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# INFECTION WITH *Strongyloides papillosus* IN SHEEP: EFFECT OF PARASITIC INFECTION AND TREATMENT WITH ALBENDAZOLE ON BASIC HAEMATOLOGICAL PARAMETERS

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**Abstract:** The aim of this study was to determine and evaluate the basic haematological parameters in conditions of natural infection of sheep with *Strongyloides papillosus*, as well as after the administration of antihelminthic albendazole (ABZ). Based on the intensity of infection with *S. papillosus* the sheep were divided into three groups: mild, moderate and high, and after that the sheep received a single dose of ABZ of 5mg/kg per body weight, per orally. Sampling of faeces and blood for parasitological and haematological assaying respectively, was performed on the 0 and the 21$^{st}$ day after the treatment with ABZ. The presence of parasitic infection with *S. papillosus* leads to a decrease of erythrocyte count, while the lowest values were established in the group with the highest intensity of parasitic infection ($p < 0.001$). After treatment with ABZ the decrease of erythrocyte count was more prominent, which was, based on comparison with control groups $C_1$ and $C_2$, unequivocally established to be the consequence of treatment with ABZ. Detected values of haematocrit and erythrocyte indices indicated the presence of parasitic infection: the lowest values were established in the group with the highest intensity of parasitic infection. After treatment with ABZ haematocrit levels in control group $C_2$ were statistically significantly lower compared to the control group $C_1$ ($p < 0.001$). In the presence of parasitic infection, the neutrophil and eosinophil counts increased almost linearly up to the value of 44.24±2.50% and 13.29±0.61% respectively, in the group of sheep with the highest intensity of parasitic infection ($p < 0.001$; compared to control group $C_1$). After treatment with ABZ the decrease of the number of these white blood cells is statistically significant ($p < 0.001$). Bearing in mind our previous research and the connection of disbalanced redox equilibrium after the treatment with ABZ with

changes, it is necessary to include antioxidative substances in the anti-parasitic treatment protocols.

**Keywords:** *Strongyloides papillosus*, albendazole, haematological parameters, sheep

# Introduction

Parasitic form of *Strongyloides papillosus* is represented by parthenogenic females present in the sheep small intestines *(Kassai, 1999)*. The infection occurs by introduction of infectious larvae (stage $L_3$) per orally, through food and water (passive) and/or by percutaneous (active) invasion of $L_3$ larvae. There is also a possibility of galactogen infection with larvae that migrated to the udder through systemic circulation right before birth *(Šibalić and Cvetković, 1996)*. Pathogenic effect of the parasite on the host is a result of the presence of migrating larvae and/or adult forms in small intestine, which damage the host's tissues mechanically and by their secretory/excretory products. Larvae that actively penetrate the host's organism by rupturing the skin in the interdigital region enable the invasion of other etiological agents *(Abott and Lewis, 2005)*. The presence of *S. papillosus* and its developmental forms leads to the disturbance of the animal's health, not infrequently inducing a sudden death syndrome in young ruminants (lambs and calves) due to heart failure. It was also established that the degree of damage directly correlates to the intensity of parasitic infection, i.e. to the number of present parasites and/or their larval forms *(Kobayashi et al., 2009; Nakanishi et al., 1993; Ura et al., 1993; Nakamura et al., 1994)*. Disturbed gastrointestinal tract motility, which occurs during the infection with *S. papillosus*, is responsible for the occurrence of clinical symptoms (anorexia, weight loss and anaemia) and sudden death in infected animals *(Kobayashi et al., 2009)*. The same authors state that the exact mechanism that leads to the animal's death in case of infection with *S. papillosus* is still unknown.

Anaemic state in case of infection with *S. papillosus* is explained by the occurrence of erosions and ulcerations of the small intestinal mucosa and the consequential development of haemorrhagic enteritis *(Šibalić and Cvetković, 1996)*. The loss of blood and disturbances of food digestion and nutrient absorption that also occur are the reason behind the slow development of young animals, progressive weight loss in adult animals and change of haematological parameters.

On the other hand, the drugs used for treatment may also have adverse (side) effects on the treated organism. The most common drug used to treat infection with *S. papillosus* is albendazole (ABZ), benzimidazole's derivate and a broad-spectrum antihelminthic, which also effects the larvae of this parasite. The

key mechanism by which ABZ achieves its effect is a result of its interaction with eukaryotic cytoskeleton protein, tubulin, by inhibiting its polymerization into microtubules *(Rufener et al., 2009)*.

