

Changes in Some Blood Biochemical and Haematological Parameters in Goats after Aminoglycoside and Aminocyclitol Treatment at Therapeutic Doses

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Abstract: The aim of the present study was to determine the changes in some blood biochemical and haematological parameters in healthy female goats after a 5-day parenteral treatment with gentamicin (4 mg/kg), tobramycin (5 mg/kg), amikacin (10 mg/kg), kanamycin (10 mg/kg), apramycin (20 mg/kg), and spectinomycin (20 mg/kg). The results indicated that aminoglycosides caused more severe alterations than aminocyclitols, especially on those parameters related to renal function. There was a tendency toward a rise in plasma creatinine and urea levels after aminoglycoside treatment, as well as a rise in urea levels after aminocyclitol administration. These antibiotics caused decreases in plasma or serum glucose, sodium and chloride levels, erythrocytes and leukocytes counts, haematocrit percentage and haemoglobin concentration. For plasma or serum total protein, total lipids, lactate dehydrogenase, alkaline phosphatase, calcium, and magnesium concentrations and differential white blood cell counts, various changes occurred. As a whole, these antibiotics have the potential to alter biochemical and haematological values in female goats after their use at therapeutic doses.

Key Words: Aminoglycosides, aminocyclitols, blood biochemical parameters, haematological parameters, goats

Introduction

Aminoglycosides and aminocyclitols are antibiotics frequently used in veterinary and human medicine against gram-negative and some gram-positive microorganisms. It has been reported that they may cause permanent or transient changes in the blood parameters related to kidney function. There are publications in sheep (1), rats (2-4), humans (5-6), and cats (7) with results supporting this hypothesis, whereas some reports confirm the opposite opinion in rabbits (8), horses (9), cats (10), mice (11), cows (12), and dogs (13). However, it is possible that aminoglycosides induce changes in some biochemical and haematological values in animals. In veterinary medicine such data exist mainly for gentamicin, but for the other members of this group and for the aminocyclitol group there are limited data (2-4,7,10,11,13). The information on ruminants is rather scarce (1,12) and for goats such experimental results are not available.

Comparative investigations of changes in biochemical and haematological parameters after aminoglycoside and aminocyclitol treatment at therapeutic doses are scarce and our work aims to fill this gap in the knowledge. Since these drugs are used for treatment of infections that also cause changes in some blood biochemical and haematological parameters, if the physician does not take into account the possible alterations caused by aminoglycosides, an incorrect diagnosis may be made and an improper medication could be administered. In our research, the possible changes in blood biochemical and haematological values after aminoglycoside and aminocyclitol treatment are studied, and an investigation of the degree of these changes is performed.

Materials and Methods

In every one of these studies a group of 6 nonlactating female goats (Bulgarian white dairy goat breed) was

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used. During the trials the goats weighed 43.71 ± 3.31 kg (mean \pm SD). Experimental animals were housed outdoor in identical conditions, according to the requirements of the species. They were fed on alfalfa hay and a concentrated grain ration. Water was supplied ad libitum.

Drugs

The drugs used in our experiments are listed in Table 1.

Experimental design

The animals were treated at intervals of 24 h for 5 consecutive days. Each group was treated with only one antibiotic. The first dose was injected intravenously and the next 4 doses were injected intramuscularly.

Blood samples for evaluation of biochemical and haematological values were collected before the experiment, on days 1, 3 and 5, and twice after the 5 days of treatment (on days 8 and 12 for amikacin, on days 10 and 17 for kanamycin, and on days 10 and 15 for tobramycin, apramycin, gentamicin, and spectinomycin). Blood samples were obtained at 7-8 h A.M. and before the goats were injected with the corresponding daily dose of antibiotic. Serum and heparinised plasma were collected after centrifugation at 1500 rpm for 20 min. Sodium, chloride, total protein, and total lipids were assayed in serum, and calcium, magnesium, urea, creatinine, lactate dehydrogenase (LDH) and alkaline phosphatase in plasma. Glucose was determined in whole blood. The measurements of the biochemical parameters (creatinine, urea, LDH, alkaline phosphatase, sodium, chloride, calcium, magnesium, total protein, total lipids, and blood glucose) were performed by spectrophotometry, using commercial laboratory kits

of Human Diagnostica (Germany). Haematological parameters (total red blood cell counts (total RBC count), haemoglobin concentration, and total white blood cell counts (total WBC count) were evaluated on the automated haematology counter Serono 150+ (USA). Differential WBC counts were done on blood smears. Statistical analysis was done using "StatMost for Windows" software (DataMost Co., USA, 1994); values were expressed as mean \pm standard error of the mean (SEM) and were compared using Tukey's test. Significance was set at $P < 0.05$.

Results

Changes in biochemical and haematological values during and after 5-day administration of aminoglycosides and aminocyclitols compared to control values (day 0) before treatment are shown in Tables 2 to 7. After administration of the antibiotics the parameters showed various changes and some of them did not vary at all. Only values that exhibited changes after administration of aminoglycosides and aminocyclitols will be discussed.

