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REVIEWS

Ovine haemonchosis: a review

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Abstract

Sheep farming is the backbone of a rural economy in developing countries, and haemonchosis is a major impediment in the way of its progress. *Haemonchus contortus* (*H. contortus*) infection persists all over the world particularly in the tropical and subtropical regions. Various review articles have been published to substantially cover one or more aspects of its morphology, prevalence, pathogenesis, symptoms, diagnosis, immune response, drug resistance, treatment, and control measure. The objective of this paper is to briefly review past and present information available in the aforementioned areas in one place to enable the readers to fully understand the problem from a broader perspective. *H. contortus* parasite harbours in abomasum of affected animal and feeds on its blood, producing mild to severe symptoms and even death in acute form. The parasite thus inflicts heavy production losses and is of economic importance. *H. contortus* has developed diverse characters over the years leading to limited success in the production of vaccines. Indiscriminate use of the anthelmintics has produced drug resistance against almost all conventional products. Efficacy of medicinal plants and non-conventional chemicals has been reported under controlled experiments; however, research on their adverse effects on growth and fertility is yet to be studied. Research on molecular tools for identification and introduction of resistant genes into the flock is also underway but still a long journey to find its field application. Crossbreeding may compromise the production traits of the existing flock. In given circumstances, a targeted selective treatment approach along with selective breeding, culling of more susceptible animals, and maintaining a good body condition score through the provision of a balanced diet remains a workable strategy to control haemonchosis in sheep.

Keywords Haemonchosis · Sheep · Barber's pole worm · Ovine

Introduction

In developing countries, the livestock sector is considered the backbone of the economy, and the small ruminants, including ovine, make its major segment (FAOSTAT 2018). Sheep are reared in rural areas for sale in the open market as a valuable source of organic meat throughout the year. Farmers, dealers, and the state also generate handsome revenue through its trading as sacrificial food animals at the occasion of annual religious festivals in Muslim countries. The demand is rapidly multiplying because of fast growth in population, increased buying power of people, and export opportunities (Rehman et al. 2017; Bai et al. 2020). Wool, skin, and hide are other by-products of this industry which significantly contribute to local as well as an export market and fetch valuable foreign exchange. Sheep milk and related dairy products also have potential in the human food market due to its peculiar health benefits (Balthazar et al. 2019; Mohapatra et al. 2019). In tropical regions, sheep farming is carried out under a semi-extensive system (Chaudary et al. 2007; Kandiwa et al. 2020) where flocks of all age groups are taken out during the day for grazing in harvested fields, along the roadside, canal banks, and foothills. Water available in stagnant reservoirs and irrigation channels is offered for drinking. Night housing consists of mud-erected sheds and paddocks. This system coupled with a high temperature-humidity index naturally exposes the animals to infestation with several gastrointestinal parasites (Swarnkar and Singh 2020; Vohra et al. 2020) which increases their susceptibility to other ailments as well. Among these parasites, *Haemonchus contortus* (*H. contortus*) is the most prevalent species which adversely affects the health of sheep leading to lower production. Commonly found effects are loss of appetite, impaired feed utilization, stunted growth,

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weakness, anaemia, poor fertility, and even death of lambs which cause major economic losses to the farmers (Emery et al. 2016; Iliev et al. 2017; Goel et al. 2020). The prevalence of *H. contortus* is around the, globe and even temperate zones are not safe due to its adapted strains (Sallé et al. 2019). Several studies and research works have been carried out on *H. contortus* infection in sheep covering various aspects of its prevalence, life cycle, pathogenesis, clinical symptoms, diagnostic methods, host immunity, treatment, control measures, and drug resistance. However, even today, this nematode remains an impediment in the way of the desired production in sheep farming. The situation demands the collection of a compendious knowledge about *H. contortus* at one place to make it readily understandable for the reader. The objective of the current article is to carry out a comprehensive review of scientific information available in the aforementioned study areas of *H. contortus* to serve as a guideline for people engaged in the sheep husbandry sector.

