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Comparative cost analysis of three injectable ivermectin preparations in the control of gastrointestinal nematodes of sheep in Makurdi, Benue State Nigeria

Mathew Adamu[1*], Paul Amuta[2], Anthony Ameh[1] and Samuel Ode[3]

[1]Department of Veterinary Parasitology and Entomology, College of Veterinary Medicine University of Agriculture Makurdi Nigeria.
[2]Department of Animal Health and Production, College of Veterinary Medicine, University of Agriculture Makurdi Nigeria.
[3]Department of Veterinary Pathology, College of Veterinary Medicine, University of Agriculture Makurdi Nigeria.

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The efficacy and comparative cost analysis of three injectable ivermectin preparations was evaluated in West African Dwarf (WAD) sheep naturally infected with gastrointestinal nematodes. Three anthelmintics: ivomec classic® (IVC), ivomec super® (IVS) and ivomec gold® (IVG) were administered at a dose rate of 200µg/kg to control gastrointestinal nematodes in three treatment groups comprising five animals each. The faecal egg counts (FEC) for each animal pre-treatment, and thereafter for a period of 16 weeks post-treatment was carried out using the modified McMaster technique. The results is a pre-treatment mean FEC for groups A, B and C of 970±550.36, 880± 279.55 and 1640±893.78 eggs per gram (epg), respectively and a mean FEC of zero for all treatment groups one week post treatment. The mean FEC of zero was maintained for 28, 35 and 56 days, respectively. A mean FEC threshold for re-treatment of 500 epg was exceeded at days 42, 49 and 84 for groups A (615±167.26), B (830±287.49) and C (737.5±448.10), respectively. The results were subjected into a deterministic model to estimate the costs of using IVC, IVS or IVG in an annual control program. The costs of a one-time treatment were $20.6, $20.8 and $21.0, respectively. The average annual costs were $82.39, $83.22 and $41.99 for groups A, B and C, respectively. Thus, veterinary service and labour are two variables that contributed more to cost of treatment when compared with the price of drugs and average weight of the animals treated.

Key words: Ivermectin, gastrointestinal nematodes, West African Dwarf sheep, efficacy, cost analysis.

INTRODUCTION

Gastrointestinal (GI) parasite infection is considered as the most important limiting factor to sheep productivity in

*Corresponding author. E-mail: mathew.adamu@gmail.com.

most parts of the world especially in developing countries (Waller, 1997; Roeber et al., 2013; Blackie, 2014; Singh et al., 2017a, b). The most common GI parasitic diseases in sheep in Nigeria are Haemonchosis, Strongyloidosis, Oesophagostomosis, Bunostomosis and Trichostrongylosis.

Haemonchus contortus has been singled out as the most important nematode of small ruminants in the tropics (Adamu et al., 2013; Singh et al., 2013; Zvinorova et al., 2016). Gastrointestinal nematode infections poses serious economic consequences to small ruminant production due to the associated morbidity, mortality, veterinary service and cost of treatment, as well as costs of other control measures (Singla, 1995; Zinsstag et al., 1998; Nwosu et al., 2007).

In ruminant production systems, parasite control has consistently shown a very high correlation with increased production (Kumar et al., 2013; Kenyon et al., 2013). Gastrointestinal nematode control strategies are almost entirely on the use of anthelmintic. The frequent use and mismanagement of these drugs has led to development of wide-spread resistance to the major groups of anthelmintic except for monepantel (Pomroy, 2006; Molento, 2009; Adamu et al., 2013; Melaku et al., 2013).

