Artykuł przeglądowy *Review*

Effect of age and food intake on the selected blood plasma/serum proteins in calves during the early postnatal period*)

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Summary

The most intense adaptive changes to the extrauterine environment occur during the first week of calves' lives. These changes involve many vital systems, including the gastrointestinal tract. Bovine colostrum contains various essential nutrients and supplies newborn calves with energy and also bioactive factors. Intestinal absorption of these molecules and its further passage into the bloodstream is only possible within the first 24 hours of life. Thus, the exact time of the first colostrum intake is crucial for the newborn calf, as it initiates a number of physiological processes, which results in, e.g., increased synthesis of endogenous proteins. The placenta of bovine species prevents the effective transfer of maternal plasma proteins to the conceptus, thus newborn calves are considered as a suitable model for the study of blood plasma protein profile changes with age and in response to the food intake. This review is intended to discuss the present state of knowledge within this subject.

Keywords: calves, postnatal period, blood plasma, proteins

The adaptation of newborn calves to the extrauterine environment requires intense structural and functional changes in many vital organs, including the gastrointestinal tract (GIT). These adaptational changes involve a transition in dietary energy sources, from a diet comprising mainly carbohydrates and amino acids to fat-rich diet. Colostrum is the first, natural food for the newborn calves. It is not only a source of nutritional substances essential for proper growth and development of an organism, but it also abounds in a wide variety of non-nutrient components responsible for initiating, controlling and supporting many biological processes (28). The composition of bovine colostrum, secreted for three days after delivery, and mature milk, produced at a later time, has a dynamic nature and it varies considerably with age, breed, nutrition, energy balance and stage of lactation (8). It seems that changes in milk composition occurring during the whole lactation period reflect changes in nutritional requirements of the young calf. The first portions of colostrum primarily contain high amounts of immunoglobulins, growth factors and oligosaccharides, which concentration dramatically decrease during the first days of lactation. At a later stage of lactation there is only an increase in the concentration of whey proteins and casein until the dry period (8).

Changes of selected calves blood plasma/serum proteins

Structural, functional and metabolic alterations occurring in calves during the early postnatal period are reflected by changes in blood plasma protein repertoire. It seems that a calf is a suitable model for the study of dynamic blood plasma protein changes, because the characteristic structure of the placenta effectively prevents maternal plasma proteins from transfer across the placental barrier. For about the first 24 hours of life, calves absorb a number of colostral macromolecules from the small intestine into the main bloodstream, including proteins and other biologically active peptides (29). There are two distinct pathways of intestinal macromolecule transport: 1) specific

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receptor-mediated transcytosis and 2) nonspecific transcytosis (25). In the hours following after birth, when the process of gut closure is completed, the small intestine is impermeable for colostral proteins.

Immunoglobulins

Among all plasma proteins, immunoglobulin G exerts the most intense age-related and diet-related changes during the early postnatal period. After birth, IgG in the blood plasma/serum is practically not present, which is mainly caused by placental structure, which isolates the foetus from maternal plasma immunoglobulins (Igs). Hence, the neonatal calf is entirely dependent on the intestinal absorption of colostral antibodies. Providing an adequate passive transfer of immunity is crucial for the survival, health and proper development of the calves (16, 31).

Intestinal absorption of intact immunoglobulins is mainly facilitated by the presence of foetal-type enterocytes and decreased proteolytic degradation of proteins due to the presence of colostral protease inhibitors (25). Moreover, the colostrum composition has an influence on the above mentioned process. It was demonstrated that feeding calves with colostrum of other species results in a much more lower immune transmission. Thus, it is postulated that colostrum contains species-specific factors that enable endocytosis across the small intestine of the newborn (27). Development of the gut microflora also contributes to lower protein absorption. Calves are born with a sterile gastrointestinal tract: however, in the hours following after birth the gut is colonised by microflora, which favour degradation of the immunoglobulins (26). The amount of immunoglobulins in the blood plasma of calves absorbed from colostrum depends on several factors, including the time and volume of the first colostrum ingestion, concentration of Igs in colostrum, methods of colostrum feeding and the absorptive capacity of the neonatal intestine (33). Much data exists in the literature concerning studies of the transfer of colostral Igs both in dairy and beef calves (9, 10, 26, 31, 33). The results of these studies clearly indicate that first colostrum feeding results in increased serum concentration of IgG, reaching a peak at 24 hour after birth. Suh et al. (33) reported that the mean serum levels of IgG at the first day of life were higher in beef calves (45 mg/ml) in comparison to dairy calves (20 mg/ml). The authors showed the gradual decline of IgG from 24 hours over 14 days of life in both dairy and beef calves. The pattern of changes of serum IgG concentration is similar to one observed in IgM and IgA. These immunoglobulins are not present in the serum of the newborn calves and its concentration increases, reaching its peak at 24 hours after colostrum feeding. Serum levels of IgM and IgA were also higher in beef calves (2.3 mg/ml for IgM, 0.9 mg/ml for IgA) than in dairy calves (1.3 mg/ml for IgM, 0.4 mg/ml for IgA) (33).

