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Mammary immunoglobulin transfer rates following prepartum milking

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ABSTRACT

Colostrum formation is thought to occur slowly over an extended period (4 wk) prepartum. Furthermore, colostrum formation is highly variable among cows in total volume, IgG_1 concentration, and mass obtained at first postpartum milking. Recent work has suggested that a rapid transfer of IgG_1 to secretions may occur if animals are milked prepartum. Our objective was to establish the concentration, mass, and mass transfer rates of IgG_1 in multiparous Holstein cows (n = 11, parity = 3.6 ± 1.1) milked prepartum (−74 to −1 h) and again around 4 h postpartum. Blood concentrations of IgG_1 were very low (<1 mg/mL) in 7 cows at prepartum milking and did not decline following prepartum milking. Cows showed variability in the capacity to recover total volume, IgG_1 concentration, and IgG_1 mass. Three groupings of cows were considered based on the time between the 2 milkings (prepartum + 4 h postpartum): long-time (−74 to −54 h, n = 3), medium-time (−25 to −17 h, n = 4), and short-time (< −13 h, n = 4) groups. The average rates of transfer of these groups were 1.4 ± 0.8, 3.0 ± 1.3, and 25.1 ± 15.8 g/h, respectively. The data indicate that a longer time between prepartum and postpartum milking is not a main factor in IgG_1 secretion transfer. Furthermore, because blood concentrations did not change after prepartum milking and the mass of blood plasma IgG_1 was not sufficient to account for the mass occurring in postpartum colostrum, a source of IgG_1 other than blood circulation appears to be present during colostrogenesis.
Key words: colostrum, immunoglobulin, mammary, transfer rates

INTRODUCTION

Colostrum immunoglobulins provide passive immunization to the newborn. The importance of adequate passive transfer for minimizing morbidity and mortality has been demonstrated (Quigley and Drewry, 1998; Weaver et al., 2000). Concentrations of IgG_1 and IgG_2 in the serum of dairy cows are approximately equal, at ∼10 to 20 mg/mL (Butler, 1974; Guidry et al., 1980), but selective mammary transfer of IgG_1 accounts for up to a ∼10-fold enhancement (Sordillo et al., 1987) in colostrum.

However, cow colostrum has extremely high animal-to-animal variation in IgG_1 concentration (11.8 to 74.2 mg/mL; Kehoe et al., 2007; Morrill et al., 2012) and mass (30 g to >2 kg; Baumrucker et al., 2010). Current explanations of this variation include endocrine effects (Casey and Plaut, 2007) and genetics (Doleschall et al., 2005; Mayer et al., 2005). Changes in serum prolactin and progesterone have little effect on colostrum IgG_1 concentration near parturition (Gross et al., 2014). Lactation number, breed of cow, length of the dry period (Pritchett et al., 1991; Tomkins and Jaster, 1991; Mansfeld et al., 2012), and method of analysis (Li-Chan and Kummer, 1997; Gelsinger et al., 2015) may also contribute to colostrum variation.

Colostrogenesis takes place mainly in the weeks before parturition, and the secreted product has high concentrations of IgG_1 (Butler, 1986). Selective IgG_1 transfer from blood to secretions occurs ∼3 wk before parturition (Brandon et al., 1971), as evidenced by ^{125}I-labeled blood IgG_1 appearing in the secretions (Sasaki et al., 1976). Sasaki et al. (1977) also showed a modest plasma IgG_1 decline from 14 to ∼5 mg/mL and indicated that IgG_1 half-life (5.5 ± 1.7 d) decreased (4.1 d) after parturition. However, this finding disagrees with current concepts of IgG_1 decline, as well as the more recently reported half-life of >20 d (Murphy et al., 2014) that is likely the result of recycling through the neonatal Fc receptor (**FcRn**) system (Kacskovics et al., 2006). Throughout the lifetime, FcRn internalizes and recycles IgG_1 in many tissues (Baker et al., 2009; Giragossian et al., 2013).

