Trakia Journal of Sciences, Vol. 3, No. 5, pp 14-16, 2005

Available online at:
http://www.uni-sz.bg

ISSN 1312-1723

Original Contribution

INVESTIGATIONS ON SOME BIOCHEMICAL AND HAEMATOLOGICAL PARAMETERS AFTER TOBRAMYCIN AND AMIKACIN TREATMENT IN FEMALE GOATS

T. Dinev[1]*, D. Kanakov[2], D. Zapryanova[1]

[1]Department of Pharmacology, Animal's Physiology and Physiological Chemistry;
[2]Department of Internal Diseases and Clinical Toxicology, Faculty of Veterinary Medicine, Trakia University, 6000 Stara Zagora, Bulgaria;

ABSTRACT

The aim of the present study was to determine the changes in some biochemical and haematological parameters after 5 days intramuscular treatment with tobramycin (5 mg/kg bw) and amikacin (10 mg/kg bw) in six healthy female goats. The results of these studies indicated that in healthy goats, both antibiotics, in therapeutic doses, caused significant rise in plasma creatinine and urea levels, lymphocyte count and decrease in sodium levels, RBC count and haemoglobin concentration ($p<0.05$). Amikacin sulphate caused significant rise in alkaline phosphatase activity; tobramycin caused significant increase in lactate dehydrogenase activity. On the whole, the results of these studies demonstrate that tobramycin and amikacin have potential for altering biochemical and haematological values in female goats after using therapeutic doses.

Key words: Amikacin, Tobramycin, Goats, Biochemical parameters, Haematological parameters

INTRODUCTION

Aminoglycosides are antibiotics, often used in veterinary and human medicine for treatment of infections caused by Gram negative and some Gram positive micro-organisms Tobramycin and amikacin belong to the group of aminoglycosides with extended spectrum of antimicrobial activity. They are insufficiently studied in veterinary medicine. Aminoglycosides with extended spectrum of activity have excellent therapeutic potential, but their applicability is limited by their nephrotoxic, ototoxic and neuroparalytic effects.

A characteristic feature of these antibiotics is their relatively low therapeutic index. The use of therapeutic doses may lead to adverse changes in biochemical and haematological indices, especially with those connected with kidney function. The physician therefore has to create a proper balance between their use as an antibiotic and these adverse effects to avoid any occasion of iatrogenicity or improper medication. In veterinary medicine such data exist mainly for gentamicin because of its wide application and its considerable nephrotoxic potential (1, 2). Such information, considering amikacin and tobramycin is rather scarce (2, 3) and for goats such experimental results do not exist. Gathering of such experimental data will prove to be useful for rational use of these antibiotics.

MATERIALS AND METHODS

In these studies a group of six non-lactating she goats (breed Bulgarian white dairy goat) was used. During the trial with amikacin the goats weighed 38.62±3.51 kg and during the experiment with tobramycin-43.12±3.39 kg. Experimental animals were housed in identical conditions, according to the requirements of the species. Food and water were supplied *ad libitum*.

The animals were injected with amikacin sulphate (Sopharma, Sofia, Bulgaria) at a dosage of 10 mg/kg bw, at intervals of 24 hours during five consecutive days. The same animals were given tobramycin (Actavis, Bulgaria) 5 mg/kg bw using the same experimental design, 40 days

*Correspondence to: Toncho Dinev, Department of Pharmacology, Animal's Physiology and Physiological Chemistry, Faculty of Veterinary Medicine, Trakia University, 6000 Stara Zagora, Bulgaria; Pnone: +359 885928707; E-mail: Dinev_sz@mail.bg

later. The first dose was administered i.v., and the next four doses were injected i.m.

Blood samples for evaluation of biochemical and haematological parameters were collected before experiment, on days 1, 3 and 5 and twice after the experiment (on days 8 and 12 for amikacin sulphate and on days 10 and 15 for tobramycin). The measurements of the biochemical parameters (creatinine, urea, lactate dehydrogenase, alkaline phosphatase and sodium) were performed by spectrophotometer, using standard laboratory tests of Human Diagnostica (Germany). Total protein and glucose were estimated by the Biuret method and ortho-toluidine method, respectively. Haematological parameters (total RBC count, haemoglobin concentration, haematocrit value, total WBC count) were evaluated using automated haematology counter Serono 150+ (USA). Differential WBC count was done from blood smears. Values were expressed as mean ± standard error and were compared using Tukey's test for statistical analysis.

