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Dynamics of hormone levels and immune activity in sheep during fasting, subsequent immobilization and the recovery period

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Abstract

Moneva, P., Yanchev, I., Tsaneva, M., Velikov, K. & Gudev, D.. (2025). Dynamics of hormone levels and immune activity in sheep during fasting, subsequent immobilization and the recovery period. *Bulg. J. Agric. Sci., 31*(3), 585–594

The object of this study was to investigate endocrine and immune responses during the four-day fast, subsequent immobilization and the recovery period in ewes. One-hundred Ile de France ewes were allocated into two groups (n = 14) according to their baseline hematocrit level: group I – low hematocrit, group II – high hematocrit level. A third (n = 10) control group was included, whose animals did not fast but were also stressed by immobilization. The effect of fasting in sheep with low and high hematocrit was examined via 4 days fasting, followed by 30 minutes of immobilization. The following parameters were measured: cortisol, growth hormone, T3, T4, estradiol-17β, N/L ratio, reticulocytes (%). Immediately before the beginning and after the end of fasting, as well as on the 7th and 20th day after fasting, the weight of the animals was recorded. Blood samples were taken via jugular venepunction before the fasting (baseline level), at 24 h of fasting, after 4 days of fasting before immobilization, immediately after immobilization, during recovery period – at d7 and d20 after fasting.

The results allow the following conclusions to be drawn: Stress exerts a specific tissue activity that, at normal levels of cortisol (in order to conserve energy), activates the immune defense by using specific mechanisms (most likely activation of 11 beta-hydroxy-steroid dehydrogenase of leukocytes) allowing activation of the inactive cortisol and realizing the redistributing effect of cortisol by binding to the leukocytes glucocorticoid receptors. The unchanged level of T3 under fasting conditions confirms our hypothesis of tissue-specific activity, because increased lipolysis during fasting is most likely associated with an increased level of reversible T3 at an unchanged level of total T3, which allows, with unchanged metabolic activity, to carry out the specific activating effect of T3 on lipid metabolism Growth hormone, like other hormones, most likely also carries out tissue-specific activity, allowing activation of lipolytic activity at unchanged growth hormone values. A directly proportional relationship between growth hormone level and hematocrit level was found, which is probably related to the stimulating effect of growth hormone on erythropoietin. An inverse relationship between T3 and growth intensity was established. The data allow us to assert that when a hormone has several biological effects and the maintenance of homeostasis in a certain stressful situation requires the suppression of one of the biological effects of the hormone and the stimulation of another, specific tissue mechanisms are used that allow the activation of a certain function against unchanged hormone level in the body.

Keywords: cortisol; GH; T4; T3; N/L ratio; fasting; stress; sheep

Introduction

Recent studies on the effects of fasting have rejected the widely accepted scientific understanding of the inevitable negative effects of starvation on health. It turns out that intermittent fasting has some stimulating and mobilizing effect on immune cells. However, these studies are still in their early stages and do not present a perception of the mechanisms through which the health effect of short-term fasting is realized.

The empirical facts stemming from the use of short-term fasting from ancient times, dictated by different religions, confirm the beneficial effect of fasting on health (Trepanowski & Bloomer, 2010; Di Francesco et al., 2018; Venegas-Borsellino & Martindale, 2018). In rodents, intermittent or periodic fasting protects against diabetes, cancers, heart disease and neurodegeneration (Goodrick et al., 1990). In humans, fasting helps reduce obesity, hypertension, asthma and rheumatoid arthritis (Longo & Mattson, 2014).

Fasting and calorie restriction are considered as an optimal intervention for improving health and lifespan, increasing resistance to stress, slowing aging and increasing longevity without the undesirable side effects associated with alternative interventions (Aris et al., 2013; Redman et al., 2018).

Recent studies in this area have shown that prolonged fasting leads to a decrease in the number of leucocytes, which, however, is associated with the differentiation of stem cells into specific white blood cells, which improves immune protection (Mendelsohn & Larrick, 2014; Takakuwa et al., 2019).

Both calorie restriction and fasting promote stress resistance in model organisms ranging from unicellular yeast to mammals, presumably by shifting energy from growth and reproduction to maintenance, recycling, and repair in order to increase cellular protection and survival (Di Francesco et al., 2018).

Current research in this area is scarce and has been conducted mainly on humans and mice. These studies suggest that the effect of fasting is triggered by changes in the number and species composition of the intestinal microflora, the products synthesized by them, as well as components of degraded microflora (Jabbar et al., 2003; Thaiss et al., 2016; Cignarella et al., 2018; Mesnage et al., 2019). Intestinal microflora signaling, as well as a sharp decline in energy and plastic substrate cause interaction between the immune system and metabolic processes, resulting in a balance between potentially conflicting processes such as the need to maintain a low metabolic level in order to conserve energy on one hand and the need for activation of energy-consuming immune mechanisms, on the other. Studies of these processes in sheep are scarce and one-sided.

The object of this study was to investigate endocrine and immune responses in ewes during the four-day fast, subsequent immobilization and the recovery.

