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Association of foot-and-mouth disease (FMD) virus vaccine elicited immune response with productive and reproductive performance in crossbred cattle

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ABSTRACT

FMD is one of the most contagious diseases of cloven-hoofed farm animals and remains a major threat to animal husbandry. In India, vaccination with the inactivated trivalent (O, A and Asia1) vaccine for the control of FMD is one proven way for protecting the livestock. In this study we tried to find the relationship between production and reproduction parameters of the crossbred cattle with FMD virus vaccine elicited immune response. In the present herd, average 305 days milk yield and daily protein yield was 2244.83 ± 80.44 kg and 2.98 ± 0.017 g, respectively. Study revealed that the vaccine response and 305 day milk yield as well as protein yield are independent of each other and they do not affect occurrence of each other. However, the association between vaccine response and part milk yield in crossbred cattle were significant in the present study. Those cattle that were in their first trimester of lactation had lower antibody titer to the FMD virus vaccine as compared to the later part of lactation or non-lactating cattle. Results of this study define the variation in vaccine response for part lactating yield; however repeated studies in different herds and locations are mandatory to avoid probability of association by chance.

Key words: Crossbred cattle, Foot-and-mouth disease, Lactation stress, Vaccine response

Foot-and-mouth disease virus (FMDV) represents one of the most devastating viruses affecting cloven-hoofed livestock including cattle, sheep, goats and pigs. The causative FMD virus is antigenically diverse having 7 distinct serotypes and many variants within them. Being a single stranded RNA virus, it conforms to the quasispecies nature with emergence and re-emergence of different genetic lineages with altered antigenicity within the serotypes, making vaccination based control programme prohibitively expensive, time consuming and difficult to achieve (Pattnaik *et al*. 2012). The management and control of the disease is a major concern worldwide.

The economic consequences of an FMD outbreak can be devastating as demonstrated by the 1997 FMD outbreak in Taiwan and the 2001 and 2007 outbreaks in the United Kingdom (Grubman *et al*. 2008). From 2009-10, in India 799 outbreaks were reported as against, 2962, 1467, 1211 and 511 outbreaks during the year 2005–06, 2006-07, 2007-08 and 2008-09 (Pattnaik 2010), respectively. Annual direct loss due to FMD in India was estimated to the tune of ₹ 20 000 crore (Pattnaik *et al*. 2012). The threat of this virus is caused by a combination of virological characteristics including high contagiousness, virus tenacity, rapidity of replication, high level of virus excretion via aerosols, and short incubation times (Summerfield *et al*. 2009). FMD gains further significance due to its trans-boundary spread and trade sanctions imposed in countries where it occurs, affecting export of livestock and their products to countries free from this disease. In India, currently FMD virus serotypes O, A and Asia1 are prevalent and the control measures involve regular vaccination with inactivated trivalent virus vaccine.

FMDV vaccine response is variable in nature and there has been a drive throughout the country to vaccinate animals against it. There has been a belief in common man that vaccinating their animals for FMDV vaccine has some detrimental effect with regards to production potential. Keeping these points in view the present study was designed to see effect of FMDV vaccine elicited immune response on production and reproduction status of crossbred cattle.

MATERIALS AND METHODS

The study population was a herd of crossbred cattle of *Bos indicus* (Hariana) × *Bos taurus* (Holstein Friesian (HF) alone or HF in combination with Jersey). Exotic inheritance

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level was more than 50%. The herd was located at Indian Veterinary Research Institute (IVRI), Mukteswar (Nainital, Uttarakhand, India) in the temperate Himalayan region of India at 29^0282 N, 79^0382 E, and has an average elevation of 2171 m (7,123 feet) above the mean sea level (msl). Animals were raised separately according to their age group. The animals were maintained on a semi-intensive system with 6 h on pasture (0800–1300 h) per day, standard ration and water *ad lib*. For newborn calves, milk was supplemented up to 3 months of age and from second week onwards green grass as well as calf starter feed was provided *ad lib*. The calf starter feed was continued up to 5 months. Calves were sent for grazing after they attained 3 months age.

