Immunogenicity of the live attenuated (Smithburn) Rift Valley fever vaccine in sheep, goats, cattle, buffaloes and camels

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In the present study, the humoral immune response developed following vaccination with the live-attenuated (Smithburn) Rift Valley fever (RVF) vaccine in sheep, goats, cattle, buffaloes and camels was investigated.

Results showed that, serum neutralizing antibody titers of RVF virus started to appear in the sera of all vaccinated animals with live-attenuated Rift valley fever vaccine after the first week post-vaccination and reached its peak after the third month of vaccination. It persisted to be higher than the acceptable limit of protection (>40) in the sera of sheep and goats in more than 6 months post-vaccination while it declined in the sera of cattle, buffaloes and camels to become lower than the acceptable limit of protection (<40) after the sixth month post-vaccination. On the other hand, the serum neutralizing antibody titers remained negative in the sera of non-vaccinated (control) animals throughout the study.

It could be concluded that, the neutralizing antibodies following vaccination of cattle, buffaloes and camels with live attenuated RVF (Smithburn) vaccine was low and of a short duration compared with those in sheep and goats. Hence, it is important to prepare a new vaccine which is safe and gives a high immune response for long period in cattle, buffaloes and camels instead of live attenuated (Smithburn) RVF vaccine to protect these animals species against this disease.

Rift Valley fever (RVF) is an acute mosquito-borne viral disease affecting animals and man it is caused by a virus that belongs to genus *Phlebovirus, Bunyaviridae,* (Kahrs, 2001). It causes high rate of abortion and neonatal mortality, primary in sheep, goats and cattle (OIE, 1996). RVF is confined essentially to Africa in association with dense populations of arthropod vectors (House *et al.,* 1992). The disease was first described by Daubney *et al*. (1931) in the Rift valley in Kenya. In Egypt, the first epidemic of RVF appeared in 1977-1978 as an acute febrile dengue like illness affecting man as well as animals (Imam and Darwish, 1977 and WHO, 1977). Further waves of the disease appeared in 1979-1980; (Abdel Gaffar *et al.,* 1979*;* Meegan *et al.,* 1979*;* El-Akked *et al.,* 1981; Seller *et al.,* 1982 and Allam, 1987) and in May 1993 up to September 1994 in Aswan, Sharkia and some other provinces in Egypt (Arthur *et al.,* 1993; Gabery *et al.,* 1994 and Abou Zaid *et al*., 1995) and recently in summer 2003 in Cidy Salem at Kafre El-Shiekh province leading to high rate of abortion in pregnant sheep, goats, cattle and buffaloes and deaths in humans with an ocular, nervous and hemorrhagic symptoms (WHO, 2003).

Control of RVF depends mainly on periodical vector control and vaccination of the susceptible animals (Kahrs, 2001). However, immunization of susceptible animals with a potent and highly immunogenic vaccine is considered the most effective mechanism for control of the disease (Wilson, 1994). Smithburn (1949) prepared live attenuated vaccine, which can protect non-pregnant animals for long period. This vaccine was proved to be immunogenic and gave good protection for sheep and goats against infection with RVF for several months (Hassan *et al.,* 2001; Shafiek, 2002 and Lilys *et al.,* 2003). However, the immunogenicity of this vaccine in other animal species is still uncertain.

The aim of the present investigation was to study the elicited humoral immune response following vaccination of sheep, goats, cattle, buffaloes and camels with live attenuated (Smithburn) RVF vaccine.

Material and Methods

Animals. Thirty-five apparently healthy animals (sheep, goats, cattle, buffaloes and camels; 7 of each) of about one-year age with no previous history of Rift Valley fever vaccination were used.

Vaccine. Live attenuated (Smithburn) RVF vaccine was kindly obtained from Rift valley fever Production Department, Serum and Vaccine Research Institute, Abbassia, Egypt.

