Feedlot gastrointestinal parasite control and anthelmintic treatment options, a review

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Abstract

Anthelmintics are an important tool in the feedlot industry. The goal of this review article is to provide the veterinary practitioner with a short summary of the important aspects of internal gastrointestinal parasite control in the feedlot. A review of economically significant gastrointestinal nematodes and the bovine liver fluke is provided, along with a discussion of treatment options and an anthelmintic efficacy assessment. Important aspects unique to the feedlot environment are addressed, including anthelmintic resistance and combination anthelmintic therapies.

Key words: bovine, feedlot, parasitology, anthelmintic, gastrointestinal nematodes, flukes

Résumé

Les anthelminthiques sont des outils importants pour l'industrie des parcs d'engraissement. Le but de cette revue est d'offrir au vétérinaire praticien un survol des aspects les plus importants du contrôle des parasites gastro-intestinaux internes dans les parcs d'engraissement. Cette revue considère les nématodes gastro-intestinaux ayant un impact économique et la douve du foie chez les bovins et comporte une discussion des options de traitements et une évaluation de l'efficacité des anthelminthiques. Les aspects uniques reliés à l'environnement des parcs d'engraissement sont mis en évidence incluant la résistance aux anthelminthiques et les thérapies anthelminthiques combinées.

Introduction

Three major classes of anthelmintics are available for the feedlot industry in the United States. These include imidazothiazoles (levamisole), benzimidazoles (albendazole, fenbendazole, and oxfendazole), and macrocyclic lactones including the first-generation avermectins (ivermectin, doramectin, and eprinomectin) and second-generation milbemycin (moxidectin). The importance of efficacious anthelmintics for the feedlot industry is well recognized. Typically, when compared to non-treated controls, deworming can be expected to improve dry matter intake, feed efficiency, and weight gain. Often an improvement in carcass quality is also observed with anthelmintic treatment. This treatment effect was shown in a single feedlot trial with over 6000 heavyweight yearling steers.[10] In this study, treatment with an injectable avermectin at feedlot entry was associated with statistically significant improvements in average daily gain (ADG), dry matter intake, feed efficiency, and carcass grading when compared to negative controls.

Bovine Nematodes

Important abomasal nematode parasites of feedlot cattle include *Ostertagia ostertagi*, *Haemonchus placei*, and *Trichostrongylus axei*. In terms of relative clinical importance, *O. ostertagi* is considered the most important helminth parasite of cattle in the United States.[2] The predilection of *O. ostertagi* for the abomasum can lead to chronic abomasitits in young cattle. Significant infections can lead to malnutrition and wasting, even in the presence of excellent nutrition.[2] Typical of ruminant nematodes, *O. ostertagi* has free-living larval stages on pasture, that following ingestion of the infective stage, develop into the fourth-stage larval (L4) forms in the abomasum. Once in the abomasum, the fourth-stage larvae may develop directly into mature adults (Type I ostertagiasis) or enter an inhibited (hypobiotic) state in the abomasal mucosa (Pre-Type II ostertagiasis).[1] The L4 enter the Pre-Type II ostertagiasis hypobiotic state when the environmental conditions are not conducive to larval survival on pasture, summer in the southern United States and winter in the northern United States. Through a mechanism that is not understood, when environmental conditions improve, the inhibited fourth stage larvae become metabolically active and quickly develop into mature adults (Type II ostertagiasis). If the inhibited L4 population in the abomasum is high, the result can be the rapid development of clinically severe ostertagiasis in previously normal feedlot animals.

In contrast to the historically recognized importance of ostertagiasis in the feedlot, pathogenic nematodes of the small intestine, especially *Cooperia* spp, have recently achieved greater recognition due to reports of anthelmintic resistance and feedlot production impact. A recent report states that based on the 2008 USDA National Animal Health Monitoring System Beef Cow/Calf survey, *Cooperia* spp have become the most prevalent parasites in the United States' cow/calf industry.[13] The report authors state that this recent development is due in part to the widespread use of macrocyclic lactones and the reduced efficacy of these products against *Cooperia* spp. Also, in the same report, the authors demonstrated in a 60-day feedlot trial that artificial infection of feedlot steers with a monoculture of *C. punctata* led to a 0.24 lb (0.11 kg) decrease in ADG (P=0.02) and a 1.5 lb (0.68 kg) daily decrease in dry matter intake, compared to controls (P=0.02).

Bovine Liver Flukes

While the importance of controlling ruminant nematodes in the feedlot is well established, the importance of the cattle liver fluke, *Fasciola hepatica*, in the feedlot is an area of some debate. In contrast to the pathogenic nematodes, the bovine liver fluke requires an intermediate snail host and has a longer life cycle.[2] The infective stage is ingested on pasture, and immature flukes migrate for several weeks in the liver parenchyma. After more than 2 months, the immature flukes develop into mature egg-producing adults in the bile ducts. Endemic fluke areas are limited by the intermediate snail host, and include coastal marsh areas of the southeastern United States, the coastal Pacific Northwest, and numerous irrigated pasture and river valleys in the southeastern and western United States. The cycle has important seasonal differences, with transmission occurring approximately mid-summer to December in the Pacific Northwest and approximately February to July along the Gulf coast.[8] Also, due to the required intermediate host, moving fluke infected cattle to the snail-free feedlot environment stops the cycle of transmission.

