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Original Research

Immunogenicity and Safety of a Classical Swine Fever Vaccine in Pigs

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Abstract

Field trial of Classical Swine Fever vaccine, manufactured by Indian Immunologicals Limited, was undertaken at Bangalore and Hyderabad Veterinary Colleges. The study was designed to assess the immunogenicity and safety in pigs. A total of 80 healthy pigs which were seronegative for Classical Swine Fever virus antibodies were used for the trial. Pigs were enrolled on the basis of eligibility criteria. Animals were randomly divided into two groups in the ratio of 3:1. Group-I, treatment group, received the vaccine and Group-II, control group, received normal saline. Immunogenicity was compared by estimating seroconversion at 30 days post- vaccination between both the groups. Safety of vaccine was assessed during vaccination and in the follow-up period