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Research Article

Persistence of Maternal Antibodies Against Foot-and-Mouth-Disease Virus in Colostrum Fed Calves Born from FMD Convalescent Vaccinated Dams Under Natural Conditions

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Abstract

Foot-and-mouth disease (FMD) is an economically devastating viral disease of cloven-footed animals that is primarily controlled through mass vaccination and bio-security measures. It is critical to know the duration of persistence of colostral antibodies known to interfere with the vaccine-induced antibody response to determine the optimal age for neonatal calves to be vaccinated for the best vaccinal efficacy. Serum samples were collected from the convalescent-vaccinated cattle (dam) at the time of calves' birth, as well as from each newborn calf four, thirty, sixty, and ninety days later. The duration of maternal antibodies against FMD virus (FMDV) structural proteins (SPs) and non-structural protein (NSP) 3AB3 in colostrum-fed calves born to dams that were vaccinated/convalescing was investigated. On calving day, 35 (92.11%) of the 38 dams tested positive for anti-3AB3 NSP antibody, while 38 (100%), 31 (81.58%), and 33 (86.84%) tested positive for anti-SP antibody log10 titre 1.8 of FMDV serotypes 'O,' 'A,' and 'Asia1,' respectively. Anti-NSP and anti-SP antibodies titre of FMD virus in serum were detected in colostrum fed calves from FMDV vaccinated dams by the fourth day and then declined to almost undetectable levels by the 90th day postpartum. The current study suggests that FMDV antibody is passively transferred and persist between 30-90 days in colostral-fed calves and nearly disappears by the 90th day after birth. Therefore, in primary vaccination regimens, the first dose of FMD vaccine may ideally be administered in caves after 3 months of age, followed by a subsequent boost 28 days later.

Keywords: Anti-SP and NSP Antibody; Colostrum; Foot-and-mouth Disease Virus; Maternal Derived Antibody (MDA); Newborn Calf

Introduction

Foot-and-mouth disease (FMD) is a contagious, economically important viral disease of cloven-hoofed livestock as well as wild herbivores like elephants, deer, gaur etc. The disease caused by FMD virus (FMDV) of the genus *Aphthovirus,* family *Picornaviridae* is characterised by fever, lameness and vesicular lesions on the tongue, muzzle, feet, and teats [1]. In endemic countries, FMD is mainly controlled by adopting biannual mass vaccination of FMDV susceptible populations and by adopting biosecurity measures. Humoral antibody response is elicited in both infected and vaccinated animals and is regarded as the most important factor in FMDV infection protection. However, the success of any vaccination program to control the disease requires comprehensive knowledge of all potential augmenting and interfering factors responsible for a desired vaccination response.

Passive immunity in newborn calves conferred by ingestion and absorption of antibodies present in colostrum from their dams is widely documented [2] and is considered nature's way of protecting the newborn during the initial phase of life. These passively transferred maternal antibodies protect neonates from various infectious diseases until their own immune system matures to respond to natural infection or vaccination. Maternal derived antibodies (MDA) passed to newborn via colostrum and receptive age of the calves are the two important factors influencing the immune response induced against any vaccine owing to the role played by colostral antibody interference [3]. These MDA are especially important for diseases that use live attenuated vaccines. The quality and quantity of antibodies ingested and absorbed from colostrum determine the duration of passive immunity against various pathogens, the higher the colostrum-antibody titre, the longer the im-

munity [2]. The duration of maternal antibodies in agriculturally important animal species lasts for about 3–6 months [4,5]. Mass immunisation in inducing immunity in young calves to protect against FMDV could be difficult, where the existence of maternal antibodies interferes with immune response of young ones [3] and owing to immature immune system. Newborn with maternal antibodies were shown to be poor responder to aqueous FMDV vaccine and this could be the reasons for vaccine failure and FMDV infection in calves [3] during the window of susceptibility and it could be upto 3-4 months. It was reported that in the presence of maternal antibodies, oil emulsion FMDV vaccines were more effective when administered at the age of 30 days [6]. Nicholls., *et al*. [7] demonstrated that in the absence of MDA, calves' immune response to FMDV inactivated vaccine was unaffected.

