Assessment, management, and control of internal parasites in beef cattle production systems

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Abstract

Gastrointestinal nematodes are important pathogens of cattle due to their negative impact on both health and productivity at the individual and herd level. Chemical control has historically been a highly effective means of controlling parasites and, as a result, is frequently the sole method of control used on many farms. Consequently, numbers of reports of anthelmintic resistance are increasing worldwide, including reports in the United States. To help monitor the efficacy of anthelmintics on individual farms, veterinarians should recommend testing for resistance to all of their producers. Alternative control strategies, such as targeted selective treatment and pasture management, should be used with good drug stewardship to slow the development or progression of anthelmintic resistance and preserve the efficacy of these drugs.

Key words: parasite management, anthelmintic resistance, refugia, fecal egg count reduction test

Résumé

Les nématodes gastro-intestinaux sont d'importants pathogènes chez les bovins en raison de leur impact négatif à la fois sur la santé et sur la productivité au niveau individuel et au sein du troupeau. Le contrôle par voie chimique s'est avéré un moyen extrêmement efficace pour contrôler les parasites et par le fait même il est fréquemment la seule méthode de contrôle utilisée dans plusieurs fermes. Par conséquent, le nombre de rapports rapportant des cas de résistance anthelminthique ne cesse d'augmenter à travers le monde incluant des rapports de cas aux États-Unis. Afin de surveiller l'efficacité des anthelminthiques au niveau de la ferme, les vétérinaires devraient recommander de tester la résistance à tous leurs producteurs. Les stratégies alternatives de contrôle, comme le traitement sélectif ciblé et le contrôle des pâturages, devraient être utilisées avec une saine gestion des médicaments afin de ralentir le développement ou la progression de la résistance anthelminthique et préserver l'efficacité de ces médicaments.

Introduction

Grazing livestock species are continuously exposed to and infected with gastrointestinal nematodes (GIN). These parasites represent an important group of pathogens because they cause health and productivity problems and are estimated to cause billions of dollars of lost productivity and drug costs globally.[27] Because of the negative consequences of infection with GIN, veterinarians and producers must develop and utilize appropriate management and control strategies to maintain herd health.

There are 5 main genera of GIN in the United States, including *Cooperia, Ostertagia, Haemonchus, Trichostrongylus,* and *Oesophagostomum*. All species have a direct life cycle, eggs are shed onto pasture in the feces, where they hatch and develop to the infective third-stage larvae. When cattle consume the infective larvae, the larvae molts, eventually developing to an adult, mating, and shedding eggs into the feces. The non-specific signs of disease, or parasitic gastroenteritis, include decreased weight gain, diarrhea, and anorexia. The eggs of this group are morphologically indistinguishable amongst species and are characterized by an oval shape, thin-shell, morula which nearly fills the egg, and range in size from 65-100 x 34-50 μm.[46] Although individual species may trend towards the upper or lower end of the size range, too much overlap in size exists to accurately and reliably differentiate eggs based on visual inspection.[46]

The 2 most important genera within this group are *Cooperia* and *Ostertagia* due to their typically high infection rate in calves and pathogenicity, respectively. *Cooperia* spp are common parasites of the small intestine of young calves; in the United States, *C. punctata* and *C. oncophora* are the most common species. While low-intensity infections are typically subclinical, uninfected calves have been reported to gain weight more rapidly and consume more feed than their infected counterparts and heavy infections can lead to parasitic gastroenteritis.[39] In dairy cattle, infection with *Cooperia* spp has been associated with decreased milk production.[19] *Cooperia punctate* and *C. pectinata* are more pathogenic than other species because their fourth-stage larvae can invade the muscoa. *Cooperia* infections are mostly limited to young animals, immunosuppressed animals, or individuals who have never been exposed to a particular species of *Cooperia* because cattle typically develop immunity to this genus by 1 year of age.[24]

Ostertagia spp, colloquially known as the brown stomach worm, are parasites of the abomasum. *Ostertagia* spp third-stage larvae molt in the abomasal glands. Then, these fourth-stage larvae enter a hypobiotic or quiescent state when environmental conditions are not ideal for survival;

in tropical and sub-tropical climates, this occurs in the hot, dry months and in temperate and sub-arctic climates, this occurs in the winter.[1] Due to their invasion of the gastric glands and the ability to undergo hypobiosis, these nematodes are the most pathogenic of the trichostrongyles in cattle. Calves infected when environmental conditions are favorable develop a condition known as type I ostertagiosis, while calves infected late in the grazing season experience type II ostertagiosis, caused by the mass emergence of encysted early fourth-stage larvae.[1,5] This syndrome is characterized by diarrhea, destruction of gastric glands, acid-base abnormality, wasting, and death.[5] Following emergence from the gastric glands, larvae develop into adults.

