Journal of Natural Sciences Research www.iiste.org
ISSN 2224-3186 (Paper) ISSN 2225-0921 (Online)
Vol.7, No.19, 2017

Comparative Efficacy of Albendazole, Tetramizole and Ivermectin Against Gastrointestinal Nematode in Naturally Infected Sheep in Sebeta, Ethiopia

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Abstract
A study was conducted to determine and compare the efficacy of the albendazole, tetramizole and ivermectin against gastrointestinal nematode in naturally infected sheep in Sebeta, Ethiopia. One hundred sixteen sheep were sampled of which 60 sheep with faecal egg count above 150 were randomly allocated into four groups, each group consisting 15 sheep were assessed to determine anthelminthic efficacy through faecal egg count reduction test (FECRT). The first group was treated with albendazole, second with tetramisole, third with ivermectin and fourth kept as untreated to serve as control. Faecal samples were collected on day first prior to administration of treatment followed by day 7 - 14 post treatment. The FECRT revealed that the presence of ivermectin resistance while albendazole and tetramizole were effective against sheep gastrointestinal nematodes in the study area. In conclusion, farmers and professionals must observe the preventive measures to avoid a wide spread of ivermectin resistance, otherwise the presence of resistant parasites and ineffective treatment may harm the productivity of sheep.
Keywords: Abendazole; Anthelminthic resistance; Fecal egg count reduction test; Ivermectin; Sheep nematodes; Tetramizole

INTRODUCTION

Livestock is the main stay of the vast majority of Ethiopian people. Among this livestock sector, small ruminant constitute a major part (Kassaye and Kebede 2010). It is also an important sector providing a significant contribution to gross domestic and export products and raw materials for industries (Adane and Girma 2008). According to recent estimates, Ethiopia is home to some 29.33 million sheep and 29.11 million goats (CSA 2015). Estimates indicated that small ruminants account for 35% of the meat and 14% of the milk consumption, as well as the biggest share of hide and skin export earnings in Ethiopia (Asfaw et al 1998).

Sheep are of great importance as major sources of livelihood and contribute to the sustenance of landless, smallholder and marginal farmers especially to the poor in the rural areas throughout the developing countries. In Ethiopia scenario, similarly like other developing countries, Sheep are very important for resource-poor smallholder systems of rural areas due to their ease of management, short generation cycles and high reproductive rates which lead to high production efficiency and significant role in provision of food and generation of cash income. They serve as a living bank for many farmers, closely linked to the social and cultural life of resource poor farmers and provide security in bad crop years (Tsedeke 2007).

However, the productivity of this huge small ruminant population remains marginal due to prevailing diseases, poor nutrition and husbandry systems, and lack of effective veterinary services (Gizaw *et al*., 2010). Gastrointestinal nematodes (GINs) constitute one of the greatest disease threats for grazing livestock worldwide. Infection with helminth parasites results in both clinical and sub-clinical diseases causing low productivity due to stunted growth, insufficient weight gain, delay of puberty, anemia, poor feed utilization and mortality (FAO 2002) hindering optimization of the economic benefits from small ruminants (Tembely et al 1997).

In Ethiopia, there are number of studies relating small ruminants and gastrointestinal nematode infections with report of widespread prevalence rate of GI helminthic infestation in different part of the country had been reported (Fikru et al 2006; Asha and Wossene, 2007; Ayalew et al 2014). To improve this problem, parasite control is usually carried out with the use of anthelmintics, often indiscriminately and without any epidemiological knowledge (Garcia et al 2016). Thus, the use of such suppressive regime added to inaccurate management strategies, contributes to the selection and establishment of parasites that are resistant to the anthelmintics (Almeida et al 2010).

As parasite resistance is an inherited trait, after every generation there may be an increase in individual parasites that would be able to survive drug treatment (Garcia et al 2016). Parasite resistance is an alarming scenario in small ruminants worldwide, but there are limited data on the magnitude of parasite resistance in sheep in Ethiopia and no data in the study area.

Therefore, the objective of this study was: to report and evaluate the of efficacy of the most used anthelmintic against gastrointestinal nematodes of sheep in NAHDIC for research purpose, Sebeta, Central

Ethiopia and its surroundings (Haro Jila Fulaso) small holder farmers.