Materials and Methods

For the purpose of determining the hematocrit levels, blood samples were collected four times from mature Ile-de-France (n = 101) sheep raised at the experimental base of the Institute of Animal Sciences, Kostinbrod. The repeated blood sampling was conducted to avoid possible errors due to the many factors that influence hematocrit values. The hematocrit was determined at 3-week intervals. After processing the obtained data, two groups (n = 14) were formed, differing in the level of hematocrit – first group (low hematocrit group) included sheep with low hematocrit values and the second (high hematocrit group) comprised sheep with high values of hematocrit. A third (n = 10) control group was included, whose animals did not starve but were also stressed by immobilization. In addition, animals were grouped according to basal levels of T3 (Triiodothyronine). The live weight of the animals was recorded. The effect of fasting on the adrenal response in sheep with low and high hematocrit was examined via 4 days fasting, followed by 30 min of immobilization. In addition, the following parameters were measured: the intensity of hematopoiesis (number of reticulocytes), the predicted hematologic (hematocrit, differential white blood cell count) and hormonal indices (cortisol, growth hormone, T3, T4, estradiol-17β). These indicators were determined immediately after the end of the fasting period and subsequent immobilization. The weight of the animals was recorded to obtain information on the degree of catabolic processes in the two experimental groups immediately before the start and after the end of fasting, as well as at 7 and 20 days after the fasting period.

Blood samples were taken via jugular venepunction before the fasting (baseline level), at 24 h of fasting, after 4 days of fasting before immobilization, immediately after immobilization, during recovery period – at d 7 and d 20 after fasting. All samples were taken at the same time to avoid the effect of the diurnal hormonal rhythm. Feeding was done according to the nutritional standards for the animal category.

The blood concentration of the tested hormones (plasma cortisol, growth hormone (GH), thyroxine (T4), triiodothyronine (T3) and estradiol-17β) were estimated by commercial ELISA kits according to manufacturer‘s instructions (NovaTec Immunodiagnostica GmbH, Germany). The optical density was read at 450 nm against blank using the microplate reader (Biotek, USA).

Hematocrit levels and leukocyte counts were determined according to the classical methods of Ibrishimov & Lalov (1984). Leukocyte subpopulations in peripheral blood were determined microscopically on Giemsa-Romanovski stained blood smears. On each blood smear were counted 400 leukocytes, including basophils, eosinophils, neutrophils, lymphocytes and monocytes. Reticulocyte counts were determined microscopically by pre-staining with New Methylene Blue dye. The results of one factor analysis are expressed as means ± S.E.M. and were analyzed by ANOVA.

Results and Discussion

Animals were grouped according to basal levels of T3 (Triiodothyronine), which is the biologically active thyroid hormone, in order to monitor the relationship between cortisol and T3.

As it can be seen from Figure 1 there is a clearly marked inverse relationship between T3 and cortisol levels determined at 24 hours from the start of fasting. This dependence does not exist in the other periods.

Our data are in agreement with the latter hypothesis of the mechanism of metabolic changes during short-term fasting, according to which cessation of dietary carbohydrate intake leads to a decrease in glucose levels, which is followed by a decrease in leptin and a subsequent decrease in hypothalamic-pituitary-thyroid activity (XHT) axis, aimed at lowering the activity of metabolism and reducing energy expenditure. Lower activity of the hypothalamic-pituitary-thyroid (HHT) axis, according to this hypothesis, activates the hypothalamic-pituitary-adrenal (HPA) axis to activate lipolysis and gluconeogenesis. The elevated cortisol level after 24 h of fasting in the low T3 animals suggests that in them the activation of lipolysis and gluconeogenesis occurs later than in the high T3 animals, in which a drop in cortisol is observed. This fact suggests that at 24 h of fasting, a complete transition to using lipids instead of carbohydrates as an energy source has not yet occurred in animals with low T3 values. It is possible that this is due to the continued influx of food substrate from the foregut, the evacuation of which to subsequent divisions of the digestive tract occurs more slowly.

Puzzling is the unchanged level of T3 immediately after the end of fasting in sheep with high basal T3 values, which are comparable to those of control animals, and the increase in T3 in sheep with low basal T3 values (Figure 2).

The sharp weight loss of the animals in the two experimental groups (Figures 3 and 4) immediately after the end of the fasting period indicates unequivocally that energy was delivered via lipolysis during the four-day fasting.

The lack of an expected decrease in the level of biologically active T3 with a view to limiting energy expenditure and stimulating the hypothalamic-pituitary-adrenal (HPA) axis may be related to the observed increase in reversible T3 in humans and a decrease in biologically active T3 during fasting (Vagenakis et al., 1975; Spaulding et al., 1976). Reversible T3 is known to be biologically inactive, with equal affinity for T3 receptors, and therefore its binding to T3 receptors sharply reduces the ability to bind biologically active T3 and realize its metabolism potentiating effect. Therefore, with unchanged T3 levels, a sharp decrease in the metabolism during the fasting period can be expected, as is the case here. Of note, animals with low basal T3 were at significantly higher weights before fasting exposure and maintained their higher weights during the 20-day recovery period. This suggests that animals with lower T3 values have a lower metabolism and better digestibility of food. Immobilization