Ivermectin (IVM) is a macrocyclic lactone with activity against GI and lung nematodes (Nolan, 2012; Campbell, 2012), as well as against ectoparasites of clinical relevance in domestic animals (Campbell et al., 1984; Shoop et al., 1995; Merola and Eubig, 2012). Ivermectin has extensive tissue distribution, low biotransformation and high plasma-GI recycling that guarantees its persistent activity. The broad spectrum of activity and wide margin of safety has made it a drug of choice for nematode and arthropod parasitism in cattle, sheep, goat, swine, dog and horses (Campbell et al., 1983). Consequently, IVM is the most widely used anthelmintic and this extensive use has led to the emergence of IVM-resistant nematode populations in several countries (Jackson and Coop, 2000; Waller, 2006; Pomroy, 2006; Molento, 2009). The efficacy of IVM against gastrointestinal parasites under different control strategies has been demonstrated (Kenyon et al., 2013).

Farmers and veterinarians should be interested in information concerning the cost analysis of using different drugs and strategies to help with decision making for better control options. The decision making process is dependent on the costs of the anthelmintic, veterinary service and labour. These three variables may change depending on cost of anthelmintic, efficacy and duration of action against GI nematodes.

Currently, there are three injectable IVM preparations in the market produced by Merial. These IVM preparations are ivomec classic®, ivomec super® and ivomec gold®. The preparations differ in composition, duration of action and price. The aim of this study was to determine the efficacy, duration of action and cost implications of these IVM preparations as demonstrated by faecal egg counts pre and post-treatment for a period of 16 weeks in a flock of sheep.

MATERIALS AND METHODS

Experimental animals and ivermectin preparations

A total of fifteen West African Dwarf sheep kept at the University Teaching and Research Farm, University of Agriculture, Makurdi were randomly selected for this experiment. The sheep included 7 rams and 8 ewes out of a herd of 35 sheep. The sheep were kept under the semi-intensive system of management. Pregnant ewes and lambs were excluded from this experiment.

The compositions of the three injectable IVM preparations used in this experiment were: Ivomec classic® (IVC) contains 1% m/v of ivermectin; Ivomec super® (IVS) contains 1% m/v of ivermectin and 10% clorsulon and Ivomec gold® (IVG) contains 3.15% m/v of ivermectin. All three formulations used were manufactured by Merial South Africa (Pty) Limited. The anthelmintic was administered at a dose rate of 200 µg of IVM per kilogram body weight according to manufacturer's instructions.

Experimental design

The fifteen sheep were randomly assigned to 3 treatment groups (A, B and C), with each group comprising 5 sheep. Sheep in group A were treated with IVC, while sheep in groups B and C were treated with IVS and IVG, respectively.

Prior to the administration of the IVM preparations, a baseline faecal examination was carried out to determine the faecal egg counts of individual sheep pre-treatment. The sheep were weighed individually using a Camry® weighing scale.

The months of August to October represent the second half of the rainy season including its peak. During this period, it is expected that *Haemonchus* L_3 are well established in grazing pasture to pose a sufficient challenge to the experimental animals. The IVM formulations were administered to the sheep in the different groups at the same dose rate of 200 µg/kg subcutaneously, as recommended by the manufacturer.

Sampling and determination of faecal egg counts

Following treatments, faecal samples were collected per rectum from all the sheep in each group once weekly for 16 weeks. Samples were placed in polythene bags, labeled and transported on ice packs to the laboratory for further processing and examination.

The faecal samples were examined for helminth eggs and the faecal egg counts (FEC) for each sample was determined using the Modified McMaster technique using saturated sodium chloride solution as the floatation medium (Hansen and Perry, 1990).

Data collection and analysis

Prior to treatment with the respective injectable IVM preparations, the FEC for each of the 5 sheep per group was examined and recorded. The mean and standard error of the mean (SEM) were calculated and recorded for each group. The FEC of each sheep in the three groups was determined once weekly for a duration of 16 weeks. The mean FEC for each group and the SEM was similarly calculated for each group weekly. The FEC of 500 epg was used as the cut-off value in this study for a repeat of treatment (the week in which the mean FEC exceeded 500 epg was referred to as "re-treatment week"). The time interval between the week of first treatment and the re-treatment week was regarded as the "duration

