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The importance of metabolic processes and immune responses in the development of pathology of cows during pregnancy and postpartum periods

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Abstract

The reproductive function of cows is ensured by a homeostasis system. The aim of this study to investigate scientific data and analyze modern practical approaches related to metabolic disorders. Also investigating immune response. The object of the research was the cows *(Bos taurus taurus)* of *Ukrainian Black-and-White dairy breed*. Using the method in groups and periods. The control group of animals (C1, n = 137) – cows with a physiological of pregnancy (248–255 days). Re-examination of control animals (C2, n = 137) was carried out during the postpartum period. The first experimental group (E1, n = 32) consisted of animals diagnosed with preeclampsia. Cows with a subclinical course of ketosis constituted the second group (E2, n = 52). The development of preeclampsia of cows was accompanied by an increase in the content of medium-sized peptides from 0.2 ± 0.01 to 0.3 ± 0.03 Mol.Wt. ($P < 0.01$), and an increase in the level of average molecular circulating immune complexes. It is proved that an imbalance in the diet and a deficiency of metabolic energy during the dry period and for 6-8 weeks after birth negatively affects the health of animals, is the cause of metabolic disorders and the manifestation of reproductive pathologies.

Key words: cows, preeclampsia, energy imbalance, metabolic disorders, reproductive pathology.

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1. Introduction

The reproductive function of cows is ensured by a homeostasis system, coordinated and harmonized function of all organs and systems, which is maintained during all their live (Duehlmeier et al., 2013; Wankhade et al., 2017; Souto et al., 2019; Klosova et al., 2019; Grymak et al., 2020). Only under such conditions will estrous cycles appear in animals. All favorable be created for early gestation, the development of pregnancy. Also the course of normal childbirth and the restoration of the body in the postpartum period (Bernabucci et al., 2005).

The functioning of the homeostasis system largely depends on the feeding conditions and the content of the dairy herd on farms. Physiological constants are especially labile during dry periods, after partum and during the of lactation (Van Saun, 2000; Castillo et al., 2005; Bomko et al., 2018; Kulyaba et al., 2019; Borshch et al., 2020). At this time the body undergoes overstressed metabolic and energy processes, a whole cascade of hormonal surges. The body is in a borderline state on the verge of "disruption" with pathology (Roche et al., 2000; Castillo et al., 2003; Zhelavskyi, 2011).

Often, an imbalance in the diet for nutrients and a deficiency of metabolic energy leads to deep metabolic disorders in the body of cows, the development of a number of dysfunctions in organs and systems. The reproductive function of animals is also no exception. The most susceptible are highly productive cows, which can cause gestosis, paresis, partum dystocia, retention of the placenta, mastitis, endometritis and other postpartum complications. Basically, postpartum complications are recorded in the first days after calving, and can subsequently develop for 6–8 weeks (transient period), which coincides with the onset of lactogenesis and the during of lactation (Lacetera et al., 2001; Castillo et al., 2003; Rossi et al., 2009; Zhelavskyi et al., 2019).

The aim of this study to investigate scientific data and analyze modern practical approaches related to metabolic disorders. Also investigating immune response in the body of cows in the during pregnant and the postpartum period.

2. Materials and methods

Clinical and experimental investigation was carried out in farms of the Khmelnitsky region of Ukraine. Studies were performed in the period 2018–2020. The object of the research was the cows *(Bos taurus taurus*) of *Ukrainian Black-and-White dairy breed*, formed on the basis of using the method in groups and periods. The control group of animals (C1, n = 137) was made up of cows with a physiological of pregnancy (248–255 days). Re-examination of control animals (C2, n = 137) was carried out during the postpartum period (from the 5th day of postpartum period) and up to 10 weeks of lactation. The first experimental group (E1, n = 32) consisted of animals diagnosed with preeclampsia (assessment of general condition, measurement of blood pressure, detection of edema and protein content in urine). Cows with a subclinical course of ketosis constituted the second group of experiment (E2, n = 52). Also determined the activity of aminotransferases (aspartate aminotransferase (AST) alanine aminotransferase (ALT). At all periods of the study studied parameters of ration (Singh, 2017).

The content of circulating immune complexes (CIC) was studied in our modification (Yablonskyi & Zhelavskyi, 2010) with differentiation of their molecular weight (PEG 6000 average molecular CICm 11S-19S). The state of endogenous intoxication was determined by the content of medium-sized peptides (MSP). A series of urological studies (pH, protein) were also performed (Singh, 2017).

The obtained data were processed statistically using the applied computer program Statistica 12.6.

