Effects of Dietary Chitosan Oligosaccharide Supplementation in Peripartum Sows on Immune Function of Sows and Piglets and Sow Gut Microbiota: Postprint

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Date: 2018-12-25T00:00:00+00:00

Abstract

This experiment aimed to investigate the effects of dietary chitosan oligosaccharide (COS) supplementation in periparturient sows on immune function of sows and piglets, as well as gut microbiota of sows. Forty healthy Yorkshire gestating sows with similar body weight, backfat thickness, parity, and expected farrowing date were selected and randomly allocated into 2 groups with 20 replicates per group and 1 sow per replicate. The control group was fed a basal diet, while the experimental group was fed a test diet supplemented with 30 mg/kg COS in the basal diet. The experimental period lasted from day 90 of gestation to day 7 postpartum. The results showed that: 1) COS supplementation in periparturient sow diets had no significant effects on sow farrowing duration, total litter size, number of live-born piglets, litter birth weight, or average piglet birth weight ($P > 0.05$). 2) COS supplementation significantly increased the contents of immunoglobulin G (IgG), immunoglobulin A (IgA), and interleukin-6 (IL-6) in sow serum ($P < 0.05$), while having no significant effects on serum immunoglobulin M (IgM), interleukin-2 (IL-2), and tumor necrosis factor- (TNF-) contents ($P > 0.05$). 3) COS supplementation significantly increased IgG, IL-2, and IL-6 contents in sow colostrum ($P < 0.05$), with no significant effects on IgA, IgM, and TNF- contents ($P > 0.05$). 4) COS supplementation significantly increased IL-2 and IL-6 contents in serum of newborn piglets ($P < 0.05$), and significantly decreased serum IgA content ($P < 0.05$). 5) COS supplementation significantly reduced the number of Salmonella in sow feces ($P < 0.05$), and tended to decrease the number of Escherichia coli in feces ($P < 0.10$). In conclusion, dietary COS supplementation in periparturient sows can improve sow gut health, increase the number of live-born piglets to a certain extent, and significantly enhance immune function of sows and newborn piglets.

Full Text

Effects of Dietary Chito-Oligosaccharide Supplementation for Perinatal Sows on Immune Function of Sows and Piglets, and Intestinal Microorganisms of Sows

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Abstract

This experiment was conducted to investigate the effects of dietary chito-oligosaccharide (COS) supplementation for perinatal sows on immune function in sows and newborn piglets, as well as on intestinal microorganisms in sows. Forty healthy Yorkshire gestating sows with similar body weight, backfat thickness, parity, and expected farrowing date were randomly allocated into two groups, each comprising 20 replicates with one sow per replicate. Sows in the control group received a basal diet, while those in the experimental group received the basal diet supplemented with 30 mg/kg COS. The experimental period spanned from day 90 of gestation to day 7 postpartum. The results demonstrated that: (1) dietary COS supplementation for perinatal sows had no significant effects on farrowing duration, total number of piglets born, number of piglets born alive, litter birth weight, or average birth weight of piglets ($P > 0.05$); (2) COS supplementation significantly increased serum immunoglobulin G (IgG), immunoglobulin A (IgA), and interleukin-6 (IL-6) concentrations in sows ($P < 0.05$), while showing no significant effects on serum immunoglobulin M (IgM), interleukin-2 (IL-2), or tumor necrosis factor- (TNF-) concentrations ($P > 0.05$); (3) COS supplementation significantly elevated IgG, IL-2, and IL-6 levels in sow colostrum ($P < 0.05$), with no significant effects on colostral IgA, IgM, or TNF- concentrations ($P > 0.05$); (4) COS supplementation significantly increased serum IL-2 and IL-6 concentrations in newborn piglets ($P < 0.05$) while significantly decreasing serum IgA concentration ($P < 0.05$); (5) COS supplementation significantly reduced fecal Salmonella populations in sows ($P < 0.05$) and tended to decrease fecal Escherichia coli populations ($P < 0.10$). In conclusion, dietary COS supplementation for perinatal sows can improve sow intestinal health, modestly increase the number of piglets born alive, and significantly enhance immune function in both sows and newborn piglets.