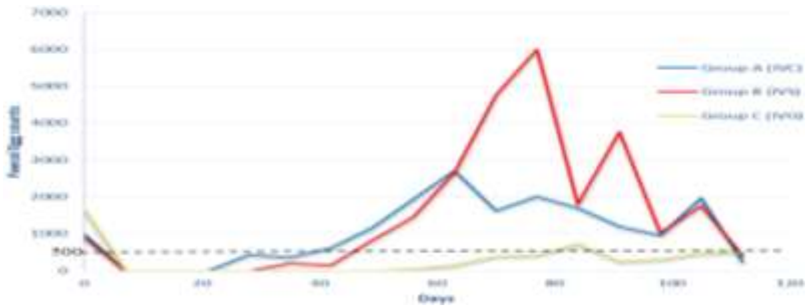

Figure 1. The mean faecal egg counts of sheep treated with three different ivermectin preparation for a 16 week period

of action" of the drug and it was noted for each group.

Economic analysis

A deterministic economic model was developed using Microsoft Excel to demonstrate the cost implications of using each of the IVM formulations with $_i$ representing the treatment groups (IVC, IVS and IVG). Table 2 shows the input values for variables used to develop the model. The calculated variables include: drug price per ml (dp_i), average weight of sheep in each group (AW_i), average dosage administered per group (DA_i), average cost of drug per treatment per group (Dc_i), veterinary service cost per group (VSc_i), labour cost per treatment per group (Lc_i), duration (weeks) till next treatment for each IVM preparation (DT_i) and number of treatments required per year (NT_i). The outcome of these calculations is the average annual cost of GI nematode control per group (ATC_i). VVc_i means veterinary visit cost.

Economic model calculations

Dc_i was calculated for each group by multiplying DA_i with dp_i as follows:

$$\mathrm{Dc}_i = \mathrm{DA}_i \times \mathrm{dp}_i \quad [1]$$

The average cost of a one-time treatment per group (Tc_i) is the sum of veterinary visit cost (VVc_i); and Dc_i, VSc_i and Lc_i for five sheep as follows:

$$\mathrm{Tc}_i = \mathrm{VV}ci + [\ \textstyle\sum_{i=1}^{5} \mathrm{Dc}_i + \mathrm{VSc}_i + \mathrm{Lc}_i] \quad [2]$$

The NT_i was determined based on the fact that the rainy season provides an environment conducive for the proliferation of GI nematodes on pasture. The rainy season usually lasts about 6 months (24 weeks) during which several life-cycles of the parasites are expected to occur. Therefore, NT_i differed between groups based on their respective DA_i as follows:

$$\mathrm{NT}_i = \frac{24weeks}{DA_i} \quad [3]$$

The average annual cost of GI parasite control for one group (ATc_i) is the product of the Tc_i and the NT_i of the respective group.

$$\mathrm{ATc}_i = \mathrm{Tc}_i \times \mathrm{NT}_i \quad [4]$$

Sensitivity analysis

A sensitivity analysis was conducted in order to determine the level of impact of some variables on the annual cost of GI parasite control for each drug. This was done by adjusting the input values of certain variables by ±20% one at a time, while all other variables remained constant at their default values. The resulting average annual cost of GI parasite control (ATc_i) from each simulated scenario was compared with the default ATc_i calculated from the values from the field experiment. Variables for which sensitivity analysis was done include: veterinary visit cost (VVc_i), veterinary service cost (VSc_i), labour cost (Lc_i), the price of the drugs (DP_i) and the average weight of the animals (AW_i).

RESULTS

The mean faecal egg count for the three groups of 5 sheep treated with the three different ivermectin preparations are illustrated in Figure 1. The pre-treatment mean FEC across the groups is as follows: 970 epg for group A, 880 epg for group B and 1640 epg for group C (Table 1). One week after treatment, all the animals in the three groups presented 0 epg on examination of faecal samples. This is indicative of the efficacy of all three IVM preparations 7 days post treatment as 100%.