Morphology

H. contortus is a nematode parasite of family Trichostrongylidae later classified as Haemonchidae (Palevich et al. 2019). Figure 1 shows its main morphological features. The adult parasite has an anteriorly tapering cylindrical body (Widiarso et al. 2018). A small oral cavity is equipped with a prominent lancet type tooth on the dorsal side for sucking capillary blood from the host stomach wall (Sambodo et al. 2018; Widiarso et al. 2018). The organism is whitish yellow in colour; however, ingested blood gives it a reddish appearance. The male bears a lobulated genital bursa at the tail end, a gubernaculum, and a pair of needle-like spicules for mating (Kuchai et al. 2012; El-Ashram and Suo 2017; Melnychuk 2019). Female has vulvular pouches towards posterior end covered with a prominent linguiform, smooth, or knobbed process (Irfan-ur-Rauf et al. 2014; Nahar et al. 2019). The blood-filled intestine in the female with the white uterus, winding around, gives the shape of a "barber's pole", the popular name used for this parasite (Saminathan et al. 2015) (Fig. 1). The average length of the male is 10–20 mm and that of the female is 18–30 mm (Roeber et al. 2013a). The eggs at an average are 70–79 μ × 45–49 μ in size (Mahmood et al. 2019). Genetic variation has given rise to so many strains of *H. contortus* (Yin et al. 2016; Sargison et al. 2019).

Prevalence

As per the latest information available, *H. contortus* originated from sub-Sahara, Africa, in wild ungulates and then evolved to spread across the globe through the movement of host

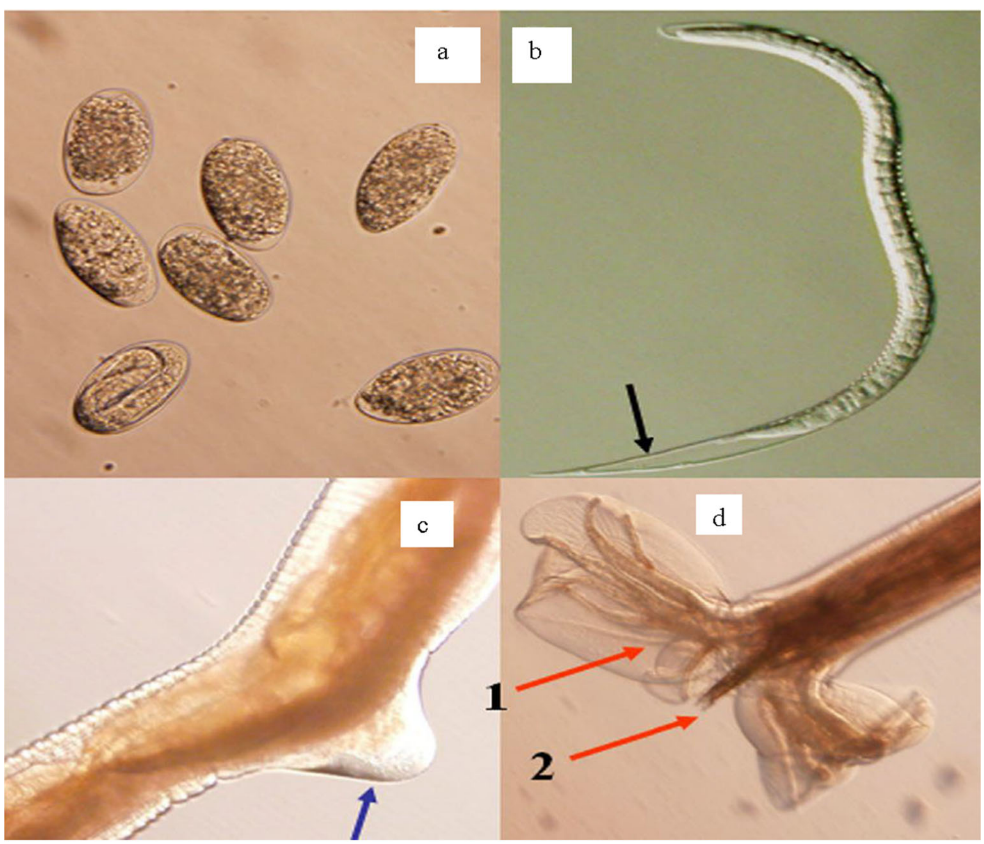

Fig. 1. *H. contortus*. (**a**) Eggs. (**b**) L_3 larva with tapering end. (**c**) Adult female, the arrow is pointing to vulval flap. (**d**) Adult male, the copulatory bursa (1) spicules (2) (El-Ashram and Suo 2017)

