

**HORMONAL STATUS AND REGULATION OF GLYCEMIA IN NEONATAL CALVES DURING THE FIRST HOURS OF POSTNATAL LIFE**

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*The aim of this study was to examine changes in some hormones concentrations in calves during the first 32 hours of neonatal life and to estimate their association with glycemia. Thirty two Holstein breed calves were selected for the study. Blood samples were taken at 30, 60 and 90 minutes postnatal. Calves received pooled colostrum: primary colostrum (1.5 L, 2 hours after birth), secondary colostrum (2 L, 14 hours after birth) and tertiary colostrum (2 L, 26 hours after birth). Blood samples were taken at hours 5, 20 and 32 of neonatal life. Concentrations of glucose, insulin, cortisol, thyroid hormones and IGF-I and abundance of IGFBP-1, IGFBP-2 and IGFBP-3 were determined in the blood serum. The  $T_3/T_4$  ratio was also calculated.*

*Calves were born hypoglycemic (glycemia was  $2.56 \pm 1.05$  mmol/L at birth). Thereafter, glycemia significantly increased ( $p < 0.001$ ) to  $3.05 \pm 0.89$  mmol/L at min 90. Glucose concentration showed a further increase after colostrum intake and was significantly higher than at the initial value in all examined periods ( $p < 0.001$ ). During the first 90 minutes of neonatal life insulinemia decreased significantly ( $p < 0.001$ ) compared to initial value ( $26.33 \pm 10.05$   $\mu$ U/L) and it measured  $18.66 \pm 5.56$   $\mu$ U/L at min 90. Cortisolemia was highest at minute 30 ( $85.08 \pm 19.36$  nmol/L) and than decreased until the end of the experiment ( $p < 0.001$ ) compared to initial values in samples obtained during the period of colostrum intake. A significantly high correlation was determined between glycemia and cortisolemia in all examined periods before the first colostrums intake ( $r^2 = 0.854$ ;  $p < 0.01$  at min 30;  $r^2 = 0.742$ ;  $p < 0.01$  at min 60 and  $r^2 = 0.551$ ;  $p < 0.01$  at min 90).  $T_4$  concentrations significantly increased during the first 2 hours, while  $T_3$  concentrations decreased, significantly from min 30 to min 90 postnatal ( $p < 0.05$ ).  $T_3/T_4$  ratio significantly increased during the first 2 hours of neonatal life. After first colostrum intake, concentrations of both hormones rose significantly compared to the initial level, but  $T_3/T_4$  ratio did not change and maintained the value determined at minute 90. IGF-1 concentrations significantly decreased during the first 2 postnatal hours. A significant positive correlation was observed between IGF-1 concentration and insulinemia ( $r^2 = 0.463$ ;  $p < 0.05$  at min 30,  $r^2 = 0.662$ ;*

*p*<0.01 at min 60 and  $r^2=0.583$ ; *p*<0.01 at min 90). IGFBP-3 abundance significantly decreased, while IGFBP-1 significantly increased in this period. IGFBP-2 abundance was highest at birth. Results presented in this study indicate that the increase in glucose concentration during the first 2 hours of neonatal life, before the first colostrum intake is mainly the result of increased activity of the adrenal cortex in cortisol secretion and extrathyroidal tissue thus providing sufficient triiodothyronine. Immaturity of mechanisms responsible for insulin secretion provides the dominance of catabolic processes. Changes of the IGF system provide a rise of glucose concentration and establishment of energy balance.

*Key words:* glycemia, hormonal status, IGF system, neonatal calves

#### INTRODUCTION

The first 24 h in newborn calves are the most critical ones for survival. Energy demands are high and physiological adjustments to the environment are great. Therefore, it is important to study those adjustments to obtain valuable information for introducing adequate feeding regime, defending neonatal diseases and improving production and to offer experimental data of animals for enriching comparative and development physiology. As glucose is the crucial energy fuel for organisms, development of homeostatic control mechanisms that maintain glucose level in the physiological range are of great importance.

