Nutrition and gut health of the young pig around weaning: what news?

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ABSTRACT

Gastro-intestinal tract (GIT) disorders, infections and diarrhoea increase at the time of weaning in young pigs. Weaning is a complex step involving many stresses that interfere deeply with feed intake, GIT development and adaptation to the weaning diet. The European ban put on in-feed antibiotic growth promoters has stimulated research on the mechanisms of GIT disorders and on nutritional approaches for preventing or reducing such disturbances. From the data accumulated over the past years, it appears that products like spray dried plasma and various organic acids are among the most effective. Other substances under study are also providing promising results. Increasing numbers of studies with prebiotics and probiotics provide evidence for the potential of these approaches. Conversely, many plant extracts and natural substances, used alone or in combinations have given frequently inconsistent results in vivo, despite their demonstrated anti-bacterial effects in vitro. Therefore, additional work is needed for precising the bioavailability of such substances.

Keywords: pig, weaning, gastro-intestinal tract, nutrition, alternative substances to antibiotics

INTRODUCTION

Gastro-intestinal tract (GIT) disorders, infections and diarrhoea increase at the time of weaning in young pigs. This causes large economic losses in the pig industry. Preventive use of antibiotic growth promoters and metal trace elements (Cu, Zn) in weaning diets has contributed largely to alleviate these problems for approximately half a century. However, increased concerned on bacterial resistance to antibiotics in humans and animals, as well as developing environmental pollution caused by high copper levels in animal slurry have progressively led to a partial and then a total ban on the preventive use of such antibiotics in feed. Despite this, medicated weaning feed are still common practice due to the lack of completely satisfactory alternative solutions for keeping post-weaning (PW) disorders under control. Antibiotic growth promoters have been shown to act through many different mechanisms.
operating both locally in the GIT and systemically (review by Anderson et al. 1999) and no one alternative substance can do the same by its own.

Weaning is a complex step involving dietary, environmental, social and psychological stresses which interfere deeply with feed intake, GIT development and adaptation to the weaning diet (reviews by Pluske et al, 1997; Lallès et al. 2004). Transient PW anorexia leads to under-nutrition and growth check. Feed intake resumption after weaning is highly variable across individuals and it takes up to 2 weeks for piglets to recover pre-weaning levels of energy intake (review by Le Dividich and Sève, 2000). The first organ suffering from nutrient shortage immediately PW is the GIT and this has dramatic consequences on its anatomy and functions, including barrier function against harmful antigens and pathogens. Therefore, diet composition and feeding management appear as critical for solving PW disorders. The aim of the present paper is to summarise recent findings on the mechanisms of GIT alterations caused by PW anorexia, and to review the most promising nutritional solutions for limiting GIT disturbances PW. This topic has been reviewed periodically (Pluske et al. 1997; Spreuwenberg and Beynen, 2003; Lallès et al, 2004, 2007a,b).

**CHANGES IN GIT PHYSIOLOGY POST-WEANING**

The most striking consequence of PW anorexia is a rapid mucosal atrophy of the small intestine which looses 20 to 30% of its weight within 2 d PW (e.g. Montagne et al. 2007). This is associated with a proximo-distal gradient reduction of villous height and surface area along the small intestine. The activities of most pancreatic enzymes (proteases and lipase) and brush border enzymes (disaccharidases and peptidases) are decreased, following specific spatio-temporal patterns.

The GIT plays a major role in the defence against harmful antigen and pathogen entry into the body thanks to a complex barrier (review by Baumgart and Dignass, 2002). It includes the secretion of fluid, minerals, mucin and immunoglobulin (IgA). Permeability of the intestinal epithelial cell monolayer is tightly regulated (review by Turner, 2006). Recent investigations around weaning revealed complex regional and temporal variations in mucosal electrical resistance and permeability along the intestines (review by Vente-Spreuwenberg and Beynen, 2003; Boudry et al. 2004). Para-cellular permeability increased in the proximal jejunum with little changes seen in the other segments. Trans-cellular permeability decreased in the proximal jejunum while it increased in the mid-jejunum. Sodium-dependent glucose absorption and secretagogue-induced chloride secretion were increased transiently PW.

Intestinal permeability and absorptive and secretory properties of the intestine are largely modulated by cellular and molecular components of immunity, e.g. mast cells and cytokines (McKay and Bird, 1999). Intestinal dysfunction PW was recently shown to involve the activation of mucosal mast cells, enteric nerves and prostanoid pathways (Moese et al. 2007). We showed
that PW anorexia results in transient over-expression of inflammatory cytokines (IL1-β, IL-6 and TNF-α) along the intestines (Pié et al. 2004). However, 7 d PW such gene expression was still elevated in the ileum and colon, suggesting an involvement of developing fermentation in these compartments. Indeed, correlations between cytokine gene expression and bacterial volatile fatty acid profiles have been recently shown (Pié et al. 2007).

