Evaluation of antiparasitic therapy directly administered for the control of canine echinococcosis in an endemic area of hydatidosis.

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Abstract

Background: Echinococcosis remains endemic despite attempts to reduce the prevalence of this disease. The objective of the study was to evaluate the results of an intervention program based on antiparasitic therapy directly administered for the control of canine Echinococcosis in an endemic area of hydatidosis.

Methods: Fecal samples of the dogs were analyzed by coproantigen using the immunoenzymatic technique for the diagnosis of echinococcosis before and after the direct and observed administration of praziquantel 5mg by kg orally in three doses every 30 days each cycle was 2 times at year for two consecutive years.

Results: Of a total of 252 dogs, 119 (47%) presented positive results to Echinococcus before the intervention. The adverse effects presented with the administration of praziquantel were: 13 (5.2%) dogs had vomiting, 6 (2.4%) dogs had diarrhea, 5 (2%) had drowsiness or lethargy, the most severe complication was death of 02 (0.8%) dogs after 7 days of the first dose. 229 dogs completed the 4 cycles of the administration of praziquantel. 03 (1.3%) dogs presented positive coproantigene after direct antiparasitic administration.

Conclusions: Antiparasitic chemotherapy administered directly to the dogs periodically managed to reduce the prevalence of canine echinococcosis.

Background

Echinococcus granulosus is the parasitic agent that causes human hydatidosis, it is found in the small intestine of its definitive host, can, which can eliminate up to one million eggs transported by feces and contaminate grasslands, when cattle mainly sheep the sheep feed on these grasslands automatically become infected, the cyst enters orally and becomes disengaged in the stomach releasing the oncosphere which migrates to the mainly viscera tissues where they develop cystically and the can is infected again when ingested Raw viscera of infected sheep, the human accidentally becomes infected by ingesting the cysts released by sick dogs [1–3]. Echinococcosis is common among people living in poor sanitary conditions in developing countries.

In Peru, the practice of sacrificing adult sheep for domestic consumption and allowing dogs to feed on infected viscera generates the ideal conditions for the persistence of this disease [4–6]. In some rural areas the prevalence of canine infection can reach up to 50% [7].

Some programs that tried to control canine echinococcosis with the massive administration of praziquantel have managed to reduce the prevalence of hydatidosis from 22.1 per 100,000 to 6.2 per 100,000, with persistence of high transmission rates in some focal areas [8, 9], while other chemotherapy studies has obtained little encouraging results, because it has not been possible to raise awareness of the need for dog prophylaxis and the lack of permanent control programs [10–13]

The objective of the study was to evaluate the results of an intervention program based on antiparasitic therapy directly administered for the control of canine Echinococcosis in an endemic area of hydatidosis.

Methods

Population

Two communities were visited in the period May 2015 to December 2017: Usibamba and Chaquicocha, belonging to the San José de Quero district, province of Concepción, located in central Peru at 4000 meters above sea level with temperatures ranging from -4°C to 16°C . These two communities have 2193 inhabitants and are endemic in human cystic hydatidosis.

The sample size was estimated at 28% prevalence of canes infested with *E. granulosus* in endemic areas [14], 95% as a confidence interval, power of 80% and adding 20% for probable losses. The sample tested was 260 stool samples, using the proportions method with the statistical program Stata v. 13.1 (Stata Corporation, Texas, USA).

Procedures:

Before the intervention, households are housed in a stratified and random manner based on the proportion of inhabitants for each community and for each street, supported by the demographic survey of the municipality of San José de Quero, on satellite images and on the map Geographical All the dogs present in each house were sampled, if the occupants of a house were absent, refused to participate in the study or had no dog, we selected a neighboring house and asked about the presence or absence of dogs. The process was continued until the sample size was completed.

Prior informed consent to the owners, the information was collected by means of a structured and validated form, as well as the measures of prevention of hydatidosis, a leaflet containing information on the importance of canine deworming was given and recently obtained samples of Fresh feces from the sticks, were collected maintaining the biosecurity measures, the samples were deposited in a bottle with 10% formalin and kept refrigerated at 4°C , then transported to the microbiology laboratory of the Institute of Tropical Medicine of the University National Mayor of San Marcos for microscopic identification. Samples of fresh feces were also collected from the fields and from the main square of the annexes in order to compare the results microbiologically.

