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Sheep drench combinations, resistance and 'refugia'

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Terms and abbreviations used

BZ: benzimidazole

LEV: levamisole

ML: macrocyclic lactones

FECRT: faecal worm egg count reduction test

Refugia: the proportion of the worm population that escapes exposure to a drench. This usually means the worms (eggs and larvae) that are on pasture.

Summary

On many, if not most, farms in NSW, 'multi-active' or 'combination' products can play an important role as highly effective drenches in an integrated parasite control program.

An advantage of combination products is the potential to delay the development of resistance. This advantage is greatest if each active in the product is highly effective on its own.

No single product can be guaranteed to be 'the best' on all farms and in all situations. It is still important to do a DrenchTest on individual properties to determine which products are appropriate.

If shown to be effective, naphthalophos-BZ/LEV combinations should be considered as an alternative to ML-only products or multi-active products containing ML.

Leaving a proportion of a mob of sheep untreated should only be done on individual properties in NSW with professional advice, especially in areas where barber's pole worm is a significant problem.

Avoid unnecessary drenching, particularly when there a few worms in refugia – e.g. during droughts or extended dry spells.

Combinations of broad-spectrum sheep drenches, 'refugia' and resistance are hot topics these days in sheep worm control.

Combinations – a good idea

Parasitologists generally agree that, if delaying resistance is the prime objective, it is better to use a combination of two or more effective broad-spectrum drenches than using these drenches on their own (Dobson and others, 2001). Such a combination will be better at killing resistant worms than the individual 'actives' acting alone, and thus the development of anthelmintic resistance will be slower.

Not a magic bullet

Combinations are not a 'magic bullet' and will not prevent development of anthelmintic resistance. Integrated parasite management – including non-chemical control options – is still strongly encouraged.

Before using drenches or combinations of drenches, they should first be tested on individual properties. The only reliable way of evaluating combination products on a property is to include the product in a FECRT ('DrenchTest'). A less accurate but still useful method is 'DrenchCheck': a worm egg count 10–14 days after routine treatment of a group of sheep. The efficacy of a multiple active product cannot be predicted reliably by extrapolating from the FECRT data for the individual actives.

Combinations and drench rotation

It is generally agreed that using unrelated drenches A, B and C in combination will be better at delaying the development of resistance than rotating (annually or otherwise) from A to B to C. Cost, however, is a consideration and needs to be weighed against the likely benefit of slower development of drench resistance. Also, for other

reasons, farmers may elect to use particular 'single-active' products in certain classes of sheep at certain times rather than 'multi-active' products. An example, discussed later, is the use of persistent drenches to control *Haemonchus* – barber's pole worm.

The 'perfect' combination

Following are attributes of an 'ideal' combination product:

- A stable and safe combination of two or more unrelated 'actives'. 'Unrelated' means they are from different 'action families', i.e. they have different modes of action. A combination of three effective 'actives' will usually be better than a combination containing two.
- Each 'active' should be highly effective, with resistance to each rare. In reality, this may be difficult to achieve. In NSW for example, about 90% of farms have resistance (efficacy <95%) to BZ ('white') drenches, about 80% have resistance to LEV ('clear') drenches, and about 60% have resistance to BZ/LEV combinations. Resistance to MLs (mectins) is now common. However, even a combination containing some actives that are only moderately effective may still be preferable (better at killing resistant worms) than drenches used individually.
- The spectrum and persistence of activity of each of the combination's components should be similar – i.e. the component 'actives' should be working against the same worm species and for a similar length of time.

In reality, however, the 'ideal' is not always achievable, and inevitably compromises have to be made.

Naphthalophos combinations

Naphthalophos (NAP) – Rametin® (Bayer), Combat® (Virbac), and Pole Vault® (Allfire Enterprises) – combinations are still an important option, particularly as an alternative to 'single-active' or 'multi-active products containing an ML. Again, NAP combinations as well as other drenches or drench combinations, need to be tested on individual farms.

If slowing the development of drench resistance is a major objective, then there is a question that needs to be asked on each farm:

'How good are the various (single- or multi-active) products at killing the sheep worms on my farm?'

Relatively few producers can accurately answer this question.

Other ML-based sheep drenches

ML sheep drenches in Australia consist of moxidectin, belonging to the 'milbemycin' subgroup of MLs; and ivermectin and abamectin, both of which are 'avermectins'.

