CHALLENGES IN THE CONTROL OF NEMATODIASIS IN SMALL RUMINANTS: A REVIEW

A. Varadharajan and R. Gnanasekar
Division of Animal Husbandry, Faculty of Agriculture,
Annamalai University, Annamalai Nagar – 608 002.
Tamil Nadu, India.

ABSTRACT

Out of various diseases affecting sheep, parasitic gastroenteritis caused by gastro-intestinal nematodes, mainly *Haemonchus contortus*, is very important for the sheep in India and is responsible for high mortality and morbidity (Yadav, 1997). The gastrointestinal nematodes of sheep include *H. contortus*, *Telodorsagia circumcinta*, *Trichostrongylus axei*, *Nematodirus* spp. and *Cooperia* spp. The proportions of each of these nematodes in sheep populations vary according to geographic location. *H. contortus* and *T. circumcincta* represent most of the parasite burdens seen in sheep, with *H. contortus* being present in highest numbers. Anthelmintic resistance is present in all of these parasites, but the prevalence is highest for *H. contortus*, making it the most economically important gastrointestinal nematodes of sheep (Fleming *et al*., 2006).

Keywords: Animal health**,** Anthelmintic resistance, Gastrointestinal nematodes, Small ruminants, Livestock productivity

INTRODUCTION

Small ruminants are important source of income for rural communities whose livelihood is largely based on livestock production (Biffa *et al*., 2006). Sheep is an important livestock species in India. India is a rich source of diverse ovine germplasm with 74 million sheep which is 6.8% of the world’s sheep population (FAOSTAT, 2010). They contribute greatly to the agrarian economy especially where crop and/dairy farming are not economical. They play an important role in the livelihood of a large percentage of small and marginal farmers and landless labours engaged in sheep rearing. However, sheep production is hindered by many factors including animal health constraints, inadequate nutrition and poor husbandry system (Sissay *et al*., 2006).

USE OF ANTHELMINTICS AGAINST GASTROINTESTINAL NEMATODIASIS

In most cases, *Haemonchus contortus* was the first nematode to develop resistance against the different anthelmintics (Fleming *et al*., 2006). There is substantial evidence that when a parasite has developed resistance to one anthelmintic from a certain class, it will usually also be resistant to other products from the same class. There is also evidence that strategic treatments have contributed to resistance development, particularly at times when the free-living component of the parasite population has been small. The most efficient way to limit the increase of anthelmintic resistance remains the reduction of the selection pressure by drugs and optimal timing to maximise their efficacy (Silvestre *et al*., 2002).

Gastrointestinal nematodes in grazing animals cause major production losses and represent an animal welfare problem worldwide. For decades, use of anthelmintics has been central in the control programmes of these parasites, as this is the only practical method to reduce the adverse effects of these nematode parasites. There are only three broad-spectrum anthelmintic classes available for treatment and control of nematodes, namely benzimidazole, imidathiazole and macrocyclic lactones. No new class with different mode of action is expected in the market in near future, as development and release of new anthelmintic may take 6–8 years and cost around US$ 30 million (Hoston, 1985). These costs have been estimated to be increased to US$ 230 million just after 9 years (McKellar, 1994). The widespread use, suppressive dosing and misuse have led to development of anthelmintic resistance (Waller, 1986) against gastro-intestinal nematodes (Singh and Yadav, 1997) posing serious limitation on use of anthelmintics, and our options are decreasing. Moreover, there is an increased consumer demand for environment-friendly products and these issues have stimulated investigations to find alternative sustainable control strategies, which are less reliant on anthelmintic input (Saddiqi *et al*., 2011). Anthelmintic resistance is defined as the 'heritable ability of the parasite to tolerate a normally effective dose of the anthelmintic' (Abbott *et al*., 2009).

The extensive use of anthelmintics for control of gastro-intestinal nematodes has resulted in the development of resistance to one or more of the widely used anthelmintics in many countries. Resistance to anthelmintics by gastro-intestinal nematodes of sheep is a widespread problem (Maroto *et al*., 2011) and has been reported to affect the health and productivity of sheep globally (Geurden *et al*., 2014). A lack of anthelmintic class rotation and, in some breeding areas, a high drench frequency, which alone or in combination, are likely to increase the risk for anthelmintic resistance (Yadav, 1997). Further, mixed grazing of sheep and goats has been evoked as a possible risk factor for the spread and emergence of anthelmintic resistance. A number of reports on anthelmintic resistance have been documented in many countries (Domke *et al*., 2011). Benzimidazole resistance in sheep was first described in 1964 (Drudge *et al*., 1964). In addition, multiple resistances to most of the anthelmintics against gastro-intestinal nematodes have also been detected in many countries (Acosta *et al*., 2012; Barbara *et al*., 2012), and these are a major concern in sheep industry (Sargison, 2012). Resistance to all classes of broad-spectrum anthelmintics available namely benzimidazoles, imidothiazoles-tetrahydropyrines and macrocyclic lactones has been reported (Ihler, 2010).