There is a paucity of literature on duration of persistence of maternal antibodies against either structural or non-structural protein of FMDV in colostrum fed neonates born from FMD convalescent vaccinated dams (know history of FMDV infection followed by vaccination) with trivalent oil adjuvanted foot and mouth disease vaccines under natural farm conditions. Thus, it is important to know the exact duration for the presence of maternal antibodies against FMDV in newborn calves, which will decide the primary vaccination regime in endemic settings like India. The purpose of this study was to determine the persistence of detectable MDA against both the structural and non-structural proteins of foot-and-mouth disease virus in colostrum-fed calves born from convalescent dams vaccinated with trivalent oil adjuvanted foot and mouth disease vaccines in natural farm settings.

Materials and Methods

Calves born from convalescent vaccinated cross-bred Holstein Friesian x native Bos indicus cattle at an organised dairy farm were studied. Cattle of this farm are regularly vaccinated against FMD (commercially available trivalent FMD vaccine against serotype of O, A, and Asia1) at every 4 months interval. Forty-eight pregnant FMD convalescent vaccinated cattle (dams) were selected for this study. Newborn calves were categorized into two groups, such as, ten calves (non-colostrum fed, group 1) and thirty-eight calves (colostrum fed regularly for 4 days, group 2). All calves in Group 2 received colostrum from their dams for up to four days after birth and were weaned after four days. Serum samples were collected from the dams at the time of birth of calf and from each calf at 4,30,60 and 90 days *post-partum*. These serum samples were analyzed for the estimation of anti-NSP antibodies and anti-SP antibodies against serotype 'O', 'A' and 'Asia1' of FMD virus using inhouse r3AB NSP indirect-ELISA [8] and LPB ELISA, respectively. Based on optical density (OD) measurement in r3AB NSP I-ELISA, percent of positivity (PP) values were calculated and PP values greater than 40 were considered positive for NSP-antibody. Log_{10} titre equal to or more than 1.8 in LPBE were considered as having a protective antibody titre [9].

Results

Measurement of anti-NSP and anti-SP antibodies titre of serotype 'O', 'A' and 'Asia1' of FMD virus in dam, control calves (non-colostral fed calves, 10) as well in colostrum fed calves were carried out by r3AB I-NSP ELISA and LPBE, respectively. All 10 non-colostral fed calves were found negative for both anti-NSP and anti-SP antibodies of FMD virus suggesting no maternally derived antibodies. Anti-NSP antibodies of FMD virus in dam as well in colostrum fed calves are presented in figure. Number of animals showing anti-structural antibody titre (log_{10} titre) of serotype 'O', 'A' and 'Asia 1' of foot-and-mouth disease virus in dams and colostral fed calves estimated by LPB ELISA presented in table.

Details of animals	FMDV Serotype 'O'	FMDV Serotype 'A'	FMDV Serotype 'Asia1'
Dams (day of calving)	38	31	33
Calves (4th day)	30	22	20
Calves (30th day)	28	22	18
Calves (60th day)	18	9	9
Calves (90th day)	0	1	2

Table 1: Number of animals showing anti-structural antibody titre (log_{10} titre ≥1.8) of serotype 'O', 'A' and 'Asia 1' of foot-and-mouth disease virus in dams and colostral fed calves estimated by liquid phase blocking ELISA.

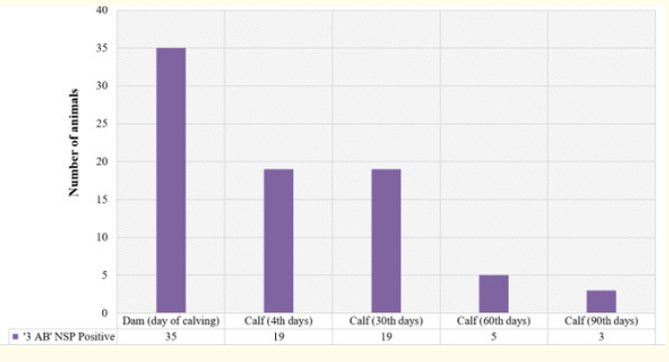

Figure 1: Number of animals showing PP Value (≥40) against 3AB non-structural protein of foot and mouth disease virus in dam (on day of calving) and colostral fed calves at 4th day, 30th day, 60th day and 90th day postpartum.