What are the attributes of the various ML products? Moxidectin in general is more potent than the avermectins. By 'potency' we mean a higher efficacy compared to other members of a drench group at a given dose rate. This dose rate is 200 µg/kg in the case of the ML-based sheep drenches. Potency – and also length of protection against re-infection – will vary depending on the species of parasite.

There is evidence that abamectin is more potent than ivermectin, but less potent than moxidectin. By virtue of potency alone, moxidectin would be expected to kill more resistant sheep worms than the avermectins. Whether moxidectin alone will kill as many resistant worms as an avermectin combination is another question and will need to be tested on individual farms. And remember that it cannot always be assumed that an ML-based product will be the treatment of choice.

We also have to consider the persistency of moxidectin and ivermectin capsules. This is both an advantage and a disadvantage. On the one hand persistency is likely to give better worm control, but possibly at the cost of greater selection for resistance compared to a short-acting drench of similar potency. This remains a contentious area.

As with many decisions in worm control, it is a matter of weighing up competing priorities.

Persistent drenches and *Haemonchus*

Most currently available combinations are short acting and provide only temporary protection against *Haemonchus contortus* – barber's pole worm. Under warm, moist conditions, this worm can be a significant threat to sheep of all ages. Under these conditions a more persistent drench may be considered desirable at some stage in the 'barber's pole season', particularly in northern NSW. Options include persistent MLs (moxidectin products, and the ivermectin or ivermectin-BZ capsules), the BZ capsule (with appropriate primer) or closantel-based drenches. However, because resistance is widespread, New England producers need to know the drench resistance status of their properties and to get professional advice on the advantages and disadvantages of these products for their particular situation.

Non-chemical options, including alternate grazing using cattle, should also be employed.

Combinations and refugia

The issue of 'refugia' is relevant regardless of whether you chose to use a multi or single-active drench product.

Worms in 'refugia' are those that escape exposure to a drench – i.e. free living stages on pasture, and worms in untreated animals, or in some circumstances, inhibited larvae within the host animal. Pasture and weather situations where there may be few worms in refugia include very hot, dry summers in some regions of Australia, crop stubbles and hay or bushfire aftermath. Whether using drenches alone or in combination, farmers should be aware that treating sheep when there are few worms in refugia probably selects more for resistance than when there are more worms in refugia.

Refugia and leaving some sheep untreated

On the matter of refugia and selection for drench resistance, there is evidence that, in Western Australian sheep raising areas for example, leaving a small proportion of sheep untreated at the summer drench will leave sufficient worms in refugia to significantly reduce selection for drench resistance without significantly compromising worm control.

However, care is required when considering this in relation to the major sheep raising areas of NSW.

Consider the following:

- 'Summer drenching' is a feature of the DrenchPlan areas (central and southern NSW), with the second summer drench being conditional on the results of worm egg count monitoring. Until recently, 'summer drenching' was also commonly practiced in southern WA as well. (This is now being modified, mainly by only drenching if worm egg counts exceed a certain benchmark.)
- WA has a 'Mediterranean' winter rainfall climate, with few worms in refugia over summer, which is hot and dry. Cereal stubbles are extensively used, with sheep being drenched and moved onto these areas in summer (November).
- In contrast, the DrenchPlan areas of NSW have non-seasonal to winter rainfall, with more summer rain on average, and probably more worms in refugia over summer than on WA sheep-wheat farms.
- Although both are 'summer drenching regions', ML resistance was first discovered in the NSW DrenchPlan area some 10 years or more after WA. This also suggests there are *significant* differences between the two regions.

Because there are significant environmental and other differences between WA and NSW, there is often more risk (with current technology) in leaving some sheep in a mob untreated in NSW. This is especially the case in areas where *Haemonchus* – barber's pole worm – is a significant problem

However, if a farmer with appropriate advice decides to adopt this strategy, it may be wise to identify the small percentage of sheep left untreated so that they can at least be monitored visually and by way of worm egg counts for indications of parasitism.

At the very least, NSW farmers should avoid treating sheep if possible in situations where there are very few worms in refugia. Most commonly this will be during prolonged dry spells or droughts, or when moving sheep onto previously ungrazed cereal stubbles.

The humble WormTest is one of the most valuable tools farmers have for sustainable worm control.

Reference

RJ Dobson, RB Besier, EH Barnes, SCJ Love, A Vizard, K Bell and LF Le Jambre (2001). Principles for the use of macrocylic lactones to minimize selection for resistance. *Aust Vet J* 79 (11):759-761

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