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Neonatal oxytocin administration and supplemental milk ameliorate the weaning transition and alter hormonal expression in the gastrointestinal tract in pigs

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ABSTRACT

The aim of this study was to investigate the influences of milk supplementation during lactation, over 1 wk after weaning, and oxytocin administration for the first 14 d of life on the pigs' response to weaning. Pigs from 20 litters were allocated to each of these 3 treatments in a randomized factorial design. Oxytocin was administered subcutaneously daily from 0 to 14 d of age at a rate of 10 I.U. per kg. The milk supplement consisted of a mixture of 25% skim milk powder offered either during lactation between 10 and 20 d of age or for the first week after weaning as a transitional diet along with dry pellets. Pigs were weaned at 21 d of age. Growth rate was measured from birth to slaughter at 140 d of age and feed intake of supplemental milk or feed from 10 to 56 d of age. Organ weights (heart, liver, stomach, and kidneys) and the gene expression of ghrelin, leptin, and glucagon-like peptides (glucagon-like peptide-1 and glucagon-like peptide-2) were measured in the stomach, ileum, and duodenum at 10, 21, and 28 d of age. Milk supplementation after weaning resulted in immediate feed intake and partially alleviated the depression in growth rate over the first 7 d postweaning ($P < 0.001$), but milk supplementation during lactation had no effects ($P > 0.1$). However, effects were only transient and disappeared once the milk liquid diet was removed. Neonatal oxytocin administration reduced weight loss over the first 2 d after weaning ($P = 0.03$), without affecting feed intake ($P > 0.1$), hence possibly reducing weaning stress. Seven days after weaning, oxytocin-treated pigs had greater stomach ghrelin and leptin expression (both $P = 0.02$), and pigs supplemented with milk after weaning had greater stomach leptin and glucagon-like peptide-2 expression ($P = 0.02$ and $P = 0.05$, respectively). Hence, neonatal oxytocin administration or postweaning milk supplementation are both effective means of enhancing gastric leptin expression and reducing weight loss at weaning, likely improving gut health during this critical period.

1. Introduction

Neonatal mammals rely on their dam for survival, through protection and the provision of food. Weaning occurs gradually in natural conditions. For feral pigs, weaning takes between 8 and 19 wk to complete [1]. This time allows the young pig to mature in its digestive and absorptive capacities and in its ability to cope with environmental challenges. However, in commercial pig production, weaning usually occurs abruptly between 3 and 4 wk of age, and the separation of piglets from the dam is usually associated with changes in their diet, physical, and social environments. These result in nutritional, thermal, immunological, and psychological challenges [2,3]. Weaning is therefore a multifactorial stressor for pigs and is

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generally associated with weight loss and increased morbidity and mortality reflective of the pigs' difficulty in coping with this challenge [4].

A variety of strategies have been attempted to facilitate the weaning transition on the pig, mostly aimed at alleviating the postweaning growth lag. Dry pelleted feed is the standard diet form given to newly weaned pigs on most farms and represents an abrupt change from the highly digestible and palatable nutrients piglets' receive from milk. Studies have shown that specific feeding regimes, such as supplementing piglets with milk during lactation [5–7] or into the early postweaning period while gradually introducing a dry pelleted feed [6,8–10], can alleviate weight loss and improve indices of gastrointestinal tract structure and function in the postweaning period.

Hormonal interventions, such as oxytocin, a mammalian peptide, could also facilitate weaning. In rats, repeated oxytocin administration induces long-lasting metabolic and physiologic changes such as increased growth [11,12], decreased corticosterone concentrations, and levels of plasma gastrin, cholecystokinin, and insulin [13,14]. In addition, oxytocin may reduce the stress response to weaning by reducing the psychological attachment to the dam and favoring self-oriented behaviors [15], although the precise mechanism by which oxytocin exerts its effect remains unclear [16]. The release of oxytocin can be stimulated by touch, warmth, and the ingestion of food [17], which are common daily occurrences for the suckling pig but become suddenly sporadic in the postweaning period.

