©2021 International Transaction Journal of Engineering, Management, & Applied Sciences & Technologies

ISSN 2228-9860 eISSN 1906-9642 CODEN: ITJEA8

International Transaction Journal of Engineering, Management, & Applied Sciences & Technologies

http://TuEngr.com

Erythrogram Indices of Vealers and the Interrelation of Their Values with the Growth Hormones' Level

Elizaveta Anatolyevna Bilan[1], Marina Arkadyevna Derkho[1*]

[1] Department of Natural Sciences, South Ural State Agrarian University, Troitsk, RUSSIAN FEDERATION
**Corresponding Author (Email: derkho2010@yandex.ru).*

Paper ID: 12A12E

Volume 12 Issue 12

Received 09 July 2021
Received in revised form 05 September 2021
Accepted 14 September 2021
Available online 21 September 2021

Keywords:
Erythrogram parameters; Cow growth hormone; Hematological profile; Principal component 1; MCV; MCH; MCHC; Traits' interrelations; Heifers; IGF-1; Holsteinized black pied calves; Forage-fed cow.

Abstract

The age-related changes in the parameters of the erythrogram and the somatotropic axis hormones in the blood of Holsteinized black pied calves during the preweaning period were studied; their interrelations were determined by the Principal Component Analysis. The objects of the study were heifers, the study material was blood. Erythrocytes, hemoglobin, hematocrit, erythrocyte indices, growth hormone (somatotropic hormone of the pituitary gland), insulin-like growth factor-1 were determined in the blood at 1, 3, and 6 months of age. It was found that the value of the erythrogram indices in the preweaning period of rearing Holsteinized black pied breed calves increases with age from 9.2 to 50.0%. By the age of 6 months, the growth hormone concentration decreases 1.80 times, and IGF-1 increases 23.35 times, determining the priority of the latter in the regulation of growth processes. Principal component analysis shows that IGF-1 directly regulates the number of erythrocytes and hemoglobin in the calves' blood.

Disciplinary: Animal and Veterinary Science, Biology.

Cite This Article:

Bilan, E. A., Derkho, M. A. (2021). Erythrogram Indices of Vealers and the Interrelation of Their Values with the Growth Hormones' Level. *International Transaction Journal of Engineering, Management, & Applied Sciences & Technologies, 12*(12), 12A12E, 1-9. http://TUENGR.COM/V12/12A12E.pdf DOI: 10.14456/ITJEMAST.2021.236

1 Introduction

A complete blood count with cell differentiation is one of the most common laboratory tests that allow getting an idea of the immune system condition in the animal body, the respiratory function of blood, and the hemostasis system [1, 2]. With the introduction of automatic hematological analyzers into veterinary laboratory practice, it became necessary to establish reference intervals for the interpretation of blood test results [3], which actualizes research in the field of age-related physiology of animals.

A hematological profile is used to assess the respiratory blood function, which allows monitoring the animal health and includes basic (erythrocytes, hematocrit, hemoglobin) and calculated parameters (average corpuscular volume of an erythrocyte, average corpuscular hemoglobin, average concentration of corpuscular hemoglobin in an erythrocyte) [4]. Like others, the level of these parameters depends on the gender and age of the animals, the breed and the direction of its productivity, the level of productivity, physiological state, environmental conditions, etc. [5]. For example, with age, the number of erythrocytes, hemoglobin, and hematocrit increases, which is especially pronounced in the early stages of postnatal ontogenesis; the level of parameters is higher in the blood of males than in females; purebred animals are characterized by higher values of indicators than hybrids; beef breeds have a higher hematological status than dairy animals; under the influence of various unfavorable factors, including pathogenic, the blood profile can change in different directions, depending on the strength of their influence [6-12]. Given the animal hematological status variability, it is very important to monitor it using a blood test. In addition, erythrogram indices are useful for the diagnosis of anemias of various etiologies [5], precise species-specific physiological parameters are required in the development, validation, extrapolation, and application of pharmacokinetic or toxicokinetic models [12]. At the same time, for farm animals, including cattle, there are a limited number of sources in which the reference boundaries of physiological parameters are determined, but only in a generalized form without considering the age, breed, direction of productivity, etc.

