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MANAGING PROLIFERATIVE ENTEROPATHY IN PIGS: CONTROLLING CHRONIC, SUBCLINICAL AND ACUTE ILEITIS

INTRODUCTION

In a typical group of pigs affected by the chronic form of porcine proliferative enteropathy (PPE), 10% will have problems with average weight gain, 40% will have various degrees of diarrhoea and many others will appear normal but will actually have low performance. In all cases of PPE (ileitis), the end result is that undervalued and poor performing pigs end up being sold.

Consider that in a typical group of finishers affected by acute haemorrhagic ileitis, 20% to 50% of pigs will have bloody faeces and may be dying. Some may have already died suddenly. If the affected pigs are pregnant, then abortions can occur. This acute form of PPE attacks many pigs in the group in a short time, so that many cases are noticed at the start and more cases may develop in the first week. The older age and high mortality of affected pigs means that the economic impact of the acute form is very high. Urgent antibiotic treatment is needed if some affected pigs are to be saved.

Even in groups affected by the less severe sub-clinical form of ileitis, measures to control PPE can have a very positive effect on the health and performance of pigs.

treat every affected animal, otherwise efficacy is not going to be optimal despite the drug used.

In acute PPE with high morbidity (many cases in the group) and high mortality, the use of injectable formulations of tiamulin or tylosin are usually recommended for the most “at-risk” pigs. This is usually followed with water-soluble formulations of tiamulin, lincomycin or tylosin to deliver a high dosage in an effective manner in the water supply of affected pigs. Pigs will generally consume water when they are sick, even though their appetite for food may be diminished.

Water delivery of medications allows a safe and quick way to deliver a reasonably accurate dosage to a large group of pigs. It also eliminates the need to alter the feed supply. In one controlled clinical study, water medication with 60 ppm of soluble tiamulin for 5 days to groups of pigs challenged with ileitis resulted in a good clinical response and reduction of lesions during the monitoring period of 2 to 3 weeks post-medication.

The use of in-feed premix formulations is also a realistic option for managing both acute and chronic clinical ileitis. Several controlled scientific studies have confirmed the beneficial effects of valnemulin, tiamulin or lincomycin premix formulations for control and prevention of ileitis on many farms across Europe. These drugs can be used with confidence for the treatment and control of ileitis.

It is important to realise that a comparison of the different methods of delivering drugs to

MANAGEMENT STRATEGIES: AN OVERVIEW

PPE is a bacterial disease caused by the Gram-negative intracellular bacterium *Lawsonia intracellularis*. It is therefore possible to use antibiotic agents that target the organism with a specific antibacterial effect. It is always important to use the correct agent at a sufficient dose and to



animals shows that injections will give the highest dose per animal, but injectable drugs are the most difficult to administer and can lead to problems associated with needle breakage. Soluble formulations give a high dose per animal, but may require specific delivery mechanisms. In-feed formulations are the easiest and cheapest to use, but may not deliver a full or high dose to all animals in a group.

The correct dose for each drug for each method of delivery must be carefully checked before it is used. It is important to realise that drugs given as a parts per million dosage in water or in feed will achieve different levels in the body of each pig treated because the bodyweight of each pig will vary with growth. It is therefore best to express the dosage of drugs on a mg of drug per kg of bodyweight dosage. For instance, valnemulin premix for treatment is best used at a rate of 3 to 4 mg/kg bodyweight. This usually corresponds to 75 ppm in feed in the late grower phase.

Other important issues to consider when evaluating antibiotic treatments include factors such as product quality, cost, the technical support provided by the product company involved, withdrawal times and other regulatory issues. These factors can vary between different countries.

ANTIBIOTIC TESTING AND ILEITIS

Studies have examined the likely minimum inhibitory concentrations (MICs) of various antibiotics against laboratory cultures of *L. intracellularis*. Valnemulin and tiamulin were shown to have low MIC values against *L. intracellularis* of 2.0 mcg/ml and 4.0 mcg/ml respectively.

The actual effect of drugs in animals with ileitis has been tested in field trials and challenge-exposure trials, which are of even more value in determining which antibiotics to recommend for ileitis than laboratory tests.

In a controlled trial in Denmark, pigs from a commercial farm with naturally occurring PPE received valnemulin (Econor® 10% Premix) at a rate providing 3.75 mg per kg bodyweight. Treatment was initiated when the prevalence of mild to moderate diarrhoea reached 20%. Valnemulin-treated pigs gained 30% more weight than untreated pigs during the treatment period; they also had better feed intake, feed conversion efficiency and significantly decreased diarrhoea. After treatment, the mean daily weight gain of valnemulin-treated pigs was nearly 3% higher than that of controls.

In a U.S. trial of finishing pigs from a commercial herd with a naturally-occurring, acute outbreak of PPE, valnemulin-treated pigs had significantly improved diarrhoea scores and significantly better bodyweights compared to controls.

Challenge-exposure studies to assess the therapeutic efficacy of oral antibiotics, in particular valnemulin, tiamulin, lincomycin or tylosin, have shown that all four drugs were efficacious against ileitis. It is possible that the drugs in fact concentrate in the correct location of the body that also contains the *L. intracellularis* bacteria.

Obviously not all antibiotics are going to be effective against each disease. The several antibiotics found *not* to be fully effective for an ileitis challenge include bacitracin, virginiamycin and salinomycin. The penicillins and fluoroquinolones likewise have proven ineffective in preliminary trials. Some of these drugs are not effective because they are aimed at Gram-positive bacteria, while others do not seem to target the correct tissues and cell location of the *L. intracellularis* bacteria.

