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Targeted selective treatment (TST): A promising approach to combat anthelmintic resistance in farm animals

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Abstract
Anthelmintic resistance is rising as a big threat for the control of gastrointestinal parasitism in farm animal production. Many strategies have been suggested to slow down the development of anthelmintic resistance and to maintain anthelmintic efficacy. One such strategy is Targeted Selective Therapy (TST) in which animals that require anthelmintic treatment alone is treated. Several methods have been suggested to selectively treat with anthelmintics. First method is based on parasitological indicator in which egg per gram (EPG) of faeces can be used to determine the existence and severity of helminth infection. Second method is based on pathophysiological indicators such as body weight and body condition score, anaemia, diarrhoea and plasma pepsinogen levels in animals with helminthic infection. In this method FAMACHA system is practical and proven farm method for anaemia evaluation in animals with hematophagous parasites. Dag score and diarrhoea score (DISCO) are based on the diarrhoea in helminth infected animals. Third method is based on the performance based indicators like milk production and live weight gain. Recently, five point check system in which eye, nose, jaw, back and tail are examined as evidence of parasitism and the selected animals are treated. In TST, only the needy animals alone are treated thereby reducing the cost of treatment, drug residues in milk and meat and spread of drug resistant genes.

Keywords: Anthelmintic resistance, Targeted Selective Therapy (TST), GI parasites, Ruminants and Small ruminants

1. Introduction

Anthelmintic resistance in gastrointestinal (GI) helminth population is now widely recognised as a major problem in small ruminants [1, 2] and in cattle [3, 4]. Since it is highly unlikely that GI parasites can ever be eradicated animal producer must learn to live with worms [5, 6].

The key approach to deal with anthelmintic resistance is to slow the development of resistance. Targeted Selective Treatment (TST) is an example of such approach where only the individual animals are treated with anthelmintics as opposed to the treatment of the entire group [7]. This approach is based on the refugia concept.

Refugia means the portion of the worm population have not been exposed to anthelmintic drugs. The aim of the refugia based approach is to reduce the use of anthelmintic and thus minimize the selection of resistant nematode alleles and thereby increasing the effective lifespan of anthelmintics for use in farm animal practice [8].

Targeted Selective Treatment (TST) can be defined as any system that selects animals on an individual basis for treatment using logical specific criteria on which this selection is made [9]. In this approach, the animals which are most likely to get benefited are included and those animals least likely to benefited are excluded.

Targeted Treatment (TT), in contrast, comprises treatment of all animals at the most beneficial times (or) circumstances for sustainable worm management [10]. Whereas, random allocation for treatment involves treatment of entire group. In this approach the healthy animals may be treated while sick animals left untreated.

The TST and TT are based on the concept of refugia. Refugia means the portion of the worm population have not been exposed to anthelmintic drugs. The aim of the refugia based approach is to reduce the use of anthelmintic and thus minimize the selection of resistant nematode alleles, thereby increasing the effective lifespan of anthelmintics [8].

The highlighted benefits of TST reported by recent studies are [11]

(i). Halving of the anthelmintic treatments

(ii). Maintenance of anthelmintic efficacy
(iii). No loss in production compared to whole flock treatment

2. Potential markers as indicators for the TST

Several methods have been suggested to selectively target anthelmintic treatments.

1. Parasitological Indicators: Egg per Gram (EPG) of faeces
2. Pathophysiological Indicators:
a. Anaemia caused by Hematophagous parasites (FAMACHA Score)
b. Dag Score
c. DISCO Score
d. Body Condition Score

3. Performance based Indicators
a. Milk Production
b. Live weight gain

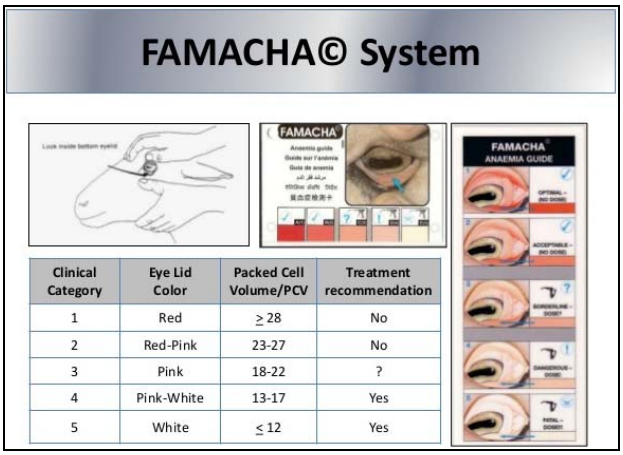
2.1. Parasitological Indicator

Faecal egg count i.e. egg per gram of faeces (EPG) of a flock may be related to actual infection in sheep and goats [12] and in young cattle [13]. Faecal testing is useful in identification of worm eggs and determination of existence and level of helminth infection (faecal floatation and egg count), determination of the parasite species (larvae culture and lectin staining tests) and determination of effectiveness of anthelmintic treatment (faecal egg count reduction test [FECRT] and larval development assay [LDA]).