animals and human intervention (Gilleard and Redman 2016; Sallé et al. 2019). All classes of ruminants are susceptible; however, aggressive distribution has been noticed in sheep and goat population (Yin et al. 2016). The parasite finds highly favourable warm and wet conditions in tropical and subtropical countries (O'Connor et al. 2006); however, over the years, prevalence has also been reported from temperate regions due to climatic changes (Emery et al. 2016; Rose et al. 2016). Incidence may vary with season, area, age, sex, breed, and body condition; however, findings of such studies are not consistent. The average larval establishment rate has been reported to be 0.24 ± 0.02 (Saccareau et al. 2017). Random examination of abomasums from abattoirs in Ethiopia (Tesfaheywet and Murga 2019) and faecal egg count (FEC) from the farms in Rwanda (Mushonga et al. 2018) revealed over 80% prevalence in sheep.

Life cycle

H. contortus passes through six stages of life which include egg, four larval stages, and the adult (El-Ashram and Suo 2017) (Fig. 2). Typical to its family, the female parasite lays numerous eggs with an average (±SE) of 1295.9 ± 280.4 per day which are passed through faeces to pastures (Saccareau et al. 2017). The eggs may die or develop to free-living larval 1st stage (L_1), 2nd stage (L_2), and infective stage (L_3) within 1–7 (Schwarz et al. 2013) days. The hatchability of eggs and development to infective larvae depend upon the availability of suitable environmental conditions (temperature range of 15–37 °C and relative humidity of 85–100%) in faecal pellets and herbage (O'Connor et al. 2006). Stage L_3 is ingested by the host where it undergoes ensheathment in the rumen and takes 2–3 weeks to develop into parasitic stage L_4. After two moultings and just before the final moult, immature adult L_5 erupts which develops a lancet to penetrate the mucosal vessels for sucking blood. The abomasum is the predilection site where the adult worms move freely. The parasite may also undergo arrested inactive phase of development in the host animal during winter called hypobiosis (Zajac and Garza 2020).

Pathogenesis and symptoms

Degree of the establishment of *H. contortus* and consequent sickness depend upon the number of infective larvae ingested, age (Saccareau et al. 2017), immunity level, and nutritional status of the host. Major pathogenic damage occurs due to the sucking of blood by the free-living parasites and eruption of ulcerative lesions in the abomasal mucosa leading to digestive syndrome and anaemic disorders (Besier et al. 2016b). The infected sheep may lose up to 30 μL of blood every day due to one parasite and even death in the pre-patent period (Emery et al. 2016). Loss of blood which is either ingested or let oozed out from the mucosal lesion to faeces leads to anaemia, which appears 10–12 days after getting infected (Roeber et al. 2013b), and a fall in packed cell volume (PCV) (Storey et al. 2017; Ferreira et al. 2019) detectable even at 4th day. The PCV value further drops by 3–6 weeks due to increased blood loss by the accelerated activity of parasites and bleeding from haemorrhagic gastritis lesions. A concurrent reduction in