Total protein. There were slight and uneven changes manifested by increases or decreases in serum protein concentrations from day 1 to day 5. After that the initial values were restored.

Blood glucose. Its level fell up to day 3 after administration of all antibiotics (with the exception of tobramycin), and after that a tendency toward returning to the starting levels was found.

Creatinine. Aminoglycosides caused elevation of its values up to day 5 followed by a decrease in plasma levels to the initial values.

Table 1. Antibiotics used in our investigation.

Antibiotic	Drug form (company, city, country)	Drug concentration	Dose (mg/kg)
Amikacin	Ampoules amikacin sulphate 2 ml (Sopharma, Sofia, Bulgaria)	25%	10
Tobramycin	Substance tobramycin 983 μ g/ml (Actavis, Sofia, Bulgaria)	10%	5
Apramycin	Phials apramycin sulphate 50 ml (Actavis, Sofia, Bulgaria)	20%	20
Gentamicin	Phials gentamicin sulphate 50 ml (Actavis, Sofia, Bulgaria)	10%	4
Kanamycin	Phials kanamycin sulphate 100 ml (Alfasan, Woerden, Holland)	25%	10
Spectinomycin	Phials spectinomycin 100 ml (Ceva, Libourne, France)	10%	20

Table 2. Changes in some blood biochemical parameters after a 5-day gentamicin treatment (4 mg/kg) administered to 6 female goats (mean \pm SEM).

Parameter	Days					
	0	1	3	5	10	15
Total protein g/l	79.94 \pm 1.4	84.45 \pm 1.21 ¹	81.09 \pm 0.47 ²	79.9 \pm 1.4 ²	81.34 \pm 0.92 ²	75.94 \pm 1.49 ^{1,2,3,4,5}
Blood glucose mmol/l	2.59 \pm 0.11	1.98 \pm 0.07 ¹	1.85 \pm 0.04 ¹	1.95 \pm 0.06 ¹	2.01 \pm 0.08 ^{1,3}	2.35 \pm 0.08 ^{1,2,3,4,5}
Total lipids g/l	2.14 \pm 0.17	2.39 \pm 0.12 ¹	2.28 \pm 0.11	2.34 \pm 0.14	2.24 \pm 0.13	2.21 \pm 0.13
Creatinine mmol/l	90 \pm 7.41	113.5 \pm 7.42 ¹	102.5 \pm 18.19	126 \pm 5.28 ^{1,3}	96 \pm 5.33 ^{2,4}	87 \pm 6.26 ^{2,4}
Urea mmol/l	6.84 \pm 0.57	8.48 \pm 0.73 ¹	7.31 \pm 1.28	8.95 \pm 0.13 ^{1,3}	8.99 \pm 0.64 ^{1,3}	6.62 \pm 0.64 ^{2,4,5}
LDH U/l	343.3 \pm 20.1	336.3 \pm 20.8	365.2 \pm 21.9	306.8 \pm 19.0 ^{1,3}	247.5 \pm 21.2 ^{1,2,3,4}	253.8 \pm 16.1 ^{1,2,3,4}
Alkaline phosphatase U/l	161.2 \pm 62.1	183.7 \pm 72.2	169 \pm 81.2	162.2 \pm 62.3	172 \pm 100.2	188.5 \pm 103.8
Calcium mmol/l	2.14 \pm 0.05	2.1 \pm 0.05	2.12 \pm 0.08	2.22 \pm 0.06 ²	2.27 \pm 0.06 ^{1,2,3}	2.36 \pm 0.04 ^{1,2,3,4}
Magnesium mmol/l	0.86 \pm 0.05	0.89 \pm 0.06	0.79 \pm 0.03 ²	0.86 \pm 0.04 ³	0.74 \pm 0.03 ^{1,2,4}	0.8 \pm 0.02 ²
Sodium mmol/l	139.67 \pm 1.98	131.83 \pm 2.3 ¹	134.33 \pm 1.93 ¹	138 \pm 3.29 ²	136.33 \pm 2.04 ²	134 \pm 1.81 ¹
Chloride mmol/l	104.5 \pm 2.26	94.83 \pm 4.33 ¹	114.83 \pm 5.98 ^{1,2}	103.5 \pm 3.32 ^{2,3}	101.67 \pm 6.68 ³	96.33 \pm 2.16 ^{1,3}
RBC count (1x10 ¹² /l)	10.92 \pm 0.79	9.96 \pm 0.89	12.2 \pm 0.682	11.45 \pm 1.082	11.25 \pm 0.5	10.83 \pm 0.28 ³
WBC count (1x10 ⁹ /l)	12.47 \pm 0.69	11.98 \pm 1.03	14.23 \pm 1.29 ^{1,2}	6.78 \pm 0.62 ^{1,2,3}	12.07 \pm 0.69 ^{3,4}	11.14 \pm 0.65 ^{3,4}
Haemoglobin (g/l)	102.5 \pm 4.43	96.33 \pm 4.95	97 \pm 5.24	71 \pm 3.31 ^{1,2,3}	95.17 \pm 4.54	94.6 \pm 4.04 ⁴
Eosinophiles (%)	4.5 \pm 0.67	3.67 \pm 0.67	4.17 \pm 0.48	5.33 \pm 1.15 ²	4.67 \pm 0.49	4.33 \pm 0.42
Band neutrophiles (%)	2.5 \pm 0.22	2.67 \pm 0.33	2.67 \pm 0.49	1.83 \pm 0.4 ^{1,2,3}	2.17 \pm 0.31	2 \pm 0.37 ^{2,3}
Segmented neutrophiles (%)	30.67 \pm 2.81	26.67 \pm 1.17	31.83 \pm 2.2 ²	29.17 \pm 3.03	34.17 \pm 4.2 ²	30.67 \pm 2.78
Lymphocytes (%)	61.83 \pm 3.41	66.33 \pm 0.8	61 \pm 2.68	63.5 \pm 3.06	59.83 \pm 4.13 ²	62.5 \pm 2.87
Monocytes (%)	0.33 \pm 0.21	0.33 \pm 0.21	0.17 \pm 0.17	0.17 \pm 0.17	0.5 \pm 0.34	0.33 \pm 0.21
Basophiles (%)	0.17 \pm 0.17	0.33 \pm 0.21	0.17 \pm 0.17	0.17 \pm 0.17	0.33 \pm 0.21	0.17 \pm 0.17

