International Journal of Pharmacology

ISSN 1811-7775

science alert

ansinet
Asian Network for Scientific Information

International Journal of Pharmacology 2 (5): 530-535, 2006
ISSN 1811-7775
© 2006 Asian Network for Scientific Information

Blood Biochemical Changes in Donkeys Naturally Infected with *Onchocerca raillieti*: the Effect of Medication with Doramectin

[1,2]H.I. Seri, [2]Husna M. ElBashir, [2]Y.H.A. Elmansoury and [2]M.M. Salih
[1]Faculty of Veterinary Science, University of Nyala, Sudan
[2]Central Veterinary Research Laboratory, Soba, Sudan

Abstract: The aim of this study is to investigate the effect of doramectin Injectable formulation on some blood biochemical constituents of the donkeys. Selected blood biochemical constituents were examined in 2 groups of donkeys naturally infected with *Onchocerca raillieti* before and after treatment with doramectin Injectable formulation. The animals received doramectin injection with the manufacturer recommended dose of 200 μg kg^{-1} body weight either subcutaneously or intramuscularly in the mid ventral part of the neck. Blood samples were collected before injection of the drug and every 4 days for 28 days after treatment. The fluctuation in the blood constituents reported in this study was within the normal values reported by other researchers. The animals did not show any side or adverse effects toward the drug under investigation.

Key words: Doramectin, donkeys, onchocerciasis, blood chemistry

INTRODUCTION

In equines, the early studies indicated that avermectins have potent anthelmintic properties including a profound effect on microfilaria (Herd and Donham, 1983; French *et al*., 1988; Mogg *et al*., 1990; Mancebo *et al*., 1997; Abdel-Wahab *et al*., 2002; ElBashir and Seri, 2004). Sudan possesses about 6,350,000 donkeys and 650000 horses (SBAR, 2000). A considerable prevalence of *Onchocerca* sp. among equidae in Sudan was very recently reported by Fadia, 2000. The use of macrocyclic lactones such as ivermectin and moxidectin open new hope for controlling of filarial infection through their potent microfilaricidal and larvicidal activities. This was especially important in human infection with *O. volvulus*.

The purpose of the experiment was to evaluate the safety of doramectin when administered via the parenteral route and to objectively record the adverse reactions to this anti-parasitic agent should they occur.

MATERIALS AND METHODS

This study was conducted during the period January to February 2004 at the premises of the department of radioisotopes, Central Veterinary Research Laboratory (CVRL), Soba, Sudan.

Animals: Twelve adult donkeys (male and female), aging 3-10 years, naturally acquired microfilariae of *O. raillieti*. Infestation was confirmed before the beginning of this study by skin snips collected from wither. The animals were housed and kept on water from tap and straw *ad libitum*.

Experimental design: Donkeys were allocated to 2 equal sized treatment groups. They were weighed and treated as follows: Doramectin-treated group1 (DRMT1) received a single subcutaneous injection of 200 μg kg^{-1} Doramectin (Dectomax® injection, Pfizer France), Doramectin-treated group 2 (DRMT2) received a single intramuscular injection of 200 μg kg^{-1} Doramectin (Dectomax® injection, Pfizer France). Injections were administered in the lateral mid-line of the neck.

Blood sample collection: Blood samples were taken from each of the 12 donkeys just before treatment and at four days interval for 28 days post treatment. All samples were collected between 09.30 and 10.30 h on the collection dates and placed in plain evacuated vacutainer tubes. Serum samples were stored at 20°C until analyses were done on a single batch.

Analytical methods: Sodium (Na) and potassium (K) concentrations of the serum were analyzed by standard flame photometry. Serum total protein, albumin and urea were analyzed using standard methods with commercial kits (Randox laboratories Ltd., United Kingdom) in spectrophotometer analyzer (Jenway 6105 U.V./vis.

Corresponding Author: Hisham Ismail Seri, Department of Clinical studies, Faculty of Veterinary Science, University of Nyala, Sudan. P. O. Box: 155 Nyala, South Darfur State, Sudan
Tel: +249915187027 Fax: +249711833123

Spectrophotometer, U. K.). Total globulins concentration was obtained by subtracting the concentration of albumin from that of total protein.