The objective of this research was to examine the effect of the intensity of infection with *S. papillosus* and treatment with ABZ on haematological parameters of sheep (erythrocyte count, haematocrit, leukocyte count, leukocyte differential count), as well as clinical significance of the resulting changes, with the purpose of possible amendments of the anti-parasitic treatment protocols used as part of the sheep health schemes. Also, we would like to emphasize that this research is a part of our previous continuous investigation *(Dimitrijević et al., 2012; Dimitrijević et al., 2015)*, of the same experimental model, but this time in course of changes of cellular components of sheep blood.

# Material and methods

### Experimental animals

All experiments involving animals were conducted in accordance with the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other (Official Daily N. L 358/1–358/6, 18, December 1986).

This study was performed in the vicinity of the city of Vranje (south-east Serbia (village Kupinince, geographic coordinates: 42°29’46.98’’ N, 21°53’50.10’’E), in a hilly-mountainous region with pastures located at altitudes between 350 and 650 m. The climate is continental, with long, cold winters and hot summers, which plays a very important role in the sterilization of pastures from infectious stages of geohelminth parasites, which also include *Strongyloides spp*. Overnight the examined sheep stayed in a shelter covered with deep litter, which represents a predisposing factor for continuous infection with *S. papillosus*. The sheep’s diet was based on daily grazing and after return to their shelter the sheep also received coarsely ground corn (cca 200 g/per day). Water and livestock salt were available *ad libitum*.

The research was carried out on Württemberg sheep (n=40), 2-3 years old, in which an infection with *S. Papillosus* was established by parasitological testing. Depending on the intensity of the infection the animals were divided into three groups ($A_1$ -mild; $A_2$ -moderate and $A_3$ -high intensity of infection with *S. papillosus*). After that the sheep were treated with ABZ, per orally, in single dose of 5 mg/kg and they are represented in results as groups $B_1$, $B_2$ and $B_3$. Control group consisted of sheep (n=10) that were negative to the presence of this parasite and after treatment with ABZ they were represented in the results as group $C_2$.

**Sampling of faeces for parasitological examination**

Samples of faeces were obtained individually from each sheep, directly from rectal ampoule, once a day for three days, packed in separate labelled plastic bags and transported in a portable refrigerator to a parasitological laboratory.
Standard keys for identification of parasites and their developmental forms based on morphological and morphometric characteristics of eggs, larvae and/or adult forms were used for detection and determination of parasites and their developmental forms. Sedimentation and flotation methods were used for coprological diagnostics *(Kassai, 1999)*. The examination of the samples was performed at magnification of 7x10 and 7x40 on Reichert microscope, Germany. The intensity of infection was established by counting the number of helminth eggs per gram of faeces using McMaster's method *(Euzeby, 1982)*.

**Sampling of blood for haematological examination**

The blood samples from sheep were obtained by punctuating *v. jugularis*, with restraining of animals, before dehelminthisation (day 0) and on the 21$^{st}$ day after dehelminthization with ABZ. The blood was sampled in plastic, sterile test tubes *(Vacuete, USA)*, using heparin as anticoagulant and it was transported in a portable refrigerator to a haematological laboratory. The blood was analysed using *Abacus Junior Vet Diatron* haemocytometer *(Mi. PLC, Hungary)*. Relative portion of individual types of white blood cells (neutrophils, eosinophils and lymphocytes) was expressed as a percentage in relationship to the total leukocyte count.

**Statistical analysis**

Statistical analysis of the results was performed by using computer program GraphPad Prism 5.00 (San Diego, CA, USA). Statistical significance of differences of the examined parameters was determined by means of the ANOVA test, followed by a Tukey test. The results were expressed as means ± standard error. Significance level was set at $p \leq 0.05$.

# Results and Discussion

Albendazole is a drug of choice for treatment of strongyloidosis and other parasitic infections (*Kassai, 1999*). Results of the examination of the intensity of parasitic infection with *S. papillosus* before and after dehelminthisation with ABZ are shown in Table 1.

