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Effect of Doramectin on Donkeys Blood Constituents

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Abstract: A study was conducted to evaluate the sub acute toxicity of Doramectin Injectable formulation in healthy donkeys. This experiment involved four groups of animals, each of five. Three treatment groups received Doramectin injection intramuscularly at 100, 200 and 300 $\mu\text{g kg}^{-1}$ body weight for seven continuous days. Blood samples were collected daily for the first week and then every week for 3 additional weeks. Results obtained from the treatment groups were compared with those of the control group. Only urea level showed significant increase ($p < 0.05$) both in the treated and control groups at the end of the experiment. The changes encountered here occurred both in treated and non treated animals and the only significant difference is reduction in urea level in the animals that received 100 $\mu\text{g kg}^{-1}$ of Doramectin when compared to that of control group. Results obtained in this study indicated that Doramectin Injectable is safe to be used in donkeys, but further studies are encouraged to be conducted to ascertain safety.

Key words: Doramectin, toxicity, donkeys

INTRODUCTION

Doramectin is a member of the avermectin family of compounds. It is known as anti-nematodal drug intended for use in ovine and bovine. Previous studies conducted in Sudan assured the therapeutic efficacy of Doramectin against gastrointestinal nematodes of sheep (Abbakar *et al.*, 2003) and in donkeys (Seri *et al.*, 2004). In a survey conducted by Karns and Luther (1984), it was determined that 366 of 3316 horses developed adverse reactions following use of Ivermectin. The present study was conducted to study the different changes that may follow injection of Doramectin intramuscularly in donkeys at three different doses for a whole week.

MATERIALS AND METHODS

Animals: Twenty clinically normal adult donkeys (12 male and 8 females) were used in this study. The ages of these animals ranged from 3 to 10 years and all had been maintained on a good herd health programme including internal parasite control prior to this trial. The donkeys were housed and kept on water from tap and straw *ad libitum*.

Experimental design: In accord with the design of this study, 3 male and 2 female animals were assigned to each of the four treatment groups. The four treatment groups

were: DRMT1, DRMT2 and DRMT3 received a daily intramuscular injection of Doramectin (Dectomax® injection, Pfizer France) for a whole week, at three different dose levels: 100, 200 and 300 $\mu\text{g kg}^{-1}$, respectively. Injections were administered in the lateral mid-line of the neck. The fourth group remained untreated as control group.

Collection of blood: Blood samples were collected before the administration of the drug and then daily for the first week after the first administration of the drug and then every week for three additional weeks. Whenever blood samples were taken they were allowed to clot, the clotted blood samples were centrifuged and sera were separated and stored at -20°C until analyzed.

Analytical methods: Serum samples were analyzed for total protein, albumin, urea, calcium and inorganic phosphorus by using commercial kits (Randox laboratories Ltd., United Kingdom) in spectrophotometer analyzer (Jenway 6105 U.V./vis. Spectrophotometer, UK). Total globulins concentration was obtained by subtracting the concentration of albumin from that of total protein.

Clinical observations: After each injection animals were monitored continuously for two hours for any adverse or side effects to the administration of the Doramectin via the intramuscular route.

Statistical analysis: Post treatment changes in blood constituents were evaluated by analysis of variance (ANOVA) with repeated measures and comparisons between means were analyzed by SPSS 11.5 for Windows.

RESULTS

No adverse clinical signs or untoward reactions to the administration of the drug were observed in any of the donkeys utilized in this trial, nor were any tissue reactions noted at the site of injection.

As shown in Table 1 there is non significant ($p>0.05$) difference between the three treatment groups and the control in total protein concentration during the whole period of the experiment. The albumin concentration as shown in Table 2 showed significant difference ($p<0.05$) at day zero (before injection of the drug) between treatment groups 2 and 4 (DRMT1 and DRMT3). At day 2 there is significant ($p<0.05$) increase in albumin concentration in treatment groups DRMT1 and DRMT2. At the last three weeks of the experiment there is no significant ($p>0.05$) difference between the treatment groups and the control.