Keywords: chito-oligosaccharide; immunity; perinatal period; sows; piglets

The perinatal period represents a particularly unique and critical phase in the sow reproductive cycle, characterized by two major aspects: first, sows experience extreme physical exhaustion and intense pain during farrowing and the immediate postpartum period; second, dramatic fluctuations in cortisol and estrogen levels before and after parturition lead to reduced numbers of lymphocytes and active monocytes, significantly impacting immune function and resulting in decreased disease resistance [1–5]. Concurrently, the perinatal period constitutes the primary timeframe for piglet mortality. Due to incomplete development of tissues, organs, and immune systems, neonatal piglets exhibit poor adaptability, with the majority of pre-weaning deaths occurring within the first three days after birth. Key factors contributing to neonatal piglet mortality include birth weight, birth order, timing of colostrum intake, and hypothermia within the first hour postpartum [6]. Since the immune system of newborn piglets is not fully developed, they must acquire passive immunity through absorption of immunoglobulin G (IgG) from colostrum [7]. Maternal milk serves as the decisive factor for survival and growth of suckling piglets, directly influencing their viability, growth, development, and body composition [8]. Colostrum is the milk secreted by sows during the final stage of pregnancy and the first few hours postpartum. Its rich natural growth factors are essential for normal development of the brain, heart, pancreas, liver, kidneys, and immature intestines, while its high immunoglobulin content can be completely absorbed by the jejunum and ileum of piglets within hours after birth, establishing passive immunity for suckling piglets [9–10]. Within hours after parturition, milk composition undergoes significant changes as colostrum transitions to mature milk, with decreases in solids and protein content and increases in lactose and fat content, accompanied by a marked reduction in immunoglobulin concentration. Consequently, mature milk primarily serves nutritional functions, with immune protection being secondary [9–10]. Perinatal sow nutrition critically impacts piglet health, and enhancing sow immunity and improving milk quality represent important strategies for reducing suckling piglet mortality, maintaining piglet health status, improving piglet performance, and increasing sow reproductive efficiency [11].

Chito-oligosaccharide (COS) is a natural alkaline polymer of glucosamine obtained through chemical and enzymatic hydrolysis of chitosan [12]. COS is readily absorbed and exhibits biological activities tens of times more potent than chitosan. Dietary COS supplementation can promote animal growth and enhance immunity, demonstrating various physiological functions including immunomodulatory, lipid-lowering, and anti-cancer effects in animals [13]. COS has been confirmed to improve growth performance in weaned piglets, likely related to its immune-enhancing, gut microbiota-modulating, and intestinal morphological and functional improvements [14–18].

Current research on COS has primarily focused on weaned piglets, with no reports investigating its effects on immune function in perinatal sows. The

objective of this study was to explore whether COS could modulate the immune status of perinatal sows and further enhance immunity in suckling piglets, thereby improving piglet survival rates.

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1. Materials and Methods

1.1. Experimental Material The COS used was water-soluble chitooligosaccharide [oligo- -(1-4)-2-amino-2-deoxy-D-glucose] with a degree of polymerization of 2–10 and purity of 10%, provided by Dalian Zhongke Glucan Biotechnology Co., Ltd.

1.2. Experimental Animals and Design Forty Yorkshire sows at day 90 of gestation, with similar parity (3rd or 4th parity) and body weight [(300 ± 15) kg], were randomly divided into two groups, each containing 20 replicates with one sow per replicate. The basal diet was a corn-soybean meal-based diet formulated according to NRC (2012) [19], with composition and nutrient levels shown in Table 1 . The control group received the basal diet, while the experimental group received the basal diet supplemented with 30 mg/kg COS (calculated as pure COS based on 10% purity).