Neonatal calves are born hypoglycemic Oltner and Breglund (1982) reported that calves are born hypoglycemic and this finding was recently confirmed by Kirovski *et al.* (2008) and Steinhoff-Wagner *et al.* (2011). Before and shortly after birth circulating concentrations of glucagon and catecholamine increase and concentration of insulin decreases (Mao *et al.*, 1994). Decreased insulin/glucagon ration stimulates glycogenolysis in the liver (Swenne *et al.*, 1994). Corticosteroids, additionally, stimulate the increase of circulating glucose mainly by impaired peripheral insulin-dependent glucose utilization (Scheuer *et al.*, 2006). There is no consistent literature data related to thyroid hormone concentrations immediately after birth (Davicco *et al.*, 1982; Stojić *et al.*, 2002; Kirovski *et al.*, 2008). That is probably due to the fact that many factors, including environmental temperature have effects on thyroid hormones concentrations. IGF - 1 concentration declines after birth (Kirovski *et al.*, 2002). A limited number of studies describes changes of concentrations of insulin-like growth factor binding proteins shortly after birth. Skaar and coworkers (1994) showed that the concentration of IGFBP-3 is higher than IGFBP-2 and IGFBP-1 immediately after birth in neonatal calves. This being opposite to most other animals and humans (Baxter and Martin, 1986; Lee *et al.*, 1991; Owens *et al.*, 1991). Changes in IGFBP ratios after parturition may influence glucose metabolism (Murphy, 2003). In humans, hypoglycemia with hyperinsulinemia is coupled with a decrease of IGFBP-3 concentration and increase of IGFBP-1 concentration (Collett-Solberg

and Cohen, 1996). Decreased IGFBP-3/IGFBP-1 ratio enables IGF-1 to pass through the capillary walls into the extracellular space. All of these changes in hormone concentrations immediately after birth, before colostrum intake, are important for glucose homeostasis. Calves are born with glycogen reserves in the liver. Since glycogen capacity in newborn calves is limited, mechanisms that increase glucose concentrations after birth through glycogenolysis may keep glycemia in the physiological range during the first 2 to 4 hours of postnatal life (Edwards and Silver, 1969). After that, circulating glucose concentrations are maintained only by an additional supply of glucose i.e. by providing colostrum to newborn calves. Colostrum contain carbohydrates, fats, proteins, peptides, minerals, vitamins, hormones, growth factors, cytokines, enzymes, polyamines and nucleotides in different amounts than mature milk (Blum and Hammon, 2000). Colostrum is richer in fat, but lower in carbohydrate than mature milk. Since carbohydrate supply from colostrum is not sufficient to cover glucose utilization, the newborn is still dependent on its own ability to produce glucose to meet the needs of the growing animal. Colostrum intake stimulates B cells of the pancreas in newborn calves to produce insulin (Hammon and Blum, 1998). It is an open question if the endocrine pancreas is completely developed in newborns and if the utilization of glucose in peripheral tissue of newborn calves is same as in adult cattle.

The aim of this study was to investigate the interrelationship between glycemia, concentrations of some hormones and IGF system in newborn calves.

#### MATERIAL AND METHODS

##### *Calves*

Immediately after birth, 32 calves (24 females and 8 males; Holstein-Friesian breed) were chosen and placed in individual boxes in a byre where the temperature ranged from 15 to 20°C. All calves were born within a 4-week period. Average birth weight was  $38.5 \pm 2.3$  kg with no significant difference ( $p > 0.05$ ) between the males ( $39.7 \pm 1.8$  kg) and females ( $38.1 \pm 2.3$  kg).

##### *Colostrum feeding*

Pools of colostrum were prepared for the first three feedings. Primary colostrum was taken up to 1 wk in advance from cows 2 to 2.5 h after calving; secondary colostrum obtained at 14 h after calving; and tertiary colostrum obtained at 26 h after calving. Calves received 1.5 L of first colostrum 2 hours after birth ( $28.0 \pm 2.29\%$  dry matter), 2 L of second colostrum 14 hours after birth ( $18.2 \pm 1.78\%$  dry matter) and 2 L of third colostrum 26 hours postnatally ( $15.9 \pm 1.44\%$  dry matter).

##### *Blood samples*

Blood samples were taken by jugular vein puncture, three times before colostrum feeding (minutes 30, 60 and 90 of postnatal life) and at 5, 20 and 32 hours postnatally. The obtained samples were placed into tubes and allowed to clot spontaneously at room temperature. The serum was decanted, centrifuged at

3000 g, portioned into aliquots of 1.5 mL, and stored in polypropylene microtubes at 20°C until analysis.

#### *Laboratory methods*

Glucose was measured spectrophotometrically using kits from Hoffman-LaRoche (Basle, Switzerland) and an automatic analyzer (Secomam CE, BP 106; Secoman, France). Concentrations of insulin, IGF-I, cortisol, triiodothyronine (T<sub>3</sub>) and thyroxine (T<sub>4</sub>) in sera were measured by radioimmunoassay (RIA; INEP-Zemun, Serbia). Intra-assay coefficients of variation (CV) ranged from 3.1% to 7.2%. Assays were performed in duplicate and samples were analyzed within the same assay run.

For the IGF-I RIA, binding proteins were removed by acidethanol treatment followed by cryoprecipitation (Breier *et al.*, 1991).