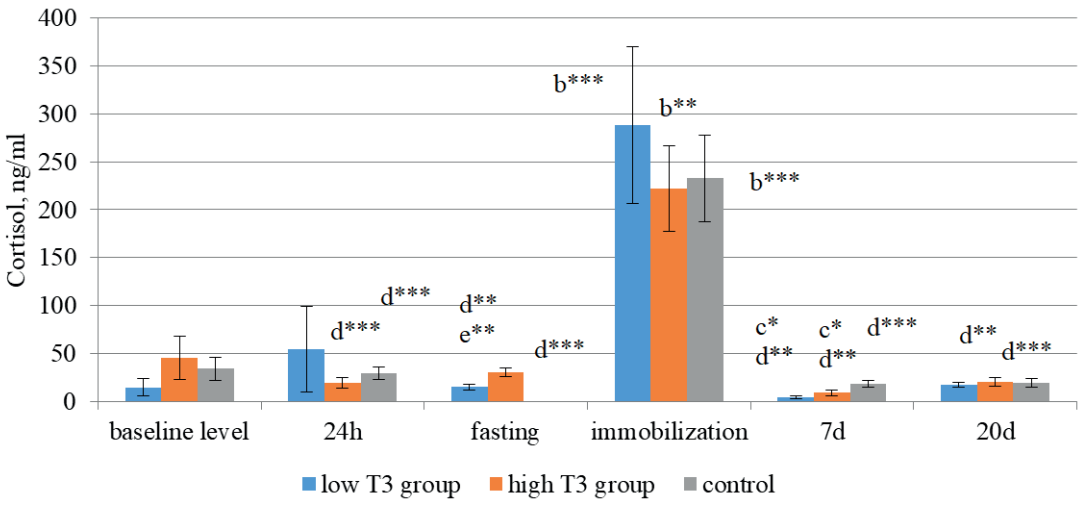

Fig. 1. Cortisol in sheep with low and high T3 values following fasting
*-P < 0.05; **-P- < 0.01; ***-P < 0.001
b – significantly different versus baseline level;
c – significantly different versus control group;
d – significantly different versus immobilization;
e – significantly different versus 7d

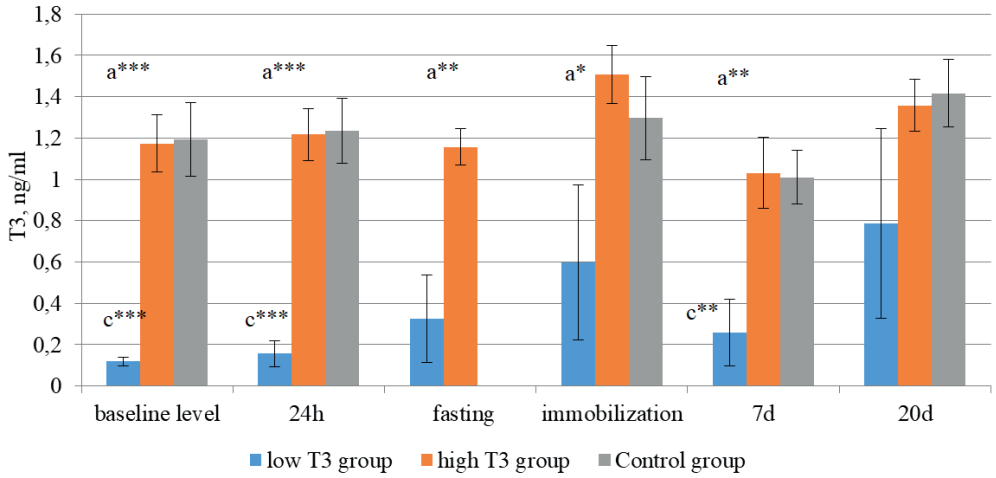

Fig. 2. T3 in sheep with low and high baseline T3 values following fasting
*- P < 0.05; **-P < 0.01; ***-P < 0.001
a – significantly different among the groups (low and high T3);
c – significantly different versus control group

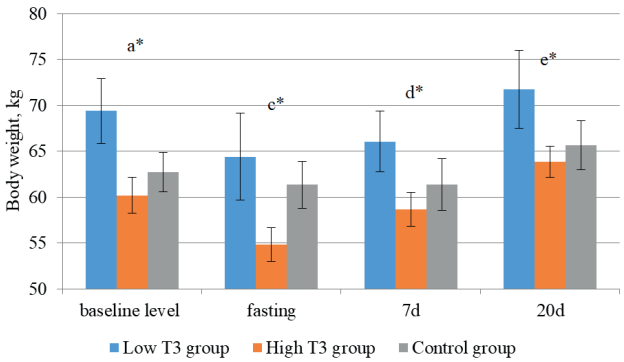

Fig. 3. Body weight in sheep with low and high T3 values following fasting
*-P < 0.05; **-P < 0.01
a – significantly different among the groups (low and high T3);
c- significantly different versus control group;
d – significantly different versus fasting (after immobilization);
e – significantly different versus 7d