Flukes can cause a disease syndrome associated with loss of condition, anemia, and hypoproteinemia leading to edematous subcutaneous swelling, especially in the intermandibular space. However, likely far more important to the feedlot industry is liver condemnation at slaughter.[2] In endemic areas, liver condemnation due to flukes can exceed 90%.[8] Treatments currently available in the United States include albendazole at 4.5 mg/lb (10 mg/kg) and clorsulon at 0.9 mg/lb (2 mg/kg) (sold in combination with ivermectin). These products will only kill the adult flukes in the bile ducts. Previously, clorsulon at a higher concentration of 3.2 mg/lb (7 mg/kg) was available for controlling the migrating immature flukes. However, currently no product is available in the United States to control the immature larval stage or prevent the subsequent liver damage.

Separate from liver condemnation, published studies demonstrating a performance advantage following fluke treatment upon feedlot entry are limited. For critical evaluation of feedlot trials with clorsulon, drug concentration is critical since 0.9 mg/lb (2 mg/kg) will only eliminate adult flukes and the 3.2 mg/lb (7 mg/kg) product is no longer available. Two feedlot studies have been reported using weaned calves or stockers that were previously grazed on pastures with a history of high fluke incidence.[8] Treatments consisted of 0.9 mg/lb (2 mg/kg) clorsulon with ivermectin (90.9 µg/lb [200 µg/kg]), doramectin alone (90.9 µg/lb [200 µg/kg]), or negative controls. In both studies, treatment with 0.9 mg/lb (2 mg/kg) clorsulon was not associated with a statistically significant difference in liver condemnation rate between treatment groups (weaned calves: 97 to 99%, stockers: 68 to 73%). In both studies, no statistically significant differences were observed in feedlot performance between the clorsulon-ivermectin group and the doramectin-only treatment group.

In contrast to these reports, a separate study reported a significant effect on feedlot performance in artificially challenged calves.[11] In this study, 60 cattle were artificially infected with 500 fluke metacercaria. For the first 69 days post-infection the cattle were grazed on pastures and then transferred to a feedlot. Upon entry into the feedlot, when the majority of infective flukes were adults, half of the animals were treated with 0.9 mg/lb (2 mg/kg) clorsulon in combination with ivermectin (90.9 µg/lb [200 µg/kg]), while the rest received ivermectin alone (90.9 µg/lb [200 µg/kg]). After 124 days on feed, clorsulon-treated cattle had a carcass adjusted total weight gain advantage of 28.5 lb (12.9 kg) with an adjusted ADG advantage of 0.23 lb (0.10 kg) (P<0.05). In summary, based on the available literature, the significance of bovine liver flukes on feedlot performance is unclear. Also, the available treatments for liver flukes are limited.

Bovine Nematode Diagnosis and Anthelmintic Selection

In the majority of feedlots, anthelmintic treatment selection for internal nematodes is based on known parasite risk, product label indications, perceived efficacy, ease of administration, and product cost. Typically, products are not tested for efficacy in the feedlot unless a case of product failure is suspected. To determine product efficacy, 2 methods are available: the controlled efficacy test and an assessment of fecal strongyle egg count before and after treatment, referred to as the fecal egg count reduction test (FECRT). The controlled efficacy test determines the actual number of worms present in animals before and after treatment by necropsying a selected population of animals pre- and post-treatment. Given the cost and expertise required for controlled studies, some version of the FECRT is the method used by most feedlot practitioners to determine product efficacy. The assumption of the FECRT is that reduction post-treatment in the fecal strongyle egg count will correlate with adult nematode killing. However, the FECRT has multiple limitations that need to be considered, including technical expertise, proper study design, test limitations, and specific parasite differences.[9] Also, since nematode genus cannot be accurately determined based on egg morphology, relative nematode genera will not be known without the technically more challenging coproculture and third-stage larval identification.[14] Since the FECRT is based on the percent of reduction in egg shedding post-treatment, the test provides no information regarding the immature inhibited fourth-stage larvae of Type II ostertagiasis. For example, a documented case of *O. ostertagi* inhibited L4 avermectin resistance would have gone unrecognized if based on FECRT results alone.[5] Also, macrocyclic lactone treatment may cause a temporary decrease in egg shedding without killing the adult parasite. Again, the result can be a significant reduction in the amount of fecal strongyle egg shedding without a corresponding adult nematode reduction.[3,15] Finally, a significant issue with the FECRT in the feedlot environment is that under long-term feedlot housing, fecal strongyle egg shedding often continues to decline without treatment.[8,10,14] This is likely due to ration change in the feedlot, lack of reinfection, and animal/immune system maturation. These factors have lead some authors to conclude that the FECRT may be invalid for feedlot operations and that an alternate method of determining product efficacy may be needed.[14] In conclusion, the FECRT may have applications in the feedlot environment but, as is the case with many clinical tests, the practitioner must interpret the results in light of the clinical condition of the subject animals and technical limits of the test.

