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Passive immunity in lambs: Serum lactoferrin concentrations as a predictor of IgG concentration and its relation to health status from birth to 12 weeks of life

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ABSTRACT

This study was designed to evaluate the potential of lactoferrin (Lf) as predictor of passive immunity by establishing correlation between serum Lf and IgG concentration determined by ELISA in healthy lambs before and after colostrum intake at various days of neonatal period, to determine the presumptive effect of serum Lf along with serum IgG levels on lamb health through comparison of values measured for healthy and diseased lambs and to evaluate the impact of colostral Lf concentrations on passive immunity and lamb health. For this purpose, blood samples were obtained from the fifty healthy lambs at birth and 1, 2, 4, 7, 14 and 28 days after birth. Additionally first day blood samples were also collected from 286 lambs. Health status of all lambs ($n = 336$) was monitored from birth to 12 weeks of life. Colostrum samples were obtained within 0–4 h of parturition from 193 the ewes related to the lambs tested in this study. Serum Lf and IgG concentrations of day 1, 2, 4, 7, 14 and 28 were significantly higher than the values of pre-suckling time in healthy lambs. There was a weak linear relationship between serum Lf and IgG concentrations in only 1, 2, 4 and 7 day-old healthy lambs ($R^2 = 0.073–0.079$) except for the first day ($R^2 = 0.213$). The multiple linear regression model moderately ($R^2 = 0.375$) estimated the serum IgG concentration as a function of the serum Lf concentration and of the age of lambs at the time of sampling [day 1, 2, 4, 7, 14 and 28] in healthy lambs during the neonatal period. The healthy lambs had significantly higher Lf concentration at 24th hour after the birth (SLfC-24) than ill lambs in the neonatal period ($P < 0.01$) and the period covering 5–12 weeks of life ($P < 0.01$). Similar results were found for SIgGC-24. The morbidity rate of lambs with SLfC-24 <800 ng/mL was 3.2 times higher in neonatal period and 1.7 times higher in the period covering 5–12 weeks of life when compared with lambs having SLfC-24 above 800 ng/mL. There was a significant ($P < 0.01$) and positive ($R = 0.261$) correlation between CIgGC and CLfC. In conclusion, our study revealed the importance of serum Lf in prevention of disease development in lambs and in prediction of passive immunity. In addition, the positive correlation between colostral Lf and IgG values may be of use in evaluation of colostrum quality.

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1. Introduction

Neonatal morbidity and mortality is an important cause of economic loss for sheep farms (Gilbert et al., 1988; Bekele et al., 1992; Gökçe and Erdoğan, 2009; Gökçe et al., 2013a), thus making this period the most critical (Massimini et al., 2006; Gökçe and Erdoğan, 2008; Gökçe et al., 2010). Lambs are born hypogammaglobulinemic and require consumption of colostrum as a source of immunoglobulin-G (IgG) in the first few days of neonatal period. This process is named as passive immunity. Numerous studies in the past three decades correlated neonatal diseases with inadequate serum IgG, in other words, failure of passive transfer (FPT) in animals and thus suggested the importance of IgG in the prevention of infections and enhancing growth performance in neonates (Vihan, 1988; Gilbert et al., 1988; Bekele et al., 1992; Massimini et al., 2006; Andres et al., 2007; Brujeni et al., 2010; Gökçe et al., 2013b). However, recent studies showed that some neonatal animals with low levels of IgG resisted diseases while some with adequate IgG did not (Gilbert et al., 1988; Basoglu et al., 1999; Tyler et al., 1999), indicating other significant components of passive immunity such as growth factors, cytokines, acute phase proteins, lactoferrin (Lf) and undefined factors (Barton et al., 2006; Orro et al., 2008; Dawes et al., 2008).

Lactoferrin is a non-heme-associated iron binding glycoprotein of the serum transferrin gene family and was first isolated from cow's milk and constitutes the largest fraction of the whey protein. It is also found in various physiological fluids including plasma, tears, saliva, vaginal fluids, semen, nasal, lacrimal and bronchial secretions, bile, gastrointestinal fluids, urine, synovial and amniotic fluids, mucosal surfaces and neutrophil granules. Lf is found in higher concentrations in colostrum when compared to milk (Legrand et al., 2004; Dawes et al., 2004; Barton et al., 2006). Colostrum intake results in increased serum Lf concentration (SLfC) in calves (Talukder et al., 2002; Hurley and Sixiang, 2000; Dawes et al., 2004), foals (Barton et al., 2006) and piglets (Harada et al., 1999) as Lf along with IgG are transferred from intestinal tract to systemic circulation trough passive absorption in newborns animals (Talukder et al., 2002; Talukder and Harada, 2006). However, no direct correlation between bovine colostral Lf and post suckle serum Lf concentration (SLfC) was also reported (Holloway et al., 2002).