Dealing with mucin and goblet cells which are important players of GIT protection, data are inconsistent. Earlier results reported a transient drop in goblet cell densities in villi but more recent results have not confirmed this (see Lallès et al. 2004).

In summary, many changes in the architecture and functions of the intestines throughout weaning have been documented. Not only digestion of diet components and absorption of nutrients, but also components of mucosal physiology and immunology are compromised. Most of these changes are highly dependent on the level of feed intake (Pluske et al. 1997). Intensive research has been carried out over the last decade for investigating how such changes may be limited through manipulating diet composition, as outlined below.

**Dietary management of GIT disorders post-weaning**

*Protein sources.* It has long been known that skim-milk powder and whey are excellent but expensive protein sources for sustaining a high growth performance in weaned pigs. Among other animal protein sources, spray dried plasma (SDP) incorporated at levels of 4-6% into starter diets is so far the most interesting commercial product stimulating PW growth rate and feed intake (van Dijk et al. 2001; Torrallardona et al., 2003, 2007). Small intestinal alterations and incidence and severity of PW diarrhoea are often reduced. Porcine SDP is more effective than bovine SDP or SDP of mixed origin. Both palatability and beneficial effects of SDP-supplemented diets are mainly related to high levels of immunoglobulin G (Pierce et al 2005), but positive effects of minor bioactive compounds cannot be excluded. It is probable that IgG prevents adhesion to potentially pathogenic *Escherichia coli* to intestinal epithelial cells. As no or little interaction were observed between SDP and antibiotics, their modes of actions may be different (Torrallardona et al. 2003, 2007). Interestingly, piglets supplemented with SDP displayed low levels of basal immune activation as seen both locally (Jiang et al. 2000; Bosi et al. 2004) and systemically (Touchette et al. 2002). SDP supplementation may or may not stimulate the growth of intestinal lactobacilli (Torrallardona et al. 2003, 2007). Finally, improved dietary protein utilisation in SDP-supplemented pigs may result from reduced protein catabolism by the enteric microflora (Jiang et al. 2000).

Bovine colostrums supplementation may provide another valuable alternative to in-feed antibiotics for protecting pig GIT. It has been shown to stimulate growth rate and voluntary feed intake PW (Luron et al. 2004). However, pair-feeding experiments revealed that most of the beneficial effects
on the GIT may be due to an increased feed intake since there were only significant effects of colostrums supplementation on gastric pH (decreased) and duodenal lactobacilli to coliform ratio (increased) (Huguet et al. 2006).

Most protein sources in feed for piglets originate from grains and bean seeds. Some plant protein sources may have adverse effects on GIT health after weaning. This has been shown for pea protein isolates which increased diarrhoea and mortality PW (Owusu-Asiedu et al. 2003a,b). Plant protein sources, in comparison to dairy ingredients, also reduced the magnitude of beneficial effects observed with SDP supplementation (van Dijk et al. 2001). Insufficiently treated soybean products are well known for eliciting antigen-specific immune-mediated gut disturbances in weaned pigs (review by Dréau and Lallès, 1999). More recent investigations have shown that seeds from legumes other than soybean (e.g. cowpea, lupine, field pea) may stimulate antibodies to dietary antigens in blood plasma (Salgado et al. 2002a) but this did not seem to affect digestion, intestinal mucosa architecture and enzyme activities (Salgado et al. 2001, 2002b). Soybean protein concentrates incorporated at high levels at the expense of soybean meals may reduce the palatability of starter diets and, therefore, growth performance (Lenehan et al. 2007).

Energy sources. In terms of energy, glucose, lactose and starch incorporated in starter diets provided essentially similar results for growth, feed intake and GIT characteristics (Vente-Spreuwenberg and Beynen, 2003). However, high levels of lactose allowed increasing incorporation of protein in weaning diets and favoured growth rate and intestinal integrity (Pierce et al. 2006, 2007). In this case, most lactose escaped digestion in the small intestine and was fermented in the large intestine. Such a diet stimulated bifidobacteria and lactobacilli and reduced E. coli counts. It also reduced protein fermentation and generation of unwanted nitrogenous compounds, while increasing butyrate production and improving small intestinal architecture (Pierce et al. 2006, 2007).

Amino acids. Amino acids (AA) display three distinct but complementary roles in the body (and GIT), most AA acting as building blocks, some (e.g. glutamine) being fuels for specific (e.g. epithelial) cells and some AA supporting important specific functions (e.g. threonine and GIT mucin). In all cases, indispensable AA need to be provided in amounts sufficient for covering pig’s requirements. Glutamine has been shown many times to improve pig performance and intestinal integrity while reducing the incidence of diarrhoea. More recent insights indicate that glutamine stimulates proliferation and reduces apoptosis of both intestinal cells and mucosal immune cells (Domeneghini et al. 2004). Densities of intestinal macrophages and intra-epithelial lymphocytes were also increased, suggesting a stimulation of both innate and acquired components of mucosal immunity. Threonine is an important component of mucin and its requirements are increased in disease states or following consumption of diets stimulating mucin secretion (Myrie et al. 2003; Bannink et...
Interestingly, dietary deficiency in threonine decreased intestinal barrier function and protein and mucin synthesis in young pigs (Hamard et al. 2007; Wang et al. 2007).