The main parameter of the animal's hematological profile is the erythrocyte. Its biological properties are not only associated with the hemoglobin it contains, which ensures the transport of respiratory gases in the bloodstream, but also the ability of cells to carry some amino acids, enzymes, glucose, immune complexes, cortisol, etc. [13-16]. In addition, the erythrocyte membrane contains many receptors for hormones [17], including hormones of the somatotropic axis (growth hormone (GR), insulin-like growth factor-1 (IGF-I) [18].

Several studies have recently appeared reflecting the effect of growth hormone on the processes of erythropoiesis. Thus, work [19] revealed that the GR / IGF-1 axis is involved in the regulation of erythropoiesis. With this, growth hormone and IGF-1 even regulate the synthesis of hemoglobin in the brain, mediating its metabolic needs [20-22]. It is assumed that the effects of growth hormone on erythropoiesis are due to its effect on the erythropoietin synthesis, due to which it controls the concentration of erythrocytes, hemoglobin, and hematocrit in the blood [23]. According to [18], there is an interrelation in the animal body between hemoglobin/hematocrit and GR / IGF-I. However, all these data are obtained in laboratory animals models.

Therefore, our study was firstly aimed at characterizing the age-related variability of the erythrogram indicators and hormones of the somatotropic axis in Holsteinized black pied breed calves during the preweaning rearing period; secondly, to identify the interrelations between erythrogram parameters and growth hormone / insulin-like growth factor-I.

2 Materials and Methods

2.1 Sample Collection and Analysis

An experimental group was formed (n=10) to carry out the work; it included heifers selected after a clinical examination (healthy) according to the principle of approximate analogs. The animals' thorough-bredness for the Holstein breed was 50%. The research period corresponded to the preweaning period of calf rearing.

Blood was obtained by vacuum method from the jugular vein. For these purposes, ready-made test tubes were used: 1) with EDTA-K3 anticoagulant (Elamed, Russia) for hematological studies; 2) without filler with a red cap (Elamed, Russia) for biochemical research. Blood was delivered to the laboratory of the veterinary clinic "Zoopuls" (Chelyabinsk) in a thermo-container at an air temperature of +2...+8°C and studied on the first day after sampling. The research material was taken from calves at 1, 3, and 6 months of age before feeding.

To determine the hormones' concentration (growth hormone, insulin-like growth factor-I) in blood serum by enzyme immunoassay, ready-made sets of reagents "DBC Growth Hormone ELISA" (Canada), "IGF-I-ELISA" (Germany) with species-specific monoclonal antibodies were used. The enzyme immunoassay was performed according to the manufacturer's instructions and the assay procedure. The strips were incubated in an ELMI ST-3 thermal shaker (Latvia) and the optical density was measured using a Mindray BA-88A microplate (China). The staining intensity formed during the enzymatic reaction was directly proportional to the concentration of hormones in the test sample.

Hematological samples' analysis was performed using a Vet Mindray BC-5150 veterinary hematological analyzer (China) with species-specific settings for cattle. It included basic and calculated erythrogram parameters: erythrocytes (RBC), hemoglobin (Hb), hematocrit (Ht), average erythrocyte volume (MCV), average corpuscular hemoglobin (MCH), average corpuscular hemoglobin concentration in an erythrocyte (MCHC).

2.2 Statistical Analysis

Statistical analysis was performed using Statistica 6.0 software. It included checking the distribution normalcy of values in the sample using the Shapiro-Wilk test, calculating the mean (X) and its standard error (Sx). The principal component method was used to assess the interrelation between the hormones' concentration and erythrogram indices [25], which made it possible to reduce the dimensionality of the correlating variables set. The similarity degree was determined using Spearman's correlation coefficient, the number of principal components - by the graphical method based on the Cattell scree test [26]. Interrelations were considered statistically significant at $P \leqslant 0.05$. The calculations were performed using the PAST package [27].

3 Results

The value of the main calves' erythrogram indicators (erythrocytes, hemoglobin, hematocrit) and the calculated indices (MCV, MCH, MCHC) depended on the age during the preweaning rearing period (Table 1). At the age of 1 month, the minimum level of erythrocytes, hemoglobin, and hematocrit in the analyzed samples was revealed. At the same time, the average corpuscular volume of an erythrocyte was on the contrary characterized by a maximum value, but the average hemoglobin amount (MCH) and the density of its filling in the cell cytoplasm (MCHC) were low.