Serum neutralization test (SNT). it was used for measurement of neutralizing antibody titers of RVF in the sera of investigated animals and was done according to Walker *et al.,* (1970). The antibody titers were calculated as the reciprocal of the final serum dilution that inhibited the CPE of 100 – 200 $TCID_{50}$ of the used virus according to Singh *et al.,* (1967).

Experimental design. animals were kept under observation for 7 days before vaccination. General clinical examination was carried out and serum samples were collected for detection of RVF antibodies. Animals of each species were randomly divided into two groups: Group (1) Five animals were vaccinated with 2 ml ($2x10^{4.5}$ $ICID_{50}$ / ml) (OIE, 1996) of live-attenuated (Smithburn) RVF vaccine.

Group (2) Two animals were kept as control (non vaccinated). Serum samples were collected from both groups of all animal species after 1, 2, 3 weeks and 1, 2, 3, 4, 5, 6 and 7 months post-vaccination and subjected to serum neutralization test for measurement of the neutralizing antibody titers of RVF virus.

Results

Means of neutralizing antibody titers, following vaccination of live-attenuated (Smithburn) Rift valley fever vaccine, in the sera of different animal species are shown in Tables 1-5 and Figures 1-5.

Table (1): Means of serum neutralizing antibody titers in sheep vaccinated with live-attenuated RVF (Smithburn) vaccine.

Vaccinal state	Means of serum neutralizing antibody titers										
	0 day	Week post-vaccination			Month post-vaccination						
		1	2	3	1	2	3	4	5	6	7
Vaccinated	-	8	16	32	64	128	256	256	256	256	256
Non vaccinated (control)	-	-	-	-	-	-	-	-	-	-	-

- = negative

Protective of titers >40 (Pini *et. al.,* 1973).

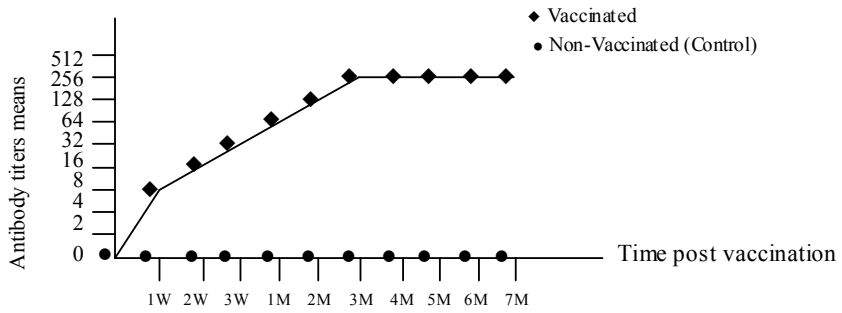

Fig. 1. Means of neutralizing antibody titers of RVF virus in the sera of sheep.

Table (2): Means of serum neutralizing antibody titers in goats vaccinated with live-attenuated RVF vaccine.

Vaccinal state	Means of serum neutralizing antibody titers										
	0 day	Week post-vaccination			Month post-vaccination						
		1	2	3	1	2	3	4	5	6	7
Vaccinated	-	4	8	16	32	64	128	128	128	128	128
Non vaccinated (control)	-	-	-	-	-	-	-	-	-	-	-

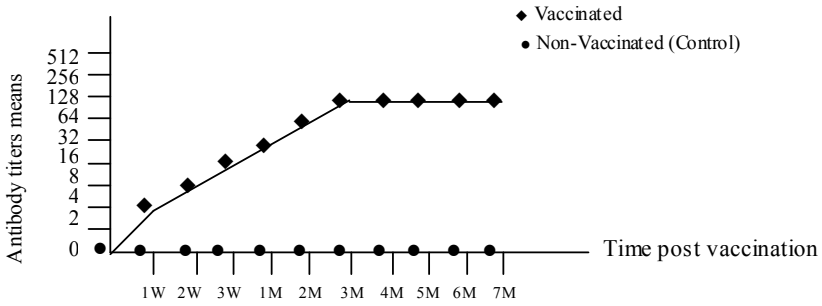

Fig. 2. Means of neutralizing antibody titers of RVF virus in the sera of goats.