**Table 1. Intensity of parasitic infection with *S. papillosus* determined based on the number of eggs/g of faeces (means ± standard error), before and after dehelminthisation with ABZ**

| | **Intensity of infection (no. of eggs/g of faeces)** | | | | | |
|---|---|---|---|---|---|---|
| | **Before treatment with ABZ** | | | **After treatment with ABZ** | | |
| **Sheep group** | $A_1$ (n=10) | $A_2$ (n=10) | $A_3$ (n=10) | $B_1$ (n=10) | $B_2$ (n=10) | $B_3$ (n=10) |
| | 832±34.7 | 1320±56.1 | 2918±146.5 | 0 | 0 | 0 |

Analysis of the results of coprological examination before and after dehelminthisation shows that the administered antihelminthic (ABZ) was 100% efficient (Table 1). This dehelminthisation result is interesting considering the data that can be found in scientific literature regarding the increasing number of cases of parasite resistance to ABZ (Rufener et al., 2009). This effect of ABZ in our study can be explained by the fact (obtained from anamnestic data regarding the sheep treatment) that this drug was used for the first time on treated animals, which greatly eliminated the possible presence of resistant forms of *S. papillosus* in the treated sheep population.

**Table 2. Values of basic haematological parameters (means ± standard error), in sheep infected with *S. papillosus*, before ($A_1$ – mild; $A_2$ – moderate; $A_3$ – high intensity of parasitic infection) and after ($B_1$ – mild; $B_2$ – moderate; $B_3$ – high intensity of parasitic infection) treatment with ABZ; $C_1$ – negative control group; $C_2$ – negative control group treated with ABZ**

| Parameter | $C_1$ (n=10) | Before treatment with ABZ | | | After treatment with ABZ | | | $C_2$ (n=10) |
|---|---|---|---|---|---|---|---|---|
| | | $A_1$ (n=10) | $A_2$ (n=10) | $A_3$ (n=10) | $B_1$ (n=10) | $B_2$ (n=10) | $B_3$ (n=10) | |
| Erythrocytes (x $10^{12}$/L) | 11.58±0.32 | 10.21±0.51 * | 9.41±0.41 ** | 8.83±0.23 *** | 9.27±0.35 + | 8.67±0.29 ++ | 8.08±0.51 + | 8.53±0.24 ### |
| Haemoglobin (g/L) | 141.25±2.32 | 137±4.32 | 131±5.19 | 119±6.61 | 135±3.41 | 130±2.28 | 101±1.81 | 110.30±3.11 |
| Haematocrit (%) | 0.48±0.02 | 0.46±0.01 | 0.44±0.02 | 0.41±0.02 ** | 0.45±0.01 | 0.44±0.01 | 0.40±0.01 | 0.40±0.02 ### |
| MCV (fl) | 45.72±0.67 | 43.29±0.71 | 42.17±0.69 | 39.59±0.60 | 43.98±0.61 | 43.81±0.59 | 44.79±0.84 | 44.80±0.64 |
| MCH (pg) | 11.85±0.12 | 10.89±0.24 | 10.71±0.15 | 8.82±0.17 | 9.90±0.12 | 9.98±0.17 | 8.15±0.09 | 10.91±0.08 |
| MCHC (g/L) | 264±9.53 | 269±12.61 | 274±15.21 * | 277±18.11 ** | 274±15.68 | 276±17.14 | 282±18.24 | 273±14.76 ## |
| Platelets (x $10^9$/L) | 273±58.21 | 299±61.93 | 350±47.73 * | 402±39.61 ** | 301±41.51 | 324±39.45 | 310±45.21 ++ | 261±47.21 |
| Leukocytes (x $10^9$/L) | 11.05±0.21 | 11.52±0.30 | 12.28±0.29 | 13.37±0.19 | 11.31±0.35 | 11.94±0.28 | 11.99±0.31 | 10.65±0.29 |
| Neutrophils (%) | 36.81±2.54 | 38.08±2.22 * | 38.51±2.89 * | 44.24±2.50 *** | 34.12±1.99 | 34.59±2.34 | 36.08±2.42 | 35.38±2.12 |
| Eosinophils (%) | 2.12±0.24 | 4.35±0.41 ** | 6.48±0.58 *** | 13.29±0.61 *** | 3.21±0.24 + | 3.59±0.81 ++ | 4.09±0.31 +++ | 1.91±0.64 |
| Lymphocytes (%) | 61.07±8.24 | 57.57±11.21 | 55.01±8.56 | 42.47±9.94 | 62.67±8.15 | 61.82±8.10 | 59.83±10.24 | 62.71±7.54 |

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ – in relationship to control group $C_1$

+ $p < 0.05$; ++ $p < 0.01$; +++ $p < 0.001$ – comparison between groups before and after dehelminthisation ($A_1$ vs $B_1$;A2 vs $B_2$; $A_3$ vs $B_3$)

## $p < 0.01$; ### $p < 0.001$ – comparison of control groups $C_1$ vs $C_2$

There is a large amount of data in the literature regarding the effects of parasitic infections on certain haematological parameters *(Saleh, 2008)*. However, the data regarding the effects and possible mechanism of action of antihelminthics used for treatment of parasitic infection are scarce, therefore, the aim of this study was to determine the changes of haematological parameters and correlate them with the possible mechanism of action of antihelminthics on certain blood cells in treated animals.