On the day of calving, 35 (92.11%) of the 38 dams tested positive for FMDV 3AB NSP antibody, whereas at 4,30,60, and 90 days post-partum, 19 (50.00%), 19 (50.00%), 5 (13.16%), and 3 (7.89%) calves tested positive for FMDV 3AB NSP antibody, respectively (figure 1).

On the day of calving, 38 (100%), 31 (81.58%), and 33 (86.84%) of the 38 convalescent vaccinated dams showed protective antibody titre (log10 titre ≥1.8) against SPs of FMDV serotypes 'O,' 'A,' and 'Asia1,' respectively (table). Similarly, protective antibody titre (log10 titre ≥1.8) against serotypes 'O,' 'A,' and 'Asia1' was recorded in calves at 4,30,60, and 90 days post-partum. It was observed that 30 (78.97%), 22 (57.89%) and 20 (52.63%) on 4th days; 28 (73.68%), 22 (57.89%), and 18 (47.36%) on 30th days; 18 (47.36%), 11 (28.95%), and 9 (23.68%) on 60th days; 00 (00.00%), 1 (2.63%), and 2 (5.26%) on 90th days post-partum number of calves showed protective antibody titre (log10 titre ≥1.8) against serotypes 'O,' 'A,' and 'Asia1', respectively (table). Furthermore, calves' antibody titres against serotypes 'O,' 'A,' and 'Asia1' dropped to $\log_{10}$ titre <1.5 after 90 days postpartum. Anti-NSP and anti-SP antibodies in colostrum fed calves were detected optimally by 4th days and thereafter the gradual decline in anti-NSP and anti-SP antibodies were observed till 90th days postpartum. The rate of decline being faster from 30th days postpartum onwards.

Discussion

In FMD-endemic countries where the disease has been controlled by regular preventive vaccination, the incidence of FMD is greatest amongst young animals [3], suggesting that calves make the most susceptible population among other groups. This may be due to the fact that calves are not vaccinated owing to poor development of their immune system and there is a low or no maternal derived antibody (MDA). Two major factors, the age of the animals before complete immune system development and the presence of MDA, may be responsible for low vaccine-induced antibody response in young stocks, as well as the lack of booster effect of vaccination. Previous research has shown that in the absence of MDA, the age of animals has no effect on their response to FMD vaccination [7]. Several studies, on the other hand, have suggested that MDA can inhibit calf response to FMD vaccination [3,10]. Therefore, it is critical to understand the kinetics of MDA decay to determine the optimal age of calves for primary FMD vaccination in neonatal calves. Hence, the goal of this study was to determine the duration of persistence of anti-FMDV antibodies transferred from vaccinated dams to calves because of colostrum feeding and also from natural FMDV exposure of dams because the vaccine does not induce sterile immunity.