3. Results and discussion

The development of pregnancy pathology in cows was accompanied by significant changes in clinical and status, as well as changes in biochemical and immunological parameters. Symptoms of preeclampsia were impaired cardiac activity, increased blood pressure, and increased breathing. The heart rate in cows increased from 68.2 ± 3.18 to 83.1 ± 1.17 beats / min ($P < 0.001$), the respiratory rate from 17.3 ± 0.45 to 19.2 ± 0.52. Systolic blood pressure: up to 120.2 ± 1.85 mmHg (systolic) and 61.5 to 68.6 ± 2.27 mmHg (diastolic) vs 117.2 ± 2.15 and 58.5 ± 1.24 in the control group (C1).

Laboratory tests of urine of cows with preeclampsia detected proteinuria (1.62 + 0.03 g/l, $P < 0.05$) and a shift in pH (7.8 ± 0.02 vs 7.3 ±0.01 in the control).

The pathological process in the body of pregnant cows was also accompanied by activation of aminotransferases: AST and ALT (Fig. 1).

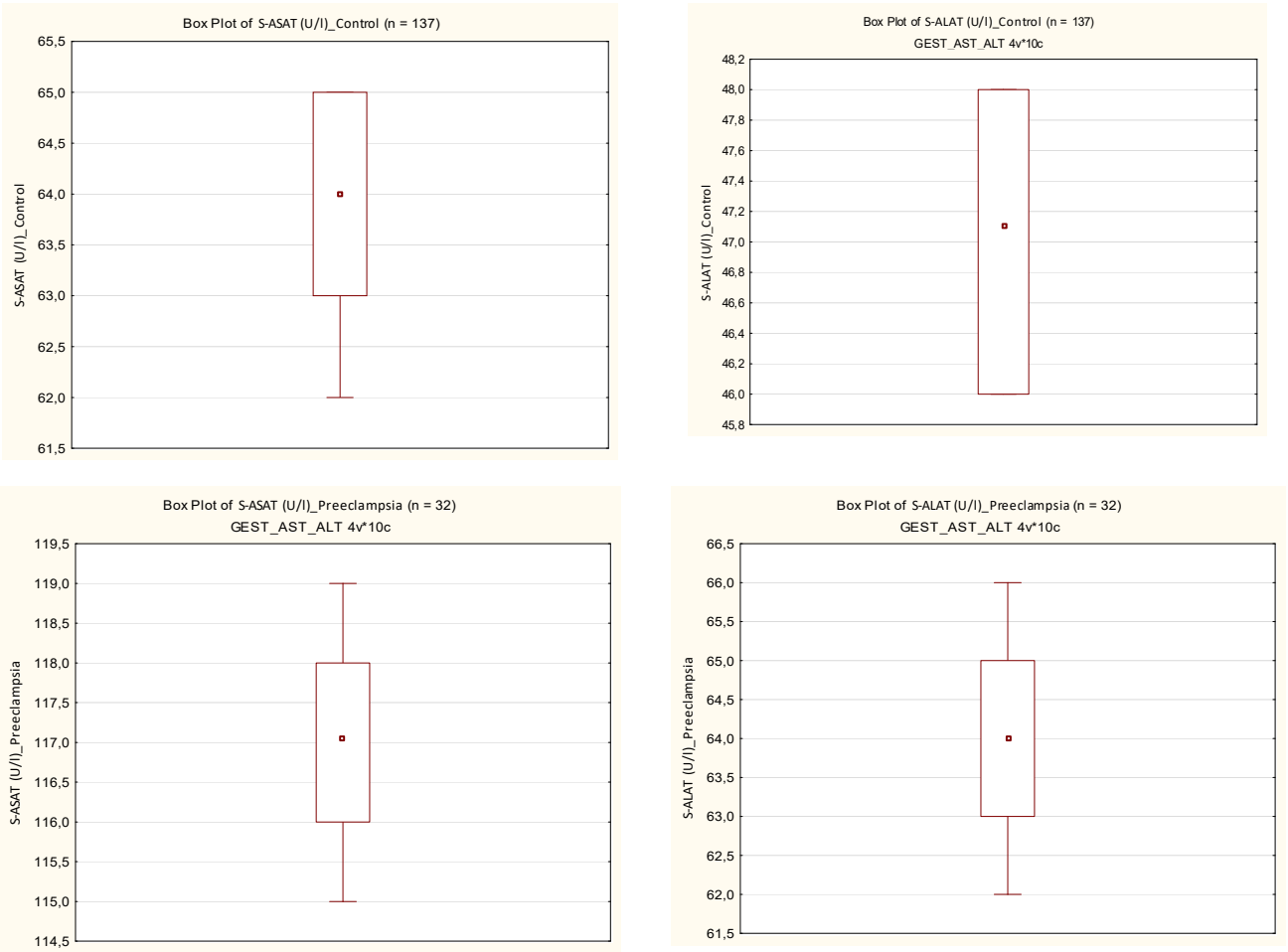

Fig. 1. Changes in the activity of aminotransferases in the blood of cows at preeclampsia (M ± m)

Activation of enzyme systems indicates the involvement in the pathology of not only the placenta but also the liver, kidneys and myocardium.