As shown in Table 3, there is significant decrease ($p<0.05$) in total globulins concentration at day 7 in DRMT1 and DRMT2 groups, on day 35 there is also significant decrease ($p<0.05$) in DRMT2. When compared with the pre treatment level it was found that there was considerable increase in total globulins concentration.

Urea concentration as shown in Table 4 showed significant increase ($p<0.05$) in day 4 in treatment group (DRMT3) when compared with the control group. At day 35 treatment group (DRMT1) showed significant ($p<0.05$) decrease when compared with control group.

As shown in Table 5 calcium concentration in the three treatment groups did not show any significant difference when compared with the control group.

Table 1: Changes in total protein concentration ($g L^{-1}$) following administration of three different doses of Doramectin injected intramuscularly in donkeys

	Control	DRMT1	DRMT2	DRMT3
Days	Mean±SD			
0	75.2±1.8	71.2±0.8	73.1±0.8	75.2±1.2
1	70.7±1.5	72.0±0.7	69.5±2.6	72.8±2.4
2	72.1±2.2	71.9± 2.0	69.6±3.7	72.5±3.2
3	73.6±2.0	69.3±3.8	70.6±1.1	71.9±2.9
4	66.9±3.7	70.7±3.4	73.1±1.7	70.4±3.1
5	75.4±2.6	73.7±1.7	75.7±0.8	71.4±3.0
6	75.1±1.1	74.8±1.2	76.4±1.5	72.9±1.5
7	75.4±1.1	74.2±1.0	73.0±1.5	77.3±1.3
14	74.2±0.8	74.3±1.0	72.1±1.1	75.2±2.3
21	73.6±1.5	73.4±2.6	76.3± 2.6	73.8±1.9
28	74.7±0.6	70.1±2.9	70.8±2.6	71.3±2.1
35	73.3±2.1	68.7±2.2	68.2± 2.7	70.2±2.4

In Table 6, the inorganic phosphorus concentration showed significant ($p<0.05$) decrease at days 4 and 6 post treatment when compared with the control group. In this study at the last three weeks there is no significant ($p>0.05$) difference between the treatment groups and the control group.

Table 2: Changes in albumin concentration ($g L^{-1}$) following administration of three different doses of Doramectin injected intramuscularly in donkeys

	Control	DRMT1	DRMT2	DRMT3
Days	Mean±SD			
0	37.2±3.8	41.5±1.4 ^a	39.8±3.1	33.1±0.6 ^b
1	37.8±1.9	36.6±3.1	34.8±2.1	34.9±1.8
2	33.2±3.9 ^a	41.5±1.8 ^b	41.2±1.2 ^b	37.0±2.3
3	40.5±4.1	41.0±3.3	37.3±2.6	40.6±2.2
4	34.3±2.1	39.9±2.7	40.7±2.7	38.5±1.5
5	37.4±2.5	43.5±1.9	38.8±4.4	39.3±4.9
6	39.0±3.0	40.4±3.5	45.5±4.6 ^a	31.7±4.8 ^b
7	31.1±0.9	37.8±2.4	36.8±2.8	36.4±3.1
14	36.6±1.9	31.6±0.6 ^a	36.7±3.4	38.8±2.3 ^b
21	29.8±1.2	27.1±1.6	31.5 ±2.5	31.4±3.3
28	29.1±3.2	28.6±3.4	27.9±2.8	28.1±1.5
35	28.7±1.8	29.5±1.3	30.4±2.6	30.9±1.1

Means on the same raw having different letter(s) are significantly ($p<0.05$) different

Table 3: Changes in total globulins concentration ($g L^{-1}$) following administration of three different doses of Doramectin injected intramuscularly in donkeys

