Strategic Control and Prevalence of Fasciola Hepatica in Cajamarca, Peru. A Pilot Study

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ABSTRACT

Fasciolosis is recognized as the major problem in cattle production in the Cajamarca region of Peru. This disease entails the highest economic losses on cattle production as well as severely impacting public health. A pilot study was conducted to test a strategic integrated control program designed to reduce the prevalence of fascioliasis in cattle in this northern region of Peru. The study was conducted over a 2-year period at 21 settlements in the district of La Encañada, province of Cajamarca, and involved 1727 producers and 8000 animals. This program involved 3 fasciolicide treatments per year, strategically timed according to the epidemiological cycle of the disease. Treatments were administered to all cattle at each of the participating sites and environmental control activities aimed at irrigation ditches and paddock drainage were used. The treatment program was supplemented by a training program and a technical assistance program to educate producers. The application of the integrated liver fluke control program led to a 49% reduction of the prevalence of Fasciola hepatica, a 38% increase in cattle live weight, and a 75% increase in milk production over the 2 years of the study.

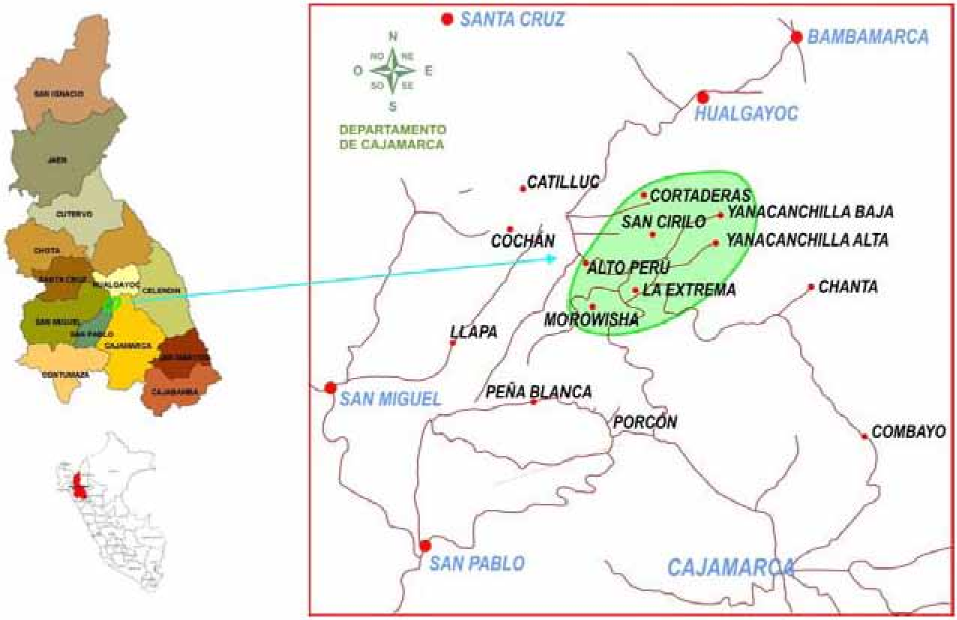
INTRODUCTION

Cajamarca is a major dairy basin in Peru whose productivity has been affected by endemic infection with *Fasciola hepatica* for many years. In one study conducted in this region, an average prevalence of 87.5% was determined (78% in cattle and 97% in sheep).[1] Producers within the region recognize fasciolosis as the most common and serious disease affecting their cattle (84%).[2] Prevalence higher than 90% in cattle has been reported in more focused studies.[3] These levels of infection are disturbing, especially when it is known that these results were obtained through coproscopic evaluations with 75% sensitivity.

Liver fluke disease is responsible for significant economic losses due to negative effects to animal health and productivity, including feed conversion, growth rate, milk production and quality, decreased reproductive capacity, reduced weaned calf weight, as well as additional losses due to liver condemnation.[4]

The first reports on the presence of *F hepatica* in Cajamarca date from the middle of the last century. From that time on, treatments have been applied first using carbon

Figure 1. *Location of the study*



tetrachloride, hexachlorethane, thiabendazole, rafoxanide, hexachlorophene, triclabendazole, nitroxinil, albendazole, closantel and other products. These drugs have been used indiscriminately without following any technical recommendations such as correct dosage, frequency, application route, etc. Treatments have been applied randomly and independently in the local herds, with no attempt to adopt an integrated parasite control program for the region.

