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Evaluation of the Efficacy of Simultaneous Vaccination of Cattle Against Rabies and Foot and Mouth Disease Viruses

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Abstract: Rabies and foot and mouth disease (FMD) are viral diseases affecting cattle in dramatic forms leading to great economic losses. To evaluate the serological response of cattle to the locally produced trivalent FMD and rabies virus vaccines when administrated separately or simultaneously, 30 native breed calves were divided into 6 groups where the 1st group was vaccinated S/C with the trivalent oil FMD vaccine by a dose of 2ml/animal. The 2nd group was vaccinated S/C with rabies vaccine by a dose of 4ml/animal. While the 3rd and 4th groups were vaccinated with the trivalent oil FMD vaccine one week before and after vaccination with the rabies vaccine respectively. Group-5 was simultaneously vaccinated with both trivalent oil FMD vaccine and rabies vaccine. While 6th group was kept unvaccinated as a control. The immune response of calves for both vaccines was monitored by serum neutralization test and ELISA. The results revealed that both inactivated rabies and trivalent FMD vaccines were safe without local or systemic post vaccinal reactions in vaccinated calves. It was observed that both vaccines were immunogenic leading protective levels of specific rabies and FMD (type O, A and SAT-2).

Key words: FMDV · Rabies · Cattle · Vaccine

INTRODUCTION

General prophylactic immunization of cattle against infectious diseases in developing countries has become a critical contribution to keep up milk and meat production and to decrease the severe economic losses. Foot and mouth disease (FMD) and rabies are two of these diseases, which could not be ignored as they have public health hazard in addition to their dramatic economic impact [1, 2].

Rabies is one of the most life-threatening zoonotic diseases in the world because it can lead to fatal encephalitis that may affect all worm-blooded animals and human [3]. It is caused by RNA virus in the Family Rhabdoviridae, genus Lyssavirus and is usually transmitted to human and animals through bites from infected animals; scratch wounds or contaminated mucous [4].

In Egypt; recently and by the expanding population, many new cities are developed which extends to the desert area. These extensions increase the chance to wild carnivores to attack farm animals and human beings [5]. Most livestock cases from rabid carnivores have been reported as accidents in which immunization of livestock was not applied, so, a rapid protection should be provided to keep the national animal wealth safe. Rabies prophylactic vaccination has been recommended for cattle by the World Organization for Animal Health (OIE) and successfully performed in rabies endemic countries [6].

Cattle are the most commonly affected species between farm animals by rabies. The clinical signs in cattle include sudden change in behavior, sexual excitement, ataxia, attacking human or each other, sudden falling after violent excretion, muscle tremors, paralysis and excessive salivation.

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Infected livestock, especially cattle act as potential risk to the veterinarians and farmers that underline the criticalness of applying rabies control measures for humans [7].

Foot and mouth disease (FMD) is a contagious viral disease affecting cloven-hoofed animals causing high economic losses because of decrease in milk production, reduced weight gain, reproductive inefficiencies and death among young ruminants [8]. The causative agent of this disease belongs to the genus Aphtovirus of the Family Picornaviridae which includes seven different serotypes A, O, Asia1, C and South African Territories (SAT) types 1, 2, 3 [9]. In Egypt, FMD is enzootic and outbreaks have been recorded since 1950. FMD serotypes 'SAT2', 'A' and 'O' were reported in the years 1950, 1972 and 2000, respectively [10]. The FMDV serotype O was the most prevalent since 1960 and onward [11]. In addition, serotype SAT2 of FMDV was later introduced into Egypt during 2012 through the importation of live animals [12].

The control of FMD based on large-scale vaccination of susceptible animals with whole virus inactivated vaccines in endemic areas was effective in limiting the spread of the disease [12, 13]. Success of the vaccination program is mainly dependent on the specificity of the vaccine that is related directly on the antigenicity of the FMDV serotypes used in the vaccine [14]. The locally produced vaccine by Veterinary Serum and vaccine Research Institute (VSVRI) is the Montanide ISA 206 trivalent inactivated vaccine, which consists of three FMDV serotypes (O Pan Asia1, A Iran O5 and SAT2/EGY/2012), is currently used in the Egyptian provinces [15].

As a trial to decrease the cost of vaccination, veterinarians suggested simultaneous vaccination with rabies and foot and mouth disease (FMD) viruses [16]. So, the present study aims to evaluate the serological response of cattle to the locally produced trivalent FMD and rabies virus vaccines when administrated separately or in mutual manner.