Table (3): Means of serum neutralizing antibody titers in cattle vaccinated with live-attenuated RVF (Smithburn) vaccine.

Vaccinal state	Means of serum neutralizing antibody titers										
	0 day	Week post-vaccination			Month post-vaccination						
		1	2	3	1	2	3	4	5	6	7
Vaccinated	-	2	4	8	16	32	64	64	64	32	32
Non vaccinated (control)	-	-	-	-	-	-	-	-	-	-	-

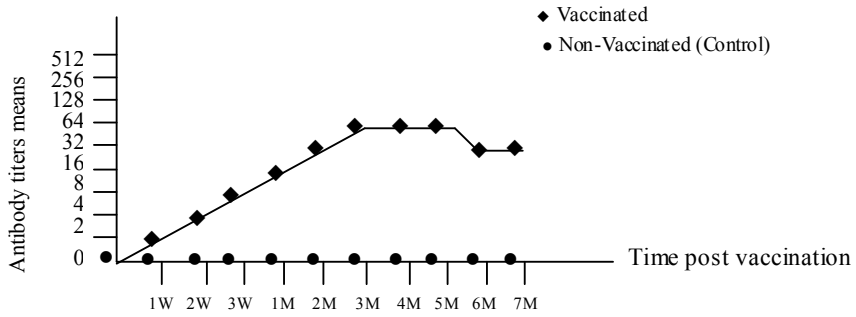

Fig 3: Means of neutralizing antibody titers of RVF virus in the sera of cattle.

Table (4): Means of serum neutralizing antibody titers in buffalos vaccinated with live-attenuated RVF (Smithburn) vaccine

Vaccinal state	Means of serum neutralizing antibody titers										
	0 day	Week post-vaccination			Month post-vaccination						
		1	2	3	1	2	3	4	5	6	7
Vaccinated	-	2	2	8	16	32	64	64	32	32	16
Non vaccinated (control)	-	-	-	-	-	-	-	-	-	-	-

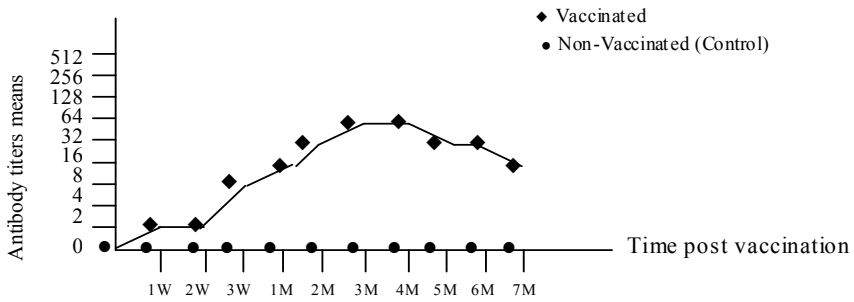

Fig. 4: Means of neutralizing antibody titers of RVF virus in the sera of buffaloes.

Table (5): Means of serum neutralizing antibody titers in camel vaccinated with live-attenuated RVF (Smithburn) vaccine.

Vaccinal state	Means of serum neutralizing antibody titers										
	0 day	Week post-vaccination			Month post-vaccination						
		1	2	3	1	2	3	4	5	6	7
Vaccinated	-	4	4	8	16	32	64	64	64	64	32
Non vaccinated (control)	-	-	-	-	-	-	-	-	-	-	-