Intensity of cattle infection by *F hepatica* in Cajamarca and its prevalence diagnosed through fecal examinations are markedly higher during February to March, August to September, and November to December. These findings show a high correlation with weather conditions, especially periods of high rainfall, which cause more humidity in paddocks and, therefore, more favorable conditions for the development and survival of the mollusk vector.[1]

Human fasciolosis has started to be recognized as a serious public health problem.[5,6] Clinical signs include fever, pain on the right side of the hypochondrium, weight loss, persistent diarrhea, and vomiting; however, many individuals are asymptomatic or only show very vague symptoms.[5]

Prevalence of this disease in humans in Cajamarca is reported to be around 16% in children, and 9% in adults, particularly among the rural human population, which is the largest demographic segment in the department of Cajamarca.[7] The danger of human infections with *F hepatica* in rural areas is highly correlated with poverty levels and small potable water distribution, which puts 2.5 million people at risk in highly endemic areas of Bolivia and Peru.[5,6] The objective of the present study was to develop strategies for the integrated control of fasciolosis, taking into consideration the epidemiological behavior of the disease in Cajamarca.

MATERIALS AND METHODS

Location

This study was carried out in 21 settlements of Cajamarca province, District of La Encañada, Department of Cajamarca – Peru, located between 3000 and 3800 meters above sea level, within the altitudinal ecological floor known as Jalca (Figure 1). The sites at each settlement were srategically selected for the study to provide a reasonable distribution of environmental conditions.

Producer Characteristics

The number of producers involved in this study was 1767 (1254 men and 513 women). People involved in this study belonged to the economic strata classified as “very poor” or “extremely poor”, according to the classification made by Foncodes.8 Families in the study area have an average of 4 children, (range 1–10). Only approximately 69% of the population has a primary education, and 45% of the population do not have access to potable water.2 The average land ownership by producer was 9 hectares. The average composition of each family farm is 8 cattle, 3 sheep, 1 horse, 11 guinea pigs, and 1 rabbit.

Ninety-five percent of the producers currently administer an average of 3 antiparasitic treatments per year (range 1–4), mainly against *F hepatica*. Of all producers who treat their cattle, only 26% treat the entire herd; 74% treat only those cattle that appear to be most infected according to external signs noticed by the producer.[2]

Before this study, calculations for antiparasitic treatment dose were made empirically as well as the selection of drug of choice. No consideration was made of the active drug or the recommended dosage or administration. Drugs used by the producers included triclabendazole, albendazole, nitroxinil, and fenbendazole.

Animals and management system

Cattle utilized in this study (N=8000) were mostly crosses between Brown Swiss and Holstein (90%), with an average live weight of 350 kg (cows in production) and an average milk production of 5.1 liters/cow/day. Cattle were maintained under uniform management and feed conditions throughout the study. The management system of these animals was extensive grazing, using mostly natural pastures. Animals without identification were earmarked to facilitate their follow up. Paddocks were irrigated by flooding, and animals drank water directly from irrigation ditches.

Sensitization and Training of Producers

At the beginning of the study, informational talks on actions to be developed and commitments needed by the producers were given at each settlement involved in the study, followed by training sessions that addressed specific topics related to fasciolosis prevention and control, such as:

- Parasites, primarily *F hepatica*, and their effects in dairy cattle
- *Fasciola hepatica* as a zoonotic disease
- Environmental control of *F hepatica*, including the correct use and administration of antiparasitic compound according to a health calendar.

The training sessions included the use of graphic and didactic manuals, addressing the most important problems caused by this parasite as well as how to prevent and control its presence on the cattle farm. A health calendar also was used, specifically focusing on controlling liver flukes. The cattle producers noted the dates they needed to meet for administration of the antiparasitic treatment, considering the technical criteria determined for Cajamarca. Follow-up visits were made to the producers’ farms to evaluate the extent of implementation of theoretical and practical knowledge imparted to them by the trainers.