FECRT could be used as a potential method to treat helminths effectively. In this method animals are treated on the basis of mean faecal egg count which is correlated with worm burden. However, this correlation may not be always true when coinfection with high egg producing nematodes such as *Haemonchus contortus* occurs with low egg producing nematodes such as *Trichostronchylus colubriformis*. FECRT also requires individual assessment, facilities and trained personnel.

2.2. Pathophysiological Indicators

a. ***The FAMACHA System***: It is the practical and proven on farm method for clinical anemia evaluation of sheep infected with hematophagus parasites especially *Haemonchus contortus* [14]. In this TST is done based on the colour of conjunctiva of small ruminants (Figure 1). This system was developed in the beginning of 1990s and widely adopted first in South Africa [15, 16].



Clinical Category	Eye Lid Color	Packed Cell Volume/PCV	Treatment recommendation
1	Red	≥ 28	No
2	Red-Pink	23-27	No
3	Pink	18-22	?
4	Pink-White	13-17	Yes
5	White	≤ 12	Yes

Fig 1: FAMACHA Chart with interpretation [15, 16]

In FAMACHA method, variation in the colour of the mucous membrane is used to detect and grade anemia as an indication of *H. contortus* infection. By grading the clinical anaemia the animals that are unable to cope with worm challenge can alone be treated. Benefits of FAMACHA include reduction in the number of anthelmintic treatments thereby reducing the cost of anthelmintic drugs, identification of susceptible and resilient animals. It also increases the refugia population thereby prolonging the effectiveness of anthelmintic drugs. However, this method can't be applied for non-haematophagous worm species and requires more time for monitoring than the treatment.

b. ***Dag Score***: Dags are the dried faeces dangling on wool or hair of sheep or goats rear end. It is scored (Table 1) between 0 (no soiling) to 5 (extensive soiling). This system of identification of sheep with repeated diarrhoea during infection with digestive tract strongyles. In Australia, the lambs are detected for dag score along the grazing season [17].

Table 1: Dag Scoring [17]

Score	Description	Action
0	No faecal soiling at all. No indication for treatment/action	None
1	Very slight soiling on edge of tail/on each side	None
2	Slight soiling on edge of tail/on each side	Usually none
3	Moderate soiling, dag formation	Consider treatment/action
4	Severe soiling, severe dag formation	Treatment recommended
5	Very severe, watery diarrhoea extending to hocks	Treatment essential

c. ***Diarrhoea Score (DISCO):*** This method is based on the dry matter of the feces at the moment of preparing faeces for faecal egg counts [12]. This is not repeatable as in dag score but score the diarrhoea at one moment in the life time of the lamb.

d. ***Body Weight and Body condition score (BCS):*** Weighing the sheep with an electronic scale and the animals with low body weight indicates low resilience for internal parasitism. However it is nonspecific and depends on many other factors like food availability.

BCS has been applied instead of FAMACHA as an index for non-hematophagous nematodes infection such as *Ostertagia*, *Trichostrongylus* etc. Body weight change measurements are an alternative to the BCS. This method has the potential for automation where more time and labour can't spend for individual animal inspection.

BCS is measured on the basis of palpating the prominence of spine and transverse process of lumbar vertebrae, rib cage, subcutaneous fat and muscle mass of sheep and goats (Table 2 and Figure 2).

Table 2: Body Condition Scoring in Goats

Score		Spineous Process	Rib Cage	Loin Eye
1	Very Thin	Easy to see and feel, sharp	Easy to feel and can feel under	No fat covering
2	Thin	Easy to feel but smooth	Smooth, slightly rounded, need to use slight pressure to feel	Smooth, even fat cover
3	Good Condition	Smooth and rounded	Smooth even feel	Smooth, even fat cover
4	Fat	Can feel with firm pressure, no points can be felt	Individual ribs cannot be felt, but can still feel indent between ribs	Thick fat
5	Obese	Smooth, no individual vertebra can be felt	Individual ribs cannot be felt. No separation of ribs felt	Thick fat covering may be lumpy and giggly