MATERIALS AND METHODS

Animals: Thirty native breed calves of about 12-18 months old belonging to a private farm located in Cairo, Egypt were found to be free from FMD and rabies antibodies as screened by serum neutralization test. These calves were randomly divided into 6 groups (5calves/group). Frist group vaccinated S/C with the trivalent oil FMD vaccine alone using a dose of 2ml/animal inoculated. second group vaccinated S/C with rabies vaccine alone using a dose of 4ml/animal inoculated. Third group was vaccinated with the trivalent oil FMD vaccine one week before vaccination with rabies vaccine. Fourth group vaccinated with the trivalent oil FMD vaccine one week after vaccination with rabies vaccine. Fifth group vaccinated simultaneously with trivalent oil FMD and rabies vaccines. The last group kept unvaccinated (Control group). All animals were kept under hygienic measures receiving balanced ration and adequate water.

Vaccines: Trivalent FMD vaccine (O; A and SAT2) and inactivated cell culture rabies vaccines were kindly supplied by Veterinary Serum and Vaccine Research Institute (VSVRI), Abbasia, Cairo. These vaccines were used for vaccination of experimental animals.

Sample Collection: Blood samples were collected from the vaccinated calves on weeks 0, 1, 2, 3, 4, 8, 12postvaccination and then every month till the protective antibody level declined. Sera were separated by incubating the clotted blood samples at 4°C for 6 h then centrifugation at 3000 rpm at for 10 min. Serum samples were then inactivated at 56°C for 30 min and stored at -20°C until used [17].

Serum Neutralization Test (SNT): The titer of neutralizing antibodies against Rabies and FMD viruses type O, A and SAT2 were measured in flat bottom tissue culture microtiter plates as described previously [18]. The SNT titer of the serum was expressed as the reciprocal of the final serum dilution which neutralized and inhibited the CPE of 100 TCID50 of the used virus.

Cell Culture Adapted Viruses: BHK cell culture adapted FMD virus type O, A and SAT2 and Evelyn Rokitniki Abelseth (ERA) strain of rabies virus were supplied by VSVRI and used for monitoring of induced antibody levels in vaccinated animals through application of SNT and ELISA.

Enzyme Linked Immunosorbent Assay (ELISA): ELISA test was performed on serum samples for determination of the FMD and rabies antibodies in the sera of vaccinated animals as per method described [19].

RESULTS

Results of Vaccinations of Cattle with Trivalent FMD Vaccine: Vaccination of cattle with the locally produced trivalent inactivated oil FMD vaccine induced specific FMD type O, A and SAT2 antibodies which were detectable by the first week post vaccination with neutralization indexes of 1.2; 0.8 and 0.3 and ELISA reading of 1.2; 1.0 and 0.85 for type O, A and SAT2 respectively. These titers reached their peaks 2.4; 2.1 and 1.8 NI and 2.6; 2.6 and 2.1 by ELISA for the three types respectively by the 12th week and remain with protective levels (Not less than 1.5 NI) up to 8-12 months post vaccination (Table 1).

Results of Vaccinations of Cattle with the Inactivated Cell Culture Rabies Vaccine: Vaccination of cattle with a single dose of the inactivated cell culture rabies vaccine resulted in induction of specific rabies neutralizing antibodies from the first week post vaccination with a mean titer of 4 that increased gradually to reach its peak (128) by the 8th week later then still unchanged till the 12th month. ELISA results showed similar behavior as SNT where the obtained mean reading on the 1st and 8th week and 12th month post vaccination were 0.5; 2.25 and 1, 25 respectively (Table 2).

Results of Vaccinations of Cattle with FMD and Rabies Vaccines: Vaccination of calves with FMD trivalent vaccine, one week before rabies vaccine did not affect the animal immune neither to FMD or rabies vaccine showing serum neutralizing index of 0.7; 0.5 and 0.4 and ELISA values of 0.6; 0.8 and 0.3 for type O, A and SAT-2 respectively by the first week recording the peak values of 2.4; 2.4 and 1.9 NI and 2.8; 2.0 and 1.9 ELISA values by the 8th week then declined to 1.6; 1.5 and 1.5 NI and 0.3; 0.3 and 0.4 ELISA values by the 12 month post vaccination (Table 3).

Also calves responded well to rabies vaccine administrated one week after FMD vaccine without any adverse effect on the vaccinated animal immune response. In this case, vaccinated animals exhibited specific rabies serum neutralizing antibodies with titers of 2 by the first week recording the peak titer (128) by the 8th week and still unchanged up to 12 months post vaccination. ELISA values were 0.9; 1.8 and 2, 2 on the same periods respectively (Table 4).

