TÜBİTAK

Turkish Journal of Veterinary and Animal Sciences

http://journals.tubitak.gov.tr/veterinary/

Review Article

Turk J Vet Anim Sci
(2013) 37: 390-394

doi:10.3906/vet-1210-33

Factors affecting colostrum quality of ewes and immunostimulation

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Received: 22.10.2012 • **Accepted:** 12.12.2012 • **Published Online:** 29.07.2013 • **Printed:** 26.08.2013

Abstract: Maternal antibodies play a major role in the development of the immune system of a young animal. Ideally, the transmission of maternal immunity to the foetus occurs in the uterus. However, in ruminants, as there is no maternal antibody transfer from the mother to her young by way of the uterus, the antibodies present in the colostrum are a vital necessity for newborn ruminants. After birth, an unhealthy neonatal period for the young animal and an unhealthy puerperal period for the mother can cause significant financial losses. In animal husbandry, due to the budget allocated for the treatment of diseases and the economic damage of breeding that can be caused by lasting problems created by disease, the importance given to preventive medicine has increased further. Therefore, in breeding, increasing the resistance against the disease agent is preferred instead of treating disease. This situation has resulted in more studies to improve the level of maternal and colostral antibodies as well as the widespread use of specific and nonspecific immunostimulants in veterinary medicine. In this review, the factors affecting the quality of ewe colostrum are discussed and the importance of colostrum quality for a newborn lamb is described. In addition, the methods used today to increase the quality of colostrum are presented.

Key words: Ewe, newborn lamb, colostrum, immunostimulation

1. Introduction

After birth the first secretion from the mammary glands is called colostrum (1). Colostrum is varied in terms of colour and the composition varies from that of normal milk. Between the second and eighth milkings, the structure of the milk gradually turns normal, and the secretion between these periods is called transit milk. In approximately 72 h colostrum turns into normal milk (2).

Colostrum plays a vital role in providing passive immunisation, thereby contributing to the development of the gastrointestinal tract, affecting the endocrine and metabolic systems and providing a source of energy for young animals to obtain heat generation to protect themselves from hypothermia (3). In addition, it has a laxative effect, which helps with the removal of meconium from the intestine (1).

While the normal milk of ruminants and ewes contains 12% solids, the same rate for colostrum is 22%. This difference is related to the density of multi-immunoglobulin. In addition, the solid material is richer in terms of casein, fat, protein, and vitamins A, B_{12}, D, and E, although it is poorer in terms of lactose. It helps to prevent the digestion of the immunoglobulins in the intestine with trypsin inhibitors (4,5). Transferrin and lactoferrin in colostrum play a role in controlling diarrhoea by binding iron and limiting the growth of some bacteria (4). Colostrum fulfils these responsibilities through the cellular (polymorph nuclear leukocytes, macrophages, lymphocytes, and natural killer cells) and humoral (lactoferrin, the lactoperoxidase–thiocyanate–hydrogen peroxide system, lysozymes, complements, and immunoglobulins) factors that it contains (6). In addition, the colostrum of ruminants and ewes contains insulin-like growth factor I (IGF-1), insulin (INS), growth hormone (GH), thyroxine (T4), triiodothyronine (T3), and prolactin (PRL) (2).

In the last 5 weeks of pregnancy, IgA, IgG, and IgMs are synthesised by plasma cells in the submucosa of the mammary gland epithelium, and at the same time IgGs taken from blood by transudation begin to concentrate in the secretions of the mammary gland by entering the gland tissue by way of pinocytosis (4,6). This condition is associated with an increase in the amount of oestrogen in the mother. The specific receptors in the mammary gland epithelium bind IgG_1 selectively and take it into the cell by transcapillary change. IgG_1 is moved through the lumen of the gland and gradually passed into the colostrum. After a while, the concentration of colostral IgG_1 reaches the level of 3–12 times serum levels and the concentration of serum IgG_1 reduces by approximately 50%. Some of the colostral IgG_1 is absorbed by the intestine, while some of it remains in the intestine and neutralises pathogenic bacteria (6).

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At the end of a short absorption period in ruminants, in order to obtain adequate levels of passive immunity, the colostrum should be of good quality. This quality is evaluated by the concentration of immunoglobulins in the colostrum (7).

