Chloroquine Phosphate in Treatment of Theileriasis in Exotic and Crossbred Cattle; A Clinico-pharmacological Approach

J. V. Anjaria, V. M. Jhala and Shersingh

Dept. of Pharmacology and Dept. of Bacteriology, Gujarat College of Veterinary Science and Animal Husbandry, GAU, Anand Campus, Anand-388 001

ABSTRACT

One hundred and nine clinical cases of Theileriasis were treated and observed. 178 treatments were given. The clinical diagnostic picture has been discussed. Six different treatments have been tried. It is observed that chloroquine phosphate in the doses of 1200, 2400 or 2800 mg. b. e. I/m with 3 g quinine dihydrochloride I/v or I/m once daily where needed, for four days gave encouraging results. The coupled immunopharmacological therapy was also tried which needed further observations. With these treatments the mortality observed was 2 per cent. (*Received on Oct. 22, 1975*).

INTRODUCTION

GUJARAT has imported the exotic breed for the cross breeding programme; and perhaps with this, it has also imported the problem of theileriasis. The stray cases were recovered in past but under the present situation the disease is rampant in Gujarat.

A plethora of literature is available on the treatment of theileriasis. Barnet (1968) has reported that theileriasis is infectious in man and animals and concluded that there is no satisfactory treatment. Gautam (1975) has put up good amount of findings before us. Rao (1973) has reported a variety of treatments like (A) Acaprin, Acriflavin and Terramycin in eight cases; (B) Acromycin and Nivaquin in four cases and (C) Berenil and Acromycin in 55 cases with inconsistant results. Mathur (1972) treated a few cases with Camoquin oral as well as intramuscular. Dhar and Gautam (1972) has reported regarding the use of Berenil and Terramycin with inconsistant results. In some clinical experiments Nivaquin was also used and did not give encouraging results. In later trials Pamaquin (oil suspension) was also used and similar results were obtained. Several immunological approaches have been tried by various workers.

The present work aims at the clinical and diagnostic approach to the theileriasis, with a view to be, of immediate help to the cattle owners to save the exotic animal in the field. Whatever the laboratory findings may be what is needed, is to spot out the subclinical cases and start the treatment without involving in any laboratory dispute. This may perhaps serve as a better solution to cater to immediate need for saving the costly animal.

METHODS

Diagnosis: The life history of theileriasis and its infectivity are wellknown. Four to five pathogenic species are generally recognised in cattle. The clinical symptomatic picture is very conspicuous to a trained eye.

The incubation period is 10 to 15 days. Presence of ticks may or may not be seen on the body of the animal. The body temp. increases and ranges from 105° F to 107° F. There is no noticeable symptom during the first few febrile days except there is drop in production. Apetite is lost, muzzle is dry, lacrimation and nasal discharge are commonly seen—superficial lymph nodes are enlarged and can be felt on palpation. Breathing is accelerated, difficult and accompanied with coughing, diarrhoea is usually present often tinged with blood and mucus. Signs of anaemia become evident and the animal starts wasting. As the disease progresses there is marked emaciation, lymph nodes often regress in size, breathing is laboured, asphyxiation sets in with froth in the nostrils. The course of the disease is fatal from 4th to 14th febrile days. The mortality rate is 94% in adult exotic breeds and in non endamic areas (British Vet. Asso. 1962).

Drugs: The use of Nivaquin has opened up the possibility of usefulness of antimalarial drugs. Chemically these drugs have a different chemical structure. The present work aims at the use of such drugs keeping in view such a structural relationship.

Some of the available antimalarials are:

1. Quinoline derivatives:
   (a) Quinine (alkaloid from Cinchona; does not contain amino group but has Quinulidine group).
   (b) 8—aminoquinoline group e.g. Pamaquine, Primaquine, Pentaquin etc. =8 (4 dimethyl-amino 1 methyl butyl amino) 6-methoxy-quinoline.
   (c) 4-aminoquinoline group:—
      i. Chloroquine phosphate (Resochin, Avloclor)=7 chloro-4(4 dimethyl amino 1 butyl amino) quinoline diphosphate.
      ii. Nivaquine=7 chloro-4 (4-dimethyl 1 methyl butyl amino) quinoline sulphate.
      iii. Camoquine (Amodiaquine hydrochloride)=4 (3 diethyl amino methyl 4 hydroxy anilino) 7 chloroquinoline.
      iv. Hydroxy quinoline sulphate (Plaquenil)=7 chloro (4-N ethyl N P hydroxyethyl amino–1 methyl butyl amino) quinoline.
2. Acridine derivatives e.g. Mepacrine. Quinacrine (Atabrine) etc.
3. Biguanide derivatives. e.g. Chlorguanide hydrochloride (Palludrine) etc.
4. Diamino pyrimidine derivatives. e.g. Pyrimethamine (Daraprim).
5. Sulphones and some sulphonamides like sulphadiazine. These are out dated.

