Veterinary Immunology and Immunopathology 178 (2016) 70–78

Contents lists available at ScienceDirect

Veterinary Immunology and Immunopathology

journal homepage: www.elsevier.com/locate/vetimm

Research paper

Natural autoantibodies in *Bos taurus* calves during the first twelve weeks of life

N. Mayasari[a,b,*], A.T.M. Van Knegsel[a], G. de Vries Reilingh[a], B. Kemp[a], H.K. Parmentier[a]

[a] Adaptation Physiology Group, Department of Animal Science, Wageningen University, P.O. Box 338, 6700 AH Wageningen, the Netherlands
[b] Faculty of Animal Husbandry, Universitas Padjadjaran, 45363 Bandung, Indonesia

ARTICLE INFO

Article history:
Received 18 April 2016
Received in revised form 30 June 2016
Accepted 1 July 2016

Keywords:
Autoantibodies
Calf
Colostrum
Maternal antibody transfer
Dry period

ABSTRACT

Natural autoantibodies (NAAb) have a role in maintaining physiological homeostasis and prevention of infections, and have been found in mammalian species tested so far. Albeit NAAb levels rise with age, little is known about the origin, function, regulation and initiation of NAAb in young animals. The present study addressed the presence of IgM and IgG NAAb binding glutamate dehydrogenase (GD), carbonic anhydrase (CA), myosin (MYO) and transferrin (TRANS) from before drinking colostrum until the first 12 weeks of life in plasma of female calves. In addition, NAAb to these four self-antigens were also measured in colostrum and in plasma of their mothers during three weeks before calving. Titers of NAAb binding GD, CA, MYO and TRANS were detected in plasma of cows before calving, in colostrum, and in plasma of calves before and after drinking of colostrum. Levels of NAAb in colostrum were positively related with levels of NAAb in plasma of cows. Before colostrum intake, levels of NAAb in plasma of calves were not related with levels of NAAb in plasma of their mother but were influenced by parity of their mother. After colostrum intake, levels of NAAb in plasma of calves in the first week of life were positively related with levels of NAAb in colostrum. Low NAAb levels in colostrum were related with low NAAb in plasma of calves in the first week of life, but after two weeks of life the relation between colostrum and plasma of calves was absent. In conclusion, NAAb are already present in the unborn calf, and levels of neonatal NAAb during the early weeks of life are affected by levels of maternal NAAb obtained via colostrum.

1. Introduction

Natural antibodies (NAb) are a humoral part of innate immunity (Matter and Ochsenbein, 2008; Vollmers and Brändlein, 2009), and have been proposed to be involved in preventing infection and maintenance of physiological homeostasis (Ehrenstein and Notley, 2010; Lutz, 2012). Natural antibodies are polyreactive with low affinity binding with various antigens (Casali and Notkins, 1989), and are present in healthy animals in the absence of antigen stimulation (Avrameas, 1991; Baumgarth et al., 2005). Natural antibodies have been divided into two classes: overt and cryptic NAb. Overt NAb bind antigens that the individual has never encountered before, such as keyhole limpet hemocyanin (KLH). Cryptic NAb or so-called natural autoantibodies (NAAb) are antibodies that bind to self-antigens or slightly changed self-antigens (neo-epitopes). Natural autoantibodies are thought to be involved in inactivation of cytokines, prevention of inflammation, clearance of metabolic waste, perform various homeostatic roles within the immune response (Cojocura et al., 2009), and have a role in the prevention of autoimmunity (Nguyen et al., 2015). Antibodies binding a variety of self-antigens such as myosin, thyroglobulin (Lutz et al., 2009), heat shock proteins (Cohen, 2013), solubilized extracts of histologically normal organs were found in humans (Stahl et al., 2000) and in healthy calves (Khobondo et al., 2015). In dairy cows, NAb binding exo-antigens (Ploegaert et al., 2011; Thompson-Crispi et al., 2013; Mayasari et al., 2015) as well as self-antigens (Van Knegsel et al., 2012) were described earlier. Little is known of the routes that lead to the production of NAAb in healthy young individuals. It was proposed that NAAb may arise by cross reactivity with the intestinal microflora (Kamada et al., 2013), are initiated by dietary compounds, directed to neo-epitopes (Lutz et al., 2009; Lutz, 2012), rest on random VDJ recombination in B-cells maintained by self-antigens (Quintana and Cohen, 2004), or reflect levels of maternal antibodies after consumption of colostrum or milk. In dairy cows, maternal antibodies are not actively transferred

* Corresponding author at: Adaptation Physiology Group, Department of Animal Science, Wageningen University, P.O. Box 338, 6700 AH Wageningen, the Netherlands.
E-mail addresses: novim001@gmail.com, henk.parmentier@wur.nl (N. Mayasari).

http://dx.doi.org/10.1016/j.vetimm.2016.07.001
0165-2427/

to the fetus before birth, but calves obtain maternal antibodies passively from the dam through colostrum during the first 24 h of life. Thus, after first colostrum intake antibody titers in calves likely reflect maternal antibody titers in colostrum during the first weeks of life until neonatal antibody production starts. Until start of neonatal antibody production, adequate and sufficient passive immune transfer of maternal antibodies via colostrum intake provides immune competence of calves, which is a prerequisite to lower the risk of diseases and infections during the pre-weaning period (Oliveira et al., 2010).