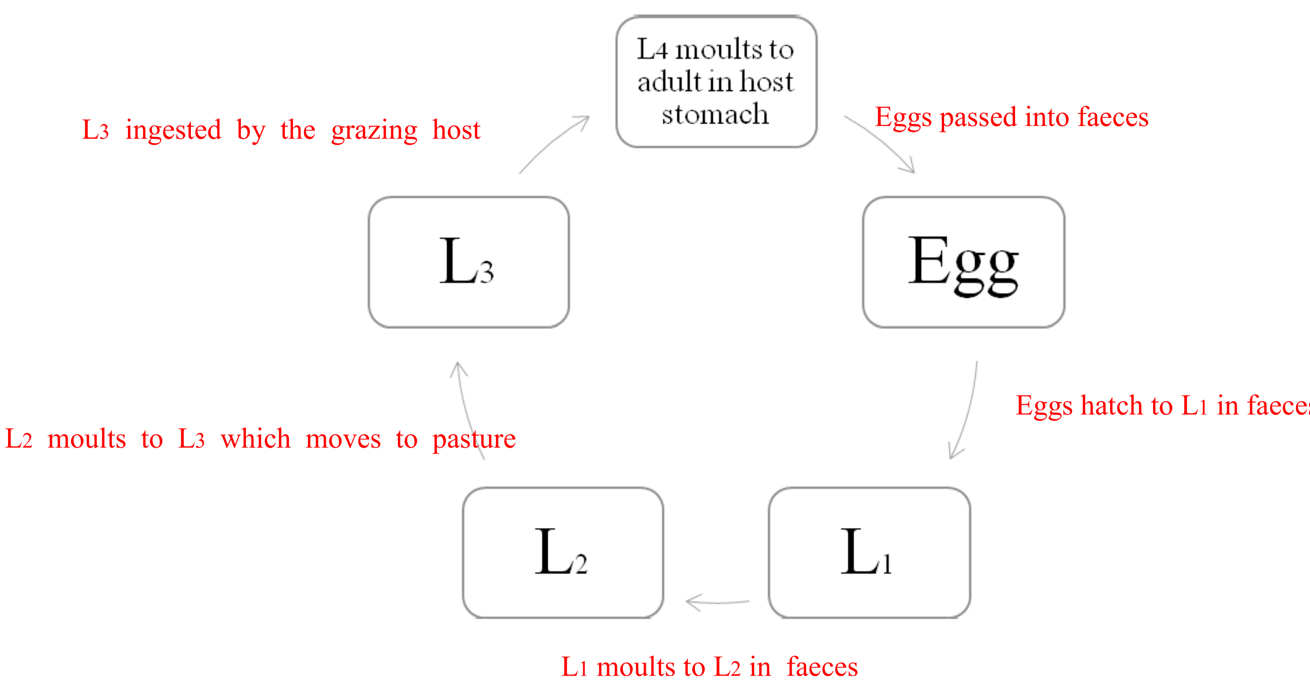

Fig. 2 Life cycle effect of *H. contortus*. Eggs hatch to L1 in faeces, L1 moults to L2 in faeces, and eggs passed into faeces

the concentration of haemoglobin and plasma protein is also observed (Swarnkar and Singh 2018). Extensive damage to abomasal mucosa affects the passage rate of ingesta, produces pain and inflammatory cytokines, and changes in gastric secretions as well as the level of gastrointestinal hormones in plasma which lead to prolonged loss of appetite (Angulo-Cubillán et al. 2007). Due to raised pH of the abomasum, rumen microbes do not get inactivated and lysed resulting in the non-availability of amino acids. Physical and chemical damage caused by the parasite induces the inflammatory response in the gastric tissues leading to a collection of numerous neutrophils, lymphocytes, and eosinophils which further aggravate the situation (Alam et al. 2020). Clinically haemonchosis can be sub-divided into hyper-acute, acute, and chronic forms. In a hyper-acute case, sudden death is the only sign. Acute form involves severe anaemia, lethargy, weakness, increased respiratory and heart rate, dark mushy faeces, loss of wool, pale to white conjunctiva, ascites, and sub-mandibular and cervical oedema. Quite recently fatal outbreaks of haemonchosis in lambs have been reported (Paul et al. 2020). Chronic disease is characterized by anorexia, loss of weight, agalactia, pallor of the conjunctiva, and mucosa (Besier et al. 2016b; Iliev et al. 2017).

Diagnosis

Diagnosis of haemonchosis can be made through the clinical picture, FAfa MAlan CHArt (FAMACHA), morphological identification of eggs and parasite, molecular techniques, haematology, immunological procedures, and post-mortem findings (Besier et al. 2016a; Zarlenga et al. 2016). FAMACHA is a popular method in tropical and sub-tropical countries which involves visual assessment of anaemia through watching colour of conjunctiva on a score of 1–5, 1 and 2 (red or pink) being normal, 3 (light pink) doubtful, and 4 and 5 (pale) being anaemic (Ferreira et al. 2019). FAMACHA scores 4 and 5 with blood PCV value ≤ 15% have been found highly sensitive, whereas scores 3–5 with PCV value ≤ 18% have been found highly sensitive for the diagnosis of haemonchosis in sheep (Ferreira et al. 2019); however, variation due to breed has been reported (Alam et al. 2020). Each diagnostic method has its limitation and advantages. Various techniques used have been reviewed in Table 1.