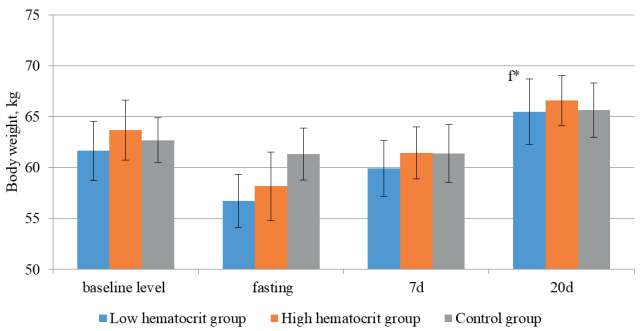

Fig. 4. Body weght in sheep with low and high hematocrit values following fasting
*-P < 0.05
f – significantly different versus fasting (after immobilization)

stress caused an increase in T3 values in all groups formed according to basal T3 values. A similar increase was noted in cortisol values (Figure 1). It should be noted that the increase in cortisol level in animals with low T3 values was distinctly greater than in animals with high T3 values. Given that a similar inverse relationship between T3 and cortisol values was also recorded at 24 h from the start of fasting, there can be no doubt about the inhibitory effect of T3 on cortisol secretion under stress. Furthermore, these data indicate that after a four-day fast, the level of the energy pool is sufficient to provide an adrenal response that is comparable to that of control animals.

During the first 7 days of recovery, the T3 level remained lower than the basal level in all three groups (Figure 2). This indicates that during the recovery period the energy storage mode is maintained, which at day 20 no longer exists and T3 values in animals with high basal T3 and control animals are close to basal values, while in animals with low basal values, a sharp increase in T3 was noted. The increase in T3 values at day 20 in the low basal T3 group suggests that the 4-day fast underlies increased metabolic activity in these animals after a 20-day recovery period, although T3 values accounted for only 50% from those of the other 2 groups.

A striking fact is that grouping animals according to T3 levels showed an inverse relationship between hormone level and live weight throughout the experimental period. These data suggest that the reduced metabolism in the animals with low basal T3 values underlies the better productive effect. This suggests that selection on the level of T3 will be accompanied by a more intense increase.

The dynamics of T4 when forming the groups according to the basal values of T4 were similar in the three groups at

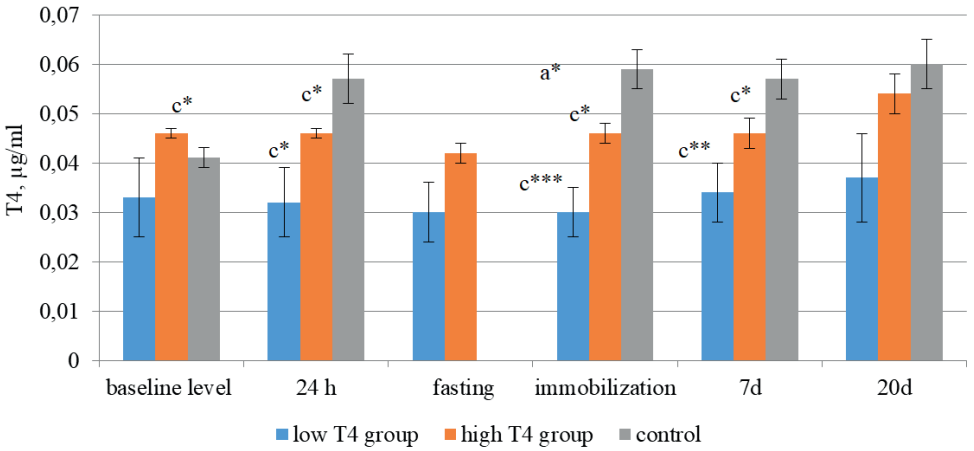

Fig. 5. T4 in sheep with low and high T4 baseline values following fasting
*-P < 0.05; **-P < 0.01; P- < 0.001
a – significantly different among the groups (low and high T4);
c – significantly different versus control group

the 24th hour, after the end of fasting, after the immobilization and on the 7th day of the recovery period, and on the 20th day a trend of increase in both experimental groups (Figure 5). It should be emphasized, however, that throughout the experimental period the level of T4 in the control group was higher than that of animals in both experimental groups and confirms our interpretation of the existence of a decreased metabolism during fasting.

It should be emphasized that when grouping animals according to hematocrit values, there is no contrast difference in T3 levels between the groups, which is probably related to the distribution of animals with low and high T3 values between the groups formed according to hematocrit values (Figure 6).

These data suggest that the level of hematocrit is not related to the level of T3, respectively to the intensity of metabolic processes. Stress by immobilization caused an increase in T3 values in all groups formed according to basal hematocrit values (Figure 6). A similar increase was observed in cortisol values (Figure 7).

Throughout the experimental period, the T4 level of the control group was higher than that of the animals in the two experimental groups (Figure 8), confirming our interpretation of the existence of reduced metabolism during fasting.

These data strongly suggest that T4 is a more reliable indicator of metabolism intensity than T3, although the latter is the biologically active hormone, whereas T4 is the prohormone from which T3 originates. Moreover, the dynamics of T4 confirm the previous interpretation of T3, according to which, at a maintained level of T3, the effect of biologically active T3 is blocked from the increasing synthesis of reversible T3, which results in a decrease in metabolism.