Anthelmintic Resistance and Combination Therapies

A key difference between pasture and feedlot parasite control is the lack of reinfection in the feedlot environment. Since the free-living larval stage is not present, if the initial arrival anthelmintic treatment is effective, additional treatment will not be needed. Also, if feedlot treatment causes the selection of anthelmintic resistant nematodes, there can be a significant effect on the individual animal, but amplification of these resistant nematodes through subsequent animals is not possible. Therefore, anthelmintic treatment in the feedlot should be considered a closed system. However, given multiple animal origins in the feedlot, the possibility of encountering anthelmintic resistant nematodes cannot be ignored.[15]

Numerous publications have documented *Cooperia* spp and *H. placei* avermectin resistance in the United States.[4,5,6,13,14] Avermectin resistant *O. ostertagi* has also been documented from a single location in California.[5] While the extent and seriousness of these newly recognized cases of anthelmintic resistance are debated, it is clear that this will be a growing problem for the feedlot industry. As these case reports increase, practitioners will have to make feedlot-specific anthelmintic treatment recommendations based on current product efficacy results. In this environment, feedlot entry combination treatments using benzimidazoles or imidazothiazoles and macrocyclic lactones continue to gain attention. The benzimidazoles or imidazothiazoles, when given at approved dose rates, do not provide effective control of the inhibited fourth-stage larvae of Type II ostertagiasis.[14] However, these products can be effective against macrocyclic lactone resistant *Cooperia* spp. Also, macrocyclic lactones can provide control of inhibited *O. ostertagi* L4. Again, the efficacy of combination products will have to be based on feedlot testing results.

Published results with combination therapies in the feedlot are varied, and dependent on many factors. In 1 feedlot study with 2647 steers on feed for 181 days, the report authors demonstrated no statistically significant difference in feedlot performance between animals treated with either an injectable macrocyclic lactone alone (moxidectin or doramectin), or a macrocyclic lactone (doramectin) in combination with a benzimidazole (oxfendazole).[7] In this trial, although a true evaluation of nematocidal efficacy required a controlled efficacy trial, a FECRT at 28 days post-treatment found no evidence of macrocyclic lactone resistance. The authors of this trial did state that there was a trend towards better animal performance and reduced egg shedding in the combination therapy group, and hypothesized that this difference might be due to the removal of non-patent nematode populations (such as inhibited larval populations). In comparison, a separate report of 2 feedlot trials with a total of 1862 yearling heifers found statistically significant improvements in feedlot performance for animals treated with a combination macrocyclic lactone/benzimidazole program, compared to a macrocyclic lactone alone.[12] In the first of these studies, heifers treated with pour-on ivermectin in combination with fenbendazole compared to pour-on ivermectin alone had statistically significant improvements in ADG, live weight, and carcass weight. In the second study, heifers treated with pour-on ivermectin and fenbendazole compared to injectable doramectin alone had statistically significant improvements in ADG, live weight, and carcass weight. It is unclear from the data provided if the observed performance advantage was due to differences in nematode anthelmintic resistance.

Conclusion

The clinical and economic importance of anthelmintics for the feedlot industry is well recognized. Ostertagiasis has historically been considered the most important helminth disease of cattle in the United States. The ability of *O. ostertagi* L4 to enter an inhibited state in Pre-Type II ostertagiasis can have a serious impact in the feedlot. Also, the fact that the immature larval stages do not produce eggs can provide a false indication of anthelmintic efficacy. The significance to the feedlot industry of a case report of avermectin resistant *O. ostertagi* inhibited fourth-stage larvae is unknown, but merits close scrutiny. In addition to ostertagiasis, *Cooperia* spp have gained more attention due to numerous reports of avermectin resistance and the apparent, previously unrecognized, clinical and economic impact in the feedlot. In comparison to the clear importance of gastrointestinal nematodes, the impact of bovine liver flukes on feedlot performance is unclear and no effective therapies are available in the United States for controlling the immature migrating stages.

As reports of apparent anthelmintic resistance continue to mount, practitioners will have to make feedlot-specific treatment recommendations. The gold standard for efficacy determination is the expensive and technically complicated controlled efficacy test. The FECRT is a tool that practitioners can readily use, but results must be considered in light of many test limitations including a typical gradual decrease in egg shedding with increasing days in the feedlot, inability to detect immature larval stages, and the potential for egg shedding reductions without concurrent worm elimination. When dealing with cases of apparent treatment failures, practitioners will have to consider the lack of anthelmintic resistance amplification in the feedlot and the unique opportunities this provides when compared to grazing situations. The use of combination treatment methodologies may have merit under certain situations, but as is the case with all treatment regimens, selections must be made on a feedlot-specific basis using all information available to the practitioner.

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