The following indicators had positive age-related dynamics in the calves' erythrogram: 1) the number of erythrocytes, which by the end of the preweaning growing period exceeded the initial level by 20.12% ($P \leqslant 0.05$); 2) the hemoglobin concentration increased by 6 months of age to 126.00 ± 1.06 g/l, exceeding the level of 1-month-old animals by 50.00% ($P \leqslant 0.05$); 3) the volume fraction of blood erythrocytes estimated by the hematocrit value changed by 9.24% ($P \leqslant 0.05$); 4) the value of the average corpuscular hemoglobin (MCH) increased from 16.73±0.81 (at the age of 1 month) to 20.89±0.05 ($P \leqslant 0.05$) pg (at the age of 6 months); 5) the average concentration of corpuscular hemoglobin in an erythrocyte increasing with age by 37.33% ($P \leqslant 0.05$).

At the same time, on the contrary, the average corpuscular volume of an erythrocyte decreased with age by 9.97% (Table 1), that is, it reached a dimensional volume that allows containing the greatest amount of hemoglobin at a high distribution density in the cell cytoplasm.

Table 1: Erythrogram indices of Holsteinized black pied calves (n=10)

Indicator	Age of heifers					
	1 month		3 months		6 months	
	X	Sx	X	Sx	X	Sx
RBC, 10^{12}/l	5.02	0.23	5.71*	0.06	6.03*	0.07
Hb, g/l	84.00	1.10	96.73*	0.98	126.00*	1.06
Ht, %	35.70	0.70	37.00	0.63	39.00*	0.69
MCH, pg	16.73	0.81	16.94	0.49	20.89*	0.05
MCHC, g/l	23.52	0.13	26.10*	0.04	32.30*	0.08
MCV, fl	71.12	0.38	64.79*	0.40	64.67*	0.12

Note: * - $P \leq 0.05$ in relation to the age of 1 month

The reference fluctuations' boundaries in the erythrogram parameters in the blood of Holsteinized black pied calves during the preweaning rearing period were represented by the following boundaries: RBC from 5.02 to 6.03 10^{12}/l, the hemoglobin from 84.00 to 126.00 g/l, hematocrit from 35.70 to 39.00%, average corpuscular hemoglobin (MCH) from 16.73 to 20.89 pg, average corpuscular hemoglobin concentration in an erythrocyte (MCHC) from 23.52 to 32.30 g/l and the average erythrocyte volume (MCV) from 64.67 to 71.12 fl.

Table 2: Dynamics of GR and IGF-1 in the blood of Holsteinized black pied calves (n=10) [28]

Indicator	Age of heifers					
	1 month		3 months		6 months	
	X	Sx	X	Sx	X	Sx
GR, ng/ml	0.82	0.03	0.60*	0.03	0.44*	0.02
IGF-1, ng/ml	0.14	0.31	1.37*	0.21	3.23*	0.18
IGF-1 / GR, conv. units	0,17	0.01	2,29*	0.11	7,26*	0.16

Note: * - $P \leq 0.05$ in relation to the age of 1 month

Growth hormones play an important role in the growth processes' regulation in the calves' body, the most significant of which are growth hormone and insulin-like growth factor-1. As it was found earlier [28], the concentration of growth hormone in calves' blood during the preweaning rearing period decreased (Table 2). At 6 months of age, the GR level was 1.80 times less than in 1-month-old calves (P⩽0.05). At the same time, on the contrary, the IGF-1 value increased and exceeded the initial level at the age of 6 months by 23.35 times (P⩽0.05). This determined the variability of the IGF-1 / GR value.

During the preweaning rearing period, the reference interval for Holsteinized Black pied calves for growth hormone and IGF-1 was 0.45-0.81 and 0.14-3.27 ng/ml.