Vaccination and sampling: As part of the regular protective scheduled vaccination programme, the animals were vaccinated (2 ml intramuscular) with trivalent (O, A and Asia1) inactivated FMD vaccine (IVRI, Hebbal Bengaluru). Whole blood was collected aseptically by jugular vein puncture from the crossbred calves on '0' day (pre-vaccination) and 28 days post vaccination (DPV) for serum separation. Serum was collected and stored at –20°C until testing.

DIVA and LPBE: Animals were tested for differentiation of infected and vaccinated animals (DIVA) test to see whether antibody raised is due to infection or vaccination. Similarly all the animals were tested for liquid phase blocking enzyme linked immunosorbent assy (LPBE) to test the antibody titer on 0 and 28 days post vaccination (DPV). Animals that gave antibody titer (Log_{10}) <1.8 were un-protected whereas those that had titer >1.8 were protected. These tests were carried out at Project Directorate on FMD, Mukteswar: (http://www.fao.org/ag/againfo/commissions/docs/training/manual/SAARC_Training_Manual.pdf).

Reproductive status and vaccine response: The reproductive status of the crossbred animals bred in the year 2010-11 was assessed (n=81). Those animals which did not conceive even after receiving 3 consecutive inseminations were defined as repeat breeders and those which conceived with 3 or less inseminations were declared as normal. Post vaccine antibody titers for 3 serotypes were assessed and an attempt to associate these titers with reproductive status of the animals was made using Chi square statistics.

Milk production status and vaccine response: The milk production status of the crossbred animals during year 2010-11 was assessed (n=40). Post vaccine antibody titers for 3 serotypes were assessed and an attempt to associate these titers with milk yield of the animals was made using ANOVA. As the animals were in different lactation order, the milk yield during 305 days was first adjusted for lactation order using LSML model 1 (Harvey 1990).

Milk protein status and vaccine response: The milk protein of the animals in milk was obtained for March 2011, in which animals were vaccinated for FMDV vaccine (n=33). Post vaccine antibody titers for 3 serotypes were assessed and an attempt to associate these titers with protein yield of the animals was made using ANOVA. As the animals were in different trimester of their lactation, the protein (average yield of morning and evening) yield was first adjusted for lactation trimester using LSML model 1 (Harvey 1990).

Lactation stress and vaccine response: The animals in their first trimester of lactation were categorized as in milk yield stress, whereas those in later phase of lactation or non-lactating were considered free from milk yield stress. In total 88 animals were used for this study. Fisher's exact test (SPSS 16.0) was employed to see whether there is any association of milk yield stress with vaccine response.

RESULTS AND DISCUSSION

In the present study all the animals were found to be negative for DIVA test indicating that the antibody raised were due to vaccination alone and not due to infection. Results of LPBE revealed that the overall protection in the herd was moderate and majority of the animals were protected for serotype O followed by serotype A and Asia 1. All the animals had log_{10} <1.5 antibody titer for pre-vaccination status; therefore there was no need to adjust the data of 28DPV titer for the previous antibody levels.

FMDV vaccine elicited immune response and reproduction and production parameters: The results revealed that the FMDV vaccine-elicited immune response and reproductive status of the animals was independent of each other. Numbers of protected individuals were higher in serotype A whereas they were less in serotype O and Asia1. Cross-classification of protected and un-protected individuals in normal and repeat breeder category did not reveal any statistically significant differences using chi-square (χ^2) test (Table 1). Therefore null hypothesis was accepted indicating that there is no relationship between FMDV vaccine elicited immune response and the reproductive status of crossbred cattle in the present study.

We studied the effect of vaccine response on 305 days lactation yield of the animals. Least squares mean (standard error) for 305 days lactation yield of the cows was 2244.83 (80.44) kg. The milk yield was significantly affected by the lactation order (P=0.013), for which data was normalized. ANOVA revealed that the FMDV vaccine induced immune response and the milk yield was independent events in

Table 1. χ^2 test of significance between FMDV vaccine elicited immune response and Reproductive status

Classification	O		A		Asia1	
of animals	#N	$R	#N	$R	#N	$R
Protected	22	7	33	14	15	7
Unprotected	32	20	21	13	39	20
χ^2 test significance (P value)	0.19		0.42		0.86	

#N: Normal breeder; $R: Repeat breeder.

