot) overnight at 4 °C. The membrane were then washed, air-dried and exposed to Kodak BioMax XAR films (Eastman Kodak Company, Rochester, NY, USA) for 15 days at –70 °C. Autoradiograms were scanned and band intensities were analysed with Imagemaster 1D Prime (GE Healthcare, Diegem, Belgium). A serum pool was used as internal standard. Band intensity of the samples is expressed relatively to the intensity measured for the standard (% of standard).

Iodination procedure

Recombinant IGF (rhIGF-I, GroPep Limited, Adelaide, Australia) was used as iodinated trace and as RIA standard. The hormone was labeled with ^{125}I-Na using the lactoperoxidase method. ^{125}I-labeled rhIGF-I was separated from iodine using a Centricon Centrifugal Filter Devices with YM-3 membranes (Millipore Corporation, Bedford, MA, USA). The specific activity was 80 µCi $µg^{-1}$.

Statistical analyses

For the performance and feed intake data, there were four repeated measures. For the blood parameters analysis was separated in two groups of piglets with two replicates for each (day 7 and day 21 for the first half of the piglets and day 14 and day 28 for the second half of the piglets). Modelling of repeated records was done using the MIXED procedure of SAS (SAS Inst., Inc., Cary, NC, USA). Analysis of variance tested treatment (Control-Colostrum) by time (days post-weaning) interactions. Bodyweight at weaning of each piglet was added as covariable in the model for the blood parameters. Effects were compared using the CONTRAST statement in the repeated MIXED analysis. The pen was used as the experimental unit for ADFI and G/F. For all the other parameters, the animal was used as experimental unit.

Pearson Correlation coefficients were determined (CORR procedure) between the growth performances and the blood hormonal concentrations.

To evaluate the effect of weaning on the blood parameters, hormonal concentrations measured during our trial from day 7 to day 28 post-weaning were compared to the values recorded on naïve piglets on day 0 by Dunnett's test.

The values presented are lsmeans ± standard error (treatment × time). The differences were declared significant at $P<0.05$.

Results

Growth performance

The ADG, ADFI and G/F for the 4-week trial are presented in Table 3. The ADG was higher for the colostrum whey supplemented pigs compared to the Control piglets ($P<0.001$) during the first week of the trial. The next 3 weeks, the ADG were similar. Finally, the ADG calculated on the total experimental period was higher for the piglets supplemented with bovine

colostrum whey (*P*=0.02). The ADFI and G/F per pen (n=4) were greater during the first week of the trial for pigs fed the Colostrum treatment compared to that of pigs fed the Control diet (respectively *P*=0.03 and *P*=0.04). For the next 3 weeks and the entire 4-week trial, feed consumption and G/F were not affected by the experimental diet.

Table 3
Body weight (BW), average daily gain (ADG), average daily feed intake (ADFI) and feed efficiency (G/F) of piglets fed a commercial diet containing milk (Control) or bovine colostrum whey (Colostrum) for 4 weeks
Körpergewicht, tägliche Zunahme, Futteraufnahme und -verwertung in den vier Versuchswochen

	Treatments			
Measurements and days	Control	Colostrum	Standard error	Significance
BW, kg (n=48)				
0	8.34	8.33	0.19	ns
7	8.89	9.51	0.24	*
14	11.0	11.5	0.29	ns
21	14.0	14.5	0.35	ns
28	17.6	18.4	0.45	ns
Significance		Time × Treatment*** , Time***, Treatment^{ns}		
ADG, g/day (n=48)				
0 to 7	81	170	15.6	***
7 to 14	297	280	14.4	ns
14 to 21	430	434	17.6	ns
21 to 28	516	548	18.9	ns
0 to 28	330	361	11.3	*
Significance		Time × Treatment*** , Time***, Treatment*		
ADFI, g/day (n=4)				
0 to 7	256	346	38.5	*
7 to 14	497	495	35.8	ns
14 to 21	791	822	46.5	ns
21 to 28	974	992	76.2	ns
0 to 28	623	665	43.2	ns
Significance		Time × Treatment*** , Time***, Treatment^{ns}		
G /F, g/g (n=4)				
0 to 7	0.31	0.48	0.078	*
7 to 14	0.56	0.61	0.023	ns
14 to 21	0.55	0.52	0.038	ns
21 to 28	0.56	0.54	0.032	ns
0 to 28	0.53	0.54	0.029	ns
Significance		Time × Treatment^{ns} , Time***, Treatment^{ns}		