**Organic acids.** Many publications have shown the beneficial effects of various organic acids (e.g. formic, fumaric, citric acids; calcium diformate) after weaning (reviews by Partanen 2001; Mroz et al. 2006). They are known for decreasing luminal pH in proximal GIT and for their bactericidal properties. Among organic acids, sodium butyrate (SB) provided orally has been little investigated despite its numerous beneficial properties in the large intestine. Spanish studies found SB to improve feed to gain ratio PW, to increase gastric DM content suggesting a delayed gastric emptying rate, but to decrease ileal and faecal digestibility of organic matter and starch (Castillo et al. 2006; Manzanilla et al. 2006). Butyrate also induced changes in the diversity and the composition of the jejunal microbiota and reduced colonic fermentation in the colon. The authors suggested an improved intestinal barrier function associated, at least partly with the observed microbial changes. French studies showed that providing piglets with SB during the suckling period rather than after weaning was more effective for improving growth performance, feed intake and diet digestibility PW, and for reducing the weight of the intestinal mucosa (Le Gall et al. 2007). These observations suggest a growth promoting effect for SB, but its mechanisms of action are currently unknown.

**Prebiotics and probiotics.** Providing diets with appropriate fermentable carbohydrates allows manipulating the GIT microbiota towards beneficial fermentation profiles and improved resistance to colonisation by enteric pathogens (review by Bauer et al. 2006). As mentioned above, lactose provided in high dietary levels does act as a prebiotic and was able to improve both pig performance and intestinal integrity (Pierce et al. 2006, 2007). A high level of lactose allowed increasing the protein content of the diet and improved pig performance. By contrast, increasing lactose in a diet already containing inulin, another fermentable carbohydrate, did not ameliorate the results obtained by the inulin diet. Supplementing weaning diets with carbohydrates of varying solubility and fermentability (inulin, lactose, sugar beet pulp, wheat starch) was shown to stimulate the growth of lactobacilli (e.g. Lactobacillus sobrius) and to improve colonic microbial stability and diversity PW (Konstantinov et al. 2004, 2006).

Lactobacilli isolated from weaned pigs have been shown to reduce gut E. coli counts and diarrhoea (Huang et al. 2004). Enterococcus faecium strongly reduced the incidence of diarrhoea in the first week PW (Taras et al. 2006). A mixture of probiotics (mainly lactobacilli) was able to reduce diarrhoea and faecal shedding of Salmonella and to improve clinical outcome in weaned pigs (Casey et al. 2007). The probiotic E. coli Nissle 1917 provided in the creep before weaning abolished diarrhoea in weaned piglets challenged with pathogenic E. coli, reduced jejunal secretory capacity and prevented the decrease in para-cellular permeability as observed after pathogen challenge.
(Schroeder et al. 2006). Fermenting feed at the farm level may be a way for providing continuously live probiotics to pigs PW but it seems that the specialised equipments required as well as risks of contamination with unwanted micro-organisms may limit the development of this strategy (Stein and Kil, 2006). Diet supplementation with live yeast improved pig performance and intestinal integrity PW (Bontempo et al. 2006).

Plant extracts and natural substances. There has been a growing interest in plant extracts and natural substances (e.g. essential oils) for controlling PW diarrhoea and GIT disorders in recent years (review by Han et al. 2006). However, the data published thus far are often inconsistent. For instance, various mixtures of essential oils and/or plant extracts increased GIT lactobacilli (Manzanilla et al. 2004) and/or decreased coliforms (Namkung et al. 2004) without major effects on pig performance (e.g. Kommera et al. 2006; Oetting et al. 2006). Therefore, more work is required on the bioavailability of such substances.

CONCLUSIONS AND FUTURE PROSPECTS
Since the beginning of the European ban on in-feed antibiotic growth promoters, many studies have investigated various nutritional approaches for preventing or reducing GIT disorders and PW diarrhoea in young pigs. It appears that two types of substances, namely spray dried plasma and organic acids represent the most satisfactory alternative solutions found thus far for limiting problems PW in the absence of preventive use of antibiotics. Other substances (e.g. butyrate) may be promising but more work is required for understanding better the underlying mechanisms. Studies with prebiotics and probiotics provide increased evidence for their beneficial effects on the pig and GIT homeostasis. Conversely, many plant extracts and natural substances display clear anti-bacterial effects in vitro but they rarely support consistent effects in vivo. Therefore more research is needed in this area for understanding these inconsistencies.

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