¹- Significantly different from the control values (day 0), P < 0.05;

²- Significantly different from day 1, P < 0.05;

³- Significantly different from day 3, P < 0.05;

⁴- Significantly different from day 5, P < 0.05;

⁵- Significantly different from day 10, P < 0.05.

Table 3. Changes in some blood biochemical parameters after a 5-day tobramycin treatment (5 mg/kg) administered to 6 female goats (mean ± SEM).

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 ^{1,2,3}	76.03 ± 1.13 ^{1,4,5}
Blood glucose mmol/l	1.96 ± 0.09	2.46 ± 0.131	2.21 ± 0.12 ^{1,2,3}	1.74 ± 0.07 ^{1,2,3}	1.92 ± 0.08 ^{2,3,4}	1.89 ± 0.06 ^{2,3}
Total lipids g/l	2.68 ± 0.04	2.56 ± 0.17	2.51 ± 0.13	2.6 ± 0.14	2.69 ± 0.11	2.53 ± 0.06
Creatinine mmol/l	85 ± 3.69	98.33 ± 4.83 ¹	101.17 ± 6.65 ¹	115.33 ± 5.58 ^{1,2,3}	97 ± 6.48 ^{1,4}	102.17 ± 5.88 ^{1,4}
Urea mmol/l	5.73 ± 0.27	6.15 ± 0.53	6.59 ± 0.24 ¹	7.78 ± 0.29 ^{1,2}	7.99 ± 0.52 ^{1,2,3}	7.3 ± 0.49 ^{1,2}
LDH U/l	284.17 ± 13.74	294.5 ± 13.6	326.33 ± 20.25 ^{1,2}	317 ± 13.89 ^{1,3}	332.5 ± 14.74 ^{1,2}	320.17 ± 17.5 ¹
Alkaline phosphatase U/l	190.33 ± 18.51	179.33 ± 17.14	159.67 ± 9.63	171.33 ± 12.76	218 ± 21.27 ^{2,3,4}	198 ± 26.63 ³
Calcium mmol/l	2.32 ± 0.03	2.29 ± 0.03	2.31 ± 0.02	2.29 ± 0.02	2.28 ± 0.05	2.34 ± 0.03 ⁵
Magnesium mmol/l	1.08 ± 0.02	1.07 ± 0.03	1.05 ± 0.05	1.09 ± 0.06	1.02 ± 0.04	1.02 ± 0.02
Sodium mmol/l	150.17 ± 2.36	148.17 ± 1.54	147.5 ± 2.62	147.17 ± 2.41	147.83 ± 2.65	145.67 ± 2.32 ¹
Chloride mmol/l	103.17 ± 2.46	103.5 ± 1.61	103.83 ± 2.56	107 ± 2.52	103.67 ± 2.06	106.17 ± 2.63
RBC count (1x10 ¹² /l)	11.8 ± 0.73	10.98 ± 0.26	10.58 ± 0.44 ¹	10.75 ± 0.51 ¹	9.5 ± 0.57 ^{1,2,3,4}	11.22 ± 0.61 ⁵
WBC count (1x10 ⁹ /l)	13.55 ± 1.09	13.67 ± 0.83	15 ± 0.86	14.67 ± 1.1	8.82 ± 0.62 ^{1,2,3}	15.45 ± 1.54 ^{1,5}
Haemoglobin (g/l)	114.67 ± 6.58	106.5 ± 5.81	105.67 ± 6.05	101.83 ± 6.78 ¹	76.33 ± 2.86 ^{1,2,3,4}	109 ± 6.14 ⁵
Eosinophiles (%)	5.67 ± 1.2	4.83 ± 0.98	4.83 ± 1.57	5.83 ± 1.68	5.5 ± 1.48	5.33 ± 1.2
Metamyelocytes (%)	0.17 ± 0.17	0.17 ± 0.17	0	0.33 ± 0.21	0.33 ± 0.33	0.17 ± 0.17
Band neutrophiles (%)	1.67 ± 0.67	2.33 ± 0.61	0.83 ± 0.4 ^{1,2}	1 ± 0.26 ²	0.83 ± 0.31 ^{1,2}	1.5 ± 0.22 ²
Segmented neutrophiles (%)	24.67 ± 1.54	27.63 ± 2.51	25.67 ± 1.48	23.17 ± 1.51 ²	21.17 ± 0.98 ^{1,2,3}	21.17 ± 1.11 ^{1,2,3}
Lymphocytes (%)	66.67 ± 2.42	64.67 ± 2.81	67.67 ± 2.36	69.17 ± 0.98 ²	71.67 ± 1.8 ^{1,2,3}	69.67 ± 2.26 ²
Monocytes (%)	0.5 ± 0.22	0.5 ± 0.22	0.83 ± 0.17	0.17 ± 0.17 ³	0.33 ± 0.21 ³	0.33 ± 0.21 ³
Basophiles (%)	0.17 ± 0.17	0.17 ± 0.17	0.17 ± 0.17	0.33 ± 0.2 ¹	0.330.21	0.17 ± 0.17