Immune response

H. contortus–infective larvae and adults, while feeding on blood in the abomasum of the host animal, also release antigenic secretions and excretions which are glycoprotein in nature. Exposure to these antigens stimulates the immune system of the host leading to activation of inflammatory, humoral, and cellular responses to reject the invading parasites (Emery et al. 2016). A large number of helper T cells appear in abomasum of *H. contortus*–infected sheep. Getting stimulated by the specific antigen, they release messenger cytokines, mostly the interleukins. These cytokines activate eosinophils, mastocytes, and globule leukocytes in peripheral mucosal tissue that is infection site as well as in blood (Robinson et al. 2010). Followed by this immediate response, the cytokines also activate B cells resulting in the production and release of infection-specific antibodies IgA and IgG1 into serum, mucosa, and saliva (Hernandez et al. 2016; Escribano et al. 2019). The mastocytes and eosinophils release inflammatory substances like histamines, proteases, leukotrienes, and prostaglandins. These mediators enhance the production of mucus, paralyse and kill the parasite, intensify smooth muscle contractions for removal of the parasite, inhibit the further establishment of third-stage larvae, and reduce egg production (Angulo-Cubillán et al. 2007; Escribano et al. 2019). Resistance level has been known to vary among various breeds and lines of sheep as resistant animals have shown a potent parasite-specific local and systemic immune response (Escribano et al. 2019). Cross-protective and added immunity has also been reported in animals previously exposed to mixed infections (González-Garduño et al. 2018).

Treatment

There are various strategies for the treatment of *H. contortus* on herd level. One common practice is periodical deworming of all the flocks with anthelmintic drugs. This approach is costly, offers the least opportunity for the development of immune response in the growing flock, and also potentiates the risk of parasite resistance. An alternate approach is targeted treatment (TT) where a targeted flock is treated with anthelmintics and others are allowed to graze on infected pastures. Another regime with a reduced cost of treatment is targeted selective treatment (TST) in which only selected animals are treated leaving remaining flock as such presumably being healthy or bearing less resistant worms, to have epidemiological benefits (Kenyon and Jackson 2012; Calvete et al. 2020). Last two strategies are labour intensive and based on inspection of individual animals, by the skilled technicians for anaemia score (FAMACHA), body condition score (BCS) (Cornelius et al. 2014), faecal egg count, or live weight gain measurement (Greer et al. 2009; Kenyon and Jackson 2012). Anthelmintics are the most commonly used drugs for the treatment of *H. contortus* throughout the world which still have adequate efficacy (Calvete et al. 2020), but the need for the choice of an effective anthelmintic to prevent the development of resistance cannot be overemphasized. Broad-spectrum substances like benzimidazoles (albendazole), imidazothiazole, and macro-cyclic lactones (ivermectin) have been known to

Table 1 Diagnostic methods

Procedure	Technique	Advantage, limitation	Reference
Clinical symptoms	History, examination, body condition score, anaemia score (FAMACHA), faecal score	Practicable in the field, non-specific	Taylor et al. (2007), Besier et al. (2016b), Zarlenga et al. (2016), Ferreira et al. (2019)
Faecal egg count and identification	McMaster method and its modifications, lectin staining, automated egg examination, FLOTAC	Easier, non-specific	Cringoli et al. (2010), Paras et al. (2018)
Larval culture, egg hatch test	Faecal incubation and identification of larvae	Laborious, not suitable for mixed infections	Coles et al. (2006), Zarlenga et al. (2016), Aguilar-Marcelino et al. (2020)
Immunological detection	ELISA, CFT, indirect-immunofluorescence, indirect haem-agglutination	Non-specific, cannot differentiate old and current infection	Hassan et al. (2019)
Visible-near infrared spectroscopy for detection of blood in sheep faeces	Detecting the presence of haemoglobin in sheep faeces	Non-specific, possible on a farm	Kho et al. (2020)
PCR, Droplet digital PCR	Real-time PCR after DNA extraction from egg flotation of faecal samples	Specific, expensive, difficult in the field	Zarlenga et al. (2016), Elmahalawy et al. (2018), Höglund et al. (2019)
Post-mortem examination	Washing of organ and sieving, identification and counting of worms	Specific	Besier et al. (2016a)