Chemical Control

Since their introduction to the market, chemical anthelmintics are heavily, and frequently solely, relied upon by producers to control parasite infections. When they were first introduced to the market, all of these products were highly effective, so producers and veterinarians did not think progressively and use them in a sustainable manner. There are 3 major classes of anthelmintics approved for the control of GIN of cattle in the United States, including macrocyclic lactones, benzimidazoles, and imidazothiazoles.

Macrocyclic lactones for cattle are available as topical and injectable products and, in the United States, include ivermectin, doramectin, eprinomectin, and moxidectin. These products are effective against a variety of nematodes and ectoparasites. The majority of products on the market are short-acting; however, a more recently developed formulation of eprinomectin[a] provides longer-acting control of GIN than other avermectin products.

Benzimidazoles, or white wormers, are available as oral formulations and include albendazole, fenbendazole, and oxfendazole. They have a broad spectrum of activity and are effective against all of the GIN, including some immature stages, as well as some cestode and trematode species, which makes them valuable in regions of the country where *Fasciola hepatica* is endemic. This anthelmintic drug class has a wide margin of safety, although albendazole has been reported to cause teratogenesis in early pregnancy. Subsequent studies in rodents and cattle have been unable to replicate this finding.[42,43] The cattle study did find that administration within 2 weeks of insemination led to decreased conception rate, but cows treated at the end of their first trimester did not demonstrate any apparent adverse effects.[43]

Levamisole is the only imidazothiazole that is commercially available for any species and is formulated as both oral or injectable medications.[5] Unlike macrocyclic lactones and benzimidazoles, levamisole is only effective for the control of nematodes.[8,32] Of the 3 classes of anthelmintics used in cattle, imidazothiazole has the lowest margin of safety.[25] Signs of intoxication include salivation, lacrimation, neurologic signs, head shaking, ataxia, muscle tremors, and death.[25]

Despite the initial high efficacy observed with these drugs, in the past 20 years there have been increasing reports of resistance worldwide in many production systems, including cattle.[6,11-14,16,20,31,35,36,40,41,45] Reports of drug failure are most common in the macrocyclic lactone drug class.

Resistance Testing

Measurement of fecal egg counts (FEC) is the standard approach for assessing strongyle-type parasite egg shedding in livestock species, and is the primary means for evaluating anthelmintic drug efficacy. Many fecal egg-counting techniques are described in the literature, varying in detection sensitivity, accuracy, precision, and technical difficulty.[2,17,34,38] Knowledge of FEC, ability to perform, or access to a diagnostic lab is crucial because the only currently available method of assessing resistance to anthelmintics at the farm level is the fecal egg count reduction test (FECRT).

For cattle, it is recommended that each treatment group has at least 15 animals with an average of 150 eggs per gram.[10] A fecal sample is collected at the time of treatment and a fecal egg count is performed on each sample. The post-treatment collection timing is dependent on which drug is being tested: levamisole 3 to 7 days, benzimidazole 8 to 10 days, macrocyclic lactones 14 to 17 days. If multiple drugs are being tested in an individual herd, it is acceptable to collect all post-treatment samples on day 14.[10] Again, following post-treatment collection, a fecal egg count is performed on each sample. Diagnosis of resistance is based on the following guidelines: if percent reduction is less than 95% and the lower confidence interval is less than 90%, that is a resistant population; if the opposite of both is true, it is a susceptible population; and if only 1 of the 2 parameters is met, then resistance is suspected but cannot be definitively diagnosed.[9]

Although FECRT are an effective method of diagnosing resistance in a parasite population, the number of FEC required can become time-consuming and expensive for producers. As a result, researchers have evaluated the accuracy of composite FEC in resistance testing and have found strong agreement and correlation between the methods.[15,23] Similar to the traditional FECRT protocol, samples should be collected at the time of treatment and at the appropriate post-treatment time. An equal weight of feces from each individual in a treatment group should be well-homogenized and FEC performed on this composite sample. FEC should be prepared and counted until 200 eggs have been observed.[30] The same number of FEC required to reach that number pre-treatment should again be counted on the post-treatment samples. Again, percent reduction can be calculated and the same guidelines applied.

Sustainable Control Strategies

Refugia
Anthelmintics will continue to play an important role in the management of GIN, but due to the rapid increase

in cases of anthelmintic resistance, there is a need to develop and apply novel approaches to manage and slow this progression. Producers use anthelmintics because of the production benefits associated with low parasite intensity in their herd, so it is necessary to develop a control strategy that allows for health and the production benefits of using anthelmintics, while preserving their efficacy over the long term. One strategy that can be adopted is the use of refugia to help slow the development of anthelmintic resistance in the parasite population.[44] Refugia is defined as the proportion of the worm population that are not selected by drug treatment. The greater the proportion of the total parasite population that are left as refugia, the slower resistance will develop. Sources of refugia include the worms in animals that are left untreated at the time of the treatment event, stages of parasites in the host that are not affected by the treatment, and eggs and immature larvae on pasture. Managing refugia is crucial for reducing the rate of resistance development, maintaining the efficacy of anthelmintics, and maintaining the same productivity.[4] Any alternative control strategy that is perceived by the producer to be financially or medically disadvantageous is unlikely to be adopted.