AN UPDATE ON REPORTS AVAILABLE ON ANTHELMINTIC RESISTANCE IN INDIA AND ABROAD

In India, the first report of anthelmintic resistance was documented against phenothiazene in *H. contortus* at State Sheep and Wool Research Station, Pashulok, Rishikesh, Uttar Pradesh (Varshney and Singh, 1976). Since then, benzimidazole resistance has been commonly reported in sheep population of India (Kumar and Yadav, 1994; Garg and Yadav, 2009) including different agro-climatic zones of northern India. However, no systematic studies have been undertaken to determine the status of benzimidazole resistance against gastro-intestinal nematodes in sheep and goats of sub-Himalyan region of northern India. The reports about the same in South India are very limited (Buttar *et al*., 2012; Harikrishnan, 2012; Rajagopal *et al*., 2013; Meenakshisundaram *et al*., 2014). Moreover, the suitability of different *in vitro* tests in detecting benzimidazole resistance has also not been studied earlier in this part of India (Rialch *et al*., 2013).

The discovery of new classes of anthelmintic compounds such as the paraherquamides, the cyclodepsipeptides (Altreuther *et al*., 2005), tribendimidine (Shu Hua *et al*., 2005) and the amino-acetonitrile derivatives (Kaminsky *et al*., 2008a) has, for the first time since the early 1980s, raised the possibility that a new class of anthelmintic could soon be released onto the New Zealand market for use in ruminants. Indeed, one of these compounds, an amino-acetonitrile derivative, monepantel (Kaminsky *et al*., 2008b), has very recently been registered here for use in sheep.

ANTHELMINTIC RESISTANCE

Maintenance of efficacy of existing anthelmintics is essential for continuing animal productivity and welfare. Moreover, an investigation on the prevalence of anthelmintic resistance in Government Sheep Breeding Farm, Hisar was last carried out by Singh and Yadav (1997). Therefore, there was a need to find out the current status of anthelmintic resistance in sheep farm because the task of selecting the drug of choice to control gastro-intestinal nematodes becomes easier if resistance status of parasite on property is known. Thus regular monitoring of status of anthelmintic resistance is required as an integral part of worm control programme (Rialch *et al*., 2013; Varadharajan and Vijayalakshmi, 2015). Further, to prolong the useful life of anthelmintics, early detection of resistance maybe greatly beneficial, as withdrawal of an anthelmintic from a farm where a low level of resistance is detected could lead to reversion to susceptibility by diluting the resistant population with susceptible or hybrid phenotype (Le Jambre *et at*., 1982; Qadri *et al*., 2015).

Further, parasitologists generally agree that if delaying resistance is the prime objective, it is better to use a mixture of two or more effective broad-spectrum drenches than using these drenches alone (Dobson *et al*., 2001). Combinations are likely to slow the development of resistance, as it is generally accepted that the mechanisms of resistance to the benzimidazole, imidathiazole and macrocyclic lactones classes of anthelmintics are different, and that, there is no, or virtually no, cross resistance between them (Coles and Roush, 1992).

The investigators found that where resistance to benzimidazole and levamisole was present to each individual drug, mixtures of fenbendazole and levamisole given simultaneously were effective in many cases. This was confirmed in a later study (Waller *et al*., 1990) for *Trichostrongylus colubriformis* and in a further report with the caution that the result would depend on the degree of resistance to each drug that was present (McKenna *et al*., 1996). Formulations permitting the simultaneous use of two or three molecules from the existing three main groups of anthelmintics are available in countries such as Australia (Q-drench® etc.), New Zealand, Uruguay and others.

CONCLUSION

Although the release of a new class of anthelmintic should remove any immediate threat to production posed by nematodes resistant to compounds currently available, history indicates that if a new drug class is simply used as a replacement for older drug classes to which resistance is already widespread, then it is inevitable that, in due course, resistance will develop to the new drug class as well. Conversely, the release of a new class of drug presents the opportunity to make changes to parasite management practices to ensure that resistance either never develops to it or takes substantially longer time to develop than the older drug classes (Varadharajan and Vijayalakshmi, 2015).