In our study we established, the same as other researchers *(Nakanishi et al., 1993)*, that the number of erythrocytes decreases with the intensity of parasitic infection reaching the lowest results in the group of sheep with high intensity of infection (8.83±0.23 x $10^{12}$/L), compared to the control $C_1$ group (11.58±0.32 x $10^{12}$/L), at the statistically significant level of $p < 0.001$. After treatment with ABZ we also detected downward trend for erythrocyte count and based on the erythrocyte count in group $C_2$ (8.53±0.24 x $10^{12}$/L), this finding was exclusively attributed to the effects of ABZ. In order to explain this finding in our study, we analysed data from literature on pharmacodynamics and pharmacokinetics of ABZ.

After peroral administration ABZ is metabolized in the sheep's organism through a two-step sulphoxidation *(Velik et al., 2004)*. Sulphoxidation is a rapid and reversible process in which the equilibrium favours formation of ABZ sulphoxide (ABZSO). ABZSO has a chiral centre and it is most likely that the formation of (+)ABZSO is influenced by flavin-containing monooxygenases (FMO). Albendazole-sulphoxide also undergoes second sulphoxidation (which occurs via cytochromes – CYP), wherein inactive metabolite albendazole-sulphone (ABZSO2) is generated *(Cristofol et al., 1998; Velik et al., 2005; Skalova et al., 2007; Capece et al., 2009)*. During the process of biotransformation of ABZ through a series of consecutive reactions on CYP and FMO (reduction, protonation, addition of oxygen, homolytic splitting of oxygen, etc.) reactive species of oxygen (ROS) and nitrogen (RNS) are generated and consequent "leakage" of these species from the biotransformation system may occur *(Guengerich, 2008)*. According to *Dubin and Goijman (1984)*, generation of ROS/RNS during redox cycling of nitroheterocyclic drugs (which also include ABZ) represents a determining factor for the intensity of peroxidative processes. Although most of the researchers in the field of pharmacokinetics of ABZ claim that practically the entire amount of this drug after peroral administration is eliminated from blood and gastrointestinal tract after 60–70 hours *(Alvarez et al., 1997; Moreno et al., 2004)*, due to the reversibility of the process ABZ↔ABZSO, the amount of ROS/RNS generated during the biotransformation of ABZ is not negligible *(Dimitrijević et al., 2012)*. Also, bearing in mind that once the peroxidative process starts it can be efficiently ended only if adequate amounts of antioxidants are present, it can be assumed that the peroxidative effect of ABZ lasts much longer than the half-life of its elimination *(Dimitrijević et al., 2012)*. In a 10-day experiment in which rats were perorally treated with ABZ *Locatelli et al.*

*(2004)* established that the treated animals were incapable of maintaining equilibrium between production and neutralization of ROS/RNS and avoiding adverse effect of these reactive species on the cellular homeostasis. In our previous study *(Dimitrijević et al., 2012)* we established that the level of oxidative stress in sheep was more prominent after the treatment with ABZ, compared to the level of oxidative stress determined in case of various intensities (mild, moderate, high) of parasitic infection with *S. papillosus*. On the other hand, detected decrease of erythrocyte count that correlates with the intensity of parasitic infection, as well as after the treatment with ABZ (Table 2) can be explained by the effect of ROS/RNS on erythrocytes. Erythrocytes are highly specialized cells that don't have nuclei (except in birds), which means that their antioxidative defence capacity is limited by the amount, i.e. the activity of the antioxidative enzymes that are already present in them. In other words, there is no *de novo* synthesis of antioxidative enzymes in erythrocytes, which shortens their half-life in conditions of disturbed redox equilibrium, considering that the erythrocyte's membrane, as part of the cell that is the most sensitive to the effects of the ROS/RNS, becomes fragile and brakes easily while traveling through the capillary network *(Burak, 2008)*.

