

The use of tylvalosin (Aivlosin[®]) in the successful elimination of swine dysentery on a farrow-to-finish herd

Succesvolle eliminatie van dysenterie met tylvalosine (Aivlosin[®]) op een gesloten varkensbedrijf

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ABSTRACT

Swine dysentery causes severe economic losses in swine industry. Eliminating the disease at farm level can become problematic when resistance of the causative agent, *Brachyspira hyodysenteriae*, against pleuromutilins is reported. In this study, the use of tylvalosin (Aivlosin[®]) in eliminating the disease in a single-site, farrow-to-finish herd was evaluated. In addition, productivity parameters and antimicrobial use were compared prior to and after implementing the elimination protocol.

On a mixed farm of 200 sows and 1500 finishers with a history of chronic dysentery, the *B. hyodysenteriae* isolate was resistant to pleuromutilins but had a low minimum inhibitory concentration for tylvalosin (2 µg/ml). Combined with a strict program for rodent control and hygiene, sows were treated with tylvalosin at a dose of 4.25 mg/kg BW daily for four weeks. The sows were washed one week after the start of the treatment before entering a clean stable. Piglets born from sows that had received this treatment, were considered free from dysentery and were kept separated from infected, untreated animals on the farm. A monitoring program with monthly sampling of sows and fatteners was installed to evaluate the absence of *B. hyodysenteriae* on the farm.

After treatment, the clinical symptoms in the treated sows disappeared and remained absent in the offspring born after the procedure. Fecal samples examined by PCR remained negative for the whole testing period (14 months after the end of the treatment) and no clinical outbreaks were reported afterwards. The feed conversion ratio improved by 12%, the mortality rate with 37% and the antimicrobial use decreased by 71.5%.

We conclude that the elimination of swine dysentery on a single-site, farrow-to-finish herd is possible using tylvalosin (Aivlosin[®]) combined with strict hygiene and rodent control. The improvements of the technical parameters in this study are not only the result of the elimination of *B. hyodysenteriae*, but also changes in management practices influenced these parameters.

SAMENVATTING

Varkensdysenterie veroorzaakt ernstige economische verliezen op aangetaste bedrijven. De eliminatie van het oorzakelijk agens, *Brachyspira hyodysenteriae*, wordt problematisch als er resistentie is tegenover pleuromutilinen. In deze studie wordt het gebruik van tylvalosine (Aivlosin[®]) geëvalueerd voor de eliminatie van dysenterie op een gesloten bedrijf. Daarnaast worden de technische parameters en het antibioticumgebruik vergeleken vóór en na de eliminatie.

Op een gemengd bedrijf met 200 zeugen en 1500 vleesvarkens met een chronisch dysenterieprobleem was het geïsoleerde *B. hyodysenteriae*-isolaat resistent tegenover pleuromutilinen en gevoelig voor tylvalosine (minimum inhibitorische concentratie, MIC, 2 µg/ml). Naast een grondige knaagdierbestrijding en strikte hygiëne werden de zeugen dagelijks gedurende vier weken behandeld met 4,25 mg/kg LG tylvalosine. Eén week na aanvang van de behandeling werden de dieren gewassen en in een gereinigde stal gehuisvest. Biggen geboren uit de aldus behandelde en gewassen zeugen werden als niet-besmet beschouwd en gescheiden gehouden van de oudere biggen en vleesvarkens. Via maandelijks staalnamen van zeugen en vleesvarkens werd het resultaat van het eliminatieprotocol opgevolgd.

Na de behandeling werden geen klinische symptomen waargenomen bij de zeugen of bij de biggen ge-

boren na de behandeling. De meststalen bleven negatief op PCR voor *B. hyodysenteriae* gedurende veertien maanden na het einde van de behandeling en ook nadien werden geen klinische symptomen meer vastgesteld. De voederconversie verbeterde met 12%, de mortaliteit bij de vleesvarkens daalde met 37% en de medicatiekost van antibiotica op het ganse bedrijf daalde met 71%.