MATERIALS AND METHODS

Study area

The study was conducted from November 2016 to April 2017 in and around Sebeta Awas woreda of Finfine Zuria special Zone, Oromia National Regional State, Ethiopia. The geographical (astronomical) location of Sebeta Awas is approximately located at 8°54'40"N latitude and 38°37'17"E longitudes, 20 km southwest of Addis Ababa with the maximum and minimum altitude of 3380 m and 180 m above sea level respectively. Eighty eight percent (88%) of the Sebeta Awas area is weynadega and 12% is dega with the relative humidity of 49.3, annual rainfall 1200mm and maximum and minimum temperature of 28oc and 11.3oc respectively. The main livestock species in the woreda are cattle, sheep, goat, horse, mule, donkey and poultry with estimated population of 151400, 25109, 20978, 4997, 2450, 26100 and 69936 respectively (Sebeta Awas Agricultural Office, 2015).

Study animals

Sixty sheep, mix of ages and sex were used for the study. These sheep were purchased from the local market in Sebeta for subsequent research purpose at National Animal Health Diagnostic and Investigation Center (NAHDIC) laboratory and the other half of the study animal were those sheep flocks owned by smallholder farmers in the study area. None of the sheep had received any anthelmintic treatment prior to the start of the experimental trial.

Design of experiment

Initial faecal samples were collected from each animal directly from rectum, placed individually sealed container and transported to NAHDIC Parasitology laboratory to perform parasite egg counts per gram employing Mc Master technique. Out of 116 sheep tested, 65 were positive but epg greater than or equal to 150 is taken into treatment and control group. Based on these the animals were randomly selected and allocated into treatment groups (Albendazole, Ivermectin and Tetramisole) and untreated (control) group. Each group consisting 15 animals were treated with Albendazole, Ivermectin, Tetramisole and a control group that received no treatment. Feacal samples were collected again from animals on days: 7-10, 10-14 and 5-7 from Albendazole, Ivermectin and Tetramisole group respectively and also from control group samples, then floatation and Mc Master technique were again employed for the second time in order to determine the drug efficacy. The details of the drugs used in the tests are presented in Table 1.

Table 1: Description of the anthelmintic drugs used in the FECRT for efficacy test

Generic Name	Trade Name	Manufacturer	Dosage mg/kg	Route of Administration
Albendazole	Albenda-QK 300 mg	Chengdu Qiankum Veterinary Pharmaceuticals Co. Ltd., China	7.5	Oral
Tetramizole HCL	Ashitetra 600 mg	Ashish Life Science Pvt Limited., India	15	Oral
Ivermectin	Ivervic 1 Injection	Shenyang Sunvictor Pharmaceutical Co., Ltd., China	0.2	Subcutaneously

Efficacy evaluation

Drug efficacy was determined by the faecal egg count reduction test (FECRT) and the percentage reduction was calculated according to the guideline provided by World Association for the Advancement of Veterinary Parasitology (WAAVP) recommendation (Coles et al 1992). The fecal nematode egg count reduction percentage (FECR%) was determined by using a formula: FECR% = 100 × (1 - Mt/Mc); Where Mt and Mc are the arithmetic mean EPG in the treated (t) and untreated control (c) groups at days 7 to 14 post treatment according to method described by Coles et al (1992) and Coles et al (2006).

Reductions in efficacy is considered to exist if the FECRT percentage of an anthelmintic treatment is <95% and the lower 95% confidence limit for the reductions is <90% (Coles et al 1992). If only one of the two criteria is met reductions in efficacy is suspected.

Data analysis

The efficacy of the anthelmintics was analyzed using the RESO 2.01 Analysis Software (Wursthorn and Martin 1990). Data was analyzed considering resistance when the effectiveness of the anthelmintic was lower than 95% and when the confidence interval was below 90% (Coles et al 2006).

RESULTS

The results for the efficacy test in sheep is shown on table 1. According to RESO software, a suspect of resistance was identified for ivermectin because the treatment revealed an egg count reduction just 97% with a lower confidence interval below 90% *i.e.* 84% while Albendazole and Tetramisole revealed an egg count reduction just above 95% (98 and 100%, respectively) with a confidence interval above 90% confirming no anthelmintic resistance.