Lf exhibit immunoregulator effect through its antimicrobial, anti-inflammatory, antioxidant and anticarsinogenic properties (Lakritz et al., 2000; Dawes et al., 2004; Larkins, 2005; Barton et al., 2006; Dawes et al., 2008; Legrand and Mazurier, 2010). Lf modulates the proliferation, maturation, migration, and activation of immune cells. It also stimulates various cytokines and decreases the formation of free radicals (Legrand et al., 2004; Puddu et al., 2009; Actor et al., 2009). Lf binds to microbial membrane components, particularly lipopolysaccharide (LPS) consequently alters permeability that leads to bacteriolysis and also neutralizes the detrimental effects of LPS through preventing expression of cellular cytokines (Lakritz et al., 2000; Sarelli et al., 2003; Larkins, 2005, Kushibiki et al., 2008, Dawes et al., 2008). In addition, oral administration of Lf affects the important immune system parameters though enhancing release of serum IgG and interleukins and interferon gamma in calves (Prgomet et al., 2007) and stimulation of mucosal immunity in mice (Debbabi et al., 1998). Studies also indicated that Lf may lead to elimination of pathogens and consequently lower the incidence of diseases in neonatal calves through iron binding mechanism, inhibition of bacterial biofilm formation (Singh et al., 2002) and proteolytic activity (Adlerova et al., 2008). Lf has a synergistic effect with some other colostral companents such as lysozyme, IgA, IgG, IgG_1 and lactoproxidase to improve immune system (Still et al., 1990; Sordillo et al., 1997; Debbabi et al., 1998; van Leeuwen et al., 2000; Sfeir et al., 2004; Larkins, 2005; Prgomet et al., 2007). Lf also has definite effects on improvement of growth performance, iron absorption and granulopoiesis (Larkins, 2005; Prgomet et al., 2007; Wang et al., 2008; Adlerova et al., 2008; Puddu et al., 2009; Tomita et al., 2009).

Lf treatment in animals experimentally challenged with pathogenic bacteria or endotoxin inhibited bacterial translocation across the intestine, thus decreased the duration and severity of disease and increased survival (Still et al., 1990; Teraguchi et al., 1995; Lee et al., 1998; van Leeuwen et al., 2000; Teraguchi et al., 2004; Barton et al., 2006). The use of Lf as an additive to calf feed also prevented neonatal diseases and increased weight gain (Joslin et al., 2002; Robblee et al., 2003; Prgomet et al., 2007). Similarly, studies in human showed that inadequate level of Lf increased the incidence of diseases compared with the individuals having adequate Lf (Breton-Gorius et al., 1980; Venge et al., 1984). In contrast, SLfC did not differ between healthy and ill foals (Barton et al., 2006) though studies are limited in animals. These results indicated that Lf supplementation has a potential to improve nonspecific immunity and strengthen host defense to protect against infection and stress in some newborns (Wang et al., 2006; Prgomet et al., 2007; Dawes et al., 2008).

Previous studies indicated that colostral Lf has an important potential role in neonatal immunity and possibility of protection against diseases. However, no observational field study determining the relationship between diseases and SLfC following colostrum intake exists. To the best of authors' knowledge, colostrum and serums Lf have not yet been measured in sheep of any age. Therefore, the potential effects of Lf on protection against diseases and on passive immunity in lambs are unknown. In addition, effects of colostral Lf on determination of passive immunity, colostrum quality and lamb health are also unexplored.

The main objectives of this study are to evaluate the potential of Lf for prediction of passive immunity by determining correlation between serum Lf and IgG concentration in healthy lambs before and after colostrum intake at various days of neonatal period, to determine the presumptive predisposing effect of serum Lf along with serum IgG levels on lamb health through comparison of values measured for healthy and diseased lambs and to compare colostral Lf and IgG concentrations and to evaluate the impact of colostral Lf on passive immunity and lamb health.

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