*P<0.05, ***P<0.001, ns not significant (P>0.05)

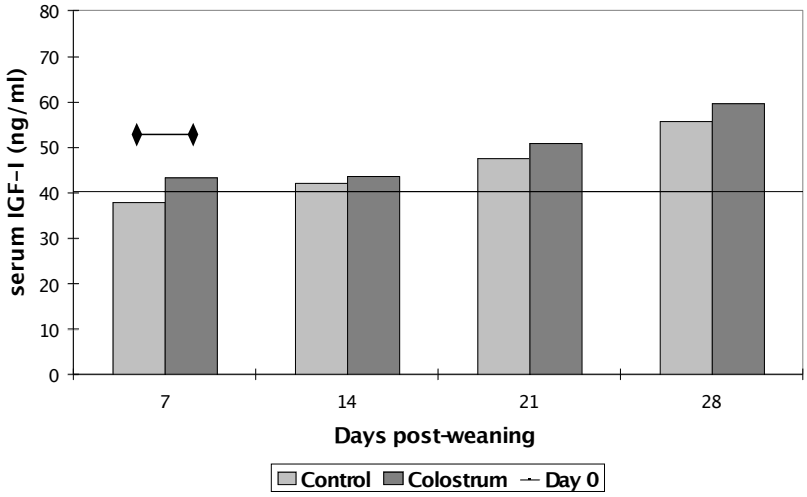
Hormonal concentrations

Figures 1, 2 and 3 represent the evolution of serum IGF-I, T_3 and T_4 concentrations during the trial. A line on each graphic represents the mean concentration measured at weaning.

IGF-I

On day 7 of the trial, the circulating IGF-I concentrations were increased by 15 % in the Colostrum-fed piglets compared to the Control treatment (P<0.05). However, the levels of

circulating IGF-I recorded in both treatments remained similar over all the trial to the mean concentration measured the day of weaning on littermates ($P>0.05$).



The horizontal line represents the mean IGF-I concentration in littermates the day of weaning (40.2 ± 8.7 ng/ml, n=15) (⧫——⧫: on the same day, mean concentrations of the two treatments are different, $P<0.05$).

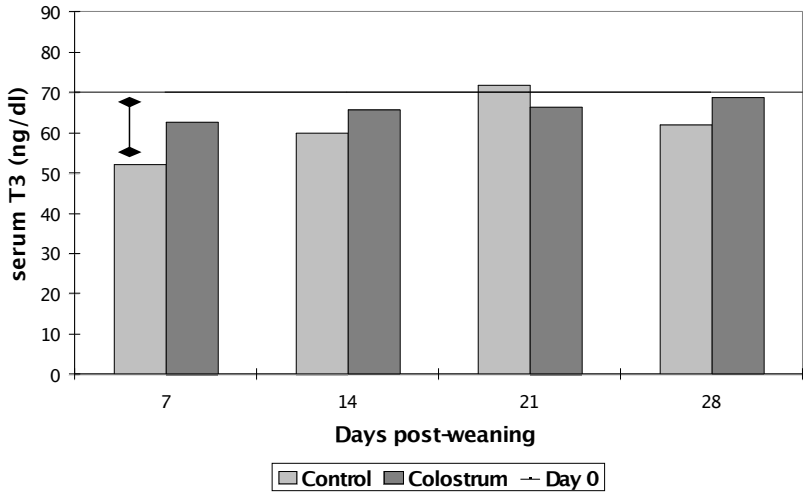
Figure 1
IGF-I concentrations in the blood serum of newly-weaned piglets fed a commercial diet containing milk (Control, n=24) or bovine colostrum whey (Colostrum, n=24) for 4 weeks
IGF-I Konzentration im Blutserum