¹- Significantly different from the control values (day 0), P < 0.05;

²- Significantly different from day 1, P < 0.05;

³- Significantly different from day 3, P < 0.05;

⁴- Significantly different from day 5, P < 0.05;

⁵- Significantly different from day 10, P < 0.05.

Table 4. Changes in some blood biochemical parameters after a 5-day amikacin treatment (10 mg/kg) administered to 6 female goats (mean \pm SEM).

Parameter	Days						
	0	1	3	5	8	12	
Total protein g/l	75.12 \pm 2.22	62.23 \pm 3.66 ¹	74.77 \pm 2.07 ²	76.37 \pm 2.252	71.68 \pm 1.49 ^{2,4}	72.52 \pm 1.46 ²	
Blood glucose mmol/l	2.36 \pm 0.2	1.97 \pm 0.05 ¹	2 \pm 0.07 ¹	2.1 \pm 0.1 ¹	1.96 \pm 0.07 ¹	2.27 \pm 0.16 ^{2,3,5}	
Total lipids g/l	2.09 \pm 0.17	2.61 \pm 0.16 ¹	2.34 \pm 0.16	2.54 \pm 0.27 ¹	2.3 \pm 0.21	2.27 \pm 0.1 ²	
Creatinine mmol/l	76.83 \pm 7.63	99 \pm 11.38 ¹	84.67 \pm 10.73	104.33 \pm 14.68 ^{1,3}	90.17 \pm 9.83	87.83 \pm 7.87	
Urea mmol/l	6.37 \pm 0.23	7.18 \pm 0.31 ¹	6.85 \pm 0.38	7.02 \pm 0.31 ¹	6.6 \pm 0.322	6.47 \pm 0.23 ^{2,4}	
LDH U/l	289.17 \pm 16.7	317.67 \pm 34.62	285 \pm 26.24	277 \pm 8.18 ²	295.5 \pm 19.51	285.33 \pm 7.56	
Alkaline phosphatase U/l	168.33 \pm 11.95	198.33 \pm 33.67	287.83 \pm 56.41 ^{1,2}	206.67 \pm 48.06 ³	203.67 \pm 46.52 ³	194.33 \pm 33.19 ³	
Calcium mmol/l	2.46 \pm 0.04	2.44 \pm 0.02	2.42 \pm 0.03	2.43 \pm 0.05	2.43 \pm 0.03	2.47 \pm 0.04	
Magnesium mmol/l	1.01 \pm 0.01	1.02 \pm 0.02	1.02 \pm 0.02	1.04 \pm 0.02	1.03 \pm 0.02	1.03 \pm 0.02	
Sodium mmol/l	153.67 \pm 0.33	147.5 \pm 1.95 ¹	150.83 \pm 1.87 ^{1,2}	146.83 \pm 1.28 ¹	152.5 \pm 0.99 ^{2,4}	151.33 \pm 1.36 ^{2,4}	
Chloride mmol/l	100 \pm 1.06	98.17 \pm 1.9	99.83 \pm 2.06	98 \pm 1.75	100.17 \pm 1.08	100.17 \pm 1.54	
RBC count (1x10 ¹² /l)	13.59 \pm 1.03	11.82 \pm 0.83 ¹	11.06 \pm 0.41 ¹	12.53 \pm 1.23	11.05 \pm 0.65 ¹	11.62 \pm 0.72 ¹	
WBC count (1x10 ⁹ /l)	14.33 \pm 1.57	12.6 \pm 1.49	12.85 \pm 1.46	12.27 \pm 0.9	10.25 \pm 0.69 ^{1,2,3}	10.65 \pm 1.24 ¹	
Haemoglobin (g/l)	134.67 \pm 7.31	118.17 \pm 5.26 ¹	116.67 \pm 5.42 ¹	119.33 \pm 3.33 ¹	118.5 \pm 5.8 ¹	111.83 \pm 4.81 ¹	
Eosinophiles (%)	3 \pm 0.58	3.67 \pm 0.95	3.33 \pm 0.95	4.33 \pm 1.12	3.67 \pm 0.8	3.17 \pm 0.48	
Metamyelocytes(%)	0.33 \pm 0.21	0.17 \pm 0.17	0.5 \pm 0.34	0.5 \pm 0.34	0.33 \pm 0.21	0.33 \pm 0.21	
Band neutrophiles (%)	1.5 \pm 0.43	1.5 \pm 0.56	2.17 \pm 0.31	2.17 \pm 0.48	1.17 \pm 0.4 ^{3,4}	1.33 \pm 0.33 ^{3,4}	
Segmented neutrophiles (%)	25.33 \pm 1.15	24 \pm 0.97	22.5 \pm 1.31 ¹	21.67 \pm 0.67 ^{1,2}	23.33 \pm 0.81	25.17 \pm 0.83 ^{3,4,5}	
Lymphocytes (%)	67.5 \pm 1.41	69.5 \pm 1.36	70.83 \pm 2.17 ¹	70.33 \pm 1.84	71.17 \pm 1.17 ¹	69.33 \pm 1.41	
Monocytes (%)	0.5 \pm 0.34	0.83 \pm 0.4	0.67 \pm 0.33	0.83 \pm 0.4	0.33 \pm 0.21	0.67 \pm 0.33	
Basophiles (%)	0.17 \pm 0.17	0.33 \pm 0.21	0.17 \pm 0.17	0.17 \pm 0.17	0 ²	0.17 \pm 0.17	