Before closures, naturally infected or vaccinated pregnant cows can provide protection to newborn calves against infection via MDA in the colostrum [11]. Before closures, within 24-36 hours after birth, intestinal cells (enterocytes) non-selectively absorb macromolecules such as immunoglobulins, and cells are unable to absorb these macromolecules after this time [12]. An immunoelectrophoretic study revealed that antibodies (-globulin) in the serum were not present in the serum of newly born calves, but they were detected 2 hours after colostrum ingestion [13]. MDA levels in the calves' serum gradually decline one month after birth, with a half-life of approximately 16 days [14]. In the event of FMD, young stock receives immediate FMDV protection after receiving MDA due to anti-FMDV antibodies in the colostrum [10]. Anti-NSP and anti-SP antibodies of FMD virus serotypes 'O,' 'A,' and 'Asia1' were found in convalescent vaccinated cattle (dams). Anti-NSP antibodies detected in these calves are not definitively indicative of passive transfer of maternal antibodies elicited during earlier infection in dams or of any in-utero acquired sub-clinical infection in calves as previously reported [15], but detection of anti-SP antibodies against the three serotypes of FMDV in these calves is indicative of passive transfer of anti-SP antibodies. The calves that received colostrum after birth had a significant increase in anti-NSP antibodies and anti-SP antibodies of FMD virus serotypes 'O,' 'A,' and 'Asia1,' which was not the case in the non-colostrum fed group of control calves, indicating that passive transfer of maternal antibody via colostrum feeding occurred. The absence of NSP antibodies in the calves in the control group ruled out subclinical infection. Following that, the titre of anti-NSP and anti-SP antibodies in these calves decreased from the 4th to the 90th day after birth, and similar findings were also reported by El-Sayed Ibrahim., *et al*. [16], who reported that passively obtained colostrum antibodies had decreased to undetectable levels due to IgG's half-life of approximately 16 days [14]. Therefore, the presence of anti-NSP antibodies as well as anti-SP antibodies for FMD virus serotypes 'O,' 'A,' and 'Asia1' in these calves suggests the passive transfer of maternal antibodies via colostrum from immunised dams to their calves. Previous research has shown that maternal antibodies can survive in calves for up to two months after birth [16,17], whereas Akhter., *et al*. [18] found MDA in calves' serum up to the age of 22-23 weeks. The immune response of newborn calves to FMDV depends on vaccine formulation and may or may not be dependent on maternal antibodies [6,7]. It has also been demonstrated that calves develop an immune response against all FMDV serotypes in the presence of maternal antibodies [19]. Poor immune response in calves with maternal antibodies may be due to the immunosuppressive effect of cortical hormones in newborn calves [20] and an underdeveloped immune system. However, no antibody (anti-NSP and anti-SP antibodies) spike was observed in non-colostrum-fed calves, even though both groups were reared in the same farm ecosystem. Therefore, the transfer of neutralising antibodies to neonatal calves against FMD was only through colostrum feeding [13], and similar findings about deficient colos-

tral antibodies in calves were also reported by earlier co-workers [4,21,22]. Under Indian socioeconomic conditions, lack of immunisation during the advanced stage of pregnancy may result in a poor reflection of MDA in newborn and, as a result, a high risk of infection in these animals.

Conclusions

The current study's findings suggest that passively transferred FMDV antibody persists for 30-60 days in colostral-fed calves and nearly vanishes after 90 days. Although the exact period of persistence of MDA in the calves in this study was observed to be quite variable, which could be due to a complex interplay among critical determinants such as antepartum titre of antibody in the dams, amount and timing of colostrum fed to the neonates, the initial titre of MDA in the neonates, and so on, MDA was apparently found to last up to 90 days postpartum in this study. Therefore, in primary vaccination regimens, the first dose of the FMD vaccine should be administered in caves after 3 months of age, with a subsequent boost 28 days later. Such a schedule may minimise MDA interference in vaccine response while not widening the gap between waning passive immunity and mounting of vaccine-induced antibodies in calves. Furthermore, the disappearance of MDA after 90 days is a natural indicator that the calf can respond efficiently to vaccine-induced immunity or natural infection.

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Ethical Approval

All procedures were performed in compliance with relevant laws and institutional guidelines and the authors declare that the present work has no animal ethics issues. All the serum samples were collected by the owner of the farm on his own interest and submitted to the institute for estimation of antibody titre against foot-and-mouth disease virus in the regularly vaccinated herd.

Authors Contribution

Conceptualization, RR and JKB; Methodology, RR and JKB; Analysis, RR; data curation, RR, JKB, JKM, writing the first draft of the manuscript, RR; writing-review-editing, RR, JKB, JKM and RPS. All authors agreed on the final version of the manuscript.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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