Vaccination with FMD trivalent vaccine, one week after rabies vaccination showed similar results to those in case of FMD vaccination, one week before rabies vaccination showing no adverse immune response to any of them. The obtained FMD-NI was 0.5; 0.6 and 0.7 by the first week to type O; A and SAT2 respectively with ELISA values 0.5; 0.8 and 0.9 on the same period respectively to the three virus types. These values reached their peak by the 8th week to be 1.8; 2.0 and 2.3 NI and 1.4; 1.5 and 1.6 ELISA values respectively. These records decline to be 1.0; 0.4 and 1.3 NI and ELISA values of 0.6; 0.8 and 0.5 by the 12th month post vaccination for the three types respectively (Table 5).

Calves which received rabies vaccine before FMD vaccine responded immunologically similar to those vaccinated with rabies vaccine alone or one week after FMD. These calves exhibited rabies neutralizing antibody titers of 4 and 128 by the 1st and 8th week post vaccination respectively and remained stable up to one year later with ELISA values of 0; 1.4 and 2.2 on the same periods respectively, reflecting no antagonizing effect of FMD vaccine on the animal immune response to rabies vaccine (Table 6).

The present obtained results revealed that both of cell culture inactivated rabies and trivalent FMD vaccines are safe inducing no local or systemic post vaccinal reaction in vaccinated cattle. Also, both vaccines were immunogenic inducing protective levels of specific rabies and FMD (Type O, A and SAT-2) as monitored by SNT and ELISA.

On the other side FMD type-O antibodies showed peak titers by the 2nd month 2.4 and 2.5 by SNT and ELISA respectively in calves vaccinated with FMD simultaneously with rabies vaccine with no change up to 8 months later. FMD type-A antibodies showed peak titers by the 2nd month of 2.2 and 2.6 by SNT and ELISA respectively in animals vaccinated with FMD simultaneously with rabies vaccine with no change up to 8 months later.

By the 2nd month post vaccination, SNT and ELISA showed the values of 2.0 and 2.2 respectively for FMD antibodies type SAT-2 in calves vaccinated with FMD vaccine simultaneously with rabies vaccine with unchanged levels up to 8 months (Table 7). Recorded rabies antibodies showed the peak titers of 128 and 1.4 by SNT and ELISA respectively in calves vaccinated with rabies simultaneously with FMD vaccine by the 2nd month remaining stable up to 12 months post vaccination (Table 8).

Table 1: Mean FMD type O; A and SAT2 antibody titers in vaccinated cattle with trivalent FMDV

	FMDV antibody titers					
	Type O		Type A		Type SAT2	
	SNT	ELISA	SNT	ELISA	SNT	ELISA
Pre-vaccination	0	0	0	0	0	0
1WPV	1.2	1.2	0.8	1.0	0.3	0.85
2WPV	1.2	1.4	1.2	1.6	0.9	1.4
3WPV	1.6	1.8	1.2	1.9	1.0	1.4
4WPV	2.1	2.0	1.6	2.0	1.0	2.0
8WPV	2.4	2.6	2.1	2.6	1.6	2.2
12WPV	2.4	2.6	2.1	2.6	1.6	2.2
4MPV	2.4	2.6	2.1	2.6	1.6	2.2
8MPV	2.4	2.0	2.1	1.8	1.6	1.9
12MPV	1.5	1.8	1.4	1.2	1.4	1.2

WPV=Week post vaccination; MPV=Month post vaccination

-ELISA reading 1.0 or more is considered positive but a reading less than 1.0 is considered negative

-FMD serum neutralizing antibody titer was expressed as serum neutralization index (SNI) where NI=0.5 is considered protective

Table 2: Rabies serum neutralizing antibody titers and ELISA readings in cattle vaccinated with the inactivated cell culture rabies vaccine

Periods post vaccination	Vaccinated calves SNT	Control calves	Vaccinated calves ELISA	Control calves
Pre-vaccination	0	0	0.03	0.03
1WPV	4	0	0.50	0.04
2WPV	8	0	0.78	0.03
3WPV	32	0	1.04	0.03
4WPV	64	0	1.36	0.03
8WPV	128	0	2.25	0.02
12WPV	128	0	2.38	0.03
4MPV	128	0	2.30	0.04
8MPV	128	0	1.76	0.03
12MPV	128	0	1.25	0.03