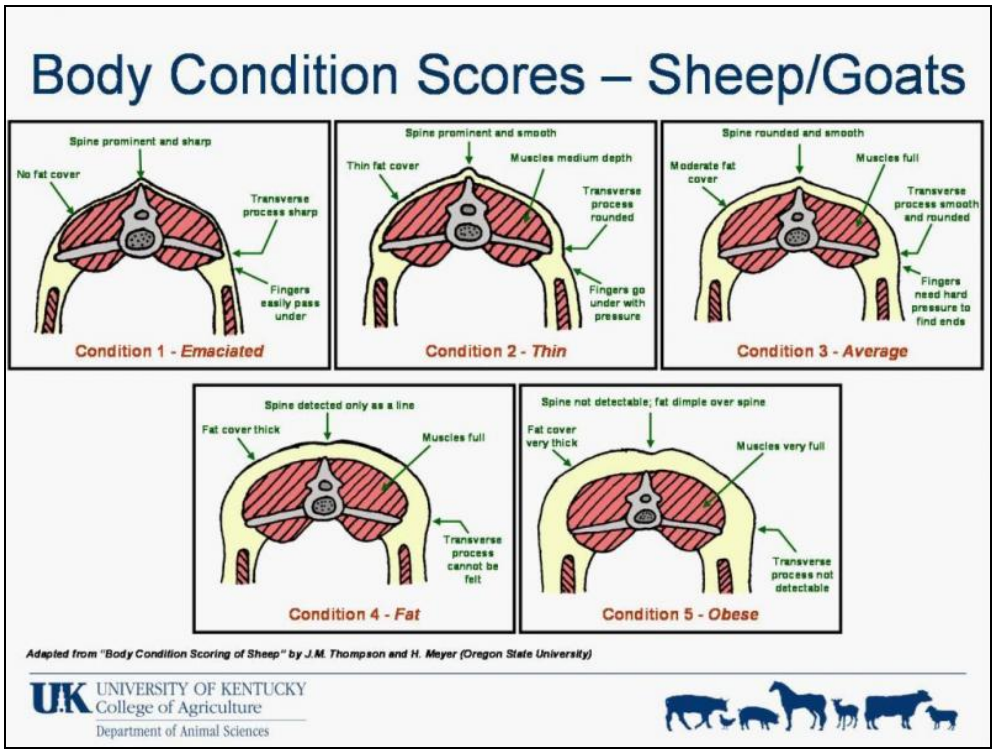


Fig 2: Body condition scoring in sheep and goats

2.3. Performance Based Indicators

I. ***Milk Production***: Epizootiological studies indicated that milk production could be an appropriate marker for TST [18].

II. ***Live weight gain***: It could be a potential marker to identify the animals for TST in areas where there are no haematophagous nematodes [19].

Investigations on effectiveness of performance based TST has been shown that it reduces the anthelmintic usage by 50% while maintaining the live weight gain of animal compared to a monthly anthelmintic treatment [11]**.** The prospects of performance based TST in dairy calves has also been stated as a feasible method.

2.4. Recent Developments in TST Indicators

a. ***5 Point Check***: Bath and van Wyk developed a system in 2009[9] for selecting the animals for treatment based on five points check (eye, nose, jaw, back and tail). The eyes are examined for FAMACHA, the nose are examined for discharge indicating nasal bots, bottle jaw or submandibular oedema for hematophagus worms and conical flukes, body condition score for worms causing weight loss and dag score or faecal fouling for worms causing diarrhoea.

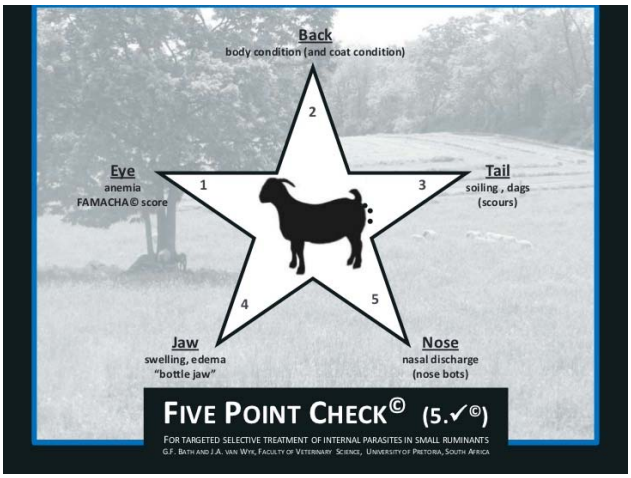


Fig 3: Five point check for TST of internal parasites in small ruminants [9]

e. ***Plasma pepsinogen concentration***: TST for Dictyocaulosis was done based on Modified Baerman's Technique and plasma pepsinogen (> 2 IU of Tyrosine /L) and faecal egg count (>200 Strongyle eggs per gram of faeces) have been treated. The author reported that there was 50% reduction in anthelmintic use in TST calves compared with control calves [20].

Disadvantages of TST

1. Difficulty and time spent on selecting the animals which need treatment
2. Possibility of reduced production
3. Need variants that complement for each farm systems

3. Conclusions

Based on the several trials on different TST methods, it is evident that TST strategies make it possible to reduce the usage of anthelmitic drugs without reducing the animals performance.

In TST, only animals which are in need are treated thereby reducing the residues in milk and meat besides the control of digestive tract parasites and control of spreading the resistance genes. Though TST necessitates evaluation of parasitic infection, pathology along the grazing season, species and age group of animals, it is a promising approach to combat anthelmintic resistance in farm animals. However, regional specific sustainable and user friendly indicators for treatment should be validated. Since the consequences of anthelmintic treatment also depend on the biology and ecology of parasites, the TST should be combined with other integrated parasite management strategies for effective control of parasites.

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