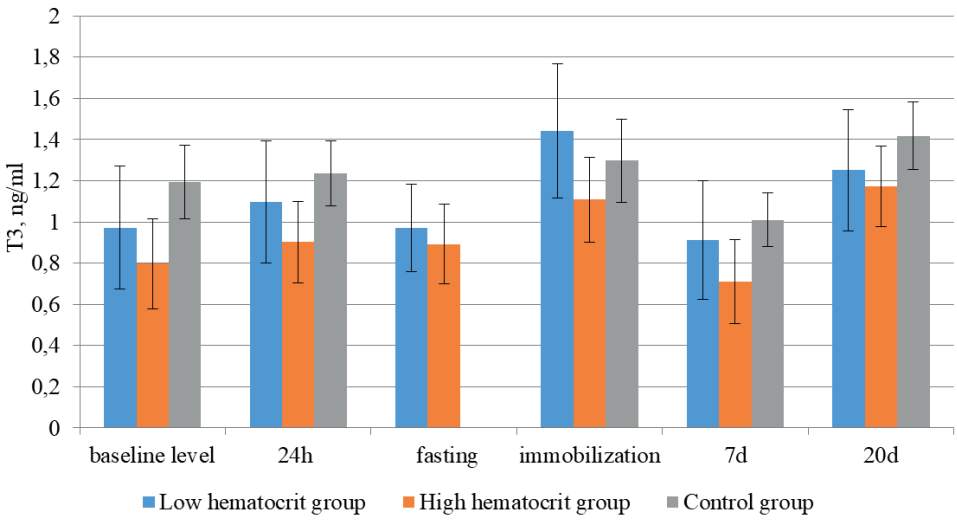

Figure. 6. T3 in sheep with low and high hematocrit values following fasting

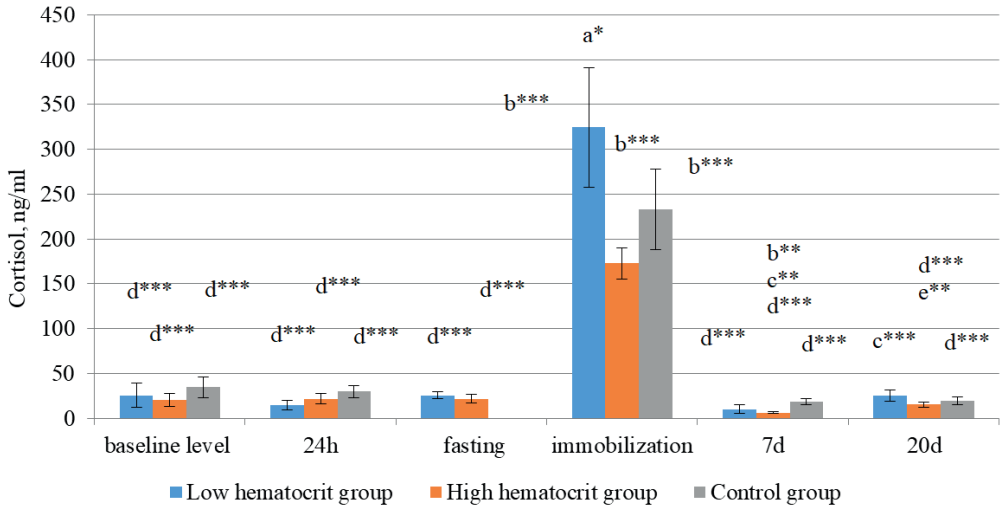

Fig. 7. Cortisol in sheep with low and high hematocrit values following fasting

a – signifificantly different among the groups (low and high hematocrit);
b – significantly different versus baseline level;
c – significantly different versus control group;
d – significantly different versus immobilization;
e – significantly different versus 7 d

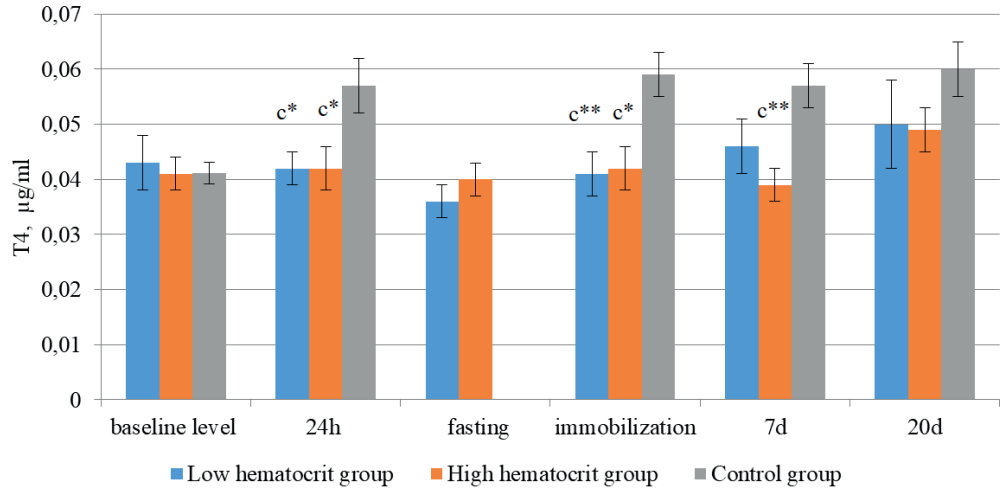

Fig. 8. T4 in sheep with low and high hematocrit values following fasting

*-P < 0.05; **-P < 0.01
c – significantly different versus control group

The dynamics of cortisol in animals grouped according to hematocrit values were similar in both experimental groups at 24 h and after fasting and were within basal values (Figure 7). Stress by immobilization caused a stronger adrenal response in the lower hematocrit group than in the other 2 groups.