The IGFBP patterns in sera were characterized by sodium dodecyl sulphate – polyacrylamide gel electrophoresis (SDS–PAGE) and ligand-affinity blotting (Hossenlopp *et al.*, 1986). Proteins were electrotransferred to nitrocellulose membrane (0.45 mm, Schleicher and Schuell), followed by autoradiography after incubation with <sup>125</sup>I IGF-I (specific activity: 36 MBq/nmol). Protein bands were putatively identified according to the mobility of reference standards: bovine serum albumin (BSA, 66 kDa), ovalbumin (45 kDa), glyceraldehyde-3-phosphate dehydrogenase (36 kDa), carbonic anhydrase (29 kDa), and chymotrypsin (24 kDa). Autoradiographic band patterns were quantitated using the GlycoBandScan program (Version 5, 1998; PROZYME, San Leandro, California, USA). The abundance of IGFBP bands was expressed in arbitrary densitometric units (ADU).

## RESULTS AND DISCUSSION

The average concentrations of glucose of calves during the first 32 hours after birth are shown in Figure 1.

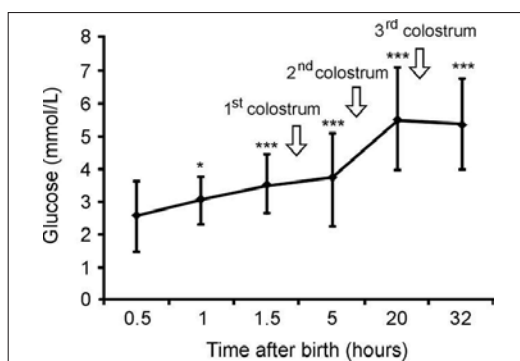


Figure 1. Changes of blood glucose concentrations during the first hours after birth in calves (mean ± SD, n = 32). \*p<0.05; \*\*\* p<0.001 compared with value at birth

Concentration of glucose at birth was  $2.56 \pm 1.05$  mmol/L. Glycemia increased to  $3.03 \pm 0.72$  mmol/L at 60 min after birth ( $p < 0.05$  compared to initial level) and  $3.5 \pm 0.89$  mmol/L at 90 min after birth ( $p < 0.001$  compared to initial level). The abrupt increase of glucose within the first 2 hours of neonatal life, before colostrum intake, indicates changes in hormonal control that provide the rise of glucose in the blood. Further increase of glucose, after colostrum intake, are expectable and are caused by suckling of colostrum rich in lactose (Steinhoff-Wagner *et al.*, 2011). Three hours after intake of the first colostrum glycemia was  $3.70 \pm 1.43$  mmol/L ( $p < 0.001$  compared to the initial level). Six hours after the intake of second colostrum glycemia was  $5.52 \pm 1.54$  mmol/L ( $p < 0.001$  compared to initial level), while 32 hours postnatally it was  $5.32 \pm 1.39$  mmol/L ( $p < 0.001$  compared to initial level). Since in this study colostrum was offered to calves at the recommended time after birth (2 to 4 hours postnatally), there was no decline of glucose concentration before colostrum intake which was previously observed by some authors (Grongnet *et al.*, 1985; Hadorn *et al.*, 1997). Our work indicates that the optimal time for first colostrum intake by calves is at hour 2 of neonatal life. Namely, if colostrum is offered to calves at this time, there will be no decline in glucose concentration and it will be maintained in the physiological range (Figure 1). It is well known that colostrum provides nutrients, and also passive immunity and growth factors that are essential for good adaptation of neonatal calf to changeable environment (Blum and Hammon, 2000).

Serum levels of insulin and cortisol are presented in Figure 2.

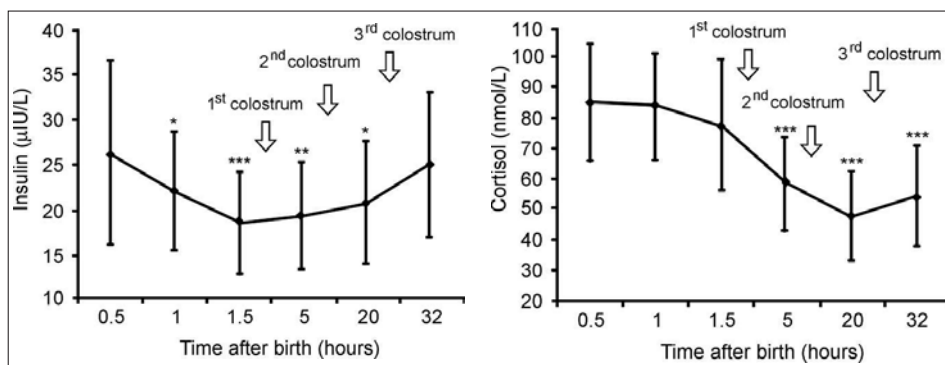


Figure 2. Changes of blood serum insulin and cortisol concentrations during the first hours after birth in calves (mean  $\pm$  SD, n = 32). \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\*  $p < 0.001$  compared with value at birth