Beside the fact that the increase of its value indicates the degree of dehydration, haematocrit is also a good indicator used for the detection of the presence of parasitic infection *(Amarante et al., 2004)* because its decreased value indicates possible presence of endoparasites. The results of this study are in concordance with this, given that we established the lowest haematocrit values in the group of sheep with the highest intensity of parasitic infection (0.41±0.02%), with statistical significance of $p < 0.01$, compared to control group $C_1$ (0.48±0.02%). Haematocrit values continue to decrease after dehelminthisation, which was in this case attributed to the effects of ABZ, given that the lowest haematocrit values were established in control group $C_2$ (0.40±0.02%), with statistical significance of $p < 0.01$, compared to control group $C_1$. Erythrocyte indices (MCV, MCH, MCHC) give information about the average cell size, the amount of haemoglobin and proportion of haemoglobin content in erythrocytes *(Radojičić, 2007)*. Slightly higher values of MCV represent a sign of cell's regenerative response, which was in our case established after dehelminthisation with ABZ, but without statistical significance ($p > 0.05$) compared to control groups $C_1$ and $C_2$ (Table 2). MCHC values are thought to be the most precise erythrocyte index and they are usually elevated in case of haemolysis, which is in concordance with our findings, given that the highest values were established in the group with the highest intensity of parasitic infection (277±18.11 g/L), with statistical significance of $p < 0.01$; compared to control group $C_1$ (264±9.53 g/L). After treatment with ABZ, we also detected an increase of MCHC values in all examined groups, but without statistical significance compared to the groups before dehelminthisation ($p > 0.05$). By comparing the MCHC values in control groups $C_1$ and $C_2$ ($p < 0.01$), we detected an increase of value of this parameter,

which unequivocally indicates the effect of ABZ and its side effect of leading to haemolysis by disrupting the delicate redox equilibrium *(Burak, 2008)*.

The presence of parasites in the host triggers the defence mechanisms. First, unspecific line of defence are neutrophils that synthesize reactive oxygen species, superoxide anion radical (O2•-), in their structures *(Saleh, 2008; Radfar, 2008)*. Superoxide dismutase (SOD) is an enzyme that neutralises superoxide anion radical (O2•-) and the product of this enzyme reaction is hydrogen peroxide ($H_2O_2$). Hydrogen peroxide, in addition to decomposition by catalase enzyme can also be homolytically decomposed in the presence of ions of transition metals such as $Fe^{2+}$ and $Cu^{+}$ *(Valko et al., 2006, 2007)*. In that case a hydroxyl radical, the most potent oxygen radical, is generated. Due to its extreme reactivity, it unselectively reacts with all the groups of organic compounds, which in case of reaction with DNA can result in mutagenesis and cancerogenesis *(Jomova and Valko, 2011, Kryston et al., 2011)*. The term "double nature" of ROS/RNS relates to the fact that in low concentrations these reactive species have beneficial effects, while in higher concentrations they may cause damage to all cellular structures and biomacromolecules *(Marnett, 1999; Stevanović et al., 2012)*.

The results of our analyses show that with the increase of the intensity of parasitic infection, the neutrophil counts increase as well, achieving the highest values in the group of sheep with the highest intensity of parasitic infection (44.24±2.50%) compared to control group $C_1$ (36.81±2.54%); $p < 0.001$. A similar trend of the count increasing with the intensity of parasitic infection was also detected for eosinophils. It is well-known that parasitic infections are followed by an increase of eosinophil count *(Radojičić, 2007)*. In our study the greatest number of eosinophils was detected in the group with the highest intensity of infection (13.29±0.61%) with statistical significance of $p < 0.001$, compared to group $C_1$ (2.12±0.24%). After treatment with ABZ the number of eosinophils decreased (Table 2), which is understandable, considering that the stimulus, i.e. parasitic infection, was no longer present.

Analysis of the platelet count established that the values were within the physiological reference values *(Radojičić, 2007)*. However, we detected that with the increase of the intensity of parasitic infection the platelet count increased as well (Table 2) reaching the highest values in the group with moderate ($p < 0.05$) and high ($p < 0.01$) intensity of infection compared to control group $C_1$. After dehelminthisation a decrease of platelet count was detected; the greatest decrease was detected in group $B_3$, with statistical significance of $p < 0.01$. This type of variations, even though they are within reference values, are probably a result of small haemorrhages caused by the presence and migration of *S. papillosus*, which have an incentive effect on bone marrow where the platelets are produced.