¹- Significantly different from the control values (day 0), P < 0.05;²- Significantly different from day 1, P < 0.05;³- Significantly different from day 3, P < 0.05;⁴- Significantly different from day 5, P < 0.05;⁵- Significantly different from day 10, P < 0.05.

Table 5. Changes in some blood biochemical parameters after a 5-day kanamycin treatment (10 mg/kg) administered to 6 female goats (mean ± SEM).

Parameter	Days						
	0	1	3	5	8	17	
Total protein g/l	71.3 ± 1.37	81.06 ± 1.11 ¹	83.52 ± 1.17 ¹	83.71 ± 2.62 ¹	80.32 ± 1.48 ^{1,3,4}	80.06 ± 1.9 ^{1,3,4}	
Blood glucose mmol/l	2.34 ± 0.22	2.13 ± 0.07 ¹	2.09 ± 0.08 ¹	1.79 ± 0.05 ^{1,2,3}	1.89 ± 0.06 ^{1,2,3}	2.11 ± 0.05 ^{1,4,5}	
Total lipids g/l	2.54 ± 0.2	2.31 ± 0.25	2.04 ± 0.18 ¹	2.68 ± 0.08 ^{2,3}	2.86 ± 0.17 ^{1,2,3}	2.6 ± 0.01	
Creatinine mmol/l	104.17 ± 5.34	111.67 ± 4.52	118.17 ± 2.29 ¹	121.17 ± 8.35 ¹	99.83 ± 5.81 ^{2,3,4}	98.83 ± 4.99 ^{2,3,4}	
Urea mmol/l	5.91 ± 0.52	6.97 ± 0.96	6.62 ± 0.96	6.31 ± 0.57	5.94 ± 0.67	5.87 ± 0.78	
LDH U/l	350.67 ± 21.95	345.5 ± 19.62	357 ± 17.34	297.83 ± 15.61	318.83 ± 18.82	339.17 ± 22.02	
Alkaline phosphatase U/l	127.83 ± 54.82	101.67 ± 29.54	111.33 ± 30.58	121.83 ± 39.91	113.33 ± 36.8	109.17 ± 36.96	
Calcium mmol/l	2.08 ± 0.04	1.94 ± 0.05 ¹	2.1 ± 0.06 ²	2.14 ± 0.04 ²	2.05 ± 0.04 ^{2,4}	1.93 ± 0.05 ^{1,3,4,5}	
Magnesium mmol/l	1.1 ± 0.03	1.04 ± 0.03 ¹	1.03 ± 0.02 ¹	1 ± 0.04 ¹	0.93 ± 0.02 ^{1,2,3,4}	1.06 ± 0.01 ^{4,5}	
Sodium mmol/l	144.17 ± 1.14	137 ± 1.55 ¹	139 ± 1.37 ¹	142 ± 1.73 ^{2,3}	137.67 ± 1.2 ^{1,4}	136.67 ± 1.96 ^{1,4}	
Chloride mmol/l	107.67 ± 4.33	103.83 ± 5.05	89.83 ± 2.14 ^{1,2}	93.67 ± 0.88 ^{1,2}	99.67 ± 4.54 ^{1,3}	94.67 ± 4.51 ^{1,2}	
RBC count (1x10 ¹² /l)	10.02 ± 1.02	9.37 ± 0.81	9.07 ± 0.82	11.24 ± 1.13 ^{2,3}	10.25 ± 1.26	11.57 ± 0.46 ^{2,3}	
WBC count (1x10 ⁹ /l)	13.33 ± 0.77	11.63 ± 1.32	11.7 ± 1.74	13.42 ± 1.18	14.05 ± 1.44	12.85 ± 1.64	
Haemoglobin (g/l)	90.5 ± 4.57	87.5 ± 4.68	83.67 ± 5.51	88.33 ± 5.12	88 ± 5.93	88.5 ± 5.73	
Eosinophiles (%)	5.33 ± 1.48	4.5 ± 0.85	5.83 ± 1.89	4.33 ± 0.61	3.5 ± 0.56 ³	3.17 ± 0.54 ^{1,3}	
Band neutrophiles (%)	1.33 ± 0.33	1.33 ± 0.42	1.17 ± 0.31	1.83 ± 0.65	2.83 ± 0.87 ^{1,2,3,4}	2.17 ± 0.31 ³	
Segmented neutrophiles (%)	22.83 ± 1.99	23.83 ± 2.95	28 ± 1.1 ^{1,2}	25.17 ± 1.38	26.5 ± 2.96	26.33 ± 2.08	
Lymphocytes (%)	69.17 ± 3.41	69.67 ± 3.4	64 ± 2.52 ²	67.67 ± 1.69	66.5 ± 3.97	67.33 ± 2.12	
Monocytes (%)	0.83 ± 0.31	0.67 ± 0.21	0.83 ± 0.31	0.67 ± 0.33	0.67 ± 0.21	0.33 ± 0.21 ^{1,3}	
Basophiles (%)	0.33 ± 0.21	01	0.17 ± 0.17	0.33 ± 0.21 ²	0.17 ± 0.17	0.33 ± 0.21 ²	