RESULTS

Tables 1 and **2** show changes in some biochemical and haematological indices during and after 5 days administration of amikacin and tobramycin compared with control values (day 0) before treatment.

The results of these studies indicate that in healthy goats, both antibiotics in therapeutic doses caused significant increase in plasma creatinine and urea levels, lymphocyte count and decrease in sodium levels, RBC count and haemoglobin concentration ($p < 0.05$). Amikacin sulphate caused significant rise in alkaline phosphatase activity, as well as fall in glucose levels. Tobramycin caused a fall in alkaline phosphatase activity and a significant rise in lactate dehydrogenase activity.

Table 1. *Biochemical and haematological values in goats, treated with amikacin sulphate (mean ± SE)*

Parameter	***Days***					
	0	***1***	***3***	***5***	***8***	***12***
Total protein g/l	75.12 ±2.22	62.23 ±3.66[1]	74.77 ±2.07	76.37 ±2.25	71.68 ±1.49	72.52 ±1.46
Glucose mmol/l	2.36 ±0.2	1.97 ±0.05[1]	2 ±0.07[1]	2.1 ±0.1[1]	1.96 ±0.07[1]	2.27 ±0.16
Creatinine µmol/l	76.83 ±7.63	99 ±11.38[1]	84.67 ±10.73	104.33 ±14.68[1]	90.17 ±9.83	87.83 ±7.87
Urea mmol/l	6.37 ±0.23	7.18 ±0.31[1]	6.85 ±0.38	7.02 ±0.31[1]	6.6 ±0.32	6.47 ±0.23
Alkaline phosphatase U/L	168.33 ±11.95	198.3 ±33.67	287.83 ±56.4[1]	206.67 ±48.06	203.7 ±46.52	194.33 ±33.19
LDH U/L	289.17 ±16.7	317.67 ±34.62	285 ±26.24	277 ±8.18	295.5 ±19.51	285.33 ±7.56
Sodium mmol/l	153.67 ±0.33	147.5 ±1.95[1]	150.83 ±1.87[1]	146.83 ±1.28[1]	152.5 ±0.99	151.33 ±1.36
Erythrocytes T/L	13.59 ±1.03	11.82 ±0.83[1]	11.06 ±0.41[1]	12.53 ±1.23	11.05 ±0.65[1]	11.62 ±0.72[1]
Haematocrit %	35.85 ±3.67	29.13 ±2.5[1]	27.22 ±1.2[1]	31.53 ±3.94	26.83 ±1.8[1]	28.58 ±2.15[1]
Leucocytes G/L	14.33 ±1.57	12.6 ±1.49	12.85 ±1.46	12.27 ±0.9	10.25 ±0.69[1]	10.65 ±1.24[1]
Haemoglobin g/l	134.67 ±7.31	118.2 ±5.26[1]	116.67 ±5.42[1]	119.33 ±3.33[1]	118.5 ±5.8[1]	111.83 ±4.81[1]
Segm. neutrophils%	25.33 ±1.15	24 ±0.97	22.5 ±1.31[1]	21.67 ±0.67[1]	23.33 ±0.8[1]	25.17 ±0.83
Lymphocytes %	67.5 ±1.41	69.5 ±1.36	70.83 ±2.17[1]	70.33 ±1.84	71.17 ±1.17[1]	69.33 ±1.41

[1]- *Significantly different from the control values (day 0), $p<0.05$*

DISCUSSION

Significant rise of creatinine and plasma urea levels after administration of both antibiotics indicates that there is an alteration of kidney function. After treatment with tobramycin more drastic increase of urea concentration is observed. With the exception of the slight rise of plasma urea levels above normal after beginning of tobramycin and amikacin administration, other values fall within the

normal range for goats (4, 5). These results are in agreement with other reported cases for tobramycin (3) and gentamicin (1, 2) treatment using therapeutic doses. Haematological parameters in both trials indicate that there is tendency toward a decrease of erythrocyte count, haemoglobin concentration and haematocrit percentage after aminoglycoside administration. Amikacin displays marked ability for increasing alkaline phosphatase activity.