It was already noted that the hormones of the somatotropic axis can regulate the hematopoiesis processes affecting the synthesis of erythropoietin. In addition, due to their adsorption-transport function, erythrocytes are able to bind a large number of hormones forming their pool in the blood [18, 23]. Therefore, it is logical to assume that the erythrogram parameters are interrelated with the hormones of the somatotropic axis. The principal component analysis was used to test this assumption. The determination of the optimal factors' number was performed using the Cattell graphical screen criterion [26]. According to the graph, the value of only one factor (Principal component 1) exceeded one, all the rest fell into the “factorial screen”. Loads of erythrogram parameters on "Principal component 1" are shown in Table 3.

Table 3: Loads of erythrogram parameters on "Principal component 1"

Indicator	Growth hormone						IGF-1					
	1 month		3 months		6 months		1 month		3 months		6 months	
	Load	P	Load	P	Load	P	Load	P	Load	P	Load	P
RBC	-0.35	0.47	-0.41	0.29	-0.15	0.67	0.75	<0.05	0.71	<0.05	0.82	<0.05
Hb	-0.08	0.79	-0.18	0.63	-0.07	0.79	0.78	<0.05	0.71	<0.05	0.82	<0.05
Ht	-0.16	0.65	-0.11	0.70	-0.25	0.62	0.54	0.17	0.62	0.09	0.39	0.45
MCH	-0.23	0.61	-0.29	0.48	-0.48	0.30	0.61	0.09	0.51	0.20	0.47	0.31
MCHC	-0.44	0.31	-0.30	0.48	-0.36	0.46	0.48	0.29	0.44	0.31	0.06	0.79
MCV	0.28	0.48	0.34	0.47	0.53	0.18	-0.36	0.46	-0.16	0.65	-0.19	0.36

The analysis revealed that the variables in the growth hormone correlation matrix for Principal Component 1 did not have statistically significant interrelations in calves at 1, 3, and 6 months of age (Table 3). Principal component 1 in the relation "Erythrogram parameters - IGF-1" had significant correlations with the number of erythrocytes and hemoglobin. Consequently, the principal components analysis made it possible to determine that of the somatotropic axis hormones, only insulin-like growth factor-1 is directly involved in the regulation of erythrogram parameters.

4 Discussion

The key parameter of the erythrogram is erythrocytes, which have practically no organelles. However, they have several metabolic pathways for energy production, the rate of which can be changed if necessary [7], which determines their sensitivity to the effects of various factors and changes in blood plasma composition [15]. Under physiological conditions, the number of erythrocytes in the bloodstream is firstly determined by their gas transport [14, 29] and, secondly, by adsorption-transport functions [30]. Therefore, during the preweaning rearing period, which is characterized by a high intensity of animal growth, the level of cells increases systematically as well as their volume fraction in the blood (hematocrit). This ensures the coverage of the body's needs for oxygen, determining the activity of aerobic processes [14]; the possibility of using substances adsorbed by erythrocytes in transcapillary and tissue metabolism; removal of metabolites, atherogenic lipids, denatured proteins, etc. [30]; regulation of substances' concentration in blood plasma due to their adsorption-desorption by cells.

The biological properties of erythrocytes are associated with the level of intra-erythrocyte hemoglobin and the morphofunctional state of cell membranes [8, 9]. According to [29], the hemoglobin molecule inside the cell enters homo- and heterotropic interactions that optimize its functional behavior in accordance with specific physiological requirements. These modulation mechanisms provide hemoglobin with the ability to perform secondary functions in relation to the main one - oxygen transport but are important for maintaining homeostasis in the body. This explains the lack of proportionality between the age-related increase in erythrocytes (by 20.12%) and hemoglobin, MCH, and MCHC (by 50.00; 24.89 and 37.32%) in the body of calves.

The membrane skeleton is important for maintaining the integrity of red blood cells and performing its functions. In this regard, a decrease in the average corpuscular volume of red cells helps to maintain the mechanical and functional integrity of red blood cells in the calves' bloodstream, allowing them to pass through the capillaries. This also indirectly indicates the absence of disturbances in the maturation and degradation of erythrocytes [15].

In general, the dynamics of erythrogram indices in calves during the preweaning rearing period indicates the physiological state of their body.