The three IVM formulations delayed re-infection for different durations. Sheep in group A treated with IVC maintained 0 epg status until day 28 post treatment, sheep in group B treated with IVS maintained 0 epg status until day 35 post treatment and sheep in group C treated with IVG maintained 0 epg status until day 56 post treatment. This implied that following clearance of infection, IVC, IVS and IVG prevented patent infection for a period of 28, 35 and 56 days, respectively.

Garg et al. (2007) reported a mean FEC of 500 epg in sheep requires anthelmintic treatment. The results in Table 1 therefore indicate the need for re-treatment on day 42 following treatment using IVC, day 49 following treatment with IVS and day 84 following treatment with IVG. The period of importance for the control of *H. contortus* is the rainy season which lasts about 6 months (180 days) on average in the study area. This implies the use of IVC and IVS will require 4 treatments per year,

Table 1. Mean faecal egg count ± standard error of the mean for groups of 5 sheep treated with IVC (Group A), IVS (Group B) and IVG (Group C).

Day	Mean FEC ± standard deviation		
	Group A	Group B	Group C
0	970±550.36	880±279.55	1640±893.78
7	0±0	0±0	0±0
14	0±0	0±0	0±0
21	0±0	0±0	0±0
28	*430±175.78	0±0	0±0
35	365±171.32	*200±187.75	0±0
42	**615±167.26	155±64.42	0±0
49	1170±436.92	**830±287.49	0 ±0
56	1945±924.37	880±279.55	*50±25.82
63	"2720±1533.59	880±279.55	150±85.63
70	1630±768.21	4765±2879.71	400±242.90
77	2020±1018.90	"6005±4205.36	425±335.91
84	1700±711.34	1800±725.95	**"737.5±448.10
91	1205±440.77	3760±2244.35	256.25±130.50
98	960±678.49	1030±615.14	312.5±124.33
105	1970±905.62	1755±874.66	475±121.79
112	230±93.01	410±137.30	512.5±250.58

*Reinfection

while farmers that use IVG will require only 2 treatments per year (Table 2). Hence, on the basis of efficacy and duration of action, IVG appears to be the more preferable choice among these injectable IVM formulations for the control of GI nematodes in a flock of sheep.

The outcome of the economic analysis shows that the average cost of a one-time treatment (Tc) for GI nematode infection using IVC, IVS and IVG for a group of 5 sheep are \$20.6, \$20.8 and \$21.0, respectively. While the average annual costs of GI nematode control using IVC, IVS and IVG for a group of 5 sheep are \$82.39, \$83.22 and \$41.99, respectively, as shown in Table 2.

A 20% increase or decrease in the average weight (AW) of the animals had the lowest impact on the average annual costs of GI nematode control (ATc) for all groups by increasing or decreasing the ATcby \$0.004 for group A, \$0.12 for B, and \$0.1 for group C. The 20% increase or decrease in veterinary service cost (VSc) had the highest impact on the ATc for all the groups by increasing or decreasing the ATc by \$4 for group A, \$4 for group B and \$2 for group C. Similarly, a 20% increase or decrease in veterinary visit costs (VVc); labour cost (Lc) and drug price (dp) increased or decreased the ATc as follows: \$3.2 for group A, \$3.2 for group B and \$1.6 for group C; \$2 for group A, \$2 for group B and \$1 for group C; \$0.04 for group A, \$0.12 for group B and \$0.1 for group C respectively (Figures 2, 3 and 4).