¹- Significantly different from the control values (day 0), P < 0.05;

²- Significantly different from day 1, P < 0.05;

³- Significantly different from day 3, P < 0.05;

⁴- Significantly different from day 5, P < 0.05;

⁵- Significantly different from day 10, P < 0.05.

Table 6. Changes in some blood biochemical parameters after a 5-day apramycin treatment (20 mg/kg) administered to 6 female goats (mean \pm SEM).

Parameter	Days					
	0	1	3	5	8	15
Total protein g/l	79.81 \pm 5.84	86.88 \pm 1.23 ¹	89.34 \pm 2.78 ¹	84.1 \pm 0.83 ³	87.04 \pm 1.82 ¹	82.78 \pm 0.91 ³
Blood glucose mmol/l	1.96 \pm 0.1	1.86 \pm 0.09	2.19 \pm 0.05 ^{1,2}	1.94 \pm 0.15 ³	1.64 \pm 0.05 ^{1,2,3}	1.8 \pm 0.12 ^{3,4}
Total lipids g/l	2.29 \pm 0.24	2.31 \pm 0.06	2.34 \pm 0.17	2.4 \pm 0.13	2.09 \pm 0.08 ⁴	2.11 \pm 0.11 ⁴
Creatinine mmol/l	103.67 \pm 7.73	99.5 \pm 7.19	100.5 \pm 5.82	104.17 \pm 4.07	95.5 \pm 3.53	105 \pm 5.85
Urea mmol/l	7.04 \pm 0.42	8.32 \pm 0.38 ¹	7.84 \pm 0.45 ¹	7.84 \pm 0.4 ¹	7.18 \pm 0.48 ²	7.39 \pm 0.41 ²
LDH U/l	348.17 \pm 12.85	373.33 \pm 28.97	411.83 \pm 28.82 ¹	369.5 \pm 23.67	371.33 \pm 17.37	316.17 \pm 31.84 ^{2,3,4,5}
Alkaline phosphatase U/l	216.17 \pm 40.88	208.33 \pm 42.03	204.17 \pm 47.06	183.67 \pm 47.43	211.5 \pm 39.11	202.33 \pm 48.79
Calcium mmol/l	2.19 \pm 0.05	2.26 \pm 0.07	2.41 \pm 0.05 ^{1,2}	2.35 \pm 0.06 ¹	2.29 \pm 0.04 ³	2.38 \pm 0.04 ^{1,2,5}
Magnesium mmol/l	103.5 \pm 1.89	99.83 \pm 3.23	102.17 \pm 3.22	96.33 \pm 2.7 ^{1,3}	95 \pm 3.61 ^{1,3}	99.17 \pm 1.8
Sodium mmol/l	137 \pm 2.41	140.33 \pm 1.54	138.83 \pm 1.3	139.5 \pm 2.32	134.17 \pm 1.14 ^{2,3,4}	138.33 \pm 2.44 ⁵
Chloride mmol/l	92.17 \pm 4.64	86 \pm 4.34	83 \pm 2.54 ¹	90.67 \pm 5.63 ³	93 \pm 2.45 ^{2,3}	89 \pm 2.45
RBC count ($1 \times 10^{12}/l$)	13.89 \pm 1.04	11.13 \pm 0.361	11.38 \pm 0.64 ¹	13.11 \pm 0.65 ^{2,3}	10.79 \pm 0.36 ^{1,4}	11.11 \pm 0.45 ^{1,4}
WBC count ($1 \times 10^9/l$)	15.5 \pm 1.59	14.62 \pm 1.35	13.72 \pm 0.96	14.42 \pm 2.18	11.7 \pm 1.28 ^{1,2,4}	12.43 \pm 1.08 ¹
Haemoglobin (g/l)	108.17 \pm 5.56	102.67 \pm 6.0	103.5 \pm 4.95	101.5 \pm 5.44	102 \pm 4.76	108.67 \pm 4.09
Eosinophiles (%)	4.33 \pm 0.42	3.17 \pm 0.6	4.83 \pm 1.51 ²	3.5 \pm 0.22	4.17 \pm 0.91	4.33 \pm 0.76
Metamyelocytes(%)	0.17 \pm 0.17	0.17 \pm 0.17	0	0	0.33 \pm 0.21	0.33 \pm 0.21
Band neutrophiles (%)	1 \pm 0.37	1 \pm 0.37	0.83 \pm 0.17	0.67 \pm 0.21	1 \pm 0.26	1 \pm 0.26
Segmented neutrophiles (%)	25.83 \pm 2.51	26 \pm 2.07	23 \pm 1.91	23.5 \pm 2.67	21.83 \pm 1.33 ^{1,2}	23.17 \pm 1.76
Lymphocytes (%)	67.83 \pm 2.44	69 \pm 1.93	70.33 \pm 3.08	71.17 \pm 2.27	71.83 \pm 1.68	72.17 \pm 1.88 ¹
Monocytes (%)	0.5 \pm 0.34	0.67 \pm 0.33	0.67 \pm 0.34	0.83 \pm 0.31	0.67 \pm 0.21	0.5 \pm 0.34
Basophiles (%)	0.33 \pm 0.21	0.17 \pm 0.17	0.33 \pm 0.21	0.5 \pm 0.34	0.17 \pm 0.17	0.17 \pm 0.17