IGFBP-2 and -3

No effect of the colostrum supplementation was observed on IGFBP-2 and -3 levels during our trial except on day 21 with a reduction of the IGFBP-2 concentration in the colostrum-fed piglets ($P<0.01$) (data not shown). Like for IGF-I, no effect of weaning was observed on the binding proteins (IGFBP-2 and -3, $P>0.05$).

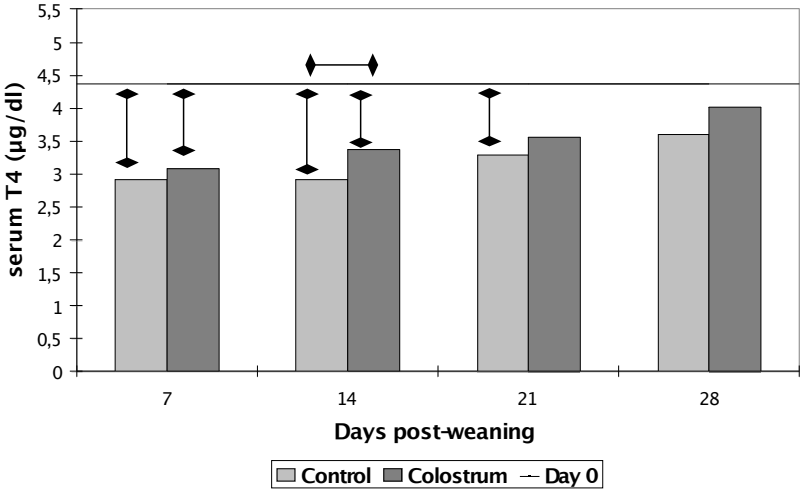
T_3 and T_4

The bovine colostrum supplementation had an effect on the thyroid response, with a higher level of circulating T_4 on day 14 of the trial for the colostrum-fed piglets compared to the Control treatment. The thyroid response was also influenced by weaning. It reduced temporarily ($P<0.05$) the levels of T_3 and T_4 in both groups of piglets compared to the mean concentration measured the day of weaning on littermates. For T_3, a decrease was only observed in the Control group on day 7 while for T_4 the initial level was recovered on day 21 for the Colostrum group and on day 28 for the Control group.



The horizontal line represents the mean T_3 concentration in littermates the day of weaning (70.2 ± 13.7 ng/dl, n=15) (↕:the concentration of the treated piglets is different of the mean concentration measured the day of weaning, $P<0.05$).

Figure 2
T_3 concentrations in the blood serum of newly-weaned piglets fed a commercial diet containing milk (Control, n=24) or bovine colostrum whey (Colostrum, n=24) for 4 weeks.
Thyroxidkonzentration (T_3) im Blutserum



The horizontal line represents the mean T_4 concentration in littermates the day of weaning (4.36 ± 1.0 µg/dl, n=15) (⧫——⧫: on the same day, mean concentrations of the two treatments are different, $P<0.05$. ↕: the concentration of the treated piglets is different of the mean concentration measured the day of weaning, $P<0.05$).

Figure 3
T_4 concentrations in the blood serum of newly-weaned piglets fed a commercial diet containing milk (Control, n=24) or bovine colostrum whey (Colostrum, n=24) for 4 weeks.
Thyroxidkonzentration (T_4) im Blutserum

Correlations

A positive correlation was established between circulating IGF-I concentrations and BW (r=0.50, $P<0.0001$) and between IGF-I and ADG (r=0.55, $P<0.0001$). For IGFBP-3 the correlations with BW and ADG are 0.46 and 0.49, respectively ($P<0.0001$), but no correlation between growth of the piglets and IGFBP-2 was observed. Finally, thyroid hormones T_3 and T_4 are correlated with BW (0.17 ($P<0.05$) and 0.27 ($P<0.001$), respectively) and ADG (both 0.26, $P<0.001$).