Treatment Program

The drug used for treatment during the study was triclabendazole administered orally at 12 mg/kg of live weight. A total of 48,000 treatments were administered to the 8000 animals. Before treatment, body weights were estimated by a tape measure that estimates animal weight according to its thoracic perimeter This tape measure has a ± 10% margin of error. The months chosen for treatment were February, May, and August, September, or November (selected according to the date of beginning of rainfall). These months were chosen because they represent the periods of highest parasite egg laying and the highest infection periods in this region. These dates were noted in the health calendar that was distributed to each producer to allow them to schedule each year's activities. The producers also were reminded to record the economic expenses for treatments, including labor costs.

Water and Irrigation Canal Management

Recognizing that water is the most important element for the success of this parasite's biological cycle, the following actions were taken to reduce its effects:

Canal cleaning: A change in the way of cleaning the irrigation canals was introduced through this project, increasing the angle of the canal banks to approximately 130° (Figure 1), thus allowing sun rays to fall the longest time possible on the bottom and sides of the ditch reducing the shaded areas where parasite's intermediate hosts are located (snails, *Fossaria viatrix*). Due to their negative phototropism, these snails tend to hide underground during times of sunlight exposure, reducing contact with water, thus contributing to breaking the *F hepatica* biological cycle.

Water management: Cattle producers also were advised to drain lands with excessive standing water.

Follow-up: Cleaning of ditches and paddock drainage were inspected at visits to each participant's property.

Coprological Examinations

Fecal samples were collected from each animal at the time of treatment and 60 days after treatment. Samples were individually identified and sent to the lab for analysis. The prevalence of *F hepatica* was determined by microscopic evaluation of a random selection of samples from 2900 of the cattle in the study. Samples were examined by the rapid sedimentation technique modified by Lumbreras et al.[9] Between 4 and 8 grams of feces were taken from each plastic container and homogenized using a stirring stick. This homogenized sample was mixed with running water and filtered in a 50-ml conical tube. The mix was transferred to a wide-neck, glass container (200 to 300 ml), and filtered through a plastic strainer. A sufficient amount of filtered water was added to fill the container and the sample was left to settle for 30 minutes. Two-thirds of the supernatant was then decanted, and the container was filled again with the same initial volume of filtered water. The same steps were repeated 3 to 5 times with a 30-minute interval until the supernatant was clear. Finally, the last sediment was poured into a glass Petri dish. This sample was observed through a microscope (10×, 100×).

Statistical Analysis

Body weight and fluke egg counts were analyzed using SPSS 10.5. A completely randomized design was used with individual animals considered as a sample of the population. Age of the cattle was not considered in the analysis because the age of many of the cattle was unknown.

RESULTS

Coprological Examinations

The initial prevalence of *F hepatica* in the cattle was 63.2%. At the end of the study only 13.6% of the cattle tested were in-

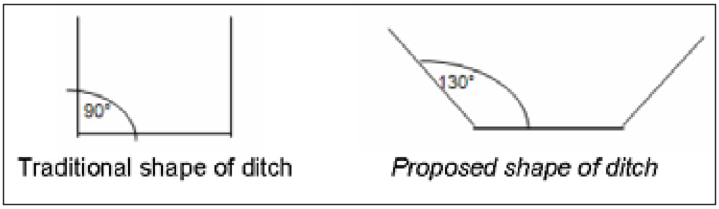
Table 1. *Results of evaluations of cattle in Cajamarca infected by Fasciola hepatica and treated strategically with triclabendazole*

	Baseline count	1st Treatment	2nd Treatment	3rd Treatment	4th Treatment	5th Treatment	6th Treatment
Positive cattle (%)	63.16[a]	43.6[b]	27.74[c]	33.78[d]	18.74[e]	8.20[f]	13.64[g]
Live weight (kg)	245.6[a]	250.43[b]	259.8[c]	270.08[d]	290.5[e]	324.34[f]	339.09[g]
Milk production (kg/mo)[1]	125,453[a]	133,320[b]	177,048[c]	200,716[d]	170,815[e]	178,264[f]	219,689[g]