Albendazole is an antihelminthic that has been very successfully used in veterinary medicine for more than 25 years. Bearing in mind its efficiency, the aim

of this study was not to emphasize the side effects of ABZ, but on the contrary, to indicate another aspect of its mechanism of action, in addition to the one that has already been described and generally accepted *(Rufener et al., 2009)*. Our research in the past five years unequivocally showed that both the presence of parasitic infection and the treatment with ABZ induce the state of oxidative stress in the organism *(Dimitrijević et al., 2012)*. Some antihelminthics are known to achieve their effect by also interfering with the metabolic processes of the parasite thus increasing the production of ROS and RNS *(Locateli et al., 2004)*. Helminths are anaerobic or in certain stages of their development optionally aerobic organisms that live in the environments with low partial pressure of oxygen. For that reason, the majority of parasites does not possess or they have lost mechanism for neutralisation of ROS and RNS during regressive evolution, or their capacity is negligible compared to aerobic organisms that during evolution developed specialized mechanisms in order to protect themselves from the toxic effects of oxygen *(Locatelli et al., 2004; Dzik, 2005)*. On the other hand, increased exposure to ROS and RNS leads the cell to the state of oxidative stress and results in a damage of biomacromolecules (lipids, proteins and nucleic acids), which may induce programmed cell death (apoptosis) leading to development of malignant cell or uncontrolled cell death (necrosis). This mechanism is the basis for development of nearly every disease *(Lykessfeldt and Svendsen, 2007)*.

## Conclusion

The results of our research indicate that the presence of infection of sheep with *S. papillosus* leads to the development of various degrees of anaemia depending on the intensity of parasitic infection, which, bearing in mind our previous research *(Dimitrijević et al., 2012; Dimitrijević et al., 2015)*, is a consequence of the development of various levels of oxidative stress depending on the intensity of parasitic infection. Dehelminthisation with ABZ further increased the degree of anaemia in all examined sheep. Bearing in mind this finding and the development of oxidative stress, phenomenon which is the basis of this condition, further research is necessary in order to define adequate treatment protocols for parasitic infections (which include administration of ABZ), first of all in terms of including substances with antioxidative properties.

# Infekcija ovaca sa *Strongyloides papillosus*: Uticaj intenziteta parazitske infekcije i terapije albendazolom na vrednosti osnovnih hematoloških parametara

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## Rezime

Cilj ovog istraživanja bio je da se utvrde i procene osnovni hematološki parametri u uslovima prirodne infekcije ovaca sa *Strongyloides papillosus*, kao i nakon primene antihelmintika albendazola (ABZ). Na osnovu intenziteta infekcije sa *S. papillosus* ovce su podeljene u tri grupe: niski, srednji i visoki intenzitet infekcije, a zatim su ovce jednokratno dobile peroralno ABZ, u terapijskoj dozi od 5 mg/kg telesne mase. Uzorkovanje fecesa za parazitološka i za hematološka ispitivanja obavljeno je nultog i 21. dana od primene ABZ. Utvrđeno je da prisustvo parazitske infekcije sa *S. papillosus* dovodi do pada broja eritrocita, pri čemu su najniže vrednosti utvrđene u grupi sa najvećim intenzitetom parazitske infekcije ($p < 0,001$). Nakon terapije sa ABZ pad broja eritrocita je izraženiji, što je nesumnjivo nastalo kao posledica terapije ABZ (na osnovu poređenja $C_1$ i $C_2$). Utvrđene vrednosti hematokrita i eritrocitnih indeksa su ukazivali na postojanje parazitske infekcije; najniže vrednosti su utvrđene kod grupe sa najvećim intenzitetom parazitske infekcije. Nakon terapije sa ABZ vrednosti hematokrita kod $C_2$ bile su statistički značajno niže u odnosu na kontrolnu grupu $C_1$ ($p < 0,001$). U prisustvu parazitske infekcije broj neutrofila i eozinofila povećava se gotovo linearno, do vrednosti od 44,24±2,50% kod neutrofila, odnosno od 13,29±0,61% kod eozinofila u grupi ovaca sa najvećim intenzitetom parazitske infekcije ($p < 0,001$). Nakon terapije sa ABZ broj ovih ćelija bele krvne loze smanjuje se statistički značajno ($p < 0,001$). Imajući u vidu naša prethodna istraživanja i povezanost narušene redoks ravnoteže posle terapije sa ABZ sa promenama utvrđenim u ovom istraživanju, neophodno je u antiparazitske terapijske protokole uključiti antioksidativne supstance.

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