REFERENCES

1. Abbott KA, Taylor MA and Stubbings LA (2012). Sustainable worm control strategies for sheep. A technical manual for veterinary surgeons and advisers, SCOPS. *In*: Sustainable Control of Parasites in Sheep 4th ed. (SCOPS), UK (KA Abbott, MA Taylor and LA Stubbings Eds.), Malvern, pp. 51.
2. Acosta TJF, Mendoza-de-Gives P, Aguilar Caballero AJ and Cuellar Ordaz JA (2012). Anthelmintic resistance in sheep farms: Update of the situation in the American continent. *Vet. Parasitol*., **189**(1): 89–96.
3. Altreuther G, Buch J, Chales SD, Davis WL, Krieger KJ and Radeloff I (2005). Field evaluation of the efficacy and safety of emodepside/praziquantel spot-on solution against naturally acquired nematode and cestode infections in domestic cats. *Parasitol. Res*., **97**: 58–64.
4. Barbara G, Hanrahan JP, de Waal DT, Patten T, Kinsella and Lynch CO (2012). Anthelmintic-resistant nematodes in Irish commercial sheep flocks – the state of play. *Ir. Vet. J*., **65**(1): 21–25.
5. Besier RB (2007). New anthelmintics for livestock: the time is right. *Trends Parasitol*., **23**: 21–24.
6. Biffa D, Jobre Y and Chaka H (2006). Ovine helminthosis, a major health constraint to productivity of sheep in Ethiopia. *Anim. Health Res. Rev.*, **7:** 107–118.
7. Buttar BS, Hari HS, Singh NK, Haque JM and Rath SS (2012). Emergence of anthelmintic resistance in an organized sheep farm in Punjab. *J. Vet. Parasitol*., **26**(1): 69–71.
8. Coles GC and Roush RT (1992). Slowing the spread of anthelmintic resistant nematodes of sheep and goats in the United Kingdom. *Vet. Rec*., **130**: 505– 510.