Strongyle was found predominantly in 56% of pre-treatment faecal examination and followed by small incidence of haemonchus (3%), trichuris (3%) and ostertagia (1%). This study revealed that great proportion of the study sheep were with light degree of infection (60%) while only small proportion were with moderate(15%) and heavy degree(25%) of strongyle type pretreatment Epg as shown in Fig. 1.

Table 2: Mean of eggs per gram in pretreatment and post-treatment, percentage of faecal egg count reduction (FECR), and 95% confidence interval after anthelmintic treatments in sheep

	Treatment groups			
Measurements	Control	Albendazole	Tetramizole	Ivermectin
Number	13	15	15	15
Mean EPG pretreatment	1515	913	673	793
Mean EPG post-treatment	2062	33	0	60
% reduction in EPG	-	98	100	97
Upper 95% CL	-	100	-	99
Lower 95% CL	-	93	-	84
Interpretation	-	Susceptible	Susceptible	Resistant

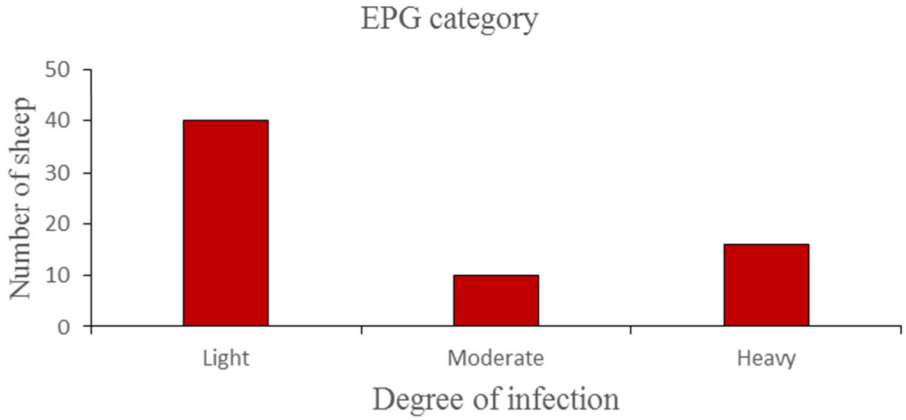

Fig 1: Degree of strongyle infection of study sheep based on EPG of pretreatment faecal sample

DISCUSSION

The fecal examination for the presence of parasite eggs in the pre-treatment fecal samples revealed that strongyle (56%) species was predominant. The result is higher than the report of Shimelis et al (2011) who had reported 37.63% of strongyle eggs in Gondar but lower than the result of Lemma and Abera (2013) and Getachew et al (2016) who had recorded 74% and 69% respectively. The prevalence of *Trichuris* (3%) in the current study was fairly in agreement with finding of Lemma and Abera (2013) who had reported that the prevalence of *Trichuris* egg as 3.7% in Asella but slightly higher than 1.5 % report by Getachew et al (2013) in Areka, Southern Ethiopia and lower than 4.5% report in western Oromia (Regassa et al 2006). Similarly, other nematodes such as haemonchus and ostertagia were also find to lesser extent.

The mean eggs per gram (EPG) revealed that 60% of the sheep were lightly while 15% and 25 % of study sheep were moderately and heavily infested respectively. This result was different from the result of Lemma and Abera (2013) who had reported that 30.04% of the sheep were lightly while 40.34% moderately and 29.62% heavily infested. This difference could be due to the difference between the management and production system of examined animals and geographical and environmental location of the study area.

Estimating the status of anthelmintic resistance is the most important step in establishing and maintaining effective parasite control of nematode parasites in livestock, especially for small ruminants. In this study, Anthelmintic efficacy tests were conducted using three brands namely; albendazole, ivermectin and tetramizole commonly available on the local markets and anthelmintic resistance was considered to be present if the percentage reduction in faecal egg counts was less than 95% and the lower limit of the 95% confidence interval was less than 90% (Coles et al 1992). If only one of these criteria is met, anthelmintic resistance is suspected.

Based on this criterion, a suspect of resistance was identified for ivermectin because the treatment revealed an egg count reduction just 97% with a lower confidence interval below 90% *i.e.* 84% while albendazole and tetramisole revealed an egg count reduction just above 95% (98 and 100%, respectively) with a confidence interval above 90% confirming no anthelmintic resistance.