Uit de gegevens van deze studie kan besloten worden dat de eliminatie van dysenterie op gesloten bedrijven mogelijk is door het gebruik van tylvalosine (Aivlosin®) in combinatie met een grondige knaagdierbestijding en een goede hygiëne. Verder wordt in deze studie de grote invloed van dysenterie op de technische parameters en de medicatiekost gedocumenteerd door de gegevens vóór en na het uitvoeren van het eliminatieprotocol te vergelijken. Veranderingen in het management kunnen echter eveneens deze parameters beïnvloeden.

INTRODUCTION

Swine dysentery, a muco-hemorrhagic enteritis caused by the spirochete *Brachyspira hyodysenteriae*, is responsible for extensive losses on affected farms. In addition to diarrhea and mortality, colonic damage results in unthrifty piglets with deteriorating feed conversion and a longer fattening period (Harris et al., 1999). The cost of production increases due to the depressed growth rate and medication costs. Once the bacteria are present, they may remain on the farm for a long period in carrier animals, in fecal material and in rodents, resulting in continuous infection of susceptible animals (Harris et al., 1999). Therefore, the elimination of swine dysentery at farm level is recommended. Elimination protocols involve treatment with antibiotics during a long period, strict hygiene and rodent control (Vyt et al., 2007; Taylor, 1980). The success rate of the protocol depends on several factors: farm structure and pig flow, susceptibility of the isolate to antimicrobials and compliance with the protocol. The presence of different age groups and the mixing of animals make elimination more challenging on single-site farms. Nowadays, in Western European countries, the number of antimicrobials that can be used to eliminate swine dysentery is limited. The pleuromutilins tiamulin and valnemulin are widely used for this purpose (Karlsson et al., 2001). However, resistance to these molecules has been reported in several countries (Vyt, 2011; Hidalgo et al., 2009; Lobova et al., 2004). In single-site, farrow-to-finish farms, the success rate of the elimination protocol using pleuromutilins on susceptible isolates has been reported to be 66% (Vyt et al., 2007). In case of strains resistant to pleuromutilins, alternative elimination protocols have to be found, when total depopulation and repopulation with dysentery free animals are not an option. Macrolides could be an alternative, but since there is widespread resistance to tylosin (Räsback et al., 2005), other molecules have to be found. In this study, the use of tylvalosin (Aivlosin®), a macrolide, was evaluated in eliminating *B. hyodysenteriae* from a single-site, farrow-to-finish farm.

MATERIAL AND METHODS

Farm history

From 2006 till 2010, a single-site, farrow-to-finish farm with 200 sows and 1500 fatteners had a problem with repeated outbreaks of dysentery in fattening com-

partments. In the sows, clinical symptoms were seldom seen. They were individually housed in one unit for gestation and in seven maternity compartments. A one-week production system was used. Piglets were weaned at 24 days of age and moved to the nurseries. Since November 2010, castration of piglets has been replaced by vaccination using Improvac® (Pfizer AH, Zaventem, Belgium). The pigs were housed in a pre-fattening unit from 20 to 35 kg of weight and in a fattening unit from 35 kg to slaughter. Maternity, nursery, pre-fattening and fattening units were used all-in/all-out except for one larger fattening unit. The gilts were raised on the farm and housed together with the fattening pigs until slaughter of the latter, and moved to the sow building at that time. The dysentery was treated successfully from 2006 till 2010 using tiamulin at 9 mg/kg BW in feed during a five-day period. No other molecules were used to treat the dysentery. Macrolides had never been used on this farm before. At the end of 2009, the clinical response to medication became insufficient. At that moment, a fecal sample of fattening pigs was submitted to the laboratory. The isolation of *B. hyodysenteriae* was performed on Trypticase Soy Agar (TSJ-BJ) with 5% sheep blood, supplemented with antibiotics (Räsback et al., 2005). Subsequently, the identification was performed using biochemical testing. Afterwards, susceptibility was tested using the agar dilution technique (Vyt, 2011). Briefly, a bacterial suspension having an OD of 1 on the scale of Mac Farland was inoculated on TSJ-BJ agar plates supplemented with serial dilutions of tiamulin, valnemulin, tylvalosin and lincomycin. The minimal inhibitory concentration (MIC) was determined as the lowest dilution where growth was inhibited.