The development of preeclampsia of cows was accompanied by an increase in the content of MSM from 0.2 ± 0.01 to 0.3 ± 0.03 Mol.Wt. (P < 0.01), and an increase in the level of average molecular circulating immune complexes (Table 1).

Table 1
The level of circulating immune complexes and medium-sized peptides (M ± m)

Value	CIC_m 11S-19S (c.u.)	MSP (Mol.Wt.)
Control group (n = 137)	89.1 ± 1.66	0.27 ± 0.01
Preeclampsia (n = 32)	111.4 ± 3.16**	0.43 ± 0.02*

Note: n – number, CICm – circulating immune complexes (average molecular size), MSP−medium-sized peptides, * − P < 0.01, ** − P < 0.001 vs healthy animals

These processes confirm the presence of overstrain, metabolic processes and the growing syndrome of endogenous intoxication and the development of immune reactions in the pathogenesis of this disease.

To date, the relationship with the genetic determination of various breeds of cows, the influence of the conditions of maintenance, exploitation and productivity on their reproductive function are being comprehensively studied. More and more information appears that the dairy herd is most susceptible to metabolic and reproductive diseases both during dead wood and in the early postpartum period (Eremina et al., 2003; Bani Ismail et al., 2008).

Numerous studies show that since the beginning of lactogenesis in dairy farms, the risk of manifestation of metabolic pathologies in cows has increased significantly, which often lead to the development of infertility. Researchers comprehensively study the etiology and pathogenesis of these disorders and often associate the onset of disease development with the moment of the greatest manifestation of negative energy balance (Roche et al., 2000; Kitabchi et al., 2004; Zhelavskyi, 2012).

Metabolic disorders of carbohydrate, protein and lipid metabolism in the early period of lactation are often accompanied by acetonemia (ketosis) and the development of Fatty liver dystrophy. A prolonged energy deficit affects a sharp reduction in milk productivity, weight loss and the development of other minor pathologies. Studies prove that with fatty dystrophy of the liver, its barrier function changes, toxic metabolites accumulate in the body, and the hormone-inactivating function of the organ is disrupted (Schlumbohm & Harmeyer, 2004; Sahoo et al., 2009).

The toxic effect of metabolites of the liver (in particular *β-hydroxybutyrate*) and a high level of insulin in the blood have been proved to have a negative effect on the development of oocytes. At the same time, a reduced level of insulin shows a decrease in lipolysis. Catecholamines, in turn, are also activators of lipid breakdown with the formation of a large amount of triacylglycerols, which increases the risk of developing fatty liver (Sathya et al., 2007; Duehlmeier et al., 2013; Wankhade et al., 2017).

It is well known that in the body of ruminants, maintaining a physiological level of glucose passes through the system of hepatic gluconeogenesis (using propionate). This energy-consuming process is directly related to lactation of cows. In the post-hotel period, an insufficient amount of dry matter in the diet leads to a sharp decrease in the level of propionate, and, consequently, a decrease in glucose synthesis. Such biochemical disturbances lead to changes in amino acid metabolism (in particular, alanine and glutamine), biochemical reactions in muscle tissue. And cause neuroendocrine disorders, including dysfunctions (most often hypofunction) of the ovaries and the development of infertility (Vannucchi et al., 2007; Beskow et al., 2008).

There is undeniable evidence that the development of prolonged sluggish (subclinical ketosis) may be the cause of infertility of cows. Often we observed this situation in the first-calf heifers of the industrial enterprises of the Khmelnitsky region of Ukraine. Subclinical ketosis (on a scale of 18–23 %) led not only to a decrease in the productivity of the dairy herd, but also caused the development of infertility. Dramatically reduced the effectiveness of artificial insemination of cows. Morbidity among heifers was 21–29 %. Persistent animals have often been diagnosed with persistent hypofunction of the ovaries, subinvolution of the uterus and the development of chronic endometritis (Bernabucci et al., 2005; Duehlmeier et al., 2013; Zhelavskyi & Dmytriv, 2018).

As practice shows in cows with a smooth physiological adaptation at the beginning of lactation after pregnancy, the risks of metabolic and energy imbalance are significantly reduced. And thus, all conditions are created for normal lactation and the resumption of estrus, the realization of a full reproductive function (Ahmed et al., 2006).

An analysis of the diets of cows of a number of industrial farms shows that in the post-hotel diet, the exchange energy in diets is often at an extremely low level (minimum of 11.0–11.5 MJ of exchange energy per 1 kg of dry matter). The energy deficit ranged from 3 to 11 %, which is especially noticeable in the body of cows at the time of the start lactation (Maynard et al., 2003; Kitabchi et al., 2013).