During the recovery period (day 7) cortisol levels in both experimental groups remained lower than baseline values and recovered on day 20 of the recovery period. The observed decrease in cortisol levels during this period coincides with the decreased T3 values and confirms our view that in this case it is a central neural system-regulated decrease in metabolism aimed at storing energy and preparing the body for possible re-exposure to fasting.

The unchanged level of cortisol at 24 h from the onset of fasting is not consistent with the hypothetical mechanism for regulating fasting metabolism, according to which the decrease in the activity of hypothalamic pituitary-thyroid (HPT) axis is accompanied by activation of the hypothalamic-pituitary-adrenal (HPA) axis.

Trafficking and redistribution of leukocyte subpopulations have been shown to be directly dependent on cortisol concentration (Dhabhar, 2002; Dhabhar et al., 2012). The stress-induced change in neutrophil/lymphocyte (N/L) ratio is currently used as an indirect indicator of stress (Davis et al., 2008; Hickman, 2017). The increase in the N/L ratio at 24 h from the onset of fasting clearly indicates the presence of stress despite unchanged cortisol levels (Figure 9). Our and published studies have found a discrepancy between the level of cortisol and the degree of change in the N/L ratio, despite the proven effect of infusion of exogenous glucocorticoids on the redistribution dynamics of leukocyte subpopulations.

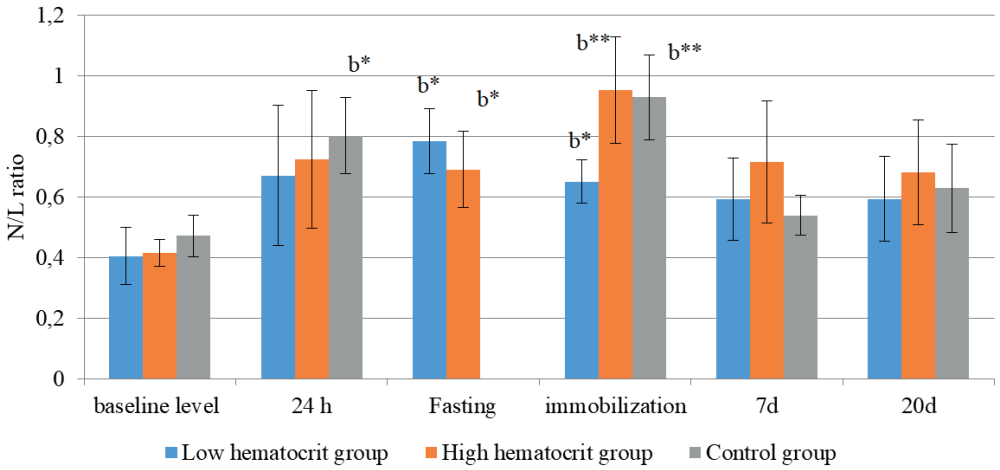

Fig. 9. Neutrophil-to lymphocyte ratio in sheep with low and high hematocrit values following fasting
*-P < 0.05; **-P < 0.01
b – significantly different versus baseline level

In our earlier study, we hypothesized that this discrepancy is due to the relationship between free (active) and protein-bound (inactive) cortisol (Moneva et al., 2019). Elastase enzyme released by neutrophil leukocytes is known to degrade transcortin. Given the increased level of neutrophils at the 24th hour, it can be assumed that, under starvation conditions, the level of the elastase enzyme increases, which in turn degrades the transcortin and thus increases the level of biologically active (free) cortisol. Thus, with unchanged levels of total cortisol, a typical stress N/L change occurs.

It is clear that the compromised concentrations of cortisol and T3 (whose increased level would lead to energy loss) during fasting and during the recovery period are predetermined by their specific metabolic effect. However, this assumption does not meet the need for a sharp reduction in energy costs, because increased levels of free cortisol will increase energy losses. It is therefore more likely to assume that it is a selective activity of cortisol to different tissues, which will allow cortisol to exert its specific effects without increasing overall energy loss. This effect of cortisol is likely to be achieved by reducing the sensitivity of glucocorticoid receptors in muscle tissue and other tissues, whose activity would increase energy loss and at the same time increase the sensitivity of these receptors in the liver and kidneys where gluconeogenesis take place and glucose delivery for erythrocytes that are devoid of mitochondria and therefore cannot use fatty acids as a source of energy. Particularly indicative of this possibility is the redistributive effect of cortisol on lymphocyte subpopulations, which occurs at low levels of cortisol and suggests that leukocyte sensitivity to cortisol is increased.