Elimination protocol

Rodent control was carried out routinely by an external company, and prior to the start of the protocol, older sows or sows with low production were culled. The piglets were sold at 20 kg of weight until the pre-fattening compartments (20 – 35 kg) were empty. After cleaning, the pre-fattening compartments were stocked with sows, and a four-week treatment period with tylvalosin at a dose rate of 4.25 mg/kg BW in feed was initiated. To prevent eating disorders when changing from pellets to medicated meal, the sows were given meal instead of pellets two weeks prior to the start of the treatment. They stayed in the pre-fattening com-

partments for 10 days while the sow unit was thoroughly cleaned with a high pressure cleaner, disinfected with Virocid® (CID Lines, Ieper, Belgium) and dried. Before moving back to the sow unit, the sows were washed outside the building using a high pressure cleaner at low pressure after soaking with sow detergent (Logic Shampoo, Agro 2000, Izegem, Belgium). The sows in the farrowing compartments were washed at weaning, and physically separated from the gestating sows by using a different row of crates. The sows of the maternity compartments were treated two weeks longer at the same dose, i.e. six weeks in total.

Piglets born in a clean maternity compartment from treated and cleaned sows were considered free of dysentery and kept separate from the compartments with older, unclean piglets by a physical barrier in the hallway and separate equipment (e.g. brushes, needles). The separation of clean piglets from older infected fatteners was continued until all contaminated animals were slaughtered. None of the gilts from the contaminated fattening units were kept. Except for the owner, no personnel was employed on the farm. Visitors as well as the herd veterinarian were obliged to wear clothes and boots of the herd before entering the stables.

Monitoring

In order to evaluate the success of the treatment in eliminating *B. hyodysenteriae*, animals were clinically observed by the herd veterinarian, and fecal samples were taken to detect the presence of the *Brachyspira hyodysenteriae*. Individual fecal samples from nine sows selected at random, were taken at 60, 120, 180, 240, 300 and 360 days after the end of the treatment. Additionally, fifteen piglets (8 to 10 weeks) and fatteners of several age groups, born from cleaned sows, were sampled every 30 days starting from 90 days after the end of the sow treatment until 360 days after the treatment. A total of 56 samples of sows and 150 samples of piglets and fatteners were examined by PCR for the presence of *tlyA* gene of *Brachyspira hyodysenteriae* (Rasbäck et al., 2006). Prior to PCR analysis, the samples were pooled by homogenously mixing 30 gram of three individual samples to a total of 68 pools.

Technical parameters and medication cost

Daily growth, feed conversion (22 kg to slaughter), mortality, slaughter weight and some other parameters (Table 1) were compared during equal periods between November 20th 2008 until December 9th 2009

Table 1. Technical parameters of fattening pigs (22 kg to slaughter) during 2009 and 2011.

| Period | Technical parameters fattening period | | |
|------------------------------------|---------------------------------------|-------------------|-------------------|
| | 20/11/08 > 9/12/09 | 2/12/10 > 8/12/11 | difference n % |
| Mean number of fatteners | 1059 | 1210 | |
| Weight at start (kg) | 22.3 | 22.8 | |
| Mean live weight at slaughter (kg) | 106.6 | 115.9 | 9.3 8.7 |
| Number pigs slaughtered | 3051 | 3008 | |
| Days to slaughter | 125 | 140 | 15 12.0 |
| Mean growth / day (kg) | 0.677 | 0.665 | |
| Amount feed / pig (kg) | 252.8 | 245.2 | -7.6 -3.0 |
| Feed conversion (FCR) | 2.999 | 2.633 | -0.366 -12.2 |
| FCR corrected for mortality | 2.960 | 2.607 | -0.353 -11.9 |
| Mortality (%) | 3.99 | 2.49 | -1.5 -37.6 |
| Feed price / kg (€) | 0.208 | 0.278 | 0.070 33.7 |

