

The use of tildipirosin in treating porcine respiratory disease complex

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A clinical condition that seems to have evolved in parallel to the modernisation of swine production is the porcine respiratory disease complex (PRDC). This respiratory complex is characterised clinically by the presence of dyspnoea, cough, acute depression, fever and nasal secretion, and essentially affects pigs at the nursery and fattening stage.

This respiratory complex is due to the interaction of multiple factors, such as the presence of bacterial and viral micro-organisms, the environment and the management system to raise pigs.

The 'appropriate' combination of these factors can deteriorate the defence mechanisms of the respiratory system and cause a severe respiratory disease.

Synergy of pathogens

This disease is caused by the interaction and synergy of viral and bacterial pathogens. The viral pathogens that are most often involved are the porcine reproductive and respiratory syndrome virus (PRRSV), the swine influenza virus (SIV), the Aujeszky's disease virus (PRV) and the porcine circovirus type two.

The main bacterial pathogens which are most often involved in the complex are *Mycoplasma hyopneumoniae*, *Actinobacillus pleuropneumoniae*, *Bordetella bronchiseptica*, *Pasteurella multocida* and *Haemophilus parasuis*. These pathogens thicken the blood-air interface (interstitial pneumonia) and/or fill the pulmonary alveoli with exudates due to the infectious process (pneumonias usually of bacterial origin) and the reaction (inflammation) that takes place in the organism.

Many measures can be implemented to solve clinical cases of

PRDC. These measures are very varied and include monitoring the environment where the animals are housed, management strategies, changes in the production flow, the implementation of strategic vaccination programmes (especially against viral infectious agents such as PRRSV, PRV, PCV2 and SIV) and the use of antimicrobial medication that could be a part of the medicine preventive programs to cope with PRDC.

Antimicrobial medication

In the case of antimicrobial medication, the basic objective is to choose the most effective agent against a specific micro-organism.

Culturing respiratory secretions and determining sensitivity to antibiotics are the best methods to design the most appropriate antibiotic treatment.

On the other hand, another question that should be answered is to what animals the antibiotic should be administered. Obviously, these drugs should be administered to all the animals that show clinical symptoms that are compatible with PRDC.

This use is a therapeutic approach to this respiratory disease and it must be applied as soon as possible for welfare and productive reasons in pig production.

In pig veterinary medicine, to preserve the health of a herd, collective antimicrobial treatments can be administered to all the animals after the observation of symptoms to individuals in situations at risk (for example all the animals in the pens where there had been PRDC clinical cases).

Metaphylactic use

This practice is referred to as metaphylaxis which corresponds to the administration of antibiotics to animals experiencing any level of bacterial disease before overt disease and could be highly recommended when a practitioner copes with PRDC taking into account the epidemiology

and the morbidity/ mortality of this disease.

The advantages and limitations of this latter approach need to be scientifically documented in a framework of risk-benefit analysis.

Tildipirosin (TD) is a new macrolide (semi-synthetic tylosin analog) that has been approved for the treatment for respiratory diseases in pigs and cattle since 2011.

The magnitude of the local accumulation and long persistence of TD in the target tissue (lung) results in a convenient treatment regimen (single administration) and positive clinical outcome rates for respiratory conditions.

This clinical efficacy can be explained by its lung selectivity and concentration vs. time profile of this macrolide in pulmonary tissue.

On the other hand, it has also been recently approved for the metaphylaxis of the swine respiratory disease at European level (EMA, 2014).

This new indication has been authorised because it has been scientifically demonstrated in a placebo controlled multi-centre field study that, following metaphylactic use of this molecule, 86% of the healthy animals remained free of clinical signs of PRDC versus 65% of the untreated control group in several trials where PRDC was confirmed in at least 30% of the pens in a farm and with a pen prevalence of PRDC equal or higher than 10%.

Choosing a strategy

According to these results, it is clear that the metaphylactic use of this molecule is soundly founded.

Moreover, it must be taken into account that these collective treatments are launched very early after the start of the infection and consequently the bacterial load targeted by the antibiotic is supposedly lower than for the strategy based on treating only animals with clinical symptoms.

Therefore, the assessment of the impact of the bacterial load on the clinical and microbiological outcomes may be a key factor in making



a decision between the therapeutic or metaphylactic strategy.

Indeed, previous studies have shown that the eradication of the targeted bacterial population needed lower concentrations of antibiotic and that the selection of resistant subpopulations of the pathogen was less frequent when a low bacterial inoculum was compared to a high inoculum.

In any case, this metaphylactic use must be only used in severe outbreaks of PRDC according to the responsible use of antimicrobials and after carrying out a risk-benefit analysis.

Finally, it has been also demonstrated with new studies the safety of this medicinal product not only in fattener pigs but also in piglets. This fact allows using this product to cope with problems associated to PRDC during all the pig rearing period.

Conclusion

In conclusion, the results of this new indication of tildipirosin support the hypothesis that the same dosage regimen given early during the time-course of a bacterial infection may lead to both more frequent clinical and microbiological cures and probably to a less frequent selection of resistant bacteria than later treatments.

By taking this element into account, further studies should now investigate at group level the impact on the overall consumption of antibiotic and on the selection of resistance, of different individual doses given to non-symptomatic animals in early 'metaphylactic' curative treatments compared to diseased animals in the later 'conventional' treatments. ■

References are available from the author on request