The fact that even on the 7th and 20th days of the recovery period, the N/L ratio remains higher than basal values (Figure 9), while the level of cortisol during this period is comparable to basal values (Figure 7) suggests that homeostatic mechanisms of regulation of metabolism at conditions of starvation, though less pronounced, continue to exert their energy-saving effect during the beginning of the recovery period.

A possible explanation for this phenomenon is that central cortisol activation (corticotropin-releasing hormone and adrenocorticotropin) is required to increase total cortisol levels, and increasing their activity may be incompatible with other physiological functions associated with reduced energy expenditure and maintenance of homeostasis in fasting. A specific example is the inverse relationship between corticotropin-releasing hormone and thyrotropin-releasing hormone, as well as multilateral central-level signaling, including leukocytes via their secreted cytokines.

Most studies in humans and mice indicate that fasting causes an initial increase in cortisol, followed by a decrease (Nakamura et al., 2016; Kim et al., 2021).

In our experiment, conclusive evidence was obtained of a statistically proven increase in the N/L ratio immediately after the end of fasting (Figure 9) at unchanged cortisol values (Figure 7).

Our interpretation of increasing the level of free cortisol at an unchanged concentration of total cortisol is in line with the need to reduce energy expenditure in fasting on the one hand and to maintain levels of free cortisol, providing glycogenogenesis in the liver and kidneys on the other.

There was a clear tendency for a lower basal level of growth hormone in sheep with a low hematocrit compared to those with a high hematocrit (Figure 10).

At 24 h after food deprivation, a tendency for a slight decrease in the growth hormone level in both groups was observed. The tendency to decrease the level of growth hormone is more pronounced immediately after the end of fasting.

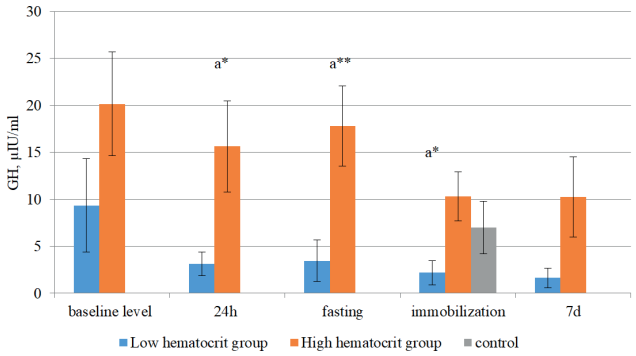

Fig. 10. GH in sheep with low and high hematocrit values following fasting
*-P < 0.05; **-P < 0.01
a – significantly different among the groups

During fasting (24 h and at the end of the four-day fasting period), the tendency of lower growth hormone values in sheep with low hematocrit values persists. Stress by immobilization did not have significant effect on the level of growth hormone. The growth hormone level after 7 days of recovery tends to be lower than the baseline values in both groups.

Most of the studies related to the study of growth hormone dynamics were conducted in humans and mice starved for 24–36 h. During this short period of fasting, an increase in the level of growth hormone has been observed, which is associated with its specific lipolytic effect (Gahete et al., 2013; Moller et al., 2009). No change in the concentration of growth hormone was observed in sheep starved for 3 days (Hua et al., 1995**)**. Most researchers are adamant that the multifaceted biological effects of growth hormone are still poorly understood and contradictory results suggest that further research is needed in a holistic context.

The decrease in growth hormone levels by the 24th hour and after the end of fasting may be associated with the need to further reduce energy expenditure, but at the same time would reduce the level of growth hormone-activated lipolysis, which is vital to ensure energy during this period. This discrepancy may be related to the established blocking effect of fibroblast-growth factor-21 (FRF-21) on the growth hormone. FRF-21 level increases upon starvation and causes resistance to growth hormone action (Inagaki et al., 2008; Fazeli et al., 2010).

Given that, along with its lipolytic effect, growth hormone exerts a certain anabolic effect and affects hematopoiesis, the immune system and other functional systems (Devesa et al., 2016); it is no surprise that its effect is blocked by fasting. Therefore, the conflicting results on the dynamics of growth hormone in fasting are not so significant.

The question of the degree of resistance of different tissues to FRF-21 remains open. Given the pronounced lipolytic effect of growth hormone and the need to maintain lipolysis as a major energy source during starvation, it can be expected that fatty tissue resistance to the lipolytic effect of growth hormone does not exist or is minimized.

These data suggest that it is necessary to study the specific resistance of different tissues to growth hormone. Moreover, our and literature data on the dynamics of growth hormone in fasting suggest that, in addition to resistance to the effect of growth hormone, the effect of other biological components, related to the realization of the biological effects of growth hormone, must be investigated.

In this regard, a mathematically proven difference in growth hormone values between animals with low and high hematocrit levels at 24 h and immediately after the end of fasting, as well as during immobilization, is of particular interest. Given the hematopoietic stimulating effect of growth hormone by increasing the secretion of erythropoietin, it may be assumed that the selection of animals according to hematocrit levels is accompanied by the selection of higher growth hormone values in animals with high hematocrit. This view is supported by the trend of higher reticulocyte percentages immediately after fasting and during the recovery period (Figure 11).