Elisa enzyme-linked immunosorbent assay, *CFT* complement fixation test, *PCR* polymerase chain reaction

create resistant parasite strains (Chaparro et al. 2017; dos Santos et al. 2019; Duarte et al. 2019). The combined use of more than one anthelmintic has been found adequately effective against resistant parasites (Borges et al. 2020). Long-acting products are though potentially effective (Ballent et al. 2019) but also have a risk of resistance development (Leathwick et al. 2006). Nevertheless, narrow-spectrum anthelimintics appear to be a better choice if they are used with absolute care. An alternate approach is to carry out 'faecal egg count reduction test' (FECRT) before choosing an anthelimintic (Salgado et al. 2019). However, an even better, time-saving, economical, and standard strategy is to carry out DNA-based testing regionally to identify resistant strains of *H. contortus* against a range of drugs (Ehrenreich et al. 2012). Studies have also been conducted to check the efficacy of other non-conventional compounds of plant origin (Zamilpa et al. 2019; Mravčáková et al. 2020) with variable success and preferred because of their non-residual effect in meat and milk. Few other substances like anti-protozoan drugs (Nixon et al. 2019), heterocyclic compounds (Nguyen et al. 2019), and organophosphate (Duarte et al. 2019) previously not used due to their toxicity have also been tried against resistant strains of *H. contortus* with success.

Parasite resistance

H. contortus has tremendous capability to develop resistance against almost all classes of anthelmintics and their combinations (Lyndal-Murphy et al. 2014), which is a major threat for sheep production through the world. This has happened due to the indiscriminate use of these chemicals leading to genetic mutations producing phenotypic variations (Chaudhry et al. 2015). Fast adaptation by this nematode to variations in climate and species of the host has also been reported (Troell et al. 2006). Elaborate information on the underlying mechanism of genetic diversification has been published (Gilleard and Redman 2016). Fortunately, the whole genome sequence of *H. contortus* has been read, and it is possible to accurately diagnose resistant strains basing on DNA testing which can make a sound basis for vaccine development (Wang et al. 2017).

Control

Due to constantly increasing drug resistance in *H. contortus* and residual effects, the control strategies which employ minimal use of synthetic anthelmintics have gained importance in the sheep industry. The experts have recommended an integrated control mechanism encompassing various approaches instead of relying on a single option to achieve enough control (Fernandes et al. 2019). Management fields like the selection of resistant lines of sheep, adoption of grazing techniques, and vaccination program have also gained significant attraction. A brief account of various control measures is given in the following sub-paras.

Pasture management

Across the globe, sheep are raised under extensive systems relying on pasture grazing. The underlying principle of this control segment is to minimize contact with infective larvae (L_3) of *H. contortus*. For this purpose, various grazing techniques have been suggested. Rotational grazing, a commonly employed practice (Whitley et al. 2014), involves the introduction of the flock to a field when the bulk of L_3 larvae has naturally diminished but such tactics are not successful in temperate countries where this stage has long survival period (Eysker et al. 2005). This system compromises the availability of forage by missing ideal periods. Cell grazing system which involves grazing of the sheep on a limited patch with high stocking density has been known to be equally effective in reducing faecal egg count of grazed animals (Ruiz-Huidobro et al. 2019). Mixed grazing of more than one host simultaneously or alternately presumably restricts the consumption of infective larvae by the specific host (Mahieu and Aumont 2009). Parallel to these interventions, *H. contortus* is also undergoing selective adaptations in its developmental and reproductive stages resulting in long inhibitive stages in the host and prolonged survival period of eggs at pastures.

Nutritional management

Provision of a well-balanced, nutritionally supplemented diet in sufficient quantity to sheep especially during late pregnancy and also to the growing lambs is an essential part of control strategies (Macarthur et al. 2014). Quality nutrition adds to the expression of resistance and resilience of host, through the provision of additional nutrients, even under infected conditions. Diet supplemented with high protein (Rocha et al. 2011), amino acids like methionine and leucine (Sakkas et al. 2013), and rumen-protected protein (Cériac et al. 2019) have been shown to boost immunity, decrease parasite proliferation, maintain production, and reduce FEC under infective conditions.

Selective breeding

Immunity against *H. contortus* expressed as FEC and PCV values is a heritable trait in sheep (Becker et al. 2020), and differences among breeds to resist infection have been known to exist. One practicable and phenotypic way is the culling of susceptible and selection of resistant animals within a flock (Gowane et al. 2020); however, it is a long-term and laborious strategy. Resistant alleles have been identified in some breeds like Red Maasai (Benavides et al. 2015; Estrada-Reyes et al. 2019), and introgression of these foreign genes through crossbreeding is an attractive workable option but should be done with utmost care so that production traits of the existing flock are not compromised. Another possible futuristic technology is the production and introduction of a sufficient number of transgenic animals having the capacity to withstand infection (Emery et al. 2016).