Out of these antimalarials they are therapeutically divided as;

i. Drugs acting on exoerythrocytic forms, used as causal prophylactics are; Primaquine, Pamaquine etc.

ii. Drugs acting on the asexual forms; Scizonticidal are; Chloroquine, Amodiaquine, Mepacrine, Quinine, Pyrimethanine etc.

iii. Drugs destroying gametocytes are; Primaquine, Pamaquine, Pentaquine, etc.

From the above explanation it was thought that as Nivaquine (4-amino quinoline-sulphate salt) has shown some inconsistant results, it would be worthwhile to screen the diphosphate salt, keeping in view the ionisation and protein binding of the drugs. Moreover, the available literature does not show any reference on the use of chloroquine phosphate. To a field worker all such drugs may seem alike but they are different chemically to a good extent and hence the trials on the chloroquine phosphate and immunopharmacological attempts were undertaken.

Observations: In the present study, 109 cases with 178 treatments of theileriasis were studied. The observations on the occurrence in different breeds and groups are presented in Table 1.

TABLE—1

Incidence of Theileriasis according to the breed and the location in Gujarat during June to September 1975.

Region	*Breed*					
	H.F. Cross	*Pure Jersey*	*Jersey cross*	*Red Danish cross*	*Kankrej*	*Total number of animals*
Baroda—1	11×2=22	—	1×3=3	—	2×2=4	18
Baroda—2	1×1=1	3×2=6	—	—	—	—
Anand area / Mogri—Dakor	5×1=5	—	1×1=1	—	—	6
Ahmedabad—1	19×3=57	2×1=2	—	1×3=3	1×1=1	—
Ahmedabad—2	3×1=3	—	—	—	—	26
Mehsana—1	9×2=18	1×2=2	—	1×2=2	—	—
Mehsana—2	24×1=24	1×1=1	8×1=8	3×1=3	12×1=12	59
Total animals treated	72	7	10	5	15	109
Total treatments	130	11	12	8	17	178
Mortality after treatment	—	1	1	—	—	2=1.8% i.e. 2%

Note:—× Multiplications show number of repeat treatments due to repeat attacks.

RESULTS AND DISCUSSION

Treatment-1 : 27 animals were treated in this group. Chloroquine phosphate (CLQ) I/m was used varying from 40 mg base equivalent to 200 mg base equivalent (mg b.e.) dose. The blood smears of all the animlas were positive. The dose range of 40 to 100 mg b.e. did not give consistant results eventhough the repeat doses were tried at 24 hourly interval. The clinical picture did not alter.

It was observed that 200 mg b.e. dose given to 9 animals brought down the clinical picture to normal in 5-7 days. 10 animals had responded in 3 days treatment also. Total treatment required about 1000 to 1200 mg b. e. of the drug.

Out of this group because of the unhygienic conditions and non control of ticks, about 10 animals got the reattack after one month. They were treated with 2000 mg b.e./ 24 hrs for 3 days, and were cured.

The supportive treatments used in this group was as follows:–

Inj. B–Complex 5 ml, Inj. Liver Ext. 5 ml for 6 days. Carminative mixtures were necessary. Some animals were given 0.17 g Iron tablets; 50 to 100, tab/orally/b.d., daily for 10 days.

Treatment-2: 20 animals were treated in this group. CLQ 800 mg b.e./ 24hrs/for 3 days was used with supportive treatment as in group-1. After 3 days no improvement was seen. As such the dose of CLQ was altered after a gap of 2 days and CLQ 2400 mg b.e./24hrs/ after 3rd day was given. 15 animals recovered on the 4th day and the blood picture and the clinical picture was clear. 5 animals did not respond to treatment and showed dullness. For the remaining 5 problematic animals following treatment was given.

CLQ 2800 mg b.e. I/m+4 g of quinine dihydrochloride I/v diluted in 30 ml distilled water. This was given for one day. I/v quinine gave a severe reaction which subsided within 30 minutes. These animals were again given the similar treatment after 5 days. In this treatment quinine was used at very slow speed of injection and the reaction was not seen. One problematic animal was also given quinine hydrochloride powder 15 g orally/once/daily for 4 days. All the five animals recovered.