For the microscopic examination of faecal samples preserved in 10% formalin, select the direct method which consists in dissolving the sample well, keeping it at rest for 5 minutes and with the help of a Pasteur pipette, a drop was taken from the bottom, then, place it on a slide, cover it with a slide cover and observe under a microscope at 10 and 40 magnification, this procedure will avoid identifying the presence of other parasites.

For the diagnosis of echinococcosis, analyze stool samples from the rods by using coproantigen analysis, using the commercial immunoenzymatic technique (ELISA) for *E. granulosus* (Cestodas

Zoonoses Research Group, University of Salford). The plates were read at 490 nm + 3 standard deviations with a kinetic microplate reader. Two positive and two negative controls are used per plate [15].

Intervention

Praziquantel 5 mg / kg was orally administered to the canes in three doses every 30 days each cycle was twice a year for two consecutive years; for the street canes the antiparasitic was combined with bread and chicken bites, a photograph was selected in each deworming process for identification. The administration of the medication went directly to the dog and under supervision, the medication was not delivered to the owner or to the health facility.

At each home visit it was reformed with the talks on prevention of hydatidosis and delivery of informative material, likewise a deworming card was delivered which was delivered to the owner and it was every time he can receive the antiparasitic treatment, likewise information is obtained from the adverse effects that the dog presented. When the owner is not found, he would visit again the next day until he found the owner and proceeded to despair.

After two years, in December 2017, we collected the stool samples again in the same way as before the intervention and took the microbiology laboratory to identify the parasite.

Results

Of a total of 252 dogs analyzed before administering the antiparasitic, 119 (47%) dogs presented positive results to *Echinococcus* in the stool sample by coproantigen study, the average age of the dogs was 33 months, the male sex it was the most frequent representing 72% of the dogs; the number of dogs chosen was related to the proportion of inhabitants in each community; in general, the average number of dogs per house was 2.4; being higher in infected dogs (2.5) compared to uninfected dogs whose average of dogs per house was 2.2 ($p = 0.0025$).

The dogs coming from the street or homeless were 21 (8.3%), of which 17 (80.9%) dogs presented positive results to the coproantigen study ($p = 0.001$). Overall, 73 dogs (29%) had ever received antiparasitic treatment in the last year, of which 27 (36.9%) dogs had a positive result for infection with *Echinococcus*; It is characteristic in these rural areas that dogs share their home with sheep raising, it was found that 79 (31%) dogs live together with sheep.

The treatment administered was independent of the result of the coproantigen test obtained, all dogs received 02 cycles of antiparasitic treatment with praziquantel per year for two consecutive years, each cycle was composed of 03 doses with a difference of 30 days between each dose: There were reported complications : 13 (5.2%) dogs had vomiting after receiving the antiparasitic, 6 (2.4%) dogs had diarrhea, 5 (2%) had drowsiness or lethargy, however, the most severe complication was the death of 02 (0.8%) dogs after 7 days of the first dose, these dogs came from the same house operated.

During the follow-up, some dogs left the study because they died (2 dogs), the owners moved to another community (4 dogs), the owners refused to continue the study (3 dogs), the owner or dog was not found for more than two months (6 dogs) and some street dogs ceased to be seen (8 dogs).

After two years, 229 dogs completed the 4 cycles of the administration of praziquantel, subsequently they were evaluated by studying stool samples to verify the presence of Echinococcus infection, the procedure was performed in the same way as before program intervention. Of the 229 samples analyzed, 03 (1.3%) dogs presented positive coproantigene after direct antiparasitic intervention, these 03 infected dogs were street dogs, 02 came from Usibamba and one from Chaquicocha.

Table 1 General characteristics of dogs before the intervention of the program.

Characteristic	n = 252	Echinococcus positive = 119 (47%)	Echinococcus negative =133 (53%)	p
Edad promedio*	33.4	33.8	33.1	0.87
Sex: male	183 (72.6%)	86 (46.9%)	97 (53.1%)	0.88
Provenance				0.011
Usibamba	141 (55.9%)	77(54.6%)	64 (45.4%)	
Chaquicocha	111 (44.1%)	42 (37.8%)	69 (62.2%)	
Average dogs per house	2.4	2.5	2.2	0.025
Street dog	21 (8.3%)	17 (80.9%)	4(19.1%)	0.001
Previously dewormed **	73 (28.9%)	27 (36.9%)	46 (63.1%)	0.09
Share sheep breeding.	79 (31.34%)	42(53.2%)	37(46.8%)	0.011

* Age in months. ** Received at least one dose of antiparasitic treatment in the last month.