Vaccination

Vaccination development using *H. contortus* larval antigen has been tried with success in the shape of reduction in FEC and lower worm burden in experimentally challenged animals (Fawzi et al. 2015). A commercial vaccine 'Barbervax' was released in Australia which has proved its efficacy in field trials (Besier et al. 2015); however, the production of its recombinant subunits has yet not been successful (Nisbet et al. 2016). Quite recently recombinant vaccine produced from *H. contortus* transthyretin domain-containing protein has been reported to induce partially protective immune responses against *H. contortus* infection (Tian et al. 2020). It is to be kept in mind that *H. contortus* has great genetic diversification (Gilleard and Redman 2016), and it may modify its antigenic structure to withstand the immune response of the host.

Targeted selective treatment

As also described in the treatment section, this system involves administering treatment to only selected animals in the flock with an anthelmintic based on periodical examination. It saves expenditures on drugs and helps to identify susceptible animals for culling (Terrill et al. 2012). The simplest technique is 'FAMACHA' in which lower eyelid of the animal is inspected to determine the degree of anaemia reflective of worm burden (Prashanth et al. 2020).

Biological control

A number of studies on biological control of *H. contortus* have been carried out. DE et al. (2016) described a larvicidal action of toxins released by the bacteria '*Bacillus thuringiensis*' against *H. contortus* which resulted in significant reduction of larvae in faecal culture after oral drench to infected lambs. Similar results were found by using spores suspension of *Bacillus circulans* (Sinott et al. 2016). Nematophagous or nematocidal action of metabolites from various fungi has also been exploited positively which has the potential to be used against *H. contortus* (de Gives and Braga 2017; Liu et al. 2020). A leguminous plant *Sericea lespedeza*, when grazed (fresh) on pastures or fed as hay (ground or pelleted), significantly reduced FEC of infected animals (Dykes et al. 2019).

Biosecurity

Strict biosecurity measures are required to prevent the introduction of resistant strains of the parasite to the flock.

Non-conventional compounds

Some non-conventional compounds with anthelmintic effects have been suggested as part of the control mechanism. Copper oxide wire particles initially used as a mineral supplement are now well-known to be effective against *H. contortus* in weaning lambs without any toxic effect (Schweizer et al. 2016; Fetene and Amante 2019). Several studies have advocated the role of condensed tannin content of various forage plants used as ‘nutraceuticals’ in controlling gastrointestinal parasites of sheep including *H. contortus* (Pathak et al. 2016; Mata-Padrino et al. 2019). A recent study in Pakistan found the extract of ‘Neem tree (*Azadirachta indica*) leaves’ highly effective against *H. contortus* under laboratory conditions (Azra et al. 2019) due to its polyphenolic flavonoids content. Another most recent study found a significant inhibition of hatchability of *H. contortus* eggs with the use of saponins extracted from forage plants of ‘*Medicago*’ species (Maestrini et al. 2020). The sheep experimentally infected with *H. contortus* and supplemented with yeast *Saccharomyces cerevisiae* for a period of 49 days showed a significant reduction of larvae and a higher number of circulating antibodies (Pinto et al. 2020).

Chemoprophylaxis

This control mechanism involves prophylactic administration of anthelmintics to all the animals during high prevalence periods of the year. This practice is more commonly adopted in tropical regions where the flocks are dewormed with regular intervals during the rainy season with a suitable product available. However, their prolonged use at a sub-lethal dose is leading to poor efficacy and development of drug resistance in the parasite (Getachew et al. 2007; Kellerová et al. 2020).

Conclusion

Haemonchosis remains a major problem in the sheep industry across the world. The organism has adapted to survive under diverse climatic conditions. Resistance has been reported against the latest available anthelmintics. Alternate compounds also have limited efficacy, and their effects on production parameters are least known. Biological control measures have their constraints. Due to diverse antigenic strains of the parasite, the recombinant production of vaccines is yet a challenge for researchers. Under these circumstances, targeted selective treatment along with culling of more susceptible animals and maintenance of good body condition score through the provision of a nutritionally balanced diet is considered the best control strategy at the herd level. Meanwhile, the scientists engaged in its related fields should carry out extensive research for the development of a potent vaccine against all strains of *H. contortus* and find a therapeutic agent which should remain effective for decades without heaving residual effects.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical review This review does not involve any human or animal testing.

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