To our knowledge, little information is present about the presence of NAAb in colostrum and in plasma of calves before colostrum intake and the relation between NAAb levels in cows and their calves during the early weeks of life. Earlier, we studied health and energy metabolism in cows with different dry period lengths. Omission of the dry period in dairy cows reduced NAb titers in colostrum compared with cows with a short (30-d) or conventional dry period (60-d) (Mayasari et al., 2015). Moreover, lower NAb titers in colostrum were reflected by lower titers of NAb binding keyhole limpet hemocyanin (KLH) and human serum albumin (HuSA) in plasma of calves in the first two weeks of life. No IgM and IgG NAb binding KLH or HuSA were detected in plasma of calves before colostrum intake. In the present study, we evaluated the level of NAAb to four self-antigens: glutamate dehydrogenase (GD), carbonic anhydrase (CA), myosin (MYO) and transferrin (TRANS) in plasma of calves before and after colostrum intake, and in plasma and in colostrum of their mother. Antibodies to those four self-antigens were found in plasma of dairy cows. Previous studies reported that self-antibodies to GD (Schulz et al., 2014) and CA (Puscas et al., 2001) are related with metabolic and health disorders in mammals. Cows with subclinical ketosis had higher non esterified fatty acid concentration and GD activation after calving (Schulz et al., 2014). Carbonic anhydrase also functions in regulation of pH and fluid balance (Badger and Price, 1994) as observed during inflammation (Mihaylova et al., 2008). Another study reported that NAAb binding MYO and TRANS in milk of cows were associated with sensitivity for mastitis (Van Knegsel et al., 2012). Myosin is a fibrous protein which has a role in muscle contraction (Schmitt, 1968). Transferrin is a serum globulin which works in the complexing and transport of iron (Crichton and Charloteauxwauters, 1987).

In the current study, it was hypothesized that NAAb binding GD, CA, MYO and TRANS are present in plasma of cows and in colostrum, but absent in plasma of calves before colostrum intake. Moreover, if omission of the dry period in cows reduced NAb titers in colostrum, NAAb titers in colostrum and in plasma of their calves may be reduced as well. Moreover, the NAAb titers in plasma of calves after colostrum intake are expected to reflect the NAAb titers of their mother (in plasma and colostrum). The present study aimed to evaluate NAAb to GD, CA, MYO and TRANS in mother and calves before and after colostrum intake until 12 weeks of age and to study relationships between these titers in mother, colostrum and the calves.

2. Materials and methods

2.1. Experimental design, animals and rations

The Institutional Animal Care and Use Committee of Wageningen University approved the experimental protocol. The registration number of the experimental protocol is 2010026. Blood and colostrum samples originated from an experiment that was designed to evaluate the effect of dry period length and ration composition on health of cows and calves. The experimental design, treatments of dry period lengths and ration composition in cows were described earlier by Van Knegsel et al. (2014). In short, Holstein-Friesian dairy cows (N = 167) were selected from the Dairy Campus research herd (WUR Livestock Research, Lelystad, the Netherlands) blocked according to parity, calving date, milk yield in previous lactation and body condition score (BCS), and randomly assigned to treatments. Treatment consisted of three dry period lengths: 0, 30 or 60 days; and two lactation rations (glucogenic or lipogenic ration). For the current study, female calves born to these cows (n = 63) were monitored.

Table 1
Distribution of cows, colostrum samples, plasma in cows and plasma of female calves (before and after colostrum intake) across the dry period length.

	n	Dry period length		
		0 days	30 days	60 days
Cows in the experiments	167	56	55	56
Colostrum	138	44	45	49
Plasma of cows (before calving)	92	30	32	30
Plasma of female calves before colostrum intake	52	19	16	17
Plasma of female calves after colostrum intake	63	23	19	21

2.1.1. Management of cows

Cows were housed in a freestall with slatted floor and cubicles and milked twice daily (at 0500 and 1630 h). Prepartum, dry cows received a dry cow ration and lactating cows received a lactating cow ration supporting 25 kg of milk per day. Forage was supplied ad libitum and consisted prepartum of grass silage, corn silage, wheat straw and a protein source (rapeseed meal or soybean meal) in a ratio of 39:25:25:11 (DM basis). Postpartum, forage consisted of grass silage, corn silage, straw, and a protein source (rapeseed meal or soybean meal) in a ratio 51:34:2:13 (DM basis). From d 10 before expected calving onwards, cows of all treatments were fed 1 kg/d glucogenic or lipogenic concentrate and increased postcalving stepwise with 0.5 kg/d until the concentration supply reached 8.5 kg/d. Main ingredient for glucogenic concentrate was corn and main ingredients for lipogenic concentrate were sugar beet pulp, palm kernel, and rumen protected palm oil. Concentrate and forage were supplied separately.

2.1.2. Colostrum sampling and management of calves

Colostrum sampling and management of the calves were described earlier (Mayasari et al., 2015). Distribution of cows, colostrum sampling, plasma samples of cows, plasma samples of female calves before and after colostrum intake across dry period length treatments group are shown in Table 1. Colostrum was collected and weighed immediately after calving from each quarter of mammary gland and pooled in one sample per cow. Calves received the colostrum from their mother via an artificial teat. Colostrum samples (n = 138; 10 ml) obtained after parturition were agitated and stored at −20 °C, until analysis.

Immediately after birth, calves were removed from the dam. When calves were born between 10.00 p.m. and 05.00 a.m. (n = 42), calves were removed from the dam at 05.00 a.m. Calves were weighed and within 24 h of life, they received four liter of colostrum in two portions from their mother. After 24 h after birth, female calves were fed with milk replacer (crude protein 22% and fat 17%) (two times a day two liter). After two days, calves were moved to the calf raising farm and were also fed milk replacer twice a day, until 60-d of life. After the first week of life, all calves were fed the same mixture of hay and grains (Agrifirm Feed, the Netherlands) based on requirements for preweaned Holstein calves. At 60-d of life, calves were weaned from milk replacer. From 60-d of life calves received a diet based on requirement for weaned Holstein calves. During first two weeks of life, calves were housed in individual hutches located