Clinical observations: All the animals were monitored continuously for 4 h post treatment and again the following day for any adverse clinical signs or untoward reactions to the administration of the doramectin via the intramuscular or subcutaneous route.

Statistical analysis: Post treatment changes in blood constituents were evaluated by paired samples t-test with repeated measures and comparisons between means were analyzed using SPSS 11.5 programme for Windows.

RESULTS

Clinical observations: None of the donkeys in this experiment exhibited signs of toxicity, nor were any tissue reactions noted at the site of injection. Suppression of appetite did not occur and the faeces remained normal throughout the study.

Laboratory analysis: Table 1-6 show the changes in total serum protein, albumin, total globulins, urea, sodium and potassium following administration of Doramectin in both treatment groups.

Table 1: Changes in total protein concentration (g L^{-1}) following administration of doramectin injection at therapeutic level in donkeys naturally infected with *Onchocerca raillieti*

	DRMT 1	DRMT 2
Days	Mean±SEM	
0	66.7±2.3[a]	70.0±2.6
4	66.6±2.6	70.8±2.8
8	65.2±2.4	70.5±2.0
12	69.5±2.5	69.5±2.2
16	72.5±1.5[b]	68.0±2.8
20	70.7±1.6[b]	71.6±3.2
24	72.9±1.8[b]	75.2±1.2
28	70.3±2.8	72.4±1.4

*Means on the same column having different asterisk with day zero are significantly ($p<0.05$) different

Table 2: Changes in albumin concentration (g L^{-1}) following administration of doramectin injection in donkeys naturally infected with *Onchocerca raillieti*

	DRMT 1	DRMT 2
Days	Mean±SEM	
0	25.0±1.7[a]	24.6±2.0
4	28.1±2.3	28.4±2.6
8	25.6±1.5	27.9±2.5
12	26.1±0.6	29.6±3.3
16	25.6±1.5	24.4±2.5
20	26.0±1.6	26.1±2.1
24	29.5±1.8[b]	28.8±1.4
28	27.3±1.3	25.7±2.8

*Means on the same column having different asterisk with day zero are significantly ($p<0.05$) different

Table 3: Changes in total globulins concentration (g L^{-1}) following administration of doramectin injection in donkeys naturally infected with *Onchocerca raillieti*

	DRMT 1	DRMT 2
Days	Mean±SEM	
0	41.6±2.4	45.4±3.4
4	38.6±1.3	42.4±4.4
8	39.5±1.9	42.6±0.6
12	43.5±2.8	39.9±1.4
16	46.9±1.3	43.6±3.3
20	44.7±1.4	45.4±2.9
24	43.4±2.1	46.4±1.9
28	43.0 ±2.6	46.7±3.4

Table 4: Changes in urea concentration (µmol L^{-1}) following administration of doramectin injection in donkeys naturally infected with *Onchocerca raillieti*

	DRMT 1	DRMT 2
Days	Mean±SEM	
0	2.51±0.38[a]	2.69±0.54[a]
4	1.71±0.31	2.13±0.34
8	2.05±0.32	2.80±0.84
12	2.80±0.34	2.62±0.68
16	2.96±0.52	3.00±0.42
20	4.97±0.51[b]	4.29±0.32
24	5.26±0.17[b]	4.77±0.43[b]
28	2.54±0.40	2.84±0.33

*Means on the same column having different asterisk with day zero are significantly ($p<0.05$) different

Table 5: Changes in sodium (mmol L^{-1}) concentration following administration of doramectin injection in donkeys naturally infected with *Onchocerca raillieti*

	DRMT 1	DRMT 2
Days	Mean±SEM	
0	125.26±1.69[a]	125.60±1.91
4	124.29±2.22	129.80±1.56
8	125.86±1.81	128.40±2.09
12	125.86±2.25	129.00±2.21
16	120.00± 1.90[b]	122.00±1.23
20	122.43±2.11	126.40±2.18
24	128.00±2.25	125.40±0.81
28	126.43±1.46	126.20±0.97

*Means on the same column having different asterisk with day zero are significantly ($p<0.05$) different