¹- Significantly different from the control values (day 0), $P < 0.05$;²- Significantly different from day 1, $P < 0.05$;³- Significantly different from day 3, $P < 0.05$;⁴- Significantly different from day 5, $P < 0.05$;⁵- Significantly different from day 10, $P < 0.05$.

Table 7. Changes in some blood biochemical parameters after a 5-day spectinomycin treatment (20 mg/kg) administered to 6 female goats (mean ± SEM).

Parameter	Days					
	0	1	3	5	8	15
Total protein g/l	84.12 ± 1.46	78.21 ± 2.09 ¹	76.04 ± 0.89 ¹	82.59 ± 1.01 ^{2,3}	78.72 ± 1.79 ^{1,3,4}	78.15 ± 1.14 ^{1,4}
Blood glucose mmol/l	2.74 ± 0.1	2.16 ± 0.07 ¹	2.06 ± 0.04 ¹	1.98 ± 0.11 ^{1,2}	2.1 ± 0.07 ¹	2.31 ± 0.05 ^{1,2,3,4,5}
Total lipids g/l	2.96 ± 0.13	2.38 ± 0.12 ¹	2.14 ± 0.1 ^{1,2}	2.71 ± 0.08 ^{1,2,3}	2.51 ± 0.1 ^{1,3,4}	2.4 ± 0.08 ^{1,3,4}
Creatinine mmol/l	93.67 ± 5.93	95.33 ± 6.38	90 ± 5.26	86.17 ± 5.69	95.33 ± 7.91	97 ± 8.15
Urea mmol/l	6.22 ± 0.45	5.97 ± 0.5	6.5 ± 0.22	7.13 ± 0.6 ^{1,2}	6.28 ± 0.25 ⁴	6.61 ± 0.13
LDH U/l	222.67 ± 29.69	205.33 ± 13.99	194.33 ± 14.15	209.17 ± 17.18	201.17 ± 15.91	234.5 ± 23.11 ³
Alkaline phosphatase U/l	115.6 ± 72.47	126.2 ± 70.26	114.2 ± 67.75	107 ± 57.06	104 ± 48.2	113.4 ± 64.13
Calcium mmol/l	2.23 ± 0.07	2.13 ± 0.11	1.9 ± 0.04 ^{1,2}	1.89 ± 0.04 ^{1,2}	1.93 ± 0.04 ^{1,2}	1.98 ± 0.02 ^{1,2}
Magnesium mmol/l	0.95 ± 0.04	1.13 ± 0.02 ¹	1.12 ± 0.04 ¹	0.98 ± 0.03 ^{2,3}	1 ± 0.03 ^{2,3}	0.97 ± 0.02 ^{2,3}
Sodium mmol/l	148.83 ± 1.89	148.83 ± 2.48	144 ± 2.44 ^{1,2}	144.5 ± 2.88	151.17 ± 2.96 ^{3,4}	147.83 ± 1.89
Chloride mmol/l	113.67 ± 7.26	93.83 ± 4.57 ¹	105.83 ± 5.74 ²	107.17 ± 3.87 ²	94.67 ± 3.4 ^{1,3,4}	105.17 ± 4.22 ^{2,5}
RBC count (1x10 ¹² /l)	13.47 ± 1.18	11 ± 0.4 ¹	11.3 ± 0.82 ¹	11.06 ± 0.4 ¹	10.36 ± 0.64 ¹	11.31 ± 0.94 ¹
WBC count (1x10 ⁹ /l)	12 ± 1.0	16.33 ± 0.71 ¹	16.5 ± 1.26 ¹	17.33 ± 1.43 ¹	14.33 ± 1.82 ⁴	14.67 ± 1.74 ^{1,4}
Haemoglobin (g/l)	112 ± 5.0	103.67 ± 5.73	98.33 ± 5.28 ¹	98.83 ± 5.49 ¹	101.5 ± 7.05 ¹	99.67 ± 6.36 ¹
Eosinophiles (%)	4.67 ± 0.45	5 ± 0.67	1.67 ± 0.27 ^{1,2}	5.83 ± 1.2 ³	3.66 ± 0.87 ³	3.5 ± 0.85 ³
Band neutrophiles (%)	1.17 ± 0.31	1 ± 0.26	3.17 ± 1.66 ^{1,2}	1 ± 0.26 ³	1.33 ± 0.33 ³	1.5 ± 0.22 ³
Segmented neutrophiles (%)	30 ± 3.47	28.5 ± 3.82	27.33 ± 3.56	30.17 ± 3.86	31.83 ± 6.0	35.5 ± 2.2 ³
Lymphocytes (%)	63.83 ± 4.09	64.83 ± 3.28	67.5 ± 3.9	62.33 ± 3.67	62.67 ± 6.71	59.33 ± 2.4 ³
Monocytes (%)	0.17 ± 0.17	0.33 ± 0.21	0.17 ± 0.17	0.33 ± 0.33	0.33 ± 0.21	0.17 ± 0.17
Basophiles (%)	0.17 ± 0.17	0.33 ± 0.33	0.17 ± 0.17	0.33 ± 0.33	0.17 ± 0.17	0