Long-term studies convincingly show (Castillo et al., 2003; Wankhade et al., 2017) that the imbalance of energy supply is one of the main links in the pathogenesis of neuroendocrine disorders. Impaired regulatory function of the hypothalamus (and other endocrine glands), trophic processes in the ovaries, and development of liver lipidosis. It has been experimentally proven that a negative energy balance in the early post-hotel period leads to a sharp decrease in the level of luteinizing hormone (LH), disruption of the ovogenesis process, and a decrease in the secretion of estrogens and progestogens. In this case, glucose deficiency also has an important role in the development of pathology (Roche et al., 2000; Sahoo et al., 2009). The accumulation in the body of a critical level of fatty acids and the formation of ketone bodies leads to obesity of the liver and impaired reproductive function in cows (Ahmed et al., 2006).

It is well known that the pancreas is actively involved in the metabolic processes of animals. Recent studies show that under the influence of insulin in the liver, an insulin-like growth factor (IGF1, insulin-like growth factor 1) is produced, which activates the formation of estrogen, stimulates the expression of specific receptors for LH, and creates the necessary conditions for ovulation (Castillo et al., 2003; Sahoo et al., 2009).

In energy metabolism, the important role of growth hormone and leptin, which actively affect fat metabolism in animals, has been proved. Experimental studies show that excessive feeding of concentrated feed (barley grain) leads

to disruption of cicatricial digestion, reproduction of pathogenic *Escherichia coli* strains and the formation of toxic metabolites (Eremina et al., 2003; Sathya et al., 2007; Zhelavskyi, 2010; Wankhade et al., 2017). The disease leads to a sharp decrease in the pH of the scar (the development of acidosis), triggering a cascade of inflammatory reactions in the body. Pathology is complicated by delayed placenta and the development of endometritis of cows (Vannucchi et al., 2007; Yablonskyi & Zhelavskyi, 2008).

There are also interesting data that the decrease in dry matter in the diet of cows is directly related to the development of postpartum endometritis. Researchers also report that disorders of protein, carbohydrate and lipid metabolism become the main cause of endocrine dysfunctions (Beskow et al., 2008). Which lead to violations of the estrus of cows and the development of infertility in them (Roche et al., 2000; Yarim & Ciftci, 2009). Over the course of all reproductive periods in the body of animals, immune responses also change. The restructuring of the immune system in the mother's body often accomoned with signs of immunosuppression (Yablonskyi & Zhelavskyi, 2009).

Modern scientists prove that a negative balance of energy and disturbances in protein metabolism can also affect immunobiological reactivity (Lacetera et al., 2001; Yablonskyi & Zhelavskyi, 2010; 2013; Wankhade et al., 2017). Our studies (the school of scientists of animal reproduction immunology under the guidance of Doctor of Biological Sciences, Professor V. A. Yablonskyi) show that in the postpartum period dysfunction occurs in the cellular and humoral immunity (Zhelavskyi, 2012; 2015; 2017; 2019). At the same time, cows are often at risk for postpartum endometritis and mastitis, which is a consequence of the inability of the immune mechanisms to withstand biotic and abiotic environmental factors. Such abnormalities were associated both with impaired phagocytic reactivity of cells and activation of the process of autophagy and apoptosis of immunocompetent cells (Kitabchi et al., 2004; Zhelavskyi & Shunin, 2017; Wankhade et al., 2017). There are publications that immune mechanisms are also involved in the pathogenesis of retention of the placenta (Castillo et al., 2003).

The main strategy for the prevention of postpartum diseases in cows and the adaptation of the body after pregnancy. As well as the creation of favorable conditions for the restoration of estrus, should be based on a balanced diet. On defeat 2–3 months' lactation in the diet of cows should be: exchange energy at the level of 11.0–11.5 MJ per 1 kg of dry matter, crude protein – 14–16.9 g per 1 MJ of exchange energy, crude fiber 17–18 %, starch 13, 5–17 % in dry matter and concertinas up to 400 g per 1 kg of milk (at 4 % fat content). During pregnant and early lactation, immunological control of the dairy herd and immunocorrection of deficient conditions of the body should also be given.

4. Conclusions

Of fundamental importance in maintaining the physiological state of the body and the functional state of the reproductive function of cows is the rational provision of livestock with nutrients from the mandatory control of energy balance. In the pathogenesis of preeclampsia an important role belongs to hormonal and metabolic disorders that occur against the background of changes in immune responses. An imbalance in the diet and a deficiency of metabolic energy during the pregnant and during the first 6-8 weeks' early lactation negatively affects the health of animals. This is the cause of metabolic disorders and the manifestation of reproductive pathologies.

Conflict of interest

The authors declare that there is no conflict of interest.

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