During the experimental period, sows were fed at 07:30 and 15:00 daily. From gestation day 90 to 1–2 days before parturition, each sow received 3.0 kg/d. Sows were transferred to farrowing crates on day 3 prepartum, with slatted floors in both sow and piglet areas and piglet heating boxes provided. Feed intake was reduced to 2.0 kg/d on days 1–2 prepartum, with no feeding on the day of parturition. Postpartum feeding levels were: day 1, 1.0 kg/d; day 2, 2.0 kg/d; day 3, 3.0 kg/d; and days 4–7, 4.0 kg/d, with free access to water. The experiment was conducted from gestation day 90 to day 7 postpartum at Zhangzhou Aonong Modern Agricultural Development Co., Ltd., Fujian Province, following strict biosecurity and management protocols.

1.3. Sample Collection 1.3.1. Sow Reproductive Performance Data Collection

At farrowing, the birth time and individual birth weight (kg) of each piglet were recorded.

1.3.2. Colostrum Collection

At 2 h postpartum, mixed colostrum samples (15 mL per sow) were collected from three teats in the anterior, middle, and posterior mammary regions into sterile EP tubes and stored at -20 °C until analysis. Prior to analysis, samples were centrifuged at 12,000 r/min for 10 min to remove milk fat.

1.3.3. Blood Collection from Sows and Piglets

On the day of parturition, umbilical cord blood was collected from nine piglets per sow and pooled into three samples by mixing equal volumes from three piglets with similar birth times (3 mL per piglet, 9 mL per pooled sample). On day 8 postpartum, fasting sows were bled via the anterior vena cava to collect 10 mL of blood. All blood samples were allowed to clot at 4 °C for 30 min, then centrifuged at 3,500 r/min for 15 min to harvest serum, which was aliquoted into 1.5 mL tubes and stored at -20 °C until analysis.

1.3.4. Fecal Collection from Sows

Fresh sow feces were collected between 07:00 and 09:00 on day 8 postpartum, placed in sterile bags, and stored at -20 °C until analysis.

1.4. Measurements 1.4.1. Sow Reproductive Performance Indicators

Farrowing duration (time interval from birth of first piglet to expulsion of placenta), total number of piglets born, number of piglets born alive, litter birth weight (sum of individual live piglet birth weights), and average piglet birth weight (litter birth weight divided by number of piglets born alive) were calculated from recorded birth times and individual piglet weights.

1.4.2. Immune-Related Indicators in Sow Serum, Colostrum, and Piglet Serum

Enzyme-linked immunosorbent assay (ELISA) kits purchased from Nanjing Jiancheng Bioengineering Institute were used to determine IgG, IgM, IgA, IL-2, IL-6, and TNF- concentrations in sow serum and colostrum and piglet serum, following the manufacturer' s protocols.

1.4.3. Fecal pH Measurement

Fresh fecal samples (5 g) were diluted with 45 mL sterile saline, and pH was measured using a pH meter.

1.4.4. Fecal Microbial Counting

Sample Dilution: Approximately 4 g of feces was aseptically transferred to a sterile flask, mixed with appropriate volumes of sterile saline to achieve 10-fold dilutions, and homogenized using a magnetic shaker for 10 min to obtain 10^{1} dilution. Subsequently, 0.5 mL of the 10^{1} dilution was transferred to 4.5 mL sterile saline to produce 10^{2} dilution, and this process was repeated to generate 10^{3}, 10 , and 10 dilutions.

Inoculation and Incubation: For *Lactobacillus* counting, 0.01 mL of 10^{2} to 10 dilutions was plated onto MRS agar in duplicate and incubated anaerobically at 37 °C for 48 h before colony counting. For *Escherichia coli* counting, 0.01 mL of 10^{3} to 10 dilutions was plated onto MacConkey agar in duplicate and incubated aerobically at 37 °C for 24 h. For *Salmonella* counting, 0.01 mL of 10^{3}

to 10 dilutions was plated onto SS agar in duplicate and incubated aerobically at 37 °C for 24 h.