DISCUSSION

This study evaluated the efficacy of three different IVM preparations in the treatment of GI nematodes in sheep as well as the onset of parasite re-infection after treatment. The efficacy of all three IVM preparations 7 days post treatment was 100% further strengthens claims about the susceptibility of GI nematodes to IVM in this region of Africa by Idika et al. (2012). Similarly, Peña-Espinoza et al. (2014) reported a 100% efficacy of IVM against *H. contortus* in small ruminants in Denmark. This finding is contrary to the report of anthelmintic resistance (AR) to all known anthelmintic groups including IVM in South Africa by Van Wyk et al. (1999). The difference may be due to a large scale sheep farming in South Africa and other southern hemisphere countries like Australia and New Zealand (Pomroy, 2006; Leathwick and Besier, 2014). These large-scale farms use IVM more frequently in GI nematode control as compared to the predominant small holder sheep farming structure in Nigeria. Periodic evaluation of the efficacy of common anthelmintic and possible resistance development by GI parasites is nevertheless important since AR has developed in sheep to all known anthelmintics except for monepantel (Kaminsky et al., 2011).

The different formulations of IVM (IVC, IVS and IVG) following clearance of infection prevented re-infection for a period of 28, 35 and 56 days, respectively. These differences in duration for re-infection to occur between treatment groups can be attributable to the different concentrations of IVM in the preparations used. The concentration of IVM in IVG may be responsible for the prolonged anthelmintic effect of IVG resulting from an extended half-life of the drug in plasma of treated sheep

Table 2. Default input values of costs and prices used in the economic analysis of the costs of GI nematode control using three different IVM preparations in WAD sheep.

Parameter	Abbreviation	Default Value ($)			Source
		IVC	IVS	IVG	
Drug Price/500 ml	DP	29.18	91.23	148.28	^OVAH S/Africa
Drug Price/ml	Dp	0.06	0.18	0.3	Calculated
Dosage (ml/kg)	D	0.02	0.02	0.02	*Merial®
Average weight (kg)	AW	16.73	16.73	16.73	Calculated
Dose Administered (ml)	DA	0.3	0.3	0.3	Calculated
Drug cost/treatment/sheep	DCT	0.02	0.06	0.1	Calculated
Drug cost/treatment/5 sheep	Dc	0.1	0.3	0.5	Calculated
Vet visit cost	VVc	8	8	8	Authors
Veterinary service cost/sheep	VSc	2	2	2	Authors
Veterinary service cost/5 sheep		10	10	10	Calculated
Labour cost/5 sheep	Lc	2.5	2.5	2.5	Authors
Cost of one-time treatment	**Tc**	**20.6**	**20.8**	**21.0**	Calculated
Duration till re-Rx of flock (wk)	DT	6	7	12	As implied from Garg et al. (2007)
No. of Rx req./year	NT	4	4	2	Calculated
Average annual treatment costs	ATc	**82.39**	**83.22**	**41.99**	Calculated

^OVAH S/Africa: Onderstepoort Veterinary Academic Hospital, Pretoria South Africa. *Merial®: The direction on the leaflets for each of the drugs was followed. $R_{\text{-treatment, wk;week, yr:year;}}$. IVC Ivomec classic, IVS Ivomec super, IVG Ivomec gold