Serum levels of insulin decline during the first 2 hours of neonatal life i.e. before colostrum intake. Initial insulinemia was  $26.33 \pm 10.05$   $\mu$ IU/L. Thirty minutes later glycemia significantly decreased ( $p < 0.05$ ) to  $22.07 \pm 6.54$   $\mu$ IU/L. Lowest insulin concentration was determined 90 minutes postnatally ( $18.66 \pm 5.56$   $\mu$ IU/L;  $p < 0.001$  compared to initial level). Since insulin is an anabolic

hormone, one of the most important adaptations to the state of starvation is the decrease of insulin concentration (Blum and Hammon, 1999). Lower insulin concentration in the circulation provides increased activity of catabolic processes, like glycogenolysis, and keeps circulating glucose within the physiological range. Calves are born with glycogen stored in the liver. Glycogenolysis is stimulated not only by decreased insulin concentration, but also increased glucagon concentration (Mayor and Cuezva, 1985). After intake of first colostrum insulin concentration increased, but not significantly since it was still lower than at the initial level. Insulinemia was  $19.36 \pm 5.89 \mu\text{IU/L}$  at hour 5 ( $p < 0.01$  compared to the initial value) and  $20.77 \pm 6.69 \mu\text{IU/L}$  at hour 20 ( $p < 0.05$  compared to initial value). Additionally, there was no statistically significant difference between insulin concentration at 90 minutes and 5 hours ( $p > 0.05$ ) and 20 hours ( $p > 0.05$ ) of postnatal life. After birth (32 hours), insulinemia was  $25.12 \pm 7.97 \mu\text{IU/L}$ , similar to the initial insulin concentration. Insulin concentration increases after intake of colostrum due to absorbed glucose which originated from digested lactose in the small intestine of calves (Steinhoff-Wagner *et al.*, 2011). Glucose stimulates B cells of the pancreas to produce insulin. Ingested colostrum increase the secretion of many gastrointestinal hormones such as gastrin, secretin, cholecystokinin (CCK), gastric inhibitory polypeptide (GIP) and vasoactive intestinal peptide (VIP) that stimulate the B cells of pancreatic islets to synthesize and release insulin (Lavine and Attie, 2010). Nevertheless, insulin concentration at hours 5 and 20 did not significantly increase. It indicates that insulin secretory mechanisms are not fully developed in newborns. Since colostrum is rich in insulin and intact insulin molecules can be absorbed during the first 24 hours of neonatal life (Kirovski *et al.*, 2008), it is possible that the absorbed insulin compensates endogen insulin deficiency.

Cortisol concentration was high at birth ( $85.08 \pm 19.36 \text{ nmol/L}$ ), probably due to the stimulation of parturition stress on the adrenal cortex (Jacob *et al.*, 2001). Thereafter, cortisol concentration decreased gradually to  $83.95 \pm 17.59 \text{ nmol/L}$  at min 60 and  $77.77 \pm 21.06 \text{ nmol/L}$  at min 90 postnatal. These results are similar to studies in earlier reports (Jacob *et al.*, 2001; Stojić *et al.*, 2002). There was a significant correlation between cortisol and glucose concentrations at 30 min ( $r^2 = 0.854$ ;  $p < 0.01$ ), 60 min ( $r^2 = 0.742$ ;  $p < 0.01$ ) and 90 min ( $r^2 = 0.551$ ;  $p < 0.01$ ). This result is in accordance with the results of Massip (1981). Although earlier studies explained this relationship through the effect of cortisol on gluconeogenesis, Scheuer and coworkers (2006) found that the increased plasma glucose concentrations, however, are not associated with the stimulation of hepatic gluconeogenic enzyme activities, but with impaired peripheral insulin-dependent glucose utilization. Decline in cortisol concentration continues after intake of colostrums and was  $58.09 \pm 15.57 \text{ nmol/L}$  at hour 5 ( $p < 0.001$  compared to initial level),  $47.49 \pm 15.02 \text{ nmol/L}$  at hour 20 ( $p < 0.001$  compared to initial level). Cortisolemia was  $54.14 \pm 16.65 \text{ nmol/L}$  at hour 32 ( $p < 0.001$  compared to initial level). These results are in accordance with Stojić *et al.* (2002), and Bittrich *et al.* (2002).

Serum levels of  $T_3$  and  $T_4$  and calculated  $T_3/T_4$  index are presented in Figure 3.

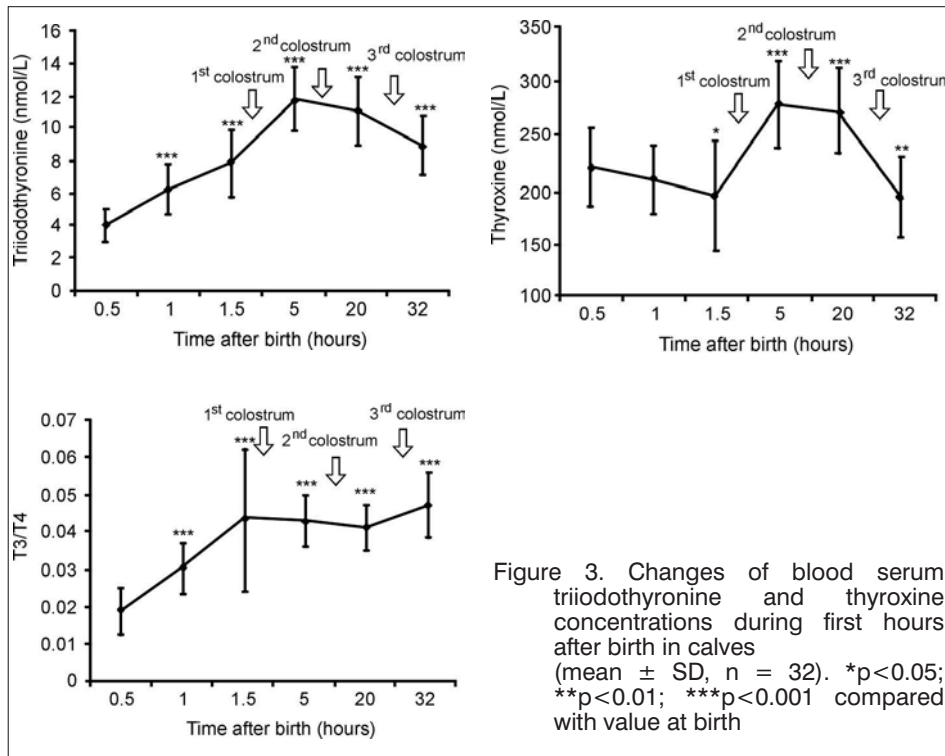


Figure 3. Changes of blood serum triiodothyronine and thyroxine concentrations during first hours after birth in calves (mean  $\pm$  SD, n = 32). \*p<0.05; \*\*p<0.01; \*\*\*p<0.001 compared with value at birth

An obviously increasing tendency of T<sub>3</sub> and decreasing tendency for T<sub>4</sub> within the first 2 hours of neonatal life, and their increase after intake of colostrums was found in this study. There is inconsistency in literature data related to the concentration of thyroid hormones in newborn calves (Davicco *et al.*, 1982; Stojić *et al.*, 2002; Kirovski *et al.*, 2008). This can be explained by the fact that the concentrations of these hormones are under a strong influence of environmental factors. Calves born during the winter period had higher concentrations of thyroid hormones than calves born in other seasons, since the cold environment stimulates the thyroid gland to synthesize and secrete more hormones in neonatal animals after parturition (Stanko *et al.*, 1991). All calves involved in our study were born in September when the average environmental temperatures were from 15 to 20°C. Thyroid concentrations within the first 2 hours were 3.99  $\pm$  1.06 nmol/L for T<sub>3</sub> and 221.56  $\pm$  39.56 nmol/L for T<sub>4</sub> at min 30, 6.23  $\pm$  1.51 nmol/L for T<sub>3</sub> (p<0.001 compared to initial level) and 210.12  $\pm$  30.95 nmol/L for T<sub>4</sub> at min 60 and 7.89  $\pm$  2.12 nmol/L for T<sub>3</sub> (p<0.001 compared to initial level) and 196.05  $\pm$  49.92 nmol/L for T<sub>4</sub> (p<0.05 compared to initial level) at min 90. After the first and second feeding with colostrum T<sub>3</sub> and T<sub>4</sub> concentrations increased and thereafter decreased at hour 32 of postnatal life. Thyroid hormones concentrations were 11.74  $\pm$  1.90 nmol/L for T<sub>3</sub> (p<0.001 compared to initial level) and 278.22  $\pm$  38.80 nmol/L for T<sub>4</sub> (p<0.001 compared to initial level) at hour 5, 11.05  $\pm$

2.13 nmol/L for T<sub>3</sub> (p<0.001 compared to initial level) and 271.42 ± 38.33 nmol/L for T<sub>4</sub> (p<0.001 compared to initial level) at hour 20 and 8.93 ± 1.87 nmol/L for T<sub>3</sub> (p<0.001 compared to initial level) and 194.55 ± 36.45 nmol/L for T<sub>4</sub> (p<0.01 compared to initial level) at hour 32 postnatal.

Good explanation concerning thyroid gland function may be provided using T<sub>3</sub>/T<sub>4</sub> ratio (Šamanc *et al.*, 2010). The T<sub>3</sub>/T<sub>4</sub> ratio is a calculated weight units ratio that reflects thyroid gland function and the potential for action of these hormones on peripheral tissues. The thyroid gland produces mainly T<sub>4</sub>, but also a small quantity of T<sub>3</sub>. In the peripheral tissues the mostly inactive T<sub>4</sub> undergoes extrathyroidal enzymatic activation by 5'deiodinase (5'D) producing the much more potent T<sub>3</sub> (Bianco and Kim, 2006). Our results show that the T<sub>3</sub>/T<sub>4</sub> ratio significantly increases after birth until colostrum intake. Thereafter, T<sub>3</sub>/T<sub>4</sub> ratio is maintained until 32 hours of postnatal life. These results indicate that activation of deiodinases in the peripheral tissues is higher during starvation in neonatal calves. When calf receives colostrum, energy balance is established and deiodinase activity decreases. That supports the earlier conclusion that colostrum should be offered to calves in the first 2 to 4 hours after birth.

Values obtained for the circulating components of the IGF system (IGF-1, IGFBP-1, IGFBP-2 and IGFBP-3) are presented in Figure 4.

IGF system in the neonates can be described by the concentration of IGF-1 and its binding proteins in the circulation (Blum and Hammon, 1999). Concentrations of IGF-1 in our study decline during the first 2 hours of postnatal life and are maintained at a significantly lower level than the initial one until hour 32 of neonatal life. Initial IGF-1 concentration was 20.95 ± 4.12 nmol/L and decreased to 18.56 ± 3.56 nmol/L (p<0.05 compared to initial level) at 60 min and to 16.25 ± 2.93 nmol/L (p<0.001 compared to initial level) at 90 min. After intake of colostrum IGF-1 concentrations were 16.25 ± 2.93 nmol/L (p<0.001 compared to initial level), 16.04 ± 2.39 nmol/L (p<0.001 compared to initial level) and 17.63 ± 2.48 nmol/L (p<0.001 compared to initial level) for hours 5, 20 and 32, respectively. Lower IGF-1 concentration is typical for the condition of negative energy balance. Hammon *et al.* (1997) showed that the somatotrophic axis is not functional in neonatal calves and that IGF-1 has a strong influence on metabolism during the first few hours of neonatal life, before intake of colostrum. In the condition of negative energy balance i.e. starvation, the concentration of IGF-1 depends on the concentration of insulin in the circulation (Rabkin, 1997). Our results confirm this, since there is a significant correlation between IGF-1 and insulin concentrations during the first 2 hours of postnatal life. Correlation coefficients between insulinemia and IGF-1 concentration were r<sup>2</sup> = 0.463 (p<0.05) for 30 min, r<sup>2</sup> = 0.662 (p<0.01) for 60 min and r<sup>2</sup> = 0.583 (p<0.01) for 90 min postnatal.

Higher levels of circulating IGF-I are usually associated with increased amounts of IGFBP-3, which forms a large tertiary complex unable to pass through the capillary walls into the extracellular space and decreased amount of IGFBP-1 which allowed IGF-1 molecules to pass into the tissue (Lelbach *et al.*, 2005). The described arrangement of IGF system components may be observed in our study at 30 min postnatally. Highest abundance of IGFBP-3 (47.09 ± 4.75 ADU/10 μL)



and lowest abundance of IGFBP-1 ( $22.05 \pm 4.86$  ADU/10  $\mu$ L) was observed at 30 min, compared to other time periods. Additionally, highest abundance of IGFBP-2 was observed immediately after birth ( $25.81 \pm 3.79$  ADU/10  $\mu$ L) which is in accordance to the stress reaction characterized by increased concentration of IGFBP-2 (Nikolić *et al.*, 2003). After birth, the abundance of IGFBP-3 significantly decreased to  $44.01 \pm 3.44$  ADU/10  $\mu$ L at 60 min ( $p < 0.05$  compared to initial value) and  $41.72 \pm 4.97$  ADU/10  $\mu$ L at 90 min ( $p < 0.01$  compared to initial value) and maintained low after intake of colostrum. IGFBP-3 abundance was  $43.14 \pm 4.98$  ADU/10  $\mu$ L at 5 hours ( $p < 0.05$  compared to initial value),  $44.66 \pm 5.06$  ADU/10  $\mu$ L at 20 hours and  $47.04 \pm 3.43$  ADU/10  $\mu$ L at 32 hours. Our results are in agreement with Hammon *et al.* (2003) and Onsouka *et al.* (2004). Hammon *et al.* (2000) showed that delaying colostrum feeding from 2 to 12 or 24 h after birth led to decreased plasma IGF-I concentrations associated with decreased IGFBP-3 concentration. IGFBP-2 abundance decreased after birth to  $24.46 \pm 3.55$  ADU/10  $\mu$ L at 60 min and to  $22.69 \pm 4.25$  ADU/10  $\mu$ L at 90 min postnatally ( $p < 0.05$  compared to initial value). After intake of colostrum, IGFBP-2 abundance

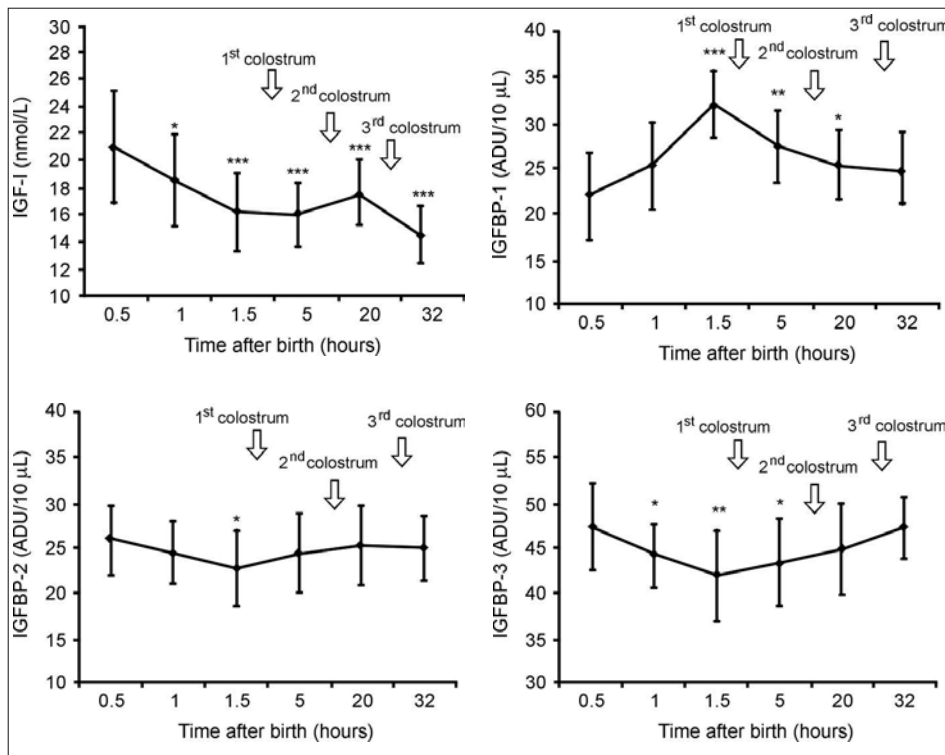


Figure 4. Changes of blood serum IGF-I concentrations (mean  $\pm$  SD, n = 32) and IGFBP-1, IGFBP-2 and IGFBP-3 abundance (mean  $\pm$  SD, n = 16) during the first hours after birth in calves. \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$  compared with value at birth

increased, but not significantly to  $24.45 \pm 4.44$  ADU/10  $\mu$ L at 5 hours, to  $25.31 \pm 4.25$  ADU/10  $\mu$ L at 20 hours and to  $25.16 \pm 3.57$  ADU/10  $\mu$ L at 32 hours. Abundance of IGFBP-1 increased during the first 2 hours of neonatal life from the initial value ( $22.04 \pm 4.86$  ADU/10  $\mu$ L) to  $25.26 \pm 4.77$  ADU/10  $\mu$ L at 60 min and  $31.99 \pm 3.76$  ADU/10  $\mu$ L at 90 min postnatally ( $p < 0.001$  compared to initial value). The presence of a positive relationship of insulin and IGFBP-1 in our work is in accordance with the well-known acute effect of insulin on its synthesis (Goswami *et al.*, 1994). IGFBP-1 abundance decreases after intake of colostrum but remains significantly higher than the initial value at 5 hours ( $27.28 \pm 4.15$  ADU/10  $\mu$ L;  $p < 0.01$ ) and 20 hours ( $25.30 \pm 3.90$  ADU/10  $\mu$ L;  $p < 0.05$ ). At hour 32 of neonatal life IGFBP-1 abundance was  $24.93 \pm 3.86$  ADU/10  $\mu$ L.

In conclusion, immediately after birth the vigorous activity of the adrenal cortex in cortisol secretion and extrathyroidal tissue in providing a sufficient level of triiodothyronine play a crucial role in the mobilization of energy reserves, promotion of catabolism and subsequent rise in glucose concentration. Additionally, immaturity of the somatotrophic axis and mechanisms responsible for insulin secretion provide dominance of catabolic processes during this period of neonatal life.

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#### **HORMONALNI STATUS I REGULACIJA GLIKEMIJE KOD NOVOROĐENE TELADI TOKOM PRVIH SATI POSTNATALNOG ŽIVOTA**

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#### **SADRŽAJ**

Cilj ovog rada je bio da se ispituju promene koncentracije pojedinih hormona kod novorođene teladi u prvim satima neonatalnog života i utvrdi njihov uticaj na glikemiju. Odabrana su 32 novorođena teleta Holštajn rase kojima je 30, 60. i 90. minuta postnatalnog života uzeta krv. Telad su bila napajana pulovima kolostruma. Pul primarnog kolostruma davan je u količinama od po 1,5 litar 2 sata nakon rođenja, dok su pulovi sekundarnog i tercijarnog kolostruma davani 12, odnosno 24 sata kasnije, u količinama od po 2 litra. Tokom perioda kolostralnog napoja, teladi je uzorkovana krv 5, 20 i 32. sata nakon rođenja. U uzorcima krvi određivana je koncentracija glukoze, insulina, kortizola, tireoidnih hormona i IGF-I,

kao i zastupljenost IGFBP-1, IGFBP-2 i IGFBP-3. Takođe je obračunat indeks konverzije  $T_3$  u  $T_4$ .

Telad su bila rođena u stanju hipoglikemije (koncentracija glukoze na rođenju je iznosila  $2,56 \pm 1,05$  mmol/l). Nakon toga, glikemija je značajno porasla ( $p < 0,001$ ) do  $3,05 \pm 0,89$  mmol/l (90. minut). Porast koncentracije glukoze je nastavljen i nakon unosa kolostruma, tako da je glikemija u svim ispitivanim uzorcima bila značajno veća u odnosu na početnu vrednost ( $p < 0,001$ ). Tokom prvih 90 minuta neonatalnog života, koncentracija insulina se značajno smanjivala ( $p < 0,001$ ) u odnosu na početnu vrednost ( $26,33 \pm 10,05$   $\mu$ U/l) tako da je 90. minuta postnatalnog života bila  $18,66 \pm 5,56$   $\mu$ U/l. Porast insulinemije nakon unosa kolostruma nije bio značajan u odnosu na vrednost određenu 90. minuta. Koncentracija kortizola je bila najviša 30 minuta nakon teljenja ( $85,08 \pm 19,36$  nmol/l) a zatim je opadala do kraja perioda ispitivanja i to značajno u odnosu na početnu vrednost ( $p < 0,001$ ) u uzorcima dobijenim nakon unosa kolostruma. Visoka pozitivna korelacija je utvrđena između glikemije i kortizolemije u svim ispitivanim terminima pre kolostralnog napoja ( $r^2 = 0,854$  u 30. minutu;  $r^2 = 0,742$  u 60. minutu i  $r^2 = 0,551$  u 90. minutu). Koncentracija  $T_4$  je značajno rasla tokom prva dva sata neonatalnog života, dok se koncentracija  $T_3$  smanjila, značajno od 30. do 90. minuta neonatalnog života ( $p < 0,05$ ). Konverzija  $T_3$  u  $T_4$  je značajno porasla tokom prva dva sata života. Nakon unosa kolostruma, koncentracija oba tireoidna hormona se povećavala (značajno u odnosu na početnu vrednost) a indeks konverzije se nije menjao, već se zadržao na vrednosti ustanovljenoj 90. minuta života. Koncentracija IGF-1 se značajno smanjivala tokom prva 2 sata neonatalnog života. Koncentracija IGF-1 je bila u visokoj pozitivnoj korelaciji sa insulinemijom ( $r^2 = 0,463$  za 30. minut,  $r^2 = 0,662$  za 60. minut i  $r^2 = 0,583$  za 90. minut). Zastupljenost IGFBP-3 se značajno smanjivala, dok se zastupljenost IGFBP-1 značajno povećavala u ovom periodu. Zastupljenost IGFBP-2 je bila najveća na rođenju. Rezultati prikazani u ovom radu ukazuju da je porast glikemije u prvim satima života, pre unosa kolostruma, prevashodno posledica pojačane aktivnosti kore nadbubrega u sekreciji kortizola i dejodinaza u ekstratireoidnim tkivima koje obezbeđuju povećanu sintezu  $T_3$ . Sistemi odgovorni za sintezu insulina nisu potpuno funkcionalni u ovom periodu, omogućavajući prevagu kataboličkih u odnosu na anaboličke procese. Promene unutar IGF sistema omogućavaju porast glikemije i uspostavljanje energetske ravnoteže.