Table 2. In vitro antimicrobial susceptibility of the *Brachyspira hyodysenteriae* isolate obtained before the start of the treatment.

| Antibiotic | MIC (µg/ml) | Breakpoint (µg/ml) | Interpretation |
|------------|-------------|-----------------------------------|-----------------------------|
| Valnemulin | 2 | > = 2 (Unpublished data Novartis) | Decreased susceptibility |
| Tiamulin | > 4 | > 4 (Ronne and Scanzer, 1990) | Decreased susceptibility |
| Tylvalosin | 2 | > 32 (Duran et al., 2009) | Susceptible |
| Lincomycin | 16 | > 36 (Ronne and Scanzer, 1990) | Intermediate susceptibility |

Table 3. Amount of antimicrobials (active substance, g or IU) used on the farm during 2009 and 2011, the indication to treatment, the category of pigs where the antimicrobial was used and the total medication costs for antimicrobials for both periods.

| Antimicrobial | Indication | Category | 2009 | 2011 |
|-----------------|--------------|-----------|----------------------|----------------------|
| Colistin | Diarrhea | Weaned | 6*10 ⁹ IU | 4*10 ⁹ IU |
| Amoxicillin | Streptococci | Weaned | 3425 g | 3237 g |
| Tiamulin | Dysentery | Fatteners | 3600 g | 0 g |
| Enrofloxacin | Diarrhea | Maternity | 160 g | 80 g |
| Ceftiofur | Respiratory | All | 135 g | 40 g |
| Lincospectin | Diarrhea | All | 12.5 g | 0 g |
| Neomycin | Infection | All | 25 g | 0 g |
| Total costs (€) | | | 3709 | 1052 |

(before treatment) and between December 2nd 2010 and December 8th 2011 (after treatment).

Parameters were calculated using Masvison[®]. The starting weights were estimated since no material was present to objectively measure groups of piglets at the start of the fattening period.

The amounts of antibiotics and the cost of these treatments were calculated by comparing invoices from 2009 and 2011.

RESULTS

The antimicrobial susceptibility of the *Brachyspira hyodysenteriae* isolate obtained in December 2009 is shown in Table 2. The isolate was considered resistant to pleuromutilins, and had a low MIC for tylvalosin. Since the elimination treatment, no signs of dysentery have been noticed in the sows, nor in the piglets born from treated sows. All fecal samples were negative by PCR for *Brachyspira hyodysenteriae*.

Technical parameters are presented in Table 1. An improvement of 12% in the feed conversion ratio (FCR) and a decrease in mortality from 3.99 to 2.49 % were noticed, resulting in a 3% lower amount of food for pigs at a 9 kg higher slaughter weight.

Comparing 2009 and 2011, an overall reduction of 71% of medication costs involving antibiotics was established (Table 3). The cost of tiamulin in 2009 was € 1318 or 35.5% of the antimicrobial costs. The cost of tylvalosin during the elimination protocol was € 6227.

DISCUSSION

In the present study, elimination of swine dysentery was attempted using tylvalosin, since the isolate was resistant to pleuromutilins. Successful treatment of the swine dysentery was described at a dose of 4.25 mg/kg BW tylvalosin (Tasker et al., 2004). No reports have been found using this molecule in elimination programs. In the literature, susceptibility has been reported between 66 % and 97 % (Vyt, 2011, Duran et al., 2009). MIC values slightly differ between studies, although the laboratory methods are similar. This phenomenon has been described for other molecules. The abundant use of pleuromutilins is considered to select for resistance (Lo-

bova et al., 2004). This phenomenon was also suggested on the farm of the present case where the clinical response to tiamulin decreased after three years of frequent treatment. Since no MIC of the isolate was made at the initial outbreak of the disease on this farm, this observation cannot be confirmed. Consequently, assessing the MIC prior to starting an elimination protocol is needed in order to comply with “Good Veterinary Practice” and prudent use of antibiotics.