Table 2. Level of significance of Fischer's test for FMDV vaccine elicited immune response and 305 day milk yield and protein yield

Results of one way ANOVA	O	A	Asia1
Level of Significance (P value) for association with 305 days Milk yield	0.182	0.727	0.278
Level of Significance (P value) for association with Milk Protein content	0.775	0.684	0.293

Table 3. χ^2 test of significance between FMDV vaccine elicited immune response and milk yield stress

Classification of animals	O		A		Asia1	
	$^{\$}$T	$^{\#}$N	$^{\$}$T	$^{\#}$N	$^{\$}$T	$^{\#}$N
Protected	4	41	3	40	1	49
Unprotected	13	30	14	31	16	22
χ^2 test significance	0.15		0.048		0.034	

$^{\$}$T signifies number of animals in their first trimester of lactation; $^{\#}$N signifies animals in later part of lactation or non-lactating.

crossbred cattle in our herd (Table 2). The least squares mean (standard error) for milk protein yield of lactating cows was 2.98 (0.017) g. The milk protein yield was affected by lactation trimester significantly (P=0.0185). However, the association between FMDV vaccine induced immune response and the milk protein yield was statistically nonsignificant (Table 2). This indicated that the milk protein yield and the vaccine response were independent events.

FMDV vaccine elicited immune response and milk yield stress: Results revealed that animals in their first trimester of lactation did not give good protection against FMDV vaccine, whereas animals that were in the later phase of lactation as well as non-lactating were comparatively better protected. The values of chi-square (χ^2) test of significance between FMDV vaccine elicited immune response and milk yield stress in crossbred cattle are presented in Table 3, indicating significant differences for serotype O (P=0.15), A (P=0.048) and Asia1 (P=0.034). These figures clearly explained the skewed distribution of animals in lactation stress for vaccine response.

The association of FMDV vaccine elicited immune response with productive (milk yield and milk protein content) and reproductive status of crossbred cattle was statistically non-significant indicating independence to each other. This might be due to the fact that these traits were governed by different biochemical pathways. Not only this, but also there is meager chance of location of the QTLs of immunological traits and production traits overlapping each other on the chromosomes. Nonsignificant genetic correlation of >0.037 between daily milk yield and antibody levels against *Mycobacterium avium* subsp. *Paratuberculosis* (Mortensen *et al*. 2004). For East Coast Fever in Kenya, no obvious differences were observed between the immunized and non-immunized cattle in their milk production (Mutugi *et al.* 1988). We could not find any other study in accordance or in contrast to present results. However there is a need to explore this area, to cross verify the results of the present experiment. Non association of these traits may also be due to less statistical power of the test owing to small data size or just by random chance. Therefore repetition of such experiments in different herds and at different locations can definitely add strength to the interpretation of such data.

Our results revealed significant differences in vaccine response among the animals which were in first trimester of lactation and those that were in later part of lactation or not in the lactation. This might be due to the fact that lactating animals in their first trimester are under great physiological stress as they have to mobilize energy and protein resources to meet the needs of production state. Although no other study with regards to FMDV vaccine response milk yield stress is available to compare our results, examples from other disease related studies have been taken. For only coliform clinical mastitis (CM) cases (*E. coli, Klebsiella,* and *Enterobacter*) within the first 50 days in milk shown milk loss for 21 d following coliform CM to be significantly less for J5 vaccinates than for controls by 6 to 15 kg/day (Wilson *et al*. 2008). In conformity with our results, in other study there was a small, but significant (P=0.05), decrease of about 1.4 litres/cow in milk production after a double vaccination with inactivated bovine herpes virus 1 (BHV1) gE-negative marker vaccine, the negative effect being slightly greater after the second vaccination (Bosch *et al*. 1997). These results indicated that there has to be some pathway that somehow correlates the vaccine response and the production status especially the milk yield stress in the animals. However, again more number of experiments repeating such studies in different herds and in different locations need to be carried out to avoid the probability of association by chance.

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