2. Development of the neonatal immune system

Ruminants' epitheliochorial placenta is impermeable for antibodies and this situation causes newborns to be devoid of immunoglobulins namely, agammaglobulinaemia, or with a very small amount of immunoglobulin, namely hypogammaglobulinaemia (8–12). Therefore, newborn ruminants are in need of the immunoglobulins that they would absorb from colostrum for passive immunity until their immune systems develop. However, the transition of immunoglobulins obtained from colostrum takes place within a limited period of time. The small intestine of lambs begins to lose the ability to absorb maternal antibodies within 24–48 h after birth (8,9,11,13,14). The end of the intestinal wall permeability to macromolecules in newborn animals is called "intestinal closure" (4,15).

3. Absorption of colostrum mechanism

Colostral absorption is defined as the passage of substances in colostrum into blood from the intestinal lumen. Newborns transfer colostrum to the intestinal canal by absorbing it. Lambs are able to absorb antitoxins of different species, polyvinylpyrrolidone (PVP), ruminant colostral proteins, and substances such as egg proteins within 48 h after birth (15). Proteins enter the intestinal epithelium of neonates through the agency of the tubulovesicular system located at the edge of epithelial cells. From here, they pass into the intestinal lymphatics and capillary vessels. Thus, these absorbed immunoglobulins, which are the structure of protein, pass into circulation and the newborn completes the transfusion of maternal immunoglobulins. However, this situation changes for each domestic animal according to selectivity and intestinal permeability. The intestine of ruminants has nonselective permeability and therefore may absorb all immunoglobulin isotypes (8,11).

4. Factors affecting intestinal closure

Immunoglobulins are highly resistant to digestion by intestinal enzymes. The trypsin inhibitor in colostrum also plays a role in the formation of this resistance (4). The average time of intestinal closure has been determined for IgG as 26.4 h, for IgM as 25 h, and for IgA as 26 h. However, it has been detected that intestinal closure may be affected by the initial time that the colostrum was taken by the newborn. It has been reported that the amount of colostrum received has no effect on intestinal closure (14).

5. Factors affecting the quality of colostrum

The quality of colostrum correlates directly with the amount of IgG it contains. This quality decreases as time goes by after birth (7). It has been reported that dairy breeds produce more colostrum than beef breeds and this colostrum is richer in terms of immunoglobulin (4,16). Likewise, in adult ewes and cows, higher levels of colostrum and colostral immunoglobulins have been detected than in youngsters (4,17,18).

Milking before birth, colostrum leaking from the mother's udder (19,20), inadequate nutrition of the mother in terms of energy during pregnancy, long-acting corticosteroid applications, and lambs not being taken care by mothers all have a negative effect on the level of colostral IgG (20). Shubber and Doxey (21) reported that there is no significant difference in terms of immunoglobulin levels in colostrum samples taken from the left and right udder lobes. Another factor affecting the quality of colostrum is the health condition of the udder. Colostrum milk from an udder with mastitis should never be given to a young animal (22).

Al-Sabbagh (22) and Gallo and Davies (23) compared the colostrum of single- and twin-pregnant ewes and determined that the colostral IgG levels in the ewes that had twin births were higher. In the study conducted by Al-Sabbagh (24), it was reported that the body weight of a ewe has a direct correlation with the concentration of IgG in colostrum samples collected 12 h after birth. In other studies it was reported that there was no correlation between the sex of the lamb and colostral IgG levels (25,26).

6. Immunostimulation

The only defence mechanism against the environmental factors of a neonatal ruminant is the antibodies obtained from colostrum. The poor nutrition of the dam, immune system suppression, and stress factors may lead to inadequate colostral immunoglobulin titres. Besides the improvement of nutritional and stress conditions, the stimulation of the immune system by exogenous methods may increase colostral immunoglobulin titres (27,28). The regulation of the immune system with some agents given to an organism exogenously is defined as "immunostimulation" and the agents used in this process are called immunostimulants (29).

Immunostimulants are analysed in 2 main groups as chemical and biological according to their origin. Both immunostimulant classes may be used for the treatment of and protection against various infections and may also be used as adjuvants that cause stronger immune responses in organisms against the vaccines administered (29,30). However, the actual expected effect of an immunostimulant is to decrease the morbidity and mortality rates and increase weight gain (30). As a result of previous studies, positive results have been reported in terms of reproductivity by administration of immunostimulants to ruminants during advanced pregnancy (30,31).