WPV=Week post vaccination; MPV=Month post vaccination

Table 3: Mean FMD type O; A and SAT2 antibody titers in vaccinated cattle with trivalent FMD vaccine one week before rabies vaccination

	FMD antibody titers					
	Type O		Type A		Type SAT2	
	SNT	ELISA	SNT	ELISA	SNT	ELISA
Pre-vaccination	0	0	0	0	0	0
1WPV	0.7	0.6	0.5	0.8	0.4	0.3
2WPV	1.0	1.4	0.8	1.2	0.6	0.6
3WPV	1.2	1.4	1.4	1.4	1.2	1.1
4WPV	1.6	1.8	1.7	1.4	1.2	1.2
8WPV	2.4	2.8	2.4	2.0	1.9	1.4
12WPV	2.4	2.8	2.4	2.0	1.9	1.4
4MPV	2.2	2.4	2.0	1.7	1.6	1.4
8MPV	2.0	0.6	1.8	0.8	1.5	1.4
12MPV	1.6	0.3	1.5	0.3	1.5	0.4

WPV=Week post vaccination; MPV=Month post vaccination

-ELISA reading 1.0 or more was considered positive but a reading less than 1.0 was considered negative.

-FMD serum neutralizing antibody titer was expressed as serum neutralization index (SNI) where NI=0.5 was considered protective.

Table 4: Rabies antibody titers in cattle vaccinated with rabies vaccine after FMD trivalent vaccine

	Rabies antibody titers			
	SNT	ELISA	SNT	ELISA
	Vaccinated cattle		Non-vaccinated cattle	
Pre-vaccination	0	0.02	0	0.01
1WPV	2	0	0	0.03
2WPV	16	0.9	0	0.03
3WPV	32	1.4	0	0.03
4WPV	64	1.6	0	0.05
2MPV	128	1.8	0	0.05
4MPV	128	2.0	0	0.06
8MPV	128	2.2	0	0.03
12MPV	128	2.2	0	0.03

WPV=Week post vaccination; MPV=Month post vaccination

Table 5: Mean FMD type O; A and SAT2 antibody titers in vaccinated cattle with trivalent FMD vaccine one week after rabies vaccination

	FMD antibody titers					
	Type O		Type A		Type SAT2	
	SNT	ELISA	SNT	ELISA	SNT	ELISA
Pre-vaccination	0	0	0	0	0	0
1WPV	0.5	0.5	0.6	0.8	0.7	0.9
2WPV	0.8	1.1	1.2	1.1	1.2	1.1
3WPV	1.0	1.1	1.2	1.1	1.4	1.2
4WPV	1.2	1.2	1.4	1.4	1.6	1.2
8WPV	1.8	1.4	2.0	1.5	2.3	1.6
12WPV	1.8	1.4	2.0	1.5	2.3	1.6
4MPV	1.8	1.4	2.0	1.4	2.3	1.6
8MPV	1.5	1.0	1.4	1.8	1.6	1.0
12MPV	1.0	0.6	0.4	0.8	1.3	0.5

WPV=Week post vaccination; MPV=Month post vaccination

Table 6: Rabies antibody titers in cattle vaccinated with rabies vaccine before FMD trivalent vaccine

	Rabies antibody titers			
	SNT	ELISA	SNT	ELISA
	Vaccinated cattle		Non-vaccinated cattle	
Pre-vaccination	0	0.04	0	0.02
1WPV*	4	0	0	0.03
2WPV	8	0.5	0	0.03
3WPV	32	0.8	0	0.03
4WPV	64	1.4	0	0.03
2MPV	128	1.4	0	0.05
4MPV	128	1.6	0	0.05
8MPV	128	2.0	0	0.06
12MPV	128	2.2	0	0.03

WPV=Week post vaccination; MPV=Month post vaccination

Table 7: Mean FMD antibody titers in calves simultaneously vaccinated with FMD trivalent and rabies vaccine

	FMD antibody titers					
	Type O		Type A		Type SAT2	
	SNT	ELISA	SNT	ELISA	SNT	ELISA
Pre-vaccination	0	0	0	0	0	0
1WPV	1.0	0.7	0.8	1.0	0.3	0.85
2WPV	1.2	1.4	1.0	1.6	0.9	1.4
3WPV	1.4	1.5	1.2	1.9	1.2	1.4
4WPV	2.1	2.0	1.6	2.0	1.0	2.0
8WPV	2.4	2.5	2.2	2.6	2.0	2.2
12WPV	2.4	2.5	2.2	2.6	2.0	2.2
4MPV	2.4	2.5	2.1	2.6	1.6	2.2
8MPV	2.4	2.0	2.1	1.8	1.6	1.9
12MPV	1.5	1.8	1.4	1.2	1.4	1.2