1.4.5. Fecal Acetate and Propionate Content Determination

Sample Preparation: Approximately 10 g of feces was placed in a 100 mL beaker with 40 mL water and 2 mL of 50% NaOH solution, heated in a steam bath for 10 min, cooled, and pH adjusted to 2 using 1:1 sulfuric acid. The solution was transferred to a 100 mL volumetric flask, diluted to volume with Milli-Q water, filtered through a Spartan 30/A 0.2 m filter, and collected in a screw-cap vial. A 10 L aliquot was injected into an Agilent 1260 Infinity HPLC system for acetate and propionate quantification.

Standard Preparation: Standards containing 0.05 g each of acetate and propionate (weighed to 0.01 g precision) were prepared identically to samples and analyzed by HPLC.

1.5. Statistical Analysis Data were initially processed using Excel 2010. Inter-group differences were analyzed using t-tests in SPSS 19.0 software, with $P < 0.05$ considered statistically significant and $P < 0.10$ indicating a significant trend. Results are expressed as means ± standard error.

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2. Results

2.1. Effects of Dietary COS on Sow Reproductive Performance As shown in Table 2 , dietary COS supplementation for perinatal sows had no significant effects on farrowing duration, total number of piglets born, number of piglets born alive, litter birth weight, or average piglet birth weight ($P > 0.05$). Compared with the control group, COS supplementation increased farrowing duration by 5.9%, total number of piglets born by 4.7%, number of piglets born alive by 2.7%, and litter birth weight by 3.3%, while average piglet birth weight remained unchanged.

Table 2. Effects of dietary COS for perinatal sows on reproductive performance of sows (n = 20)

Item	Control group	Experimental group	P-value
Farrowing duration (h)	4.39 ± 0.41	4.65 ± 0.60	0.72
Total number of piglets born	16.47 ± 1.09	17.24 ± 1.11	0.63
Number of piglets born alive	14.89 ± 0.95	15.29 ± 0.99	0.76
Live born litter weight (kg)	17.51 ± 0.95	18.08 ± 1.17	0.71
Born individual weight (kg)	1.20 ± 0.04	1.20 ± 0.05	0.98

In the same row, values with different small letter superscripts indicate significant difference ($P < 0.05$), while values without superscripts indicate no

significant difference (P > 0.05). The same applies below.

2.2. Effects of Dietary COS on Sow Serum Immune Parameters As presented in Table 3 , dietary COS supplementation for perinatal sows significantly increased serum IgG, IgA, and IL-6 concentrations (P < 0.05), while showing no significant effects on serum IgM, IL-2, or TNF- concentrations (P > 0.05).

Table 3. Effects of dietary COS for perinatal sows on serum immune indicators of sows (n = 20)

Item	Control group	Experimental group	P-value
IgG (mg/mL)	8.96 ± 1.00	13.62 ± 1.60	0.03
IgA (mg/mL)	1.93 ± 0.23	3.01 ± 0.26	0.01
IgM (mg/mL)	4.18 ± 0.37	4.71 ± 0.50	0.42
IL-2 (ng/L)	30.74 ± 2.73	33.13 ± 3.22	0.58
IL-6 (ng/L)	34.28 ± 3.58	54.33 ± 6.09	0.01
TNF- (ng/L)	64.70 ± 6.03	72.74 ± 8.09	0.45

2.3. Effects of Dietary COS on Sow Colostrum Immune Parameters As shown in Table 4 , dietary COS supplementation for perinatal sows significantly increased colostral IgG, IL-2, and IL-6 concentrations (P < 0.05), while showing no significant effects on colostral IgA, IgM, or TNF- concentrations (P > 0.05).