The preweaning rearing period is important in shaping the future productivity of heifers [31]. At this age, a somatotropic axis is formed in their bodies consisting mainly of growth hormone, IGF-1, and IGF-2, and associated carrier proteins and receptors. It is the main regulator of the growth and development of cattle during the postnatal ontogenesis periods, including the development of the mammary gland [32].

By the end of the preweaning rearing period, the concentration of IGF-1 in the blood of heifers of the Holsteinized Black pied breed increased 23.35 times, and the growth hormone - decreased 1.80 times. At the same time, the level of IGF-1 significantly prevailed over the concentration of growth hormone. This suggests that IGF-1 is a priority factor in stimulating the growth of the heifers' bodies. At the same time, during the animal's development and the formation of physiological systems' functions, various tissues and organs (liver, kidneys, heart, intestinal tract, adrenal glands, spleen, etc.) contribute to the formation of its concentration in the blood [33]. In addition, according to [34], the multidirectional age-related variability of growth hormone and IGF-1 promotes protein synthesis in the animal body and also indicates the ability of growth hormone to realize its biological effects not only through IGF-1.

Firstly, the processes of the organism's growth and development, especially in the early periods of postnatal ontogenesis, are regulated by hormones of the somatotropic axis [23]; secondly, aerobic redox processes covering the energy consumption of growth processes are provided due to the gas and adsorption-transport functions of erythrocytes [14, 29, 30]; based on these, the authors attempted to identify the interrelation between these traits by the principal components analysis. Only one factor (Principal component 1) was statistically significant in the Cattell screen test.

Factor loads on the Principal component 1 of growth hormone were not statistically significant. This indicated that the hormone did not directly affect the formation of the red blood cell pool in the body of calves during the preweaning rearing period. At the same time, of the variables used (erythrogram parameters) for the Principal component 1 in the IGF-1 correlation matrix, reliable interrelations at 1, 3, and 6 months of age were characteristic of erythrocytes and hemoglobin. Consequently, growth hormone realizes its effects on the hematopoietic organs by inducing the synthesis of insulin-like growth factor-1. Similar results were obtained [35] in experiments on mice. The authors found that IGF-1 is able to increase the proliferation of committed bone marrow progenitor cells and reduce the rate of their death. The effect of growth hormone on the hemoglobin synthesis in the cells of the animal body by means of IGF-1 was also noted in [18, 20]

5 Availability of Data and Material

Data can be made available by contacting the corresponding author.

6 Ethical Statement

The studies were approved by the Bioethics Committee of the South Ural State Agrarian University and carried out in accordance with the principles of humane animal treatment.

Animals. The work was carried out in the conditions of the APC "Koelginskoe" named after Shundeev I.N. (Chelyabinsk region) in 2019-2020 The agricultural enterprise is one of the leading ones in the Chelyabinsk region, specializing in dairy farming in addition to the plant growing. For these purposes, it accommodates about 2,400 forage-fed cows, the gross milk yield per day is more than 70.0 tons. The breeding work of the enterprise is aimed at Holsteinization of black pied cattle by artificial insemination with Holstein bulls' semen. The technology of keeping young animals provides for their rearing up to 3 months of age in individual houses with individual feeders and a courtyard. Subsequently, group keeping is used in group cages of 10 heads each. Free access to food and water. The conditions for keeping animals comply with the VIZh standards [24].

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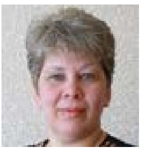
Bilan Elizaveta Anatolyevna a postgraduate student at the Department of Natural Science Disciplines of the Federal State Budgetary Educational Institution of Higher Education "South Ural State Agrarian University" in the direction 06.06.01 Biological Sciences, profile Physiology. In 2018, she graduated with honors from the South Ural State Agrarian University. Research interests: age physiology, hormonal regulation of metabolism.



Professor Dr. Derkho Marina Arkadyevna is Professor and Head of the Department of Natural Science Disciplines of the Federal State Budgetary Educational Institution of Higher Education "South Ural State Agrarian University". She holds a Doctor of Biological Sciences, from the Moscow State Academy of Veterinary Medicine and Biotechnology. K.I. Scriabin. Her research interests are Ecological Biochemistry, Age Physiology, Neuro-humoral Regulation, Adaptation Processes, Biotechnology of Food Production.