¹- Significantly different from the control values (day 0), P < 0.05;

²- Significantly different from day 1, P < 0.05;

³- Significantly different from day 3, P < 0.05;

⁴- Significantly different from day 5, P < 0.05;

⁵- Significantly different from day 10, P < 0.05.

Urea. Increased levels were measured between day 1 and day 5 after treatment with all antibiotics followed by a return to the initial values.

Total lipids. Slight and uneven changes in total lipids were measured, and there was a tendency toward regaining the initial values after cessation of treatment.

LDH. The highest levels were determined between day 1 and day 3, and afterwards a tendency toward a decrease in plasma levels to the initial values was observed. Spectinomycin did not cause any alterations.

Alkaline phosphatase. Its values varied widely in the different experiments. Only amikacin showed a marked ability to increase alkaline phosphatase activity.

Calcium, magnesium, sodium, and chloride. There were slight and uneven changes in these parameters. As a whole, antibiotics administration tended to decrease serum sodium and chloride levels.

Haematological parameters. All antibiotics (excluding kanamycin) caused decreases in RBC counts, total WBC counts, and haemoglobin concentrations. There was not a tendency toward a return to the initial values after drug administration. In differential WBC counts slight and uneven changes occurred after antibiotic administration: lymphocyte percentage was unaltered or increased, and neutrophil percentage was usually decreased.

Discussion

Creatinine and urea values are primarily connected with kidney function. According to our data for these indices, it appears that gentamicin shows the highest potential to alter renal function. Tobramycin has slightly less influence on these 2 blood parameters than gentamicin at this dose. Kanamycin caused higher increases in urea concentration than amikacin, but the tendency for plasma creatinine concentration was the opposite. Therefore, these 2 aminoglycosides expressed

almost equal ability to change these parameters. After aminocyclitol administration only increased urea levels were observed. These results are in agreement with other reports for comparative investigations of plasma creatinine and urea levels after gentamicin (2-6,11), tobramycin (3,5,6), amikacin (3,4,11), and kanamycin treatment (11). There are no such data for aminocyclitol antibiotics. The changes in plasma creatinine and urea levels might be due to accumulation of aminoglycosides and aminocyclitols in the renal cortex (14). Gentamicin, amikacin, tobramycin, and apramycin increased urea levels slightly above reference values for goats and this may have some clinical significance (15). Creatinine levels were within the normal range during the whole experiments with both aminoglycosides and aminocyclitols (16).

The observed tendency toward decreases in blood glucose and insignificant changes in total protein levels was in agreement with other investigations (10,11). According to other reports, there was a slight rise in alkaline phosphatase and LDH activity (10), as observed in our research.

These experiments confirmed our hypothesis that, in therapeutic doses, some drugs may cause changes in some haematological and biochemical values, and therefore may be the reason for incorrect diagnoses and improper medication. Our results could be regarded as data providing information about the possible changes that might occur and could be useful when continuing administration of aminoglycosides and aminocyclitols is needed. Although in the present paper we did not perform any statistical analysis between different antibiotics for the rates of change, we can conclude that aminoglycoside antibiotics are more powerful factors in changing the blood parameters investigated than aminocyclitols and especially those connected with renal function.

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