Table 2. Canes infected by Echinococcus granulosus: comparison before and after the intervention.

	Infected dogs before the intervention = 119	Infected dogs After the intervention = 3
Echinococcus positive	119 (47.2%)	3 (1.2%)
Provenance		
Usibamba	77 (64.7%)	2 (66.6%)
Chaquicocha	4 (3.4%)	1 (33.4%)
Street dog	17 (14.3%)	3 (100%)

Discussion

Cystic hydatidosis is still considered as an unattended zoonotic disease with great economic impact in rural areas (16) and in communities with cold weather that favors the viability of Echinococcus eggs in the environment for several months [17–18].

In some countries it is considered a reemerging disease, because it is very difficult to control or eliminate, mainly in more remote areas and difficult to access. Massive treatment with praziquantel has proven effective in some countries and in others not so much due to the different schemes they use, non-compliance with doses, non-supervision of medication administration, non-permanent and non-periodic programs. Many of these programs are costly in financial terms, but beneficial in terms of disease expenses, but poorly assessed in relation to impact [19–21].

Direct administration ensured the correct dose and frequency or administer a second dose in case of vomiting to ensure compliance with antiparasitic treatment, because our objective was to evaluate the results of an intervention program based on antiparasitic therapy directly administered for control of canine Echinococcosis. The initial prevalence of 47% was evidenced and after the intervention, two years later, the prevalence was reduced to 1.3% in the two rural communities.

Praziquantel is effective in the treatment of echinococcosis, reduces the burden of infection in dogs and indirectly in sheep, but does not protect against future reinfections if the treatment is not continuous and cyclic, so it can explain the poor decrease in prevalence in places where short deworming schemes are prophylactic and discontinuous.

The use of praziquantel as preventive chemotherapy, that is to say to administer periodic treatment in populations at risk, is approved by the World Health Organization to reduce the disease burden of some pathology such as schistosomiasis, whose objective is to prevent infected hosts from developing the chronic disease and cure mild symptoms [21–24]. Although reinfection can occur after treatment, it is still considered the main effective measure in the fight against echinococcosis.

Praziquantel is the treatment of choice against Echinococcus, it seems to be a safe medication with good tolerance levels, safety, easy to administer but with little effect on young stages of parasites [25–26], with some adverse effects evidenced in the study as vomiting, diarrhea and lethargy that were self-limited; However, the efficacy of praziquantel depends on the host's immune response, and the severity of side effects may increase in hyperinfested dogs after administration of the antiparasitic causing a severe inflammatory response [27], this may explain the death of two dogs that They received praziquantel at the first dose.

Attempts to eliminate canine echinococcosis take years because effective control has not been achieved, however in some countries they have been reduced to undetectable levels thanks to the sustained effort of programs based on continuous deworming.

Some limitations found in the study is that the positive coproantigen test may be higher than reported because this test does not usually detect low parasite loads in the stool [28], however to compare the response to the antiparasitic was used the same test before and after administration of praziquantel.

The advantages of this intervention study is that infection surveillance in dogs is non-invasive through the stool samples collected from the ground (29). This control program was only applied in two

communities and we do not have data to evaluate the gradual response in time after the two years of intervention, because the study ended, the application of the program being necessary on longer and more sustained time scales to evaluate Response and reinfection rates.

Conclusions

Antiparasitic chemotherapy administered directly to the dogs periodically and sustainably managed to reduce the prevalence of canine echinococcosis and is considered the main effective measure.

Abbreviations

Kg: kilogram; °C: centigrade degree; E. granulosus: Echinococcus granulosus; %: percentage; WHO: World Health Organization

Declarations

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Authors' contributions

RM performed the study design and data analyses. JC, LC performed experimental assays and data analysis. LC, EC, YC, MN performed data collection and analysis; AH performed in tests; LB performed clinical diagnostics; CI performed data collection and manuscript preparation; CR performed study design, data analysis and manuscript preparation. All authors read and approved the final manuscript.

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Availability of data and materials

The dataset supporting the findings of this article is available from the corresponding author upon request.

Ethics approval and consent to participate

The study protocol was approved by The Local Ethic Medical Committee (CEI No. 21-2015/OCDI-HRDCQ-DAC). Written informed consents were obtained from the participants and owners of the dogs.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

Graph N ° 1 Percentage of dogs infested by *Echinococcus granulosus* before and after the intervention, San José de Quero district, Concepción.