Treatment-3: After the experience of treatment 1 and 2, 13 animals with clinical symptoms and blood smear positive with, temp. ranging between 105° f to 106° f were treated directly with the higher dose.

CLQ 2800 mg b.e./day 3 g quinine dihydrochloride (diluted) I/v once daily for four days was given. The infection was cleared out on 3rd day and all the animals were normal.

Treatment-4: 10 animals with temp. ranging between 105° f to 107° f were taken up. 9 animals were treated and one was kept as control (untreated, for want of drug). In this group Nivaquine 40 ml+Terramycin 40 ml was given for 4 days. The animals did not respond. After a gap of two days, these animals were divided into 2 groups. *Group 4* A: Having 9 animals, was given CLQ 1200 mg b.e.+Acromycin 2000 mg+15 ml Belamyl for 4 days. Animals did not respond. Then all the animals were given

the following treatment as in 4 B. None of the treated animlas then died. *Group 4 B:* 24 cows in milk were given, CLQ 2800 mg b.e.+3 g quinine dihydrochloride I/m for 4 days. All the animals were negative blood smear picture and normal by 5th day.

Treatment-5 : 10 milking cows in the light infection detected earlier were treated with CLQ 1200 mg b.e.+3g quinine-dihydrochloride I/m/once/daily for 5 days, and responded nicely to the treatment and all animals became normal.

Treatment-6: With CLQ 1200 mg b.e.+3 g quinine dihydrochloride I/m daily for 4 days and immunotherapy was tried. 50 ml blood was collected from a blood smear positive case and was mixed with 50 ml saline and thoroughly shaken, till haemolysed and erythrocytic forms were thrown in saline. 20 ml of this suspension was injected subcutaneously in animals with clinical signs and in febrile condition. 5 cases were treated and encouraging results were seen. This seems to be an easy field work immunopharmacological approach, which need further trails and observations.

Out of 109 animlas treated only two animals have died. The mortality was upto 2% after this treatment.

Observation on Milch Cows: In milch cows the production drops for two days when CLQ 2800 mg b.e. is given. With CLQ 1200 mg b.e. drop in production is not noticed. Another peculiar symptom noted was a transient oedematous mastitis after a week or 10 days of the treatment for 1 or 2 days which yielded to local therapy. This was partly an oedematous swelling of the mammary gland and glycerine magsulph paste and iodex relieved the symptoms. No other big damage was noticed.

Observation on Pregnant Cows: CLQ 2800 mg b.e. with 3 g quinine was given in some pregnant cows. Two pregnant animals aborted out of which in one cow a still born calf was recovered. In pregnant animals therefore a low does long term therapy may be beneficial or change to high dose as the stretagy demands.

Observation on Calf Treatment: CLQ 600 mg b.e. and 1200 mg b.e. along with two doses with 1.5 g quinine dihydrochloride gave satisfactory results. Plain CLQ treatment in earlier cases was also responsive.

Supportive Therapy: In all cases of theileriasis the supportive therapy equally plays an important role. Inj. whole liver extract: Glucose saline, oral iron therapy, inj. Imferon, oral dosing of phosphomin with iron and carminatives whenever necessary have helped the treatment. Haematinics and Vitamin B Complex play a considerable role in each treatment.

ACKNOWLEDGEMENTS

The authors wish to express their sincere thanks to all the cattle owners who helped for this study for the supply and purchase of drugs on demand, which could make this study possible.

REFERENCES

Barnet, S. F. 1968. Theileriasis. Infectious disease of man and animals by Weinmann and M. Ristic **2** : 269. Through Gautam, O. P. 1975 No. 3.

Dhar, S. and O. P. Gautam, 1972. Paper read at 14th conference of research workers in animal diseases at Mathura Nov., 25-26, 1972.

Gautam, O. P. 1975. Souvenir papers at summer institute on the emerging diseases of exotic and crossbred amimals. HAU, Hissar. July, 1975.

Mathur, S. C. 1972. Theileriasis in Jersey, bulls. *Indian Vet. J.* **48** : 962.

Rao, S. G. 1973. Treatment of Theileriaisins exotic breed and crossbred bovines *Indian Vet. J.* **50** : 1-104.

British Vet. Assos. 1962. Hand book on tropical diseases. Mansfield Street, London, p. 156.