Based on declining concentrations of blood IgG_1, colostrum formation is thought to begin 3 to 4 wk before parturition (Brandon et al., 1971). However, individual cows might start colostrogenesis at different times prepartum. Relative to specific IgG_1 transfer mechanisms,

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we have hypothesized that a slow rate of transfer from blood to mammary secretions, coupled with variable lengths of the colostrogenesis period among animals, contribute to this variation (Baumrucker and Bruckmaier, 2014). Recent evidence suggests that colostrum formation starts earlier than 4 wk prepartum (Chandra et al., 2013). Mammary secretion IgG_1 concentrations were significantly higher than blood concentrations within 8 d (Winger et al., 1995; Stark et al., 2015) after the start of an induced lactation protocol similar to that used by (Macrina et al., 2011) with nonpregnant dairy cows. Initiation of colostrogenesis may be important, because different animals may start the process at different times, and if the process is slow, animals with an earlier start may gain much higher concentrations and mass, accounting for some of the documented animal variation (Baumrucker et al., 2014a). A difference in colostrogenesis start time may be related to circulating concentrations of steroids, differential sensitivity of their receptors in the mammary glands, or both, but recent work has shown little, if any, effect of progesterone decline on the end of colostrogenesis and the start of lactogenesis (Gross et al., 2014).

In a preliminary experiment, we separately milked the mammary gland quarters of a pregnant dairy cow ~26 h before parturition and again 4 h after parturition. We found that IgG_1 mass from the quarters was ~100% recovered at 4 h postpartum (total of ~30 h; Baumrucker and Bruckmaier, 2014), suggesting that transfer of IgG_1 can be very fast. In a recent study of pregnant cows with a standard dry period, we extended the data to show that IgG_1 transcytosis can be a rapid process in the mammary glands of some animals after prepartum milking, with some interesting changes in composition (Gross et al., 2014). Milking prepartum (−74 to −1 h) produced an average IgG_1 concentration that was equivalent to that of control animals milked postpartum. In prepartum-milked cows, the overall mass of IgG_1 was independent of the time between the 2 milkings, and IgG_1 mass was not different between the 2 milkings. Total colostrum mass was similar for prepartum-milked (sum of 2 milkings) and control animals (1 milking) (Gross et al., 2014). These findings showed that the transcytosis mechanism of IgG_1 can be very fast but extremely variable between animals. The objectives of the current study were (1) to critically examine the animal-to-animal variation in IgG_1 transfer from blood to mammary gland secretions obtained from dairy cows milked once before parturition and again after parturition; and (2) to define the blood plasma concentration decline and mammary appearance and establish IgG_1 transfer rates into the first milked postpartum colostrum. We hypothesized that prepartum milking would induce an increased flux of IgG_1 from blood to mammary secretions that would appear as a blood concentration decline and recovery.

MATERIALS AND METHODS

Animals and Experimental Procedures

The experiment was conducted in accordance with the guidelines of Swiss law on animal production and approved by the Veterinary Office of the Canton Fribourg, Switzerland (permit no. 2011–40-FR). The study included 11 multiparous Holstein dairy cows (parity 3.6 ± 1.1) that were milked before parturition in the same season of 2012 and were part of a larger group of animals that has been reported (Gross et al., 2014). One cow from the previously reported group (Gross et al., 2014) was excluded due to missing samples. In the present study, our goal was to milk cows at approximately 24 h before estimated parturition to maximize secretion volume for the calf, and then again 4 h after calving. The actual prepartum milking (**C1**) occurred from −74 to −1 h before calving; the second milking (**C2**) occurred at 4.6 ± 0.3 h postpartum. Prepartum and postpartum milking colostrum mass was recorded, and proportional samples were frozen at −20°C until analysis. Starting at 4 d before expected parturition, blood samples were taken from the jugular vein 3 times daily at 0600, 1400, and 2200 h until calving, and 1 additional sample was collected shortly before postpartum milking. Blood samples were collected in 9-mL evacuated tubes coated with EDTA and kept on wet ice until centrifugation at 2,500 × g for 15 min at 4°C to harvest plasma. Plasma was subsequently stored at −20°C until analysis. Animal blood volume was calculated assuming 55 mL/kg of BW (Reynolds, 1953), and plasma volume was assumed to be 55% of blood volume.

Milk and Plasma Sample Analysis

Colostrum IgG_1 concentration was determined using a modified ELISA (Bovine IgG_1 ELISA Quantitation Set; Cat. No. E10-118; Bethyl Laboratories Inc., Montgomery, TX), as described previously (Baumrucker et al., 2014a). Blood IgG_1 and IgG_2 were determined using kits E10-118 and E10-117, respectively. Results were expressed as IgG concentration in milligrams per milliliter or total grams (mass).

Statistical Analysis

Data were analyzed using the CORR and MIXED procedures in SAS (version 9.2; SAS, Institute, Inc.,