Data with different superscript letters are significantly different ($p \leq 0.01$)
[1]Source: Nestlé Perú. S.A.

fected, representing a reduction of more than 49% (Table 1). A clear negative trend is shown for the presence of *F hepatica* throughout the study, with a strongly negative correlation coefficient (r = -0.92), using the regression equation: Y (% estimated prevalence) = 62.46 – 8.155 × number of treatments, with a percentage of predictability of 85%. This indicates that with each treatment the prevalence of *F hepatica* decreased at a rate of 8%. There is a statistically significant difference ($p \leq 0.01$) in the prevalence of *F hepatica* among all treatment times over the 2 years of the study.

Figure 2. *Modifications of ditches to aid in liver fluke control by creating less favorable environment for fluke vectors*



Live Weight

The live weight average of the animals in the study increased from 245.60 to 339.09 kg, an increase of 38% (Table 1). This factor exhibited a positive trend, with a strongly positive correlation coefficient (r= 0.96) regarding the number of treatments, with a regression equation: Y (estimated live weight) = 217.2 + 16.39 × number of treatments, with a predictability factor of 93%. This indicates that with each treatment, live weight of animals increased an average of 16 kg, representing 7% of the initial weight. This average included young and adult animals, with similar proportions of each age group within and among sites. Increases in mean live weights between successive treatment times were statistically significant ($p \leq 0.01$).

Milk Production

Analysis of milk production was performed on milk samples collected from all cattle in the study one month following each treatment. Monthly milk production increased from a total of 125,453 kg to 219,689 kg, an increase of 75% (Table 1). Milk production relationship with treatments is highly positive (r= 0.84) and has the following predictive equation: Y (milk production) = 11,984 + 13,084 × number of treatments, with a confidence index of 70%. It was determined that this population increased its milk production by 13,084 kg per treatment, representing an increase of 10%.

Relationship between variables under study (prevalence, live weight and milk The highest correlation found was between the prevalence of liver fluke and live weight variables, which is strongly negative (r= -0.86). Prevalence of liver fluke and milk production also had a negative relationship (r= -0.74). The relationship between milk production and live weight is positive (r= 0.73).

Treatment-associated Costs

Treatment-associated costs decreased by 30%, which included several factors including savings for a more accurate calculation for treatment through live weight measurement, reduction of fixed costs of labor since treatment was administered to all animals at the same time within the herds, rather than treating animals randomly when clinical signs were observed, and a lower price of the antiparasitic product since cost was negotiated in bulk.

DISCUSSION

Strategies used to control fasciolosis mostly depend on the extent and seasonality of disease transmission, the intermediate host's ability to survive climatic conditions, and husbandry practices of cattle farmers in their management systems.[10]

Therefore, the control of *F hepatica* is very difficult considering that the presence of this parasite is closely related to climatic conditions, which are out of the control of cattle farmers. These problems are further enhanced because the parasite control program is carried out in real conditions by small producers with limited economic resources. In general, the producers involved in this study had very low levels of education and technical knowledge. In most cases, their cattle management practices are inefficient regarding general cattle production and disease prevention and control program, with little to no access to technical support.

In spite of the aforementioned factors, results of this study provide evidence that implementing integrated parasite control programs for these dairy cattle producers through training, technical assistance, strategically timed treatments, and improved drainage techniques for ditches and fields provided substantial benefits through vastly improved fasciolosis control, showing a marked decrease in the prevalence of *F hepatica* from 63.16% to 13.64% over a 2-year period. The prevalence of *F hepatica* was reduced by 8% per treatment, using a program of 3 treatments a year.