WPV=Week post vaccination; MPV=Month post vaccination

Table 8: Mean Rabies antibody titers in calves vaccinated simultaneously with the cell culture inactivated rabies and trivalent FMD vaccines

	Rabies antibody titers			
	SNT	ELISA	SNT	ELISA
	Vaccinated cattle		Non-vaccinated cattle	
Pre-vaccination	0	0.04	0	0.02
1WPV	4	0	0	0.03
2WPV	8	0.5	0	0.03
3WPV	16	0.8	0	0.03
4WPV	32	1.4	0	0.03
2MPV	128	1.4	0	0.05
4MPV	128	1.6	0	0.05
8MPV	128	2.0	0	0.06
12MPV	128	2.2	0	0.03

WPV=Week post vaccination; MPV=Month post vaccination

DISCUSSION

Rabies and foot and mouth disease are viral diseases affecting cattle in dramatic forms resulting in huge economic losses [20]. Vaccination against viral infection is the corner stone to eradicate or minimize the disease incidence. In countries where the disease is endemic, extraordinary measures of eradication are not easy to be applied. Control is based on a strict system of immunization and quarantine, using vaccines specific for the type and subtype of the circulating virus [15]. Vaccines containing one or more viruses are produced in several countries [21].

So, there is a suggested vaccination of cattle with rabies vaccine on the time recommended for their vaccination with the trivalent FMD vaccine and accordingly, the present study was designed to investigate the validity of mutual vaccination of cattle with the tow vaccines regarding the levels of induced immunity against both viruses in vaccinated cattle.

Through the present study, following up the levels of FMD antibodies in cattle vaccinated with the trivalent FMD vaccine alone, it was found that all vaccinated animals exhibited specific FMD antibodies which were detectable by the first week post vaccination with neutralization indexes of 1.2; 0.8 and 0.3 and ELISA reading of 1.2; 1.0 and 0.85 for type O, A and SAT2 respectively .These titers reached their peaks 2.4; 2.1 and 1.8 NI and 2.6; 2.6 and 2.1 by ELISA for the three types respectively by the 12th week and remain with protective levels (Not less than 1.5 NI) up to 8-12 months post vaccination. These results agreed with those obtained by El-Sayed *et al*. [22] and Selim *et al*. [23] they reported that the mean antibody titers against FMD in vaccinated animals was at one week post vaccination (0.9 log10) by SNT, whereas, the mean peak titers (1.9 log10) by SNT were detected by the 6th week post vaccination. Also Abu Bakr (24) reported that the neutralizing antibody titers against O1/3/93 in sheep vaccinated with bivalent gel adjuvant FMD vaccine (A, O) achieved in a protective level from the 2nd WPV (1.38 log10) till the 18th WPV (1.26 log10). In this El-Sayed *et al*. [22], Selim *et al*. [23] and Abu Bakr [24] suggested that FMD ELISA antibody titer of1.3 log10 was considered protective.

Vaccination of cattle with a single dose of the inactivated cell culture rabies vaccine resulted in induction of specific rabies neutralizing antibodies from the first week post vaccination with a mean titer of 4 that increased gradually to reach its peak (128) by the 8th week then kept unchanged till the 12th month. ELISA showed similar results as SNT where the obtained mean titers were 0.50; 2.25 and 1.25 on the 1st and 8th week and 12th month post vaccination respectively. These results were confirmed by the findings of Khodier *et al*. [21] and Khodier [25] who stated that the cell culture inactivated rabies vaccine, is safe for all animal species and clarified that the protective neutralizing antibody titer should not be less than 1:5.

Vaccination of calves with FMD trivalent vaccine, one week before rabies vaccine did not affect the animal immune response neither to FMD or rabies vaccine showing serum neutralizing index of 0.7; 0.5 and 0.4 and ELISA values of 0.6; 0.8 and 0.3 for type O, A and SAT-2 respectively by the first week recording the peak values of 2.4; 2.4 and 1.9 NI and 2.8; 2.0 and 1.9 ELISA values by the 12th week then declined to 1.6; 1.5 and 1.5 NI and 0.3; 0.3 and 0.4 ELISA values by the 12 month post vaccination showing no antagonizing effect of rabies vaccine on the animal response to FMD vaccine.Parallel to these results; also calves responded well to rabies vaccine administrated one week after FMD vaccine without any adverse effect on the vaccinated animal immune response. In this case vaccinated animals exhibited specific rabies serum neutralizing antibodies with titers of 2 by the first week recording the peak titer (128) by the 8th week and keeping unchanged up to 12 months post vaccination. ELISA values were 0.9; 1.8 and 2.2 on the same periods respectively.