In present study, treatments with albendazole revealed susceptibility with 98% of reduction of the nematode egg in the post-treatment fecal analysis with a confidence interval above 90% confirming very good efficacy of tested products. This finding was in agreement with the report of Sheferaw and Asha (2010); Aga et al (2013); Sibhatu et al (2011); Terefe et al (2013); Melaku et al (2013) who reported the effectiveness of albendazole against treatment of nematode parasite with percent of reduction in 99.34%, 98%, 100%, 96%, 99.08%, respectively. However, our finding was disagreement with the report of Getachew et al (2016) in Areka Agriculture Research Centre, Yidnekachew (2015) in Haromaya University flock of sheep in Eastern Ethiopia and Aga et al (2013) in Horro sheep from Western Oromia who had reported faecal egg count reduction of 90.05%, 87% and 98% with lower confidence interval below 90%. The difference of the current and the previous studies in the efficacy of albendazole against nematode treatment might be attributed to several factors such as poor quality drugs, continuous under dosages treatments at the sheep dose rate by farmers due to low bioavailability in sheep, misuse and inappropriate treatment by owners. Such factors have been also suggested to contribute to lower efficacy Papadopoulos (2008); Chandrawathani et al (2004); Saeed et al (2007).

In this study, tetramizole had a very good efficacy in reducing gastrointestinal nematodes with percent faecal egg count reduction of (100 %) in sheep. This finding is an agreement with the result of Shefarew et al (2013); Getachew et al (2016); Terefe et al (2013); Sibhatu et al (2011); Niguse et al (2014); Sheferaw and Asha (2010) and Aga et al (2013) who reported the effectiveness of tetramizole with percent of reduction of 97.5%, 98.5%, 98.5%, 100%, 100%, 100% and 100%, respectively. On the other hand, this result is different from the study of Kumar (2014) in Pakistan and Melaku et al (2013) in North Gondar of Ethiopia where the lowest efficacy of tetramizole with 24% and 74.29% percent of reduction recorded respectively. The differences of the efficacy of those tested drugs from other studies could be due to the difference in the frequency, dosage, misuse of drugs and ways of utilization of the drugs among the sheep on station and at farmers hand in addition to the difference study locations.

Ivermectin was not effective in reducing fecal egg count in the current study in sheep with the lower confidence limit of 84%. This finding was in agreement with the result of Getachew et al (2016), Kumsa and Abebe (2009), Melaku et al (2013), and Singh et al (2012) who had reported lower efficacy of ivermectin in sheep. However, this result was disagreement with Sheferaw *et al* (2013) in Dale District, and Hamdullah et al (2014) who reported a 96.7%, and 98% efficacy of ivermectin respectively. The discrepancy between the current and previous study might be associated to high frequency of anthelmintic treatment of these drugs against nematode parasite in the study area. As explained by Magona and Musisi (2002) utilization of limited group of drugs for a long period at high frequency may favor the development of resistance. Moreover, sheep raisers do not have any idea on anthelmintic rotation (Niguse et al 2014) that favors anthelmintic resistance.

CONCLUSION AND RECOMMENDATIONS

Parasite control is usually carried out with the use of anthelmintics, often indiscriminately and without any efficacy evaluation technique. In this study, gastrointestinal nematodes of sheep in the study area were susceptible to albendazole and tetramizole fully effective. On the other hand, ivermectin showed lower efficacy for sheep nematode in the study area.

Based on the above conclusion, the following recommendations are forwarded:

- Avoid frequent and unnecessary treatments of anthelmintics, opting instead for strategic deworming
- Farmers should be educated with proper veterinary extension about the importance of use of efficacious anthelmintics.
- Give adequate advice for the farmers and persons who are in contact to animals to use anthelmintic drugs which are more effective
- Further studies are needed to assess the status of efficacy of widely used anthelmintic drug in different agro-ecology, species of animals and management systems with economic impact of the problem.

Acknowledgements

We would like to extend our heartfelt appreciation to National Animal Health Diagnostic and Investigation Centre staff especially for their cooperation in using the animals for this research and all rounded Support.

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