Alpha-1-fetoprotein and albumin

Significant changes in blood plasma concentrations of α_1-fetoprotein (AFP) and albumin are observed during fetal development and early postnatal life in cattle. AFP is the predominant plasma protein in the bovine foetus. It is mainly synthesised by the yolk sac and at the later period by the foetal liver. Smith et al. (30) have demonstrated that concentration of AFP in foetal bovine plasma reaches the highest values (4 mg/ml) in the 3-4 month of foetal period, which is followed by significant decrease until birth.

On the other hand, the plasma concentration of albumin is relatively low in the foetal bovine plasma (14). Judah and Thomas (15) reported that albumin is initially synthesised as a preproalbumin in the endoplasmic reticulum of the hepatocytes and it is further converted into the proalbumin form. Proalbumin possesses an additional hexapeptide attached to the N-terminal polypeptide chain (in bovine: Arg-Gly--Val-Phe-Arg-Arg). Degradation of this sequence by proteases in the Golgi apparatus results in formation of the mature form of albumin, which is immediately secreted from the hepatocytes. The results from a previous studies (19, 38) indicate that the most dynamic increase in plasma albumin concentration occurs from the moment of birth (mean value 21 mg/ml) until the seventh day of calves life (mean value 27 mg/ml). At a later time, only slight changes in concentration of this protein are observed. The albumin synthesis by the liver is enhanced due to increased dietary amino acids supply (4). According to Akker et al. (1) high plasma level of this protein in the early neonatal period helps to maintain the metabolic balance in newborns. Aside from its fundamental role as a transporter that binds and carries amino acids (AAs) albumin also provides for temporary storage of AAs, which prevents them from oxidation. In the situation of low protein intake or increased protein demands of growing organism, free AAs are released from AA-albumin complexes (1).

Similar chemical and physical properties and also existence of amino acid sequence homology between these two proteins indicate that AFP is the fetal analogue of albumin. Moreover, these proteins exert congenial biological functions displayed by ability to bind similar molecules such as bilirubin, copper and fatty acids (35).

Protease inhibitors

Blood plasma concentrations of protease inhibitors increase dynamically in calves during perinatal and neonatal period. From all protease inhibitors, α_1-antitripsyne (AAT) is considered as the most abundant protein in the blood plasma of many farm animals, including cattle. The main functions of this protein is to inhibit the activity of the serine proteases (trypsin, chymotrypsin) and also to inactivate elastase, which is released by neutrophils in response to inflammatory reactions (5). In the available literature there is a lack of information concerning changes in plasma α_1-antitrypsin concentration in calves during the early postnatal period. Martin et al. (21) reported that the concentration of AAT in the blood plasma of fetal pigs is 15-fold higher compared with mature individuals. Nevertheless, during the first two weeks of piglets' lives, a statistically significant decrease of plasma α_1-antitrypsin concentration is observed (21).

Fetuin-A, the protein which is considered as a main glycoprotein in the blood plasma of bovine fetuses, shows a similar pattern of changes. Its concentration gradually decreases a few days before calves birth and also during the first two weeks of postnatal life (20). Fetuin-A exerts a wide range of biological functions, including: lipid transport during the foetal period, trypsin activity inhibition, as well as apoptosis induction (7, 37). The results of a study conducted by Heiss et al. (10) indicate that fetuin-A also binds to calcium and phosphorus. Moreover, the authors imply that this protein might possibly play a role in maintaining homeostasis of these macroelements during fetal and early postnatal period (11).

Acute phase proteins

Acute phase reactants constitute another group of proteins which show relevant changes in concentration in the blood plasma of calves during early postnatal development (23). Acute phase proteins (APP) are produced by the liver of the neonates and represent the first line of defence against potential pathogens (24). The plasma profile of APP differentiate between the species. In cattle, these proteins include: haptoglobin (Hp), ceruloplasmin (Cp), fibrinogen (Fb), α_1-acid glycoprotein (AGP), α_1-antitripsyne, serum amyloid A (SAA) and fetuin-A (5). APP elicit an array of biological functions such as: limiting tissue damage during the inflammatory process, inhibiting excessive platelet aggregation, deactivating free radicals (Cp), may also participate in blood coagulation and fibrinolysis processes and in protection against iron losses (Cp, Fb, Hp). Additionally, acute phase proteins enhance nonspecific immune response through increased activation of leukocytes and the complement system (18).