Discussion

The inclusion of bovine colostrum whey in the weaning diet improved growth performance, feed intake and feed efficiency (respectively by 100, 30 and 50 %) the first week after weaning compared to the control piglets. These results agree with literature (see BOUDRY *et al.* 2008 for a review).

Concomitantly with the increase in growth performance and feed consumption, an increase in serum IGF-I was observed during the first week post-weaning. Insulin-like growth factor-I is a potent growth factor that has been associated with a wide range of anabolic processes. It has been shown to stimulate proliferation, differentiation and numerous other cellular functions in many different tissues (SIMMEN *et al.* 1998, RENAVILLE *et al.* 2002). Consequently, IGF-I is believed to be important in the regulation of growth and development (OWENS *et al.* 1999, DONOVAN *et al.* 2004, NEBDAL *et al.* 2000). The positive correlation between circulating IGF-I and the growth rate of our piglets confirms this.

CARROLL *et al.* (1998) showed a decrease in piglet serum IGF-I levels the first days after weaning. They associated this reduction in IGF-I with the underfeeding at weaning since BUONOMO and BAILE (1991) observed that fasting induces a decrease of blood IGF-I levels in pigs. In fact, CLEMMONS and UNDERWOOD (1991) showed that the nutritional status exerts a direct influence on circulating IGF-I, with blood IGF-I being closely related to the energy intake. Thus, during the first week of our experiment, the increase of serum IGF-I in the colostrum treatment is at least partly explained by the higher feed ingestion reported for this treatment over the same period.

Only two studies on bovine colostrum supplementation in newly-weaned piglet diet with measure of circulating IGF-I and controlled ingestion were found. LE HUEROU-LURON *et al.* (2003), showed an increase in circulating IGF-I for colostrum-fed piglets weaned at 7 days of age. While HUGUET *et al.* (2006) didn't highlight any effect of bovine colostrum on the ADG and the plasma IGF-I concentrations in 21 day-old weaned piglets. In this last study, the same amount of feed was distributed to the control and colostrum-fed piglets but unexpectedly the consumption of colostrum-fed piglets was lower than for the control piglets. From these results, it seems that bovine colostrum may induce an increase of circulating IGF-I independently of the feed consumption, however, a new study, with limited feed ingestion, is necessary to confirm this.

Like reported by others (ELFSTRAND *et al.* 2002), we measured a high level of IGF-I in the bovine colostrum powder used in the present study (2 500 ng/g). Considering the homology between the bovine and porcine IGF-I amino acid sequence (TAVAKKOL *et al.* 1988), one explanation for the increased circulating IGF-I level in the colostrum-fed piglets would be

the assimilation of colostral IGF-I. However, according to findings of others (DE RODAS 1995, DONOVAN 1997), this suggestion was dismissed. First of all, even if the content in IGF-I in bovine colostrum is very high compared to the other feedstuffs of the piglet diet, our colostrum-fed piglets received approximately 2 µg of IGF-I/kg of BW per day during the first week post-weaning. This concentration was probably too low to increase significantly circulating IGF-I as DE RODAS *et al*. (1995) observed no effects on circulating IGF-I by administrating 8 µg of IGF-I/kg BW per day to 26 day-old weaned piglets. Moreover, DONOVAN *et al*. (1997) showed that orally administered IGF-I does not contribute significantly to circulating IGF-I concentrations of the neonatal piglet.