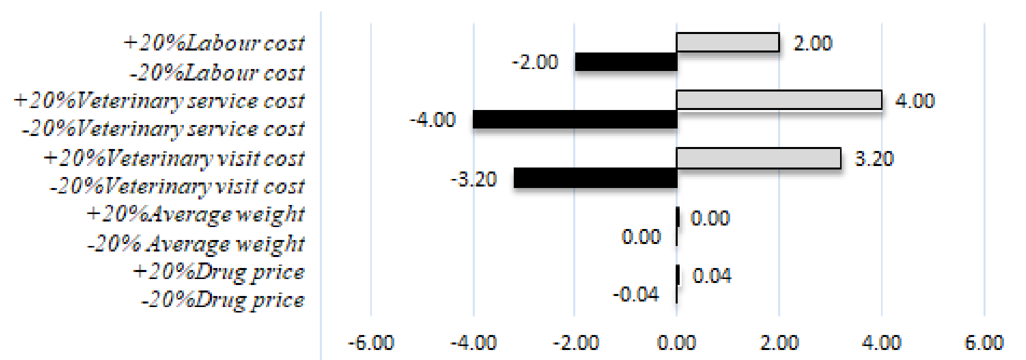

Figure 2. Turnado graph showing sensitivity analysis for Group A treated with Ivomec Classic®. Tornado graphs showing sensitivity analysis of cost variables. The values displayed are the differences between the average annual costs of GI nematode control in the normal scenario (with default prices for all cost variables) and the average annual costs of GI nematode control in a group of 5 WAD sheep under scenarios in which the value of one cost variable is altered. The negative values represent reduced marginal costs compared to the normal scenario, while the positive values represent additional marginal costs compared to the normal scenario in US Dollars.

(McKellar and Marriner, 1987; Garg et al., 2007).

The economic model used to evaluate the comparative cost analysis of the three IVM preparations shows that in spite of the relatively large difference in price between the drugs (that is, $119.10 between the cheapest option, IVC and the most expensive option, IVG), the consequential difference in the average costs of a one-time treatment for a group of 5 sheep was relatively small, that is, $1.40 between the cheapest option (IVC) and the most expensive option (IVG). This may be due to the proportion of treatment costs attributable to the cost of the drug used was only about 0.5, 1.5 and 2.4% for IVC, IVS and IVG, respectively. Whereas, other complementary costs that make up the treatment costs contributed much more. The proportion of treatment costs attributable to veterinary service cost is almost 50% for all three treatment options. A scenario manipulation of the model showed that the cost of veterinary services would account for as much as 75% of treatment costs in a flock of 50 sheep kept under the same circumstances as those in the current study. The relatively high cost associated with veterinary services make farmers to by-pass professionals there

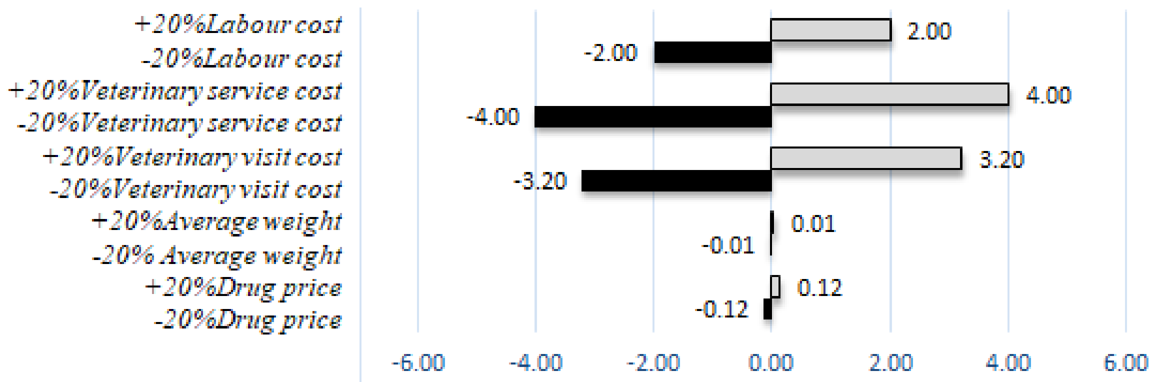

Figure 3. Turnado graph showing sensitivity analysis for Group B treated with Ivomec Super®. Tornado graphs showing sensitivity analysis of cost variables. The values displayed are the differences between the average annual costs of GI nematode control in the normal scenario (with default prices for all cost variables) and the average annual costs of GI nematode control in a group of 5 WAD sheep under scenarios in which the value of one cost variable is altered. The negative values represent reduced marginal costs compared to the normal scenario, while the positive values represent additional marginal costs compared to the normal scenario in US Dollars.