In the same way, animals vaccinated with FMD trivalent vaccine, one week after rabies vaccination showed similar results to those vaccinated with FMD alone or one week before rabies vaccination without an adverse immune response to any of them. The obtained FMD-NI was 0.5; 0.6 and 0.7 by the first week to type O; A and SAT2 respectively with ELISA values 0.5; 0.8 and 0.9 on the same period respectively to the three virus serotypes. These values reached their peak by the 12th week to be 1.8; 2.0 and 2.3 NI and 1.4; 1.5 and 1.6 ELISA values respectively. These records decline to be 1.0; 0.4 and 1.3 NI and ELISA values of 0.6; 0.8 and 0.5 by the 12th month post vaccination for the three serotypes respectively.

Calves which had received rabies vaccine before FMD vaccine responded immunologically similar to those vaccinated with rabies vaccine alone or one week after FMD exhibiting rabies neutralizing antibody titers of 4 and 128 by the 1st and 8th week post vaccination respectively and remained stable up to one year later with ELISA values of 0; 1.4 and 2.2 on the same periods respectively reflecting no antagonizing effect of FMD vaccine on the animal immune response to rabies vaccine.

Confirming that there is no antagonizing effect between the trivalent FMD and inactivated rabies vaccines on the immune response of cattle, the present obtained results revealed that FMD type-O antibodies showed peak titers by the 3rdmonth (2.4 and 2.5) by SNT and ELISA respectively in calves vaccinated with FMD simultaneously with rabies vaccine with no change up to 8 months later.

FMD type-A antibodies showed peak titers by the 3rd month of (2.2 and 2.6) by SNT and ELISA respectively in animals vaccinated with FMD simultaneously with rabies vaccine with no change up to 8 months later.

By the 3rd month post vaccination, SNT and ELISA showed the values of (2.0 and 2.2) respectively for FMD antibodies type SAT-2 in calves vaccinated with FMD vaccine simultaneously with rabies vaccine with unchanged levels up to 8 months.

On using the inactivated bivalent oil ISA 206 FMD vaccine the detectable FMD type A antibodies started from the 1st WPV reaching a protective titer (1.63 log10) by the 3rd WPV while the peak titer (2.5 log10) was recorded on the 6th WPV. This titer declined gradually reaching zero level by 47 WPV. This titer declined gradually reaching zero level by 46 WPV. In this respect, these results agreed with those obtained by Selim *et al*. [23], Abu Bakr [24] and Jamal *et al.* [26].

Recorded rabies antibodies showed the peak titers of 128 and 1.4 by SNT and ELISA respectively in calves vaccinated with rabies simultaneously with FMD vaccine by the 2nd month remaining stable up to 12 months post vaccination. Similar results were obtained in case of single vaccination of cattle with rabies vaccine alone; before; after or simultaneously with FMD vaccine in agreement with those recorded by Khodier *et al.* [21], Khodier [25] and El-Karamany [27]. In addition, Edries [28] showed that such vaccine was able to induce immunity in vaccinated animals lasted for one year post vaccination with high levels of antibodies. There are no available data discuss simultaneous vaccination of cattle with FMD and rabies vaccines but Khodeir *et al*. [21] found that sheep vaccination with the inactivated cell culture vaccine did not antagonize sheep immune response to Rift valley fever vaccine inducing similar levels of specific rabies and Rift Valley fever antibodies to those induced in case of single vaccination.

Results of this study indicate that an effective post exposure prophylaxis (PEP) protocol for unvaccinated domestic animals exposed to rabies includes immediate vaccination against rabies. This PE schedule has proven to be effective for control of rabies and domestic animals. Bourhy *et al*. [29] stated that rabies is preventable by timely administration of PEP. Moreover, Khodeir and Daoud [30] showed that post exposure immunization of animals should be carried out as soon as possible on time post exposure recommended the same periods.

In conclusion, this study records that there was no antagonizing effect between the trivalent FMD vaccine and rabies vaccine on the immune response of cattle to each of them and they could be used simultaneously in countries where these diseases are endemic to reduce the cost of vaccination.

Authors' contribution: all authors contributed equally in designing and performing the experiments, analyzing the data and writing the manuscript.

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