Even if the colostral IGF-I were probably not absorbed and had a limited systemic effect, it is likely that they had a local action within the intestine. MORGAN *et al*. (1996) demonstrated the presence of IGF-I receptors throughout the 28 day-old weaned piglet intestine. The colostral IGF-I may thus exert their biological function in the intestine of the weaned piglet, e.g. gut growth and development (expression of brushborder enzymes) (MORGAN *et al*. 1996). In their studies, HUGUET *et al*. (2006 and 2007) and KING *et al*. (2007 and 2008) reported a beneficial effect of bovine colostrum on the intestinal mucosa integrity. These effects on the intestinal structure may increase the nutrient intake and perhaps partly explain the higher feed efficiency observed in the Colostrum treatment.

Another growth factor present in bovine colostrum which is implicated in circulating IGF-I is the GH. Treatment of growing pig with this hormone was reported to elevate serum IGF-I and IGFBP-3 and depress IGFBP-2 concentrations (ETHERTON 2004). We didn't measure the level of GH in the bovine colostrum powders used in the present studies but according to SCAMMEL (2001), it is very low (<1 µg/l), meaning that our colostrum-fed piglets received less than 1 ng of GH/kg BW per day during the first week of the present study. The lowest levels found in the literature with an effect on circulating IGF-I is 35 µg/kg of BW per day to growing pigs (about 60 kg) (COLEMAN *et al*. 1994). Moreover, according to DUNSHEA *et al*. (1999) and RYBARCZYK *et al*. (2007), the response to GH is much lower in young piglets.

The fact that IGF-I/IGFBP complexes account for virtually all the circulating IGF-I in growing pigs, suggests that the increase in serum IGF-I is due in part to the effect of bovine colostrum on serum IGFBPs. However, in the present study, the effects of bovine colostrum observed on the IGF-I during the first week of the trial were not observed on their binding proteins. It is possible that changes in IGF-I levels are detected earlier than changes in IGFBP-2 and -3 because the IGF-I RIA is more sensitive than the 125I-IGF ligand blots used to detect IGFBP-2 and -3 (HATHAWAY *et al*. 2003). The reduction in IGFBP-2 levels on day 21 for the best growing group (colostrum treatment) is in accordance with the results of NEBDAL *et al*. (2000) who showed in a transgenic mouse model that IGFBP-2 is a potent inhibitor of skeletal muscle growth.

The circulating thyroid hormones (T_3 and T_4) were decreased by weaning in our trial. This may be due to the low feed intake the first week post-weaning as SAGGAU *et al*. (2000) and WIECEK *et al*. (2010) showed that a period of limited feed supply is paralleled by a low level of thyroid hormones. This permits the body to spare energy by reducing basal metabolic rate (HORNICK *et al*. 2000). Pre-weaning levels of T_3 and T_4 are recovered respectively 1 and 3 weeks after weaning for the colostrum-fed piglets while in the control diets they are recovered after 2 weeks for T_3 and 4 weeks for T_4. Thus, it is possible that bovine colostrum, by inducing

a higher feed intake, allowed a faster recovery of T_3 and T_4 circulating concentrations than the Control treatment. The delayed response of T_4 may be explained by a lower and slower response of this hormone to nutritional changes compared to T_3 (BUONOMO and BAILE 1991).

The decrease in thyroid hormones may contribute to the reduction of circulating IGF-I levels as they exert permissive actions on IGF-I synthesis and receptor binding. They stimulate IGF-I synthesis in the liver and potentiate the effects of GH and IGF-I synthesis (RAJARAM *et al*. 1997).

From this study, we may conclude that the physiological effects of bovine colostrum supplementation on the hormonal response of the newly weaned piglet are, at least in part, consequent of the positive action of bovine colostrum on feed intake and can be one of the explanations (with the better feed efficiency) of the higher growth performance.

Practical implications for animal nutrition

The results of this study demonstrate that bovine colostrum has a high growth promoting activity during the first days post-weaning: its introduction in the diet at a level of 2 % induces significant increases in food intake and growth performance of the piglets. This observation is really of great importance for pig producers as many problems are still associated to weaning in the modern pig husbandry, such as growth depression and occurrence of diarrhea (VAN BEERS-SCHREURS and BRUININX 2002).

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