TREATMENT FAILURES

Occasionally, use of some of the drugs mentioned, such as tylosin, are used against ileitis

in farm outbreaks, but do not seem to be fully effective. Sometimes, this is thought to mean that *L. intracellularis* is becoming “resistant” to the drug. However, investigation of these situations usually reveals that either:

- Pigs were underdosed; for example, older larger pigs got an inadequate in-feed amount. This is most commonly seen in sows during hot weather, when feed intake is below normal.
- Pigs had concurrent infection with ileitis and another disease, such as swine dysentery or colitis.
- Pigs had some other disease or nutrition problem that is confused with ileitis.
- The antibiotic is given too late to be effective in preventing intestinal damage.

Another common problem occurs when antibiotics are administered to groups of “clean” pigs, which then develop acute or severe PPE after they are taken off the antibiotics as might occur before they are transported. In these situations, it is clear that the medicated pigs are not getting the chance to develop active immunity to the disease and remain naïve and susceptible. Older pigs are more likely to get acute PPE, so that this strategy presents a great danger when gilts and other animals are kept on antibiotics.

TIMING ANTIBIOTICS FOR TREATING ILEITIS

Ileitis usually affects a high proportion of pigs within a building — at least 20% is typical — requiring ongoing clinical attention. It is vital that effective treatment be administered to affected and in-contact pigs when actual disease is occurring. As noted before, the antibiotics known to be effective in both controlled field and challenge-exposure trials include valnemulin, tiamulin, tylosin and lincomycin.

It is no longer considered appropriate to use

antibiotics for long periods of time during the growing and finishing period. In the case of ileitis, this tactic may actually make the situation worse because it lowers the exposure of pigs to the endemic disease and, hence, lowers immunity in each group to the disease.

If antibiotics are to be used, they should be administered in a “targeted” manner. On farms where ileitis is common (endemic), the most appropriate means of targeted use may be after a known period of exposure. This allows for natural exposure and some immunity to develop.

However, it can be difficult to establish when an outbreak starts and when that suggested time-point relates to the build-up of bacteria in the group. In other words, the infection can build up slowly or quickly, with variations in disease onset. This variation can occur on different farms and importantly on the same farm between different groups in the same building. As a result, antibiotics might be added too late to stop damaging clinical signs and poor performance.

The most appropriate means of targeted use depends on the pattern of infection on each farm and when infection and disease are occurring. The use of blood serology and faeces testing may pinpoint when pigs have developed antibodies or excretion of the organism and have therefore already had exposure to *L. intracellularis*. The goal is to initiate antibiotic treatment shortly after actual exposure starts to develop in the group of pigs. For example, on many smaller continuous-flow European farms; *L. intracellularis* infections start to build up in growers at about 8 weeks of age. The medication strategy would be to add one of the effective antibiotics into the feed at around 8 to 10 weeks of age at the standard dose for 3 weeks. Hopefully, this will reduce or limit clinical signs while the group of pigs are exposed to the disease and develop some level of natural immunity.

Other possible medication strategies aimed at controlling ileitis, such as medicating sows, have not been fully evaluated. Many sows have only low levels of infection and “clearance” of the infection by medication has not been convincingly demonstrated for any antibiotic tested in pigs. It is most likely that the environment of many pig farms contains a sustained level of *L. intracellularis* infection “embedded” in the buildings, which acts to re-introduce the infection to many new groups of pigs at various ages.

leading to a high environmental load. So far, it has not been possible to eliminate *L. intracellularis* from pig-raising systems. The most effective types of disinfectants tested to date include the tetrammonium compounds and iodine-type products. Rigorous cleaning may help establish clean and dirty zones on farms. However, once a farm is infected with well-adapted enteric bacteria like *L. intracellularis*, *Brachyspira* or *E. coli*, these pathogens often spread easily around the site and remain embedded for many years, leading to on-going, year-to-year problems.

FEED ADDITIVES

When added to feed, additives such as heavy metals (copper, zinc), probiotics, acids or enzymes have not been shown to have any effect on ileitis. Although some inhibitory effect on microbial agents is likely at high levels of inclusion, these levels tend to reduce feed palatability for sensitive pigs. The removal of many anti-bacterial growth promoters from routine usage in European pigs in the last 10 to 20 years has corresponded with a rise in the use of the above types of compounds, but has also coincided with a rise in the proportion of European farms positive for ileitis.

ILEITIS VACCINE DEVELOPMENT

For intracellular bacterial pathogens like *L. intracellularis*, live attenuated bacteria offer the most “natural” immunity and are widely considered the best vaccine approach. An attenuated live vaccine formulation of *L. intracellularis* was therefore developed (Enterisol® Ileitis).

Because it is a live bacteria intended for oral administration, it is best administered in the middle of a 7-day, antibiotic-free period. That way, any antibiotics in the pig’s system would be eliminated and would not kill any vaccine bacteria prior to its uptake. Outside that 7-day period, oral antibiotics, such as valnemulin or tiamulin, can be readily administered to vaccinated pigs without any disruption in vaccine efficacy. Bacitracin or other anti-Gram positive drugs would not have a negative effect on vaccine efficacy, even if used right through the vaccine administration period. Many operations find that an antibiotic-free period can be readily developed 1 to 4 weeks after weaning to allow for live vaccine use.

It is possible that vaccines for ileitis will foster the development of new ileitis control and eradication programmes, ultimately yielding better control of PPE and reduced losses for pork producers.

ILEITIS ERADICATION PROGRAMMES

A number of preliminary studies have tried to establish a PPE eradication programme, but none have yet proved to be fully effective. The programmes have generally used disinfection and improved sanitation, similar to those aimed at controlling swine dysentery, along with antibiotic administration to numerous pigs on the farms.

The factors that set off a clinical outbreak in any one group of pigs may be some combination of poor immunity and poor hygiene or sanitation,