Table 6: Changes in potassium (mmol L^{-1}) concentration following administration of doramectin injection in donkeys naturally infected with *Onchocerca raillieti*

	DRMT 1	DRMT 2
Days	Mean±SEM	
0	3.47±0.10[a]	3.68±0.15[a]
4	4.11±0.22[b]	4.28±0.21
8	4.67±0.26[b]	4.50±0.21[b]
12	4.26±0.23[b]	4.26±0.16[b]
16	4.56±0.17[b]	4.50±0.31[b]
20	4.40±0.29[b]	4.36±0.21[b]
24	4.59±0.27[b]	4.02±0.09
28	4.60±0.18[b]	4.32±0.08[b]

*Means on the same column having different asterisk with day zero are significantly ($p<0.05$) different

In treatment group 1 (DRMT1) there is significant ($p<0.05$) increase in total serum protein, urea level and potassium concentration when compared with pretreatment level. Sodium concentration showed significant ($p<0.05$) reduction, while serum albumin showed fluctuation in level through the four weeks of the experiment.

In treatment group 2 (DRMT 2) there is non significant ($p>0.05$) increase in total serum protein concentration, while urea and potassium concentration showed significant increase ($p<0.05$). Albumin and sodium concentration showed fluctuation in level during the course time of the treatment.

In both treatment groups we could observe that there is parallel increase in total protein, urea and potassium level following the administration of the drug.

DISCUSSION

Under the conditions of this study, doramectin appears to be safe and free from producing untoward effects when administered parenterally at 200 μg kg^{-1} of body weight. The total absence of adverse clinical signs and the lack of change beyond the normal clinical values in the biochemical values post dosing indicate that a drug related toxicosis did not occur. Here in this study the significant increase in total protein concentration observed in the animals treated subcutaneously is within the normal range and does not exceed the values of the second group of animals treated intramuscularly. Similar results were obtained in camels injected subcutaneously with Ivermectin (Ibrahim *et al*., 1981; Hisham, 1999) and in sheep after injection of Ivermectin at three times the recommended dose i.e., 600 μg kg^{-1} body weight (Shadad, 1997). The simultaneous increase in globulin level is partially in agreement with the results obtained following injection of Ivermectin in camels (Ibrahim *et al*., 1981; Hisham, 1999). In a similar fashion albumin level is normal. Similar non significant increase in total protein and albumin level was reported in horses treated with Ivermectin intramuscularly (Herd and Kociba, 1985). The significant ($p<0.05$) increase in urea blood level observed in days 20 and 24 of the experiment was also observed in horses 8 days following injection with Ivermectin intramuscularly (Herd and Kociba, 1985). In this experiment, at day 28 the level of urea returned below that of day zero. Significant increase in urea level was reported in sheep treated with Ivermectin at three times the recommended dose level (Shadad, 1997). Sodium level in the two treated groups showed different results such that in animals treated subcutaneously the sodium level showed transient and significant ($p<0.05$) decrease in day 16 when compared with pretreatment level, but in days 20, 24 and 28 there was no significant increase. In the other group where the animals were treated intramuscularly, there was significant ($p<0.05$) increase in sodium level immediately after treatment till day 12 and then non significant increase. Herd and Kociba (1985) observed significant decrease in potassium level 4 days following injection of Ivermectin, but the level returned to the pretreatment level after that. In this study there is significant ($p<0.05$) increase in potassium level till the end of the experiment. Here in this study, we do agree with the justification that the fluctuations in these parameters are due to nutrition and management (Herd and Kociba, 1985), because all parameters reported here did not exceed normal ranges.

The minor alterations in blood constituents observed in this study appear to be biologically insignificant, although some are statistically significant. They are within the normal range suggested by different authors in donkeys' worldwide (Nayeri, 1978; Zinkl *et al*., 1990; Gupta *et al*., 1994; French and Patrick, 1995; Jordana *et al*., 1998). These constituents are subject to variation with changes in feeding, handling and husbandry and the alterations may not be drug related.

CONCLUSION

We conclude that doramectin injectable formulation in parasitized animals does not seem to affect kidney or liver functions adversely. It may be safe to use this dosage level, but further studies need to be carried out before a final word can be cast.

ACKNOWLEDGMENTS

The financial support to this study was jointly secured by the Central Veterinary Research Laboratory, Soba (CVRL), Sudan and German Academic Exchange Service (DAAD). Due thanks are extended to staff members of the Department of Radioisotopes (CVRL).

REFERENCES

Abdel-Wahab, T.M., A.A. Abou-Rawash, A.Y. Desouky and M.A. Harfoush, 2002. Efficacy of Ivermectin (oral paste) against *Onchocerca cervicalis* infection in donkeys: Parasitological and histopathological study. Proceedings of the 10th Scientific Congress. Faculty of Veterinary Medicine. Assiut University, Egypt, pp: 220-235.

ElBashir, H.M. and H.I. Seri, 2004. Efficacy of Doramectin injectable against *Onchocerca raillieti* microfilariae in donkeys (*Equus asinus*), in Khartoum State. Sudan. Proceedings of 11th scientific congress. Faculty of Veterinary Medicine. Assiut University, Egypt, 5-7 December 2004, pp: 30-35.

Fadia, Y.A., 2000. Studies on equine onchocerciasis in Southern Darfur State. M.V.Sc. Thesis. University of Khartoum.

French, D.D., T.M. Klei, C.S. Foil, R.I. Miller, L.D. Foil, M.R. Chapman and J.J. McClure, 1988. Efficacy of Ivermectin in paste and injectable formulation against microfilariae of *O. cervicalis* and resolution of associated dermatitis in horses. Am. J. Vet. Res., 49: 1550-1554.

French, J.M. and V.H. Patrick, 1995. Reference values for physiological and biochemical parameters in domestic donkey (*Equus asinus*). Equine Vet. Edu., 7: 33-35.

Gupta, A.K., J.P. Varshney and P.K. Uppal, 1994. Comparative studies on biochemical indices in different breeds of equines. Ind. Vet. J., 71: 26-30.

Herd, R.P. and J.C. Donham, 1983. Efficacy of ivermectin against *Onchocerca cervicalis* microfilarial dermatitis in horses. Am. J. Vet. Res., 44: 1102-1105.

Herd, R.P. and G.J. Kociba, 1985. Effect of Ivermectin on equine blood constituents. Equ. Vet. J., 17: 142-144.

Hisham, I.S.F., 1999. Some pharmacotoxic aspects of Ivermectin in camels (*C. dromedaries*). M.V.Sc. Thesis, University of Khartoum, Sudan.

Ibrahim, M.S., A.R. Mohamed, F.A. El-balkemy, H. Omran and M.F. El-Mekkauri, 1981. Studies on the relation between the effect of ivomec® as a parasitic control and the general health condition of camels. Res. Bull. No. 375 Oct. 1981 Zagazig university Egypt.

Jordana, J., P. Folch and R. Cuenca, 1998. Clinical biochemical parameters of the endangered Catalonian donkey breed: Normal values and the influence of sex, age and management practices effect. Res. Vet. S., 64: 7-10.

Mancebo, O.A., Z.H. Verdi and G.M. Bulman, 1997. Comparative efficacy of moxidectin 2% equine oral gel and Ivermectin 2% equine oral paste against *Onchocerca cervicalis* microfilariae in horses with naturally acquired infection in formosa (Argentina). Vet. Parasitol., 73: 243-248.

Mogg, T.D., C.C. Pollitt, J.P. Willmore and H. Thompson, 1990. Efficacy of avermectin B1 given orally against equine intestinal strongyles and Onchocera microfilaria. Aust. Vet. J., 67: 399-401.

Nayeri, G.D., 1978. Blood characteristics of the adult donkey. Zbl. Vet. Med. A., 25: 541-547.

SBAR., 2000. Statistical Bulletin for Animal Resources. Ministry of Animal Resources, 10: 14.

Shadad, S.A.I., 1997. Pharmacological studies on Ivermectin in ewes. Ph.D Thesis, University of Khartoum.

Zinkl, J.G., D. Mae, P.G. Merida, T.B. Farver and J.A. Humble, 1990. Reference ranges and the influence of age and sex on hematologic and serum biochemical values in donkeys (*Equus asinus*). Am. J. Vet. Res., 51: 408-413.