Table 2. *Biochemical and haematological values in goats, treated with tobramycin (mean ± SE)*

Parameter	***Days***					
	0	***1***	***3***	***5***	***10***	***15***
Total protein g/l	79.43 ±1.12	78.02 ±1.49	78.43 ±1.14	80.64 ±1.45	82.11 ±2.27[1]	76.03 ±1.1[1]
Glucose mmol/l	1.96 ±0.09	2.46 ±0.13[1]	2.21 ±0.12[1]	1.74 ±0.07[1]	1.92 ±0.08	1.89 ±0.06
Creatinine µmol/l	85 ±3.69	98.33 ±4.83[1]	101.17 ±6.65[1]	115.33 ±5.58[1]	97 ±6.48[1]	102.17 ±5.88[1]
Urea mmol/l	5.73 ±0.27	6.15 ±0.53	6.59 ±0.24[1]	7.78 ±0.29[1]	7.99 ±0.52[1]	7.3 ±0.49[1]
Alkaline phosphatase U/L	190.33±18.51	179.33±17.14	159.67 ±9.63	171.33 ±12.76	218 ±21.27	198 ±26.63
LDH U/L	284.17 ±13.74	294.5 ±13.6	326.33 ±20.25[1]	317 ±13.89[1]	332.5 ±14.74[1]	320.17 ±17.5[1]
Sodium mmol/l	153.67 ±0.33	147.5 ±1.95[1]	150.83 ±1.87[1]	146.83 ±1.28[1]	152.5 ±0.99	151.33 ±1.4
Erythrocytes T/L	11.8 ±0.73	10.98 ±0.26	10.58 ±0.44[1]	10.75 ±0.51[1]	9.5 ±0.57[1]	11.22 ±0.61
Haematocrit %	28.75 ±2.11	26.32 ±0.81	26.25 ±1.47	26.42 ±1.71	22.27 ±1.65[1]	27.3 ±1.92
Leucocytes G/L	13.55 ±1.09	13.67 ±0.83	15 ±0.86	14.67 ±1.1	8.82 ±0.62[1]	15.45 ±1.54[1]
Haemoglobin g/l	114.67 ±6.58	106.5 ±5.81	105.67 ±6.05	101.83 ±6.78[1]	76.33 ±2.86[1]	109 ±6.14
Segm. neutrophils %	24.67 ±1.54	27.63 ±2.51	25.67 ±1.48	23.17 ±1.51	21.17 ±0.98[1]	21.17 ±1.11[1]
Lymphocytes %	66.67 ±2.42	64.67 ±2.81	67.67 ±2.36	69.17 ±0.98	71.67 ±1.8[1]	69.67 ±2.26

[1]-*Significantly different from the control values (day 0), $p<0.05$*

These experiments have confirmed our hypothesis on the possibility that therapeutic doses of some drugs may cause changes in haematological and biochemical parameters and therefore could constitute treatment hazards. These results might be accepted as a starting point for future experiments in a direction aimed at inculcating safety measures in aminoglycoside use.

REFERENCES

1. Lashev, L. and Lasarova, S., Pharmacokinetics and side effects of gentamicin in healthy and *pseudomonas aeruginosa* infected sheep. *J vet Pharm Ther*, 24: 237-240, 2001.
2. Ramsay, E. C. and Vulliet, R., Pharmacokinetic Properties of Gentamicin and Amikacin in the Cockatiel. *Avian Dis*, 37: 628-634, 1993.
3. Jernigan, A. D., Hatch R. C. and Wilson R. C. Pharmacokinetics of tobramycin in cats. *Am J Vet Res*, 49: 608-612, 1988.
4. Georgiev, I., Georgieva, T. and Georgiev. G., Endocrine control of lactation. KOTA, Stara Zagora, 2002.
5. Petkov, P., Nikolov, Y., Tsokova, L. and Sabev S., Propaedeutics of Internal Noninfectios Diseases in domestic animals (guidance for practical work with students). SD KONTRAST, Stara Zagora, 2001.