This experiment aimed to determine the influence of milk supplementation during lactation, over 1 wk after weaning, and of oxytocin administration for the first 14 d life on the pigs' feed intake, growth rate, organ weights, and the gene expression of hormones released from the gastrointestinal tract, with an emphasis on ghrelin, leptin, glucagon-like peptide-1 (GLP-1), and glucagon-like peptide-2 (GLP-2). The hypothesis of this study was that pigs supplemented with milk, during lactation or after weaning, or pigs administered with exogenous oxytocin would show greater feed intake in the first 7 d after weaning, greater growth rate, and greater expression of these gastrointestinal hormones.

2. Materials and methods

The project was approved by the Victorian Department of Primary Industries Ethics Committee in accordance with the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes.

2.1. Animals and milk supplementation during lactation

Pigs were allocated to treatments in a 2 × 2 × 2 × 2 randomized factorial design with the respective factors being sex (male vs female), injection (oxytocin vs saline), preweaning dietary treatment (supplemented with milk during lactation vs unsupplemented), and postweaning dietary treatment (pellets vs pellets plus milk).

Twenty large white × landrace multiparous sows of mixed parities suckling 10 to 12 pigs were randomly allocated to one of the 2 treatments: pigs were either supplemented with milk or were unsupplemented and relied solely on suckling the sow. The liquid supplement consisted of a mixture of 25% skim milk powder (SMP) and water. The SMP was available from day 10 of lactation to weaning (day 21). The SMP was reconstituted by adding 1 part powdered SMP (Murray Goulbourn, Melbourne, Victoria, Australia) to 4 parts warm tap water; 20 mL of a live probiotic (Yakult Australia Pty Ltd, Dandenong, Victoria, Australia) was added per liter as a source of *Lactobacillus casei* Shirota strain to prevent diarrhea. The SMP mixture was stored at 4°C and used within 2 d. The supplement was delivered by a gravity feed system that was designed to minimize spillage and contamination by feces and urine [6].

2.2. Oxytocin administration

Within each litter, pigs were allocated at birth into pairs of the same sex based on similar live weight. Within each litter, 2 female and 2 male pigs of each pair (n = 40 per sex) were injected subcutaneously with oxytocin (Ilium Syntocin, Troy Laboratories, Glendenning, New South Wales, Australia) daily from 0 to 14 d of age at a rate of 10 I.U. per kg of body weight (equivalent to 20 μg per kg). The other 2 female and 2 male pigs of the pairs (n = 40 per sex) were injected subcutaneously with 0.9% saline in the same manner and same quantity as the control. These pigs were used for live measurements. Any additional pig in the litter also received injections of either oxytocin or saline, and 117 pigs were later euthanized for the collection of tissue samples and measurements of gene expression.

2.3. Weaning and milk supplementation postweaning

Pigs were weaned at 21 d of age into individual weaner crates to measure their feed intake. Forty pigs were fed ad libitum a high quality weaner pelleted diet, Ultrawean 75 (digestible energy [DE]): 16 MJ/kg, crude protein [CP]: 24%, total lysine: 1.0%; Ridley AgriProducts, Pakenham, Victoria, Australia), whereas 40 other pigs were fed the same diet but also supplemented with the same SMP mixture as a transitional diet. Over the 7 d postweaning, the dry matter content of the SMP mixture was gradually increased by the inclusion of less milk and more dry pelleted feed (Ultrawean 75) until pigs were completely offered the dry pelleted diet. Accordingly, for the first 2 d postweaning, pigs were offered 1 L of SMP mixture. On the third day postweaning, 200 g of Ultrawean 75 was added and the amount of pelleted diet increased by 100 g/d until day 7, whereas the amount of the SMP mixture decreased proportionately. From the end of the first week after weaning, all pigs were fed ad libitum Ultrawean 100 (DE: 16 MJ/kg, CP: 24%, Lysine content: 0.9%; Ridley AgriProducts) for another week before being changed to an ad libitum high quality weaner mash from the third week to 56 d of age (DE: 14.5 mj/kg, CP: 23%, total lysine: 1.0%; Riverbank Stockfeeds, Leongatha, Victoria, Australia). At 56 d of age, pigs were returned to the herd, housed in 1 shed in groups of 10 in 3.0 × 3.4 m pens and fed conventional grower (DE: 14.3 MJ/kg, CP: 18.7%, total lysine: 0.6%; Riverbank Stockfeeds) and finisher diets (DE: 13.0 MJ/kg, CP: 18.2%, total lysine: 0.5%; Riverbank Stockfeeds) until slaughter.