Most of the work in refugia treatment strategies has been done in sheep production systems, however, given the similar parasite species composition and life history and management of cattle, it is likely that the same principles would apply to this type of production system.[4,22,26,33] A study in New Zealand found that leaving a portion of the population untreated over 3 grazing season led to a significant decrease in drug resistance as compared to treating all the animals.[29] Importantly, several studies suggest that applying refugia-based strategies does not significantly reduce herd/flock productivity.[2,7,18] Although the percentage of the herd that should be left untreated is dependent on the efficacy of the treatment, the general recommendation is to leave 10% untreated. The producer or veterinarian, should select the animals that appear the healthiest at the time of anthelmintic application to be left untreated. The individuals left untreated do not need to remain the same over time. Mature cows do not have the same parasites as calves, so it is important that 10% of each type is left untreated.

The concept behind refugia-based approaches is that the untreated animals will shed parasites onto the pasture that have not been exposed to anthelmintic. The untreated animals will likely harbor a mixture of susceptible and resistant worms, but these parasites will not be selected for the development of drug resistance. If the drug used on the treated animals is highly effective, the number of eggs being shed by the untreated, refugia group will be greater than the few eggs being shed by the treated animals. This will allow for a dilution effect of the resistant genes in the population and will help producers maintain a susceptible population of parasites. For this strategy to be impactful, it is necessary for the deworming protocol to be highly effective, so that the majority of GIN that remain in the population are susceptible,

so if the refugia group is too small or the drug used is not highly effective, the benefit of refugia will be lost.

Other management strategies

In addition to selective treatment of animals, producers can use other management strategies to help lengthen the efficacy of chemical anthelmintics. The majority of parasite larvae live in the bottom 2 inches of grass. Keeping grass taller and rotating animals off pastures before they become overgrazed can reduce exposure to infective larvae.

Ensuring that each animal is receiving an appropriate dose of drug is necessary for adequate control. Under-dosing animals is believed to be a contributing factor in the selection of anthelmintic resistance. This can be achieved by appropriately training and educating whoever is applying the drug so that all of the drug gets in, or on, the animal. Equipment should be calibrated, so there is less of a risk of a mechanical cause of under-dosing. Ideally animals should be weighed individually or all animals should be dosed to the heaviest in the group.

Treatment Recommendations

Cow-calf

The refugia-based approach should be used for cow-calf production systems. It is important to understand that calves and mature cattle do not harbor the same parasites and that resistance develops at the species level. In a mixed population of GIN, it is possible to have some species that are resistant and some that are susceptible to an anthelmintic. Calves can be infected with any of the GIN, but typically, *Cooperia* is the most common genus. Mature cattle are more likely to have immunity to *Cooperia*. *Ostertagia* spp is a major concern for all ages of cattle. Because of these observed differences in parasite communities, when selecting animals to be left untreated, calves and mature cattle should be treated as separate herds. For both groups, 10% of the herd should be left untreated to reduce the development of resistance.

While it should not be used as a solo method of overcoming anthelmintic resistance, concurrent therapy with 2 drugs from different drug classes can be used to help prolong the efficacy of the currently available drugs. Modeling studies have shown that the use of 2 drugs simultaneously can slow the development of resistance, as long as resistance is not too prevalent in the population.[3,29,37] In a field trial, sheep parasites with existing resistance to ivermectin and levamisole did not become more resistant to either drug following concurrent therapy.[28] There is a concern that if concurrent therapy alone is recommended to producers, without careful guidance, they may unintentionally use this method inappropriately and parasites resistant to multiple drug classes will be selected. Concurrent therapy used with other alternative control strategies, including pasture management and targeted, selective treatment plans would be more beneficial than concurrent therapy alone.

Feedlot

Animals in feedlots have different needs than cow-calf operations. All animals should be treated with concurrent therapy upon arrival to the feedlot to reduce parasite intensity in all animals. Although they may still shed resistant parasites, these animals are not on pasture and will not be continuously exposed to GIN. As in any other situation, ensuring the proper dose is given will reduce parasite populations as much as possible and be beneficial for productivity.

Conclusions

Appropriate management of gastrointestinal nematodes is vital for optimal health and productivity of cattle. Adequate resistance testing and application of an integrated approach to control should be used to help preserve the efficacy of chemical anthelmintics for the future. Veterinarians and producers should work together to develop an ideal management strategy taking into account what drugs have been used on the farm previously, resistance status of the parasite population, and type of livestock system.

Conflict of Interest

The authors declare no conflict of interest.

Endnote

[a]LongRange®, Boehringer-Ingelheim Ingelheim, Germany

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