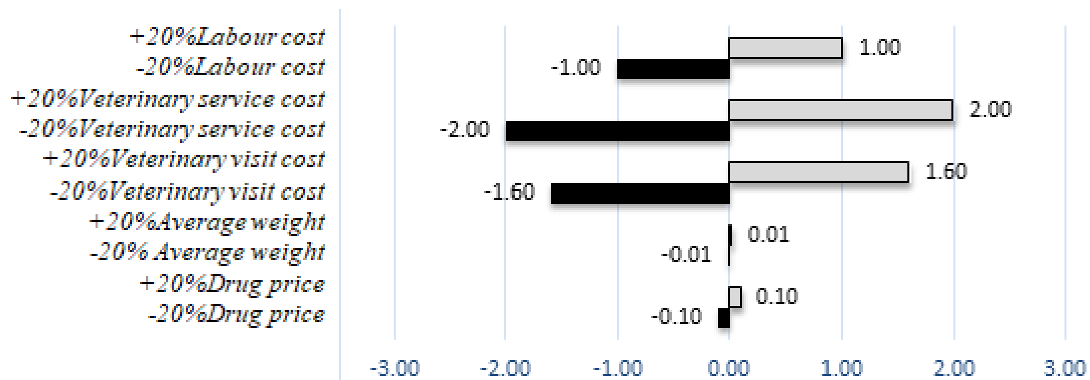

Figure 4. Turnado graph showing sensitivity analysis for Group C treated with Ivomec Gold®. Tornado graphs showing sensitivity analysis of cost variables. The values displayed are the differences between the average annual costs of GI nematode control in the normal scenario (with default prices for all cost variables) and the average annual costs of GI nematode control in a group of 5 WAD sheep under scenarios in which the value of one cost variable is altered. The negative values represent reduced marginal costs compared to the normal scenario, while the positive values represent additional marginal costs compared to the normal scenario in US Dollars.

by administering the drugs or employing the services of unqualified individuals (quacks). This abuse of the veterinary profession may increase the risk of anthelmintic resistance as a result of the use of incorrect dosages and routes of administration, as well as the practice of sub-optimal control strategies. Most farmers do not consider the cost of their labour (time and energy spent on catching and restraining the sheep during treatment) into account. This is taken for granted, but this study considered this an important input as persons may be employed to perform the duty. The farmer may perform the duty himself, the time spent should be valued based on the value of other profitable activities he/she could have been engaged in during the period. In the current study, labour costs accounted for about 12% of treatment costs, which is much more than the cost of the drugs, indicating that they should not be overlooked. The sensitivity analysis buttresses the fact that veterinary services and labour costs are the highest contributors to the overall costs and should be considered more importantly in the choice of control strategy, rather than the price of the drug which is usually the major consideration by farmers.

The major reason for which IVG emerged as a cheaper option, this is less than half the cost of either IVC or IVS is when used for an annual control programme. The sheep were protected for 12 weeks, indicating that the treatment procedure will only need to be carried out twice a year as against four times when compared with the other two options used. This reduction in the frequency of treatment cuts down the cost of the procedure such as veterinary services and labour by 50%. This will reduce the exposure of the anthelmintic and possibly delaying the onset of anthelmintic resistance. Famers may be more willing to employ the services of a vet when the costs of veterinary services are lowered. To optimize the cost of anthelmintic control, the choice of anthelmintic should be based on the efficacy and duration of action of the drug.

Conclusion

The GI nematode parasites in circulation among West African Dwarf (WAD) sheep in the study area may not have developed resistance to ivermectin. The IVG confers a longer duration of protection when compared with IVC and IVS formulations. While IVG is costly than both IVC and IVS in a one-time treatment of GI nematodes in sheep, it is much cheaper to use in an annual control programme of GI nematodes of sheep in the study area. Veterinary service and labour costs contributed more to treatment costs than the price of the anthelmintic in GI nematode control. Thus, the decision for choice of anthelmintic for optimization of the cost analysis of GI nematode control should be based on the efficacy and duration of action of the drug rather than its price.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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