9. Dobson RJ, Besier RB, Barnes EH, Love SCJ, Vizard A, Bell K and Le Jambre L (2001). Principles for the use of macrocyclic lactones to minimize selection for resistance. *Aust. Vet. J.*, **79**: 759–761.
10. Domke AV, Chartier C, Gjerde B, Leine N, Vatn S, Osterås O and Stuen S (2011). Worm control practice against gastro-intestinal parasites in Norwegian sheep and goat flocks. *Acta Vet. Scand*., **13**: 53– 29.
11. Drudge JH, Szanto J, Wyant ZN and Elam G (1964). Field studies on parasitic control in sheep: Comparison of thiabendazole, ruelene and phenothiazine. *Am. J. Vet. Res*., **25**: 1512–1518.
12. FAOSTAT (2010). FAOSTAT Agriculture Data. Food and Agriculture Organization Statistics, Rome, Italy.
13. Fleming SA, Craig T, Kaplan RM, Miller JE, Navarre C and Rings M (2006). Anthelmintic resistance of gastrointestinal parasites in small ruminants. *J. Vet. Intern. Med.*, **20**: 435–444.
14. Garg R and Yadav CL (2009). Genotyping of benzimidazole susceptible and resistant alleles in different populations of *Haemonchus contortus* from Himalayan and sub-Himalayan regions of North-West India. *Trop. Anim. Health Prod*., **41**(7): 1127– 1131.
15. Geurden T, Hoste H, Traversa PJD, Strake S, *et al.* (2014). Anthelmintic resistance and multidrug resistance in sheep gastro-intestinal nematodes in France, Greece and Italy. *Vet. Parasitol*., **201**(1– 2): 59–66.
16. Harikrishnan TJ (2012). Management of anthel-mintic resistance in GI helminthes of sheep and goats in Tamil Nadu – the way forward. Proceeding, International Conference on Holistic Approaches for Combating Anthelmintic Resistance – an update in parasitology. *Vet. Parasitol*., **189**(1): 46–53.
17. Hoston IK (1985). New developments in nematode control. The role of animal health products Industry. *In*: Resistance in Nematodes to Anthelmintic Drugs (N Anderson and PJ Waller Eds.), pp. 117–125. CSIRO, Melbourne.
18. Ihler CF (2010). Anthelmintic resistance. An overview of the situation in the Nordic countries. *Acta Vet. Scand.*, 52(1): 1–24.
19. Kaminsky R, Ducray P, Jung M, Clover R and Rufener L (2008a). A new class of anthelmintics effective against drug-resistant nematodes. *Nature*, **452**: 176–180.
20. Kaminsky R, Gauvry N, Schorderet Weber S, Skripsky T and Bouvier J (2008b). Identification of the amino-acetonitrile derivative monepantel (AAD 1566) as a new anthelmintic drug development candidate. *Parasitol. Res*., **103**: 931–939.
21. Kumar R and Yadav CL (1994). Prevalence of fenbendazole resistance in ovine nematodes in North West India. *Trop. Anim. Health Prod*., **26**(4): 230–234.
22. Le Jambre LF, Martin PJ and Jarrett RG (1982). Comparison of changes in resistance in *Haemonchus contortus* egg following withdrawal of thiabendazole selection. *Res. Vet. Sci*., **32**: 38– 43.
23. Maroto R, Jimenez AE, Romero JJ, Alvarez V, De Oliveira JB and Hern´andez J (2011). First report of anthelmintic resistance in gastro-intestinal nematodes of sheep from Costa Rica. *Vet. Med. Int*., **145**: 3–12.
24. McKellar QA (1994). Chemotherapy and delivery, systems helminths. *Vet. Parasitol*., **54**: 249–258.
25. McKenna PB, Allan CM and Taylor MJ (1996). The effectiveness of benzimidazole-levamisole combination drenches in the presence of resistance to both benzimidazole and levamisole anthelmintics in New Zealand sheep. *N.Z. Vet. J*., **44**(3): 116–118.
26. Meenakshisundaram A, Anna T and Harikrishnan J (2014). Prevalence of drug-resistant gastrointestinal nematodes in an organized sheep farm. *Vet. World*, **7**(12): 1113–1116.
27. Qadri K, Ganguly S, Wakchaure R, Sharma S, Kumar A and Kumar P (2015). Resistance to anthelmintic medications in animals: A review. *Ann. Pharma Res*., **3**(09): 144–147.
28. Rajagopal A, Radhika R, Shameem H and Devada K (2013). Detection of anthelmintic resistance in small scale goat rearing units in Thrissur. *J. Vet. Anim. Sci*., **44**: 51–53.
29. Rialch A, Vatsya S and Kumar RR (2013). Detection of benzimidazole resistance in gastrointestinal nematodes of sheep and goats of sub-Himalayan region of northern India using different tests. *Vet. Parasitol*., **198**(3–4): 312–318.
30. Saddiqi HA, Jabbar A, Sarwar M, Iqbal Z, Muhammad G, Nisa M and Shahzad A (2011). Small Ruminant inherited resistance against G.I. nematodes: A case of *Haemonchus contortus* in Faisalabad, Pakistan. *Parasitol. Res.*, **109**: 1483–1500.
31. Sargison ND *(*2012*)*. Pharmaceutical treatments of gastrointestinal nematode infections of sheep– future of anthelmintic drugs. *Vet. Parasitol.*, **189**: 79–84.
32. Shu Hua X, Hui-Ming W, Tanner M, Utzinger J and Chong W (2005). Tribendimidine: a promising, safe and broad-spectrum anthelmintic agent from China. *Acta. Trop.*, **94**: 1–14.
33. Silvestre A, Leignel V, Berrag B, Gasnier N, Humbert JF, Chartiere C and Cabaret J (2002). Sheep and goat nematode resistance to anthelmintics: Pros and cons among breeding management factors. *Vet. Res*., **33**(5): 465–480.

34. Singh S and Yadav CL (1997). A survey of anthelmintic resistance by nematodes on three sheep and goat farm in Hisar (India). *Vet. Res. Commun*., **21**: 447– 451.
35. Sissay MM, Aset A, Uggla A and Waller PJ (2006). Anthelmintic resistance of nematode parasite of small ruminants in eastern Ethiopia, exploitation of refugia to restore anthelmintic efficacy. *Vet. Parasitol*., **135:**337–346.
36. Varadharajan, A and R. Vijayalakshmi (2015). Prevalence and seasonal occurrence of gastrointestinal parasites in small ruminants of coastal areas of Tamil Nadu. Int. J. Adv. Res. Biol.Sci. 2(2): 21–25.
37. Varadharajan, A and R. Vijayalakshmi (2015). Emergence of anthelmintic resistance in naturally infected goats of Cuddalore district, Tamil nadu. G.J.B.A.H.S. 4(1):101-104.
38. Varshney TR and Singh YP (1976). A note on development of resistance of *Haemonchus contortus* worms against phenothiazine and thiabendazole in sheep. *Indian J. Anim. Sci*., **46**: 666–668.
39. Waller PJ (1986). Anthelmintic resistance in sheep nematodes. *Agric. Zool. Re*v., **1**: 333–373.
40. Waller PJ, Dobson RJ and Haughey KG (1990). The effect of combinations of anthelmintics on parasite populations in sheep. *Aust. Vet. J*., **67**(4): 138–140.
41. Yadav CL (1997). Premature ovine births caused by *Haemonchus contortus. Indian Vet. J*., **74**: 983–984.