Table 4. Effects of dietary COS for perinatal sows on colostrum immune indicators of sows (n = 20)

Item	Control group	Experimental group	P-value
IgG (mg/mL)	2.73 ± 0.37	8.92 ± 1.99	0.01
IgA (mg/mL)	0.87 ± 0.12	1.12 ± 0.18	0.27
IgM (mg/mL)	2.39 ± 0.49	1.80 ± 0.27	0.29
IL-2 (ng/L)	9.75 ± 1.43	16.27 ± 2.57	0.04
IL-6 (ng/L)	32.27 ± 3.41	43.05 ± 3.73	0.04
TNF- (ng/L)	32.16 ± 5.33	31.55 ± 4.41	0.93

2.4. Effects of Dietary COS on Newborn Piglet Serum Immune Parameters As indicated in Table 5 , dietary COS supplementation for perinatal sows significantly increased serum IL-2 and IL-6 concentrations in newborn piglets (P < 0.05) and significantly decreased serum IgA concentration (P < 0.05), while showing no significant effects on serum IgG, IgM, or TNF- concentrations (P > 0.05).

Table 5. Effects of dietary COS for perinatal sows on serum immune indicators of neonatal piglets (n = 20)

Item	Control group	Experimental group	P-value
IgG (mg/mL)	1.87 ± 0.26	1.86 ± 0.13	0.97
IgA (mg/mL)	0.35 ± 0.06	0.18 ± 0.04	0.03
IgM (mg/mL)	1.20 ± 0.22	1.06 ± 0.08	0.56
IL-2 (ng/L)	5.31 ± 0.75	8.07 ± 0.66	0.02
IL-6 (ng/L)	6.88 ± 0.78	9.54 ± 0.38	0.01
TNF- (ng/L)	12.91 ± 2.41	14.34 ± 1.90	0.64

2.5. Effects of Dietary COS on Sow Fecal pH and Microbial Populations As presented in Table 6 , dietary COS supplementation for perinatal sows significantly reduced fecal Salmonella populations ($P < 0.05$) and tended to decrease fecal E. coli populations ($P < 0.10$), while showing no significant effects on fecal pH or Lactobacillus populations ($P > 0.05$).

Table 6. Effects of dietary COS for perinatal sows on fecal pH and microbial population of sows (n = 20)

Item	Control group	Experimental group	P-value
Lactobacilli [log (CFU/g)]	6.67 ± 0.09	6.80 ± 0.10	0.34
Escherichia coli [log (CFU/g)]	6.13 ± 0.17	5.85 ± 0.22	0.09
Salmonella [log (CFU/g)]	7.14 ± 0.15	5.91 ± 0.11	0.01
Fecal pH	6.44 ± 0.18	6.59 ± 0.08	0.48

2.6. Effects of Dietary COS on Sow Fecal Acetate and Propionate Contents As shown in Table 7 , dietary COS supplementation for perinatal sows had no significant effects on fecal acetate or propionate concentrations ($P > 0.05$).

Table 7. Effects of dietary COS for perinatal sows on fecal acetate and propionate contents of sows (n = 20)

Item	Control group	Experimental group	P-value
Acetate	11.68 ± 0.40	11.49 ± 0.48	0.76
Propionate	4.28 ± 0.33	3.88 ± 0.33	0.40

3. Discussion

The present results indicate that dietary supplementation with 30 mg/kg COS during the perinatal period (from day 90 of gestation to day 7 postpartum) had no significant effects on farrowing duration, total number of piglets born, number of piglets born alive, litter birth weight, or average piglet birth weight. Long et al. [21] similarly reported that supplementing sow diets with 30 mg/kg COS during late gestation (from day 85 of gestation to farrowing) did not significantly affect reproductive performance, though it tended to shorten farrowing duration. In contrast, Cheng et al. [22] found that supplementing sow diets with 40 mg/kg COS throughout the reproductive period (from mating to weaning at day 21 postpartum) significantly improved total number of piglets born, number of piglets born alive, litter birth weight, and average piglet birth weight. These three studies yielded different results regarding sow reproductive performance. Our feeding protocol and results align closely with those of Long et al. [21] but differ somewhat from Cheng et al. [22], possibly due to differences in supplementation timing. Reportedly, 40% of embryonic mortality in pregnant sows occurs before day 20 of gestation [23], which represents the most critical determinant of litter size. Both Long et al. [21] and the current study initiated COS supplementation during late gestation (days 85–90), whereas Cheng et al. [22] began supplementation at mating. Therefore, COS supplementation during early gestation may enhance reproductive performance, whereas supplementation limited to late gestation shows no significant effects. The influence of COS on reproductive performance may be related to its immune-enhancing properties.