	Control	DRMT1	DRMT2	DRMT3
Days	Mean±SD			
0	38.0±4.1	29.7±1.1 ^a	33.3±2.9 ^b	42.1±1.4
1	32.9±2.3	35.4±3.4	34.7±1.0	37.9±1.4
2	38.9±5.5	30.4±1.0	28.4±3.6	35.5±4.6
3	33.2±5.0	28.3±6.8	33.3±1.7	31.2±4.9
4	32.5±5.4	30.8±4.5	32.3±3.8	32.0±4.4
5	33.0± 5.2	3.0.3±0.8	36.9±4.3	32.1±5.7
6	36.2±2.5	34.5±4.2	30.8±4.2	41.2±5.1
7	44.3±1.5 ^a	36.4±1.7 ^b	36.2±2.7 ^b	40.9±2.4
14	37.7±2.2	42.7±0.6 ^a	35.4±3.3 ^b	36.4±2.0
21	43.8±2.0	39.9±1.3	41.7±2.0	42.4±3.0
28	45.6±2.8	41.5±6.0	42.9±2.6	43.2±2.7
35	44.6±3.5 ^a	39.2±1.1	37.8±1.7 ^b	39.3±1.7

Means on the same raw having different letter(s) are significantly ($p<0.05$) different

Table 4: Changes in urea level ($mmol L^{-1}$) following administration of three different doses of Doramectin injected intramuscularly in donkeys

	Control	DRMT1	DRMT2	DRMT3
Days	Mean±SD			
0	2.25±0.51	1.96±0.33	1.71±0.27	2.26±0.40
1	2.21±0.61	2.12±0.17	1.79±0.23	2.24±0.10
2	3.06±0.49	3.14±0.27	2.92±0.41	3.29±0.27
3	3.49±0.31	3.48±0.19	3.60±0.47	3.94±0.21
4	2.94±0.22	2.44±0.26 ^a	2.72±0.42	3.73±0.54 ^b
5	3.72±0.48	2.58±0.62	2.58±0.66	2.84±0.29
6	2.41±0.37 ^a	2.39±0.47	2.68±0.34	3.57±0.08 ^b
7	1.85±0.19	1.93±0.33	2.49±0.40	2.56±0.27
14	3.62±0.27	3.03±0.42	2.99±0.69	3.69±0.41
21	1.79±0.58	1.61±0.38	1.78±0.67	2.34±0.85
28	3.36±0.67	2.17±0.52 ^a	3.07±0.32	4.19±0.66 ^b
35	5.11±0.72 ^a	3.13±0.09 ^b	4.03±0.73	5.52±0.43

Means on the same raw having different letter(s) are significantly ($p<0.05$) different

Table 5: Changes in calcium level (mmol L⁻¹) following administration of three different doses of Doramectin injected intramuscularly in donkeys

	Control	DRMT1	DRMT2	DRMT3
Days	Mean±SD			
0	2.49±0.04	2.45±0.07	2.58±0.05	2.55±0.09
1	2.49±0.03	2.54±0.07	2.57±0.02	2.54±0.06
2	2.61±0.05	2.60±0.04	2.60±0.04	2.70±0.03
3	2.61±0.05	2.63±0.05	2.59±0.05	2.63±0.04
4	2.58±0.02	2.61±0.10	2.61±0.03	2.67±0.04
5	2.50±0.02	2.56±0.08	2.57±0.04	2.53±0.05
6	2.25±0.08	2.31±0.03	2.44±0.08	2.35±0.06
7	2.20±0.19	2.45±0.08	2.28±0.08	2.17±0.08
14	2.40±0.21	2.39±0.24	2.33±0.06	2.33±0.18
21	2.34±0.17	2.39±0.09	2.08±0.08	2.39±0.15
28	2.33±0.17	2.23±0.08	2.49±0.23	2.29±0.10
35	2.34±0.08	2.25±0.06	2.46±0.19	2.27±0.08

Table 6: Changes in inorganic phosphorus concentration (mmol L⁻¹) following administration of three different doses of Doramectin injected intramuscularly in donkeys