Based on the clinical observations and the negative PCR results during one year after finishing the sow treatment, the elimination of dysentery on this farm has been considered successful. Besides good susceptibility to tylvalosin, other factors are considered important in achieving this success. First, temporarily selling piglets at 20 kg of weight to empty the pre-fattening units (20 to 35 kg) will have lowered the infection pressure and created the opportunity to establish a physical distance between the piglets born from treated sows and older piglets and fatteners with the disease. Secondly, the thorough cleaning of the sow unit was important to prevent re-infection from the environment. Moving out all animals for cleaning followed by emptying the slurry pits and washing the sows prior to returning proved to be a good strategy.

The protocol on this farm was based on an elimination protocol for this type of farm which has been described earlier (Vyt et al. 2007). Instead of treating for six weeks with the last three weeks at half the dose as described, a treatment with tylvalosin for four weeks at 4.25 mg/kg BW was preferred in order to reduce the risk of resistance selection. In this type of protocol, the farmer’s awareness of the possible risks of carry-over from the older, infected fatteners to the clean animals, is crucial. Detailed explanation prior to the start of the protocol and frequent follow-up by the herd veterinarian are important in order to maintain an optimal separation of both animal groups for several months.

The comparison of technical parameters before and after the elimination protocol emphasizes the impact of dysentery on growth. Feed conversion from 22 kg to slaughter improved dramatically, and although the slaughter weight was 9.3 kg higher, the amount of feed in the fattening period decreased by 3%. The decreased feed costs in the absence of dysentery was 12%. The part

of this improvement that is due to the elimination of dysentery cannot be exactly quantified in this field case, since commercial and zootechnical changes are inevitable when using data of a long time period. Although there were no changes in genetics or in vaccination scheme, and although no other diseases were recorded in that period, the influence of using Improvac® on growth cannot be discriminated (Oliver et al., 2003). Based on these data, the impact of dysentery on productivity can be estimated. To produce a 70 kg meat gain during the fattening period, the absence of *Brachyspira hyodysenteriae* results at current feed price in a gain of € 8.85 per fattening pig. For 3000 pigs slaughtered a year, a reduction of the feeding cost of € 26550 was achieved by eliminating dysentery. Especially at the current high feed prices, feed conversion has a large impact on profitability which makes it important to lower disease pressure and eliminate diseases such as dysentery. In the literature, data on the effect of the elimination of swine dysentery on technical parameters are scarce. In an earlier study, Wood and Lysons (1988) found an even higher decrease in feed conversion of 0.58 and calculated a comparable £7.31 (€ 8.73) increase in feed costs. Detailed differences in technical parameters before and after disease elimination as presented in this study can be an important tool for practitioners to motivate farmers to eliminate swine dysentery.