In previous sheep studies, the prevalence of liver flukes was reduced significantly (75% to 1%) after 5 treatments were administered annually during a 3-year period.[10] In another study performed in France, the number of annual treatments were reduced from 4 to 3 in the second year of a control campaign, and the prevalence of liver fluke infections were reduced from 93% to 5%.[11]

Parasite control programs based on the use of anthelmintics that are efficacious against several stages of liver fluke are considered cost effective, especially in endemic areas. Triclabendazole, used in the present study, is highly effective against early immature, immature, and adult stages of Fasciola and is considered one of the most effective drugs available to treat fascioliasis, with efficacy ranging from 90% to 100%.[10] However, it is necessary to bear in mind that resistance has been reported in the region of Cajamarca due to its intensive and indiscriminate use.[12] This serious problem has also been reported by other investigators in different other parts of the world.[13-18] In response to this problem of benzimidazole resistance, clorsulon has recently been introduced in Cajamarca as an injectable fasciolicide for cattle, given in combination with 1% ivermectin for other parasites. In studies using the clorsulon ivermectin formulation to treat artificial and natural infections of *F hepatica* in the USA, efficacy was 97 to 99% against adult flukes.[19]

It is also important to consider that because triclabendazole is the only fasciolicide available for human use, any development of resistance to this drug may also affect human infections, leaving the human population unprotected with no drug available for treating these infections.[13]

Strategic treatments for cattle vary mainly by transmission period seasonality as determined by individual weather conditions of each area, such that recommendations vary from 1 to 5 annual treatments.[20] Three or four treatments per year administered intensively to the cattle to reduce the level of infection, and once the infection is reduced to very low levels, the number of dosages a year may be reduced.[10]

Results of the present study confirm that it is important to set schedules to 3 strategically timed treatments per year in Cajamarca, taking into consideration the months of higher rainfall and humidity when parasite egg laying is higher. A longer interval between treatments is possible during dry months where egg laying is reduced and transmission is more limited due to restrictive weather conditions. For Cajamarca, as shown previously the months to consider for administering flukicide treatments are February to March, August to September, and November to December.[21] During these months of more rainfall, more cercariae are produced by the intermediate host, and conditions are adequate for further development of metacercariae.[22,23]

The extent of reduction in milk production will depend on the animal's parasitic burden.[24] Many studies have reported milk production reductions of 8% to 14% when cattle are infected with *F hepatica*.[4,25,26] Moderate to high infection levels affected production by as much as 16% to 20%, mainly as a result of poor feed conversion, and 8% may be recovered after successful treatment.[4,24] Milk production within the scope of the study, according to the parasite control program implemented in this study, increased by 75%, with a 10% increase rate per treatment .

Moderately infected cattle experience significant reductions of live weight, described to be between 8% and 9%.[25,26] Weight gains in treated cattle in the present study are very close to the losses described by these researchers. This level of weight loss can also be observed in animals with light infections that do not show clinical signs.[26] More severe weight loss is observed in infected animals maintained on a poor diet.

Reduced weight gain of liver fluke-infected animals is directly connected to feed efficiency and depression of appetite. Appetite depression might be related to damage in the liver parenchyma at the time of immature liver fluke migration, which increases glutamate dehydrogenase and aspartate aminotransferase.[27] Live weight of animals in the present study was increased through strategic treatments by 38%, a 7% increase per treatment. Previous studies have shown that when treating with fasciolicides a weight gain increase of between 8% and 18% can be recorded in cattle.[28,29]

Liver fluke disease also causes chronic blood loss, often resulting in a normochromic normocytic anemia. It is known that liver flukes can produce blood losses between 0.2 and 0.5 ml per day associated with hypoglycemia.[30] Significant blood losses with consequent loss of metabolizable energy are associated with the inability to retain nitrogen due to increased urinary excretion and diminished intestinal absorption, which will contribute to decreased weight gain.[31,31] Structuring integrated parasite control programs to reduce the field population and activity of the intermediate host, in addition to the control of the infections in cattle through successful anthelmintic treatments, maximizes the result of intervention in this disease as previously reported by Asrat and co-workers.[32] Our results also confirm that cleaning ditches and draining paddocks with greater humidity limit survival of pre-parasitic stages of the parasite and their vectors in pastures.[33]

Positive effects found in this study resultant of the implementation of integrated parasite control programs show the need and potential benefits of putting regional programs into place, involving massive bovine populations with the support of cattle producers, dairy industry and the region's political authorities.

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