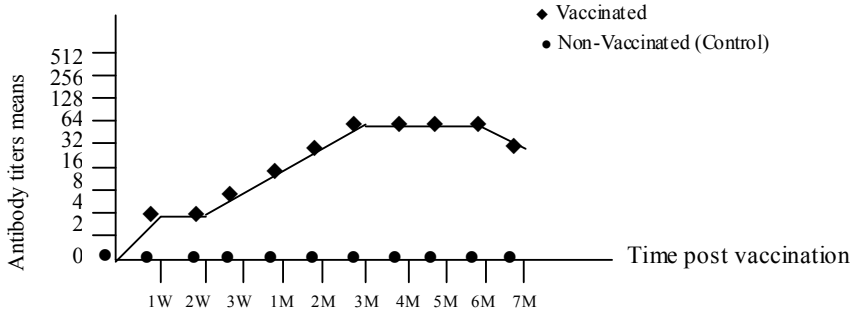

Fig. 5: Means of neutralizing antibody titers of RVF virus in the sera of camels.

Discussion

Rift valley fever is one of the most serious zoonotic viral disease causing devastating epidemics among sheep, goats, cattle and human (Kahrs, 2001). A relatively solid and potentially life long immunity was developed following recovery from natural infection or successful vaccination with RVF (Wilson, 1994). Both live attenuated and inactivated vaccines have been developed for protection of sheep and cattle against Rift valley fever. The inactivated vaccine is effective and safe to the pregnant animals but it gives short period of immunity and needs two doses to protect them for 6 months (El-Nimr, 1980). The live attenuated Rift valley fever (Smithburn) vaccine has long period of immunity which can extend for more than 2 years (Smithburn, 1949). In this study, the neutralizing antibodies in the sera of sheep, goats, cattle, buffaloes and camels following vaccination with live attenuated (Smithburn) Rift valley fever vaccine were determined using virus neutralization test. Results showed that the neutralizing antibodies titre started to appear in the sera of vaccinated sheep and goats after the first week post vaccination, and reached its peak after the third month of vaccination and remained higher than the acceptable limit of protection (>40) for more than 6 months post-vaccination (Tables 1 & 2 and Figures 1 & 2). This finding gets in a agreement with the finding recorded by OIE (1996) and Shafiek (2002) in sheep and Hassan *et al*., (2001) and Lilys *et al.,* (2003) in goats who reported that the neutralizing antibody in sheep and goats vaccinated with Smithburn live attenuated RVF vaccine were at the protective level (>40 as mentioned by Pini *et al.,* 1973) from the first month post-vaccination till 3 years. Likewise, means of the serum neutralizing antibodies of RVF virus in the serum of cattle, buffaloes and camels following vaccination with live attenuated (Smithburn) RVF vaccine started to appear after the first week and reached its peak after the third month post-vaccination, but declined gradually to become less than the acceptable limit of protection (<40) after sixth months post-vaccination (Tables 3, 4 & 5 and Figures 3, 4 & 5). This means that this vaccine cannot stimulate the immune system of these species for long duration to produce enough antibodies. This finding confirms the finding of Swanepoel (1981); Elian *et al.,* (1996) and Shafiek *et al.,* (2004) who said that the live attenuated (Smithburn) Rift valley fever vaccine is poorly immunogenic in cattle. On the other hand, the serum neutralizing antibody titers RVF in the sera of non vaccinated contact (control) animals remained negative throughout the study (Table 1-5 and Fig. 1-5). This means that, there is no lateral transmission of infection with vaccinal strain from the vaccinated to non vaccinated contact animals.

From the above mentioned results, we can say that humoral immune response following vaccination of cattle, buffaloes and camels with live attenuated (Smithburn) vaccine is low and of short duration if compared with those in sheep and goats. This might be due to the poor immunogenicity of the Smithburn vaccine in other animal species. Therefore, it is important to prepare a new vaccine which is safe and gives a high immune response for long period in cattle, buffaloes and camels instead of live attenuated (Smithburn) RVF vaccine to protect these animal species against this disease.

Such findings clarify the urgent need to prepare safe and highly immunogenic vaccine for immunization of cattle, buffaloes and camels.

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