Another important aspect of eliminating a disease such as swine dysentery is the reduction of antimicrobial use after elimination, not only because of the effect on the production cost of frequent treatments (Wood and Lysons, 1988), but also because of the risk of induction of antimicrobial resistance and subsequent spread of resistance genes (McEwen and Fedorka-Cray, 2002). In the present study, a reduction of the costs of antimicrobials of 71% was achieved. This reduction cannot be explained completely by stopping tiamulin treatments. It can be speculated that medication for the treatment of diarrhea (colistin, enrofloxacin, lincospectin) diminished since the disturbing influence of dysentery on the intestinal content disappeared. Furthermore, stopping castration of piglets and changing to vaccination (Improvac®, Pfizer, Zaventem, Belgium) are responsible for the decrease of preventive medication for the treatment of streptococcal disease. The reduction of treatment of respiratory diseases may be explained by the effect of tylvalosin (used in the treatment of sows) on *Mycoplasma hyopneumoniae* which was present on this farm, subsequently reducing its transmission from sows to piglets. If the large reduction of antimicrobial usage is the result of the above mentioned speculations or simply due to lowered infection pressure by selling piglets between 20 and 35 kg could not be objectively determined. In addition, the influences of reduced infection pressure, of the decrease of other gastro-intestinal and respiratory problems and the influence of intact boars on the increased productivity parameters could not be determined separately in this on-farm setting. In line with prudent use of antibiotics and based on the data in the present study, the elimination of dysentery with

a well-defined antimicrobial treatment should be preferred to continuous treatments over a period of several years.

In conclusion, the results of this study confirm that tylvalosin can be used to eliminate swine dysentery on single-site, farrow-to-finish farms at a dose of 4.25 mg/kg BW given daily for four weeks. Therefore, tylvalosin, a macrolide, may be an alternative treatment in cases of pleuromutilin resistance of *Brachyspira hyodysenteriae*. Although the exact contribution could not be discriminated from other influences, the elimination of dysentery resulted in improved technical parameters as well as in a reduction of the cost of antimicrobial treatments.

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Uit het verleden

VERVELLEN OM EEUWIG TE LEVEN

Uit het epos van Gilgamesj (Sumerië, omstreeks 4650 jaar geleden)

De vroegst opgeschreven mythe (oudste versie rond 1750 vóór onze jaartelling ten tijde van koning Hammoerabi, maar nog ouder dateerbaar) eindigt werkelijk triestig. De grote held en halfgod koning Gilgamesj had na de dood van zijn vriend, de sterveling Enkidoe, gezworen dat hij het geheim van de onsterfelijkheid zou vinden en tot zijn geliefde volk in de sterk ommuurde stad Oeroek aan de Eufraat te brengen. En, inderdaad, na een reeks onbeschrijfelijke avonturen was hij erin geslaagd de bloem van de eeuwige jeugd te plukken op de bodem van de diepe zee. Maar dan loopt het mis.

De lange reis naar Oeroek verliep nochtans eerst nog voorspoedig. Gilgamesj hield de bloem in zijn hand en geen gevaar kon hem bedreigen. Af en toe snoof hij de verrukkelijke geur ervan op. Op een middag kwam hij, moe en stoffig, bij een fris meertje wonderlijk blinkend midden in de woestijn. Hij trok zijn kleren uit en legde de kostbare bloem voorzichtig op een steen bij het water en nam een duik. Na een poosje waadde Gilgamesj naar de oever, net op tijd om te zien hoe een slang, aangetrokken door de geur, met de bloem van de eeuwige jeugd in zijn bek verdween. Hoe hij ook zocht, de bloem bleef onvindbaar. Naakt zat hij neer bij het meertje en weende.

Diep ongelukkig keerde koning Gilgamesj naar Oeroek terug. Niets kon hem opvrolijken. 'Hiervoor heb ik gezwogen,' vertelde hij zijn volk. 'Hiervoor heb ik gevochten met een verschrikkelijk monster en heb ik mijn krachten gemeten met de Hemelstier. Hiervoor heb ik mijn dierbare vriend Enkidoe zien afdalen naar de plek vanwaar terugkeer niet mogelijk is. Hiervoor - om het eeuwige leven te brengen aan slangen en niet aan mijn beminde volk!'

NvdR. Men neemt aan dat de oude opvatting dat slangen eeuwig zouden leven, zijn oorsprong vindt in hun vermogen hun oude huid af te werpen en met een nieuw en jeugdig velletje verder te leven. Het *Journal of Herpetological Medicine* en de beoefenaren van deze jonge tak van de diergeneeskunde houden er een andere mening op na.

Luc Devriese