Major immunostimulants are typically microbial preparations that can be captured easily by macrophages such as mycobacteria, anaerobic coryneforms (*Corynebacterium cutis*, *Propionibacterium acnes*, etc.), and some plant carbohydrates that have a fungal origin (32,33). Activation of macrophages has been performed primarily in order for the preparation that was given to have an immunostimulant effect on the organism. For the preparation given to the organism to have an effect, inflammation is the first response of the body against pathogens. First, the polymorphonuclear cells (granulocytes) migrate to the region and then invasion of macrophages takes place. Macrophage activation is then stimulated either as a result of direct interaction with antigens or by way of bacterial endotoxins (34). When these immunostimulants are captured and digested by macrophages, they stimulate the macrophages to synthesise cytokines such as interleukin-1 (IL-1), tumour necrosis factor (TNF), and interleukin-6 (IL-6). After the release of these cytokines, lymphocytes are activated and lymphokines such as interleukin-2 (IL-2) and interferon-γ (IFN-γ) are released. At the end of all of these stages, resistance to viral infection, natural killer cell (NKC) activity, production of antibodies, inflammation reactions, and the level of wound healing increase (30,35–38).

7. Some immunostimulants and their mechanisms

The effect of levamizol used as an anthelmintic on the immune system arises as the result of a cascade of events such as phagocytosis, chemotaxis, lymphocyte production, lymphokinesis production, delay of hypersensibility, and the formation of interferon and antibodies (39,40).

It has been reported that β-glucan, which is a structural component of the fungal cell wall, has an immunostimulant effect by increasing the activity of NKCs, macrophages, and lymphokine-secreting T-helper cell activity (41,42).

OM-85 (LW-50020, SL-04), which includes lyophilised bacteria lysate obtained from *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Klebsiella pneumoniae*, *Klebsiella ozaenae*, *Staphylococcus aureus*, *Staphylococcus viridans*, and *Neisseria catarrhalis*, has the property of activating the capacity of polymorphonuclear cells, phagocytic ability of macrophages, and activation of dendritic cells and B lymphocytes after it is given to an organism. After all of these, it exhibits the immunostimulant effect by stimulating cytokines such as interferon-γ, which has an important role in fighting infections (41,43).

Today cytokines can be obtained using recombinant DNA technology and can be used to stimulate the immune system (44). It has been reported that disruptions in the production of IL-2 may cause severe immune deficiency (45,46). Therefore, exogenous application of the cytokine is expected to activate the immune system (44).

It has been reported that vitamin C (20 mg/kg) administered to ruminants increases the neutrophil oxidative mechanisms and antibody-dependent cellular cytotoxicity mediated by neutrophils (24). Vitamin E, which can be added to the diet or administered as an injectable, and selenium support the immune system by ensuring the stimulation of antibody synthesis, increasing the migration of leukocytes to the infection region, strengthening the capacity of phagocytosis, and preventing the harmful effects of reactive oxygen on the cell membrane (47).

It has been reported that the agents obtained by ultrasound from lysates of *Corynebacterium cutis commune* are easily phagocytised by macrophages after the administration of organisms; stimulate the secretion of TNF, IL-1, and IL-6 by macrophages; and enable the release of lymphokines, IL-2, and IFN-γ by affecting secondary lymphocyte function and therefore reactivation of the immune system. With increasing immunity it is expected that the rates of morbidity and mortality caused by bacterial and viral infections will reduce and it is expected that weight gain will be observed as a result of improving health care and nutrition. Turna Yılmaz et al. (48) reported increases in concentrations of colostral IgG at 0, 36, and 72 h after birth by administration of *C. cutis lysate* to pregnant ewes on day 140 of gestation.

8. Conclusion

All organisms just after birth are exposed to some harmful microorganisms and various stress factors in environmental conditions. The weakness in the newborn immune system makes it easy for these factors encountered after birth to cause some infections in the body. For the fight against these factors, the antibodies in colostrum provide the greatest support to newborns. Therefore, it is suggested that immunostimulation application for pregnant ewes during pregnancy in order to reduce postnatal morbidity and mortality rates, increase the live weight gain, and obtain immunoglobulin-rich colostrum will be helpful.

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