The dynamics of estradiol were characterized by a downward trend in both groups immediately after the end of fasting, while a decrease was observed only in animals with high hematocrit values on the 24th hour of fasting (Figure 12).

The sharp rise in estradiol in animals with low hematocrit at 24 h from the onset of fasting may be associated with the start of the estrous cycle in some animals in the group immediately before the fasting exposure, whereas in other animals in the group the trend is downward. Fasting is known to suppress the function of gonadotropic hormones and is thought

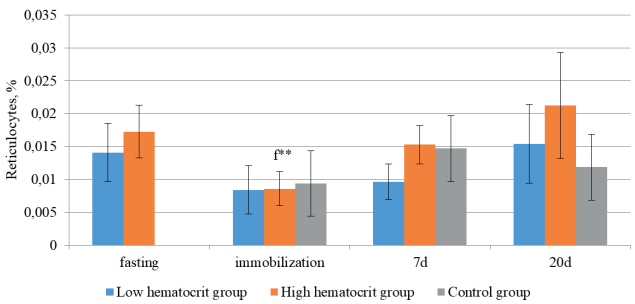

Fig. 11. Reticulocytes in sheep with low and high hematocrit values following fasting
**P < 0.01
f – significantly different versus fasting

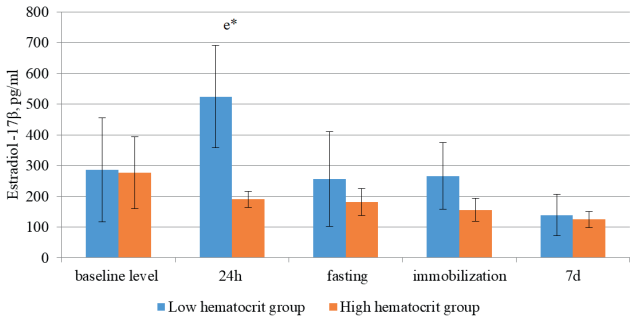

Fig. 12. Estradiol- 17β in sheep with low and high hematocrit values following fasting

*- $P < 0.05$

e – significantly different versus 7d

to be accomplished by a sharp decrease in glucose and leptin levels during fasting (Crane et al., 2007). Our data suggest that the inhibitory effect of fasting on gonadal function is prevented by an estrous cycle started prior to the onset of fasting.

The dynamics of the studied hormones allow us to formulate a new concept for the mechanism of action of these hormones in fasting, which explains the contradictory data on the dynamics of cortisol and the realization of specific hormonal effects in unchanged or slightly altered hormonal plasma values.

According to our concept, each of the tested hormones exhibits selective activity to the tissues, whose functional activity is particularly important for providing energy homeostasis in fasting. When some of the effects of a given hormone are simultaneously associated with vitally important functions (energy production through lipolysis) and those whose activity is not vitally important and is associated with an increase in metabolism and an increase in energy expenditure (muscle tissue), are activated mechanisms that increase the resistance of tissues, the activation of which is associated with a significant loss of energy, and increase the sensitivity of tissues (in this case, adipose tissue), the activation of which is necessary to maintain the supply of energy.

The most convincing argument to support this concept is the distribution effect of glucocorticoids on leukocyte subpopulations and in particular the change in the N/L ratio. There can be no doubt that with unchanged levels of cortisol after four-day fasting period (which saves energy), an increases in the N/L ratio is observed.

This concept is in line with the well-established understanding that the short-term effect of stress has a positive effect on the activity of the immune system. The fact that there is a redistribution of leukocyte subpopulations, typical of short-term stress to different organs and tissues, in order to protect the body without increasing cortisol, indicates that the sensitivity of glucocorticoid receptors of different leukocyte subpopulations is increased.

Conclusions

Stress exerts a specific tissue activity that, at normal levels of cortisol (in order to conserve energy), activates the immune defense by using specific mechanisms (most likely activation of 11 beta-hydroxy-steroid dehydrogenase of leukocytes) allowing activation of the inactive cortisol and realizing the redistributing effect of cortisol by binding to the leukocytes glucocorticoid receptors.

The unchanged level of T3 under fasting conditions confirms our hypothesis of tissue-specific activity, because increased lipolysis during fasting is most likely associated with an increased level of reversible T3 at an unchanged level of total T3, which allows, with unchanged metabolic activity, to carry out the specific activating effect of T3 on lipid metabolism.

Growth hormone, like other hormones, most likely also carries out tissue-specific activity, allowing activation of lipolytic activity at unchanged growth hormone values. A directly proportional relationship between growth hormone level and hematocrit level was found, which is probably related to the stimulating effect of growth hormone on erythropoietin.

An inverse relationship between T3 and growth intensity was established.

The data allow us to assert that when a hormone has several biological effects and the maintenance of homeostasis in a certain stressful situation requires the suppression of one of the biological effects of the hormone and the stimulation of another, specific tissue mechanisms are used that allow the activation of a certain function against unchanged hormone level in the body

These studies provide a definite direction for investigating the mechanisms of specific tissue activation in various physiological conditions in animals.

These are the first studies of its kind to demonstrate the presence of specific tissue activation at unchanged levels of the hormone in the blood.

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