Farrowing is controlled by complex physiological and endocrine activities and represents a process of extreme fatigue, intense pain, and various metabolic disorders [23]. During the perinatal period, most animals exhibit increased disease incidence, likely due to increased susceptibility to pathogens resulting from compromised immunity. Dramatic fluctuations in cortisol and estrogen levels before and after parturition have been confirmed to affect the immune system. The number of monocytes and immunoglobulin-producing monocytes in gilt blood decreases significantly during farrowing, with immunoglobulin levels showing high correlation with cortisol concentrations [4,24]. Consequently, perinatal sow immunity is markedly reduced. Studies have demonstrated that oligosaccharides can modulate blood immunoglobulin concentrations [25]. Huang et al. [26] investigated COS effects in broilers and found that dietary supplementation with 100 mg/kg COS promoted immune organ development and significantly increased blood immunoglobulin concentrations, indicating COS can enhance broiler immunity. Dang et al. [27] studied COS effects in weaned piglets and observed that 50 mg/kg COS supplementation significantly increased blood IgG, IgA, IgM, and TNF- concentrations while decreasing IL-6 levels. Both in vitro and in vivo studies have shown that COS exhibits potent immune-activating properties by activating macrophage Toll-like receptor-4 (TLR4) [28]. Our results demonstrate that 30 mg/kg COS supplementation during the perinatal

period significantly increased sow serum IL-6 concentration, suggesting that COS activated macrophages in sows, leading to increased cytokine secretion. Macrophages can activate B cells through helper cells to generate responses [29]. The observed significant increases in sow serum IgG and IgA concentrations may result from COS activation of B cells via macrophages.

Brambell [30] reported that neonatal cattle, goats, sheep, horses, donkeys, and pigs have low or absent maternal antibody levels and primarily acquire maternal antibodies through ingestion of colostrum within the first few hours postpartum. In our study, immune parameter concentrations were highest in sow serum, intermediate in colostrum, and lowest in piglet umbilical cord blood (approximately one-fifth of sow serum concentrations). Minimal immunoglobulin transfer occurs across the placenta between sows and piglets; instead, large quantities are transferred across the mammary barrier into colostrum during the initiation of lactation. Our results show that 30 mg/kg COS supplementation improved immune parameters in sow serum and colostrum (colostral IgM and TNF- concentrations decreased slightly but not significantly), consistent with trends observed in sow serum. In piglet umbilical cord blood, IL-2, IL-6, and TNF- concentrations mirrored trends in sow serum and colostrum, whereas IgG, IgA, and IgM concentrations decreased. The differential responses of immunoglobulin concentrations in sow serum, colostrum, and piglet cord blood to COS supplementation reaffirm that immunoglobulin transfer between sows and piglets occurs primarily through colostrum and that enhanced sow immunity through COS supplementation can be transferred via colostrum.

Kong et al. [31] reported that 500 mg/kg COS supplementation in weaned piglets significantly increased Lactobacillus populations in the ileum and colon while reducing colonic E. coli populations. Yang et al. [15] found that 200–600 mg/kg COS supplementation in weaned piglets significantly increased cecal Lactobacillus populations and decreased E. coli populations on day 7 post-weaning. Our results show that 30 mg/kg COS supplementation during the perinatal period significantly reduced fecal Salmonella populations and tended to decrease E. coli populations in sows, with no significant effects on fecal pH or Lactobacillus populations. Differences between our findings and previous studies may be related to COS dosage and animal model. Overall, COS demonstrates beneficial effects on gut microbiota in animals.

4. Conclusion

Dietary COS supplementation for perinatal sows (from day 90 of gestation to day 7 postpartum) can improve sow intestinal health, modestly increase the number of piglets born alive, and significantly enhance immune function in both sows and newborn piglets.

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Note: Figure translations are in progress. See original paper for figures.