From all the above mentioned APP, the concentration of α_1-acid glycoprotein, serum amyloid A and haptoglobin demonstrate the most intense changes in the blood plasma of calves during the first week of postnatal life. Itoh et al. (13) reported that the plasma AGP levels were the highest immediately after birth and gradually decreased during the first three days of calves' lives. Similar results were obtained by Orro et al. (23). The authors noted that the highest plasma concentration of α_1-acid glycoprotein occurred at birth (13,18 mg/ml) and was followed by a gradual decrease, reaching a value of 0.9 mg/ml on the seventh day of life. Orro et al. (23) also demonstrated that the concentration of serum amyloid A in the blood plasma of calves was relatively low immediately after birth (0.06 mg/ml) and significantly increased on the third day of life (0.09 mg/ml). Also plasma haptoglobin values are very low at birth and increase during the first week (23). These results are in accordance with similar studies conducted by Alsemgeest et al. (2). Dobroszycka (6) postulates that increased expression of haptoglobin is caused by elevated hemolysis of fetal erythrocytes and haptoglobin is known to reduce the oxidative and peroxidative potential of free haemoglobin. The high plasma concentration of haptoglobin during the first fourteen days of calves' lives was also demonstrated by Knowles et al. (17).

The factors directly responsible for the hepatic synthesis of acute phase proteins are not yet well defined. Nevertheless, it is postulated that the birth trauma may have a great influence on that phenomenon. Cellular stress-inducing factors activate the hypothalamic-pituitary-adrenal axis as well as the sympathetic nervous system (SNS). Black (3) claims that the above-mentioned stimuli may induce secretion of proinflammatory cytokines and glucocorticoids, which in turn may lead to an increased synthesis of APP. Another possible factor which may be responsible for increased plasma concentration of acute phase proteins in the newborn calves is the absorption of colostral proinflammatory cytokines. In a study conducted by Yamanaka et al. (36) with newborn calves, it was found that immediately after birth, IL-6 in the blood plasma is not present. The authors also demonstrated a rapid increase in plasma IL-6 level in calves within 24 hours after the first colostrum intake. Probably free pro-inflammatory cytokines absorbed from colostrum directly stimulate APP synthesis and/or activate the circulating lymphocytes and neutrophils. Nagahata et al. (22) postulate that probably hepatic production of APP is one of the mechanisms involved in the compensation of a functionally immature immunological system during the early neonatal period, which facilitate adaptation to extrauterine life.

Lactoferrin

Lactoferrin (Lf) is a glycoprotein which exerts both bacteriostatic (elicits high iron binding affinity, thus prevents from its utilisation by invading bacteria) and also bactericidal (binds to bacterial lipopolysaccharides and destroys its cell membranes) effects (28). Moreover, Lf elicits antiviral (against a wide variety of DNA and RNA viruses), antifungal (particularly against the *Candida* type of fungus) and antiinflammatory actions (32). It should be emphasised that lactoferrin may act synergistically with immunoglobulins, leading to increased antibacterial protection (28). The other function attributed to lactoferrin is participation in many immunological processes including: regulation of leukocyte cytotoxic activity and lymphocyte proliferation (12). Hurley and Sixiang (12) demonstrated that immediately after birth, the lactoferrin concentration in the serum of calves was approximately 1.09 μg/ml. The first colostrum intake resulted in a 10-fold increase in serum Lf levels. These changes persisted for the next 8-12 hours and were subsequently followed by a gradual decrease until the second day of calves' lives (12). The authors suggested that the observed increase in serum lactoferrin concentration was probably caused by its absorption from the colostrum and it was not the result of a transitory release of endogenous Lf into the main bloodstream (12). Similar results were obtained by Talukder et al. (34). The authors found that the concentration of lactoferrin in the blood plasma of calves was relatively low at birth (0.20 μg/ml) and dramatically increased (10-fold) after 6 hours after the first colostrum intake. This tendency was sustained for the first 12 hours of life.

It is clear that the plasma protein profile is profoundly modified in the first days of life, which is mainly influenced by colostrum intake. Among the reported changes, acute phase proteins deserves particular attention. It seems that observed alterations in both plasma APP and in the other above described proteins are a part of the mechanism involved in facilitating normal adaptation to extrauterine life.

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