	Control	DRMT1	DRMT2	DRMT3
Days	Mean±SD			
0	0.96±0.06	0.80±0.13	1.16±0.10	0.90±0.07
1	0.94±0.07	0.95±0.11	0.84±0.05	0.94±0.06
2	1.29±0.04	1.15±0.12	0.98±0.11	1.23±0.25
3	1.32±0.18	1.10±0.07	0.98±0.12	1.05±0.10
4	1.36±0.11 ^a	0.81±0.08 ^b	1.05±0.11 ^c	1.01±0.09 ^d
5	1.13±0.13	1.00±0.16	1.27±0.09	1.01±0.07
6	1.03±0.11	0.89±0.10 ^a	1.20±0.04 ^b	1.10±0.10
7	1.06±0.14	1.09±0.07	1.07±0.09	1.21±0.11
14	1.16±0.20	0.94±0.05	0.89±0.04	1.01±0.08
21	1.35±0.06	1.23±0.18	1.21±0.08	1.22±0.10
28	1.34±0.04	1.13±0.14	1.16±0.07	1.13±0.06
35	1.33±0.04	1.13±0.05	1.15±0.08	1.12±0.04

Means on the same raw having different letter(s) are significantly (p<0.05) different

DISCUSSION

The present study showed that there were no significant difference between the three treatment groups and the control in total protein concentration has been observed during the whole period of the experiment. The fluctuation in total protein concentration in the control and treated groups did not exceed the normal range suggested by other researchers (Nayeri, 1978; Gupta *et al.*, 1994; French and Patrick, 1995; Jordana *et al.*, 1998; Mori *et al.*, 2003). Herd and Kociba (1985) reported that non significant difference in total protein concentration was also observed in horses injected intramuscularly with Ivermectin. The albumin concentration showed significant difference (p<0.05) at day zero (before injection of the drug) between treatment groups 2 and 4 (DRMT1 and DRMT3). At day 2 there was significant (p<0.05) increase in albumin concentration in treatment groups DRMT1 and DRMT2. During the last three weeks of the experiment there was no significant difference between the treatment groups and the control. These results are in agreement with other findings in horses (Herd and Kociba, 1985).

There was a significant (p<0.05) decrease in total globulins concentration at day 7 in DRMT1 and DRMT2 groups, as well as on day 35 within DRMT2. When compared with the pre treatment level it was found that there was considerable increase in total globulins concentration which agrees with the findings of Hisham (1999) in camels, Herd and Kociba (1985) in horses.

Urea concentration showed a significant (p<0.05) increase on day 4 in treatment group (DRMT3) when compared with the control group. At day 35 treatment group (DRMT1) showed significant decrease when compared with control group. Herd and Kociba (1985) reported similar significant increases in urea level in horses treated intramuscularly with Ivermectin.

Serum calcium level in the three treatment groups did not show any significant difference when compared with the control group. Herd and Kociba (1985) reported significant decrease in calcium level 4 days after the treatment, but the level returned to the pre treatment level at day 8 post treatment.

Inorganic phosphorus level showed significant (p<0.05) decrease at days 4 and 6 post treatment when compared with the control group. Herd and Kociba (1985) reported significant decrease in inorganic phosphorus level 4 days post treatment. In this study during the last three weeks there was no significant difference between the treatment groups and the control group with respect to phosphorus levels.

Minor alterations in blood constituents observed in our study appear to be biologically insignificant, although statistically significant. The same alterations occurred in the control group to some extent, which means that they are subjected to variations in changes with feeding, handling and husbandry and the alterations may not be drug related (Herd and Kociba, 1985). Normal levels of calcium, phosphorus, sodium, creatinine, bilirubin and glucose were also observed in horses given up to 12 mg kg⁻¹ body weight Ivermectin (Herd and Kociba, 1985).

In this trial no untoward effects were observed nor did any of the post treatment blood chemistry values suggest any degree of toxicosis. Results obtained in this study indicated that Doramectin Injectable is safe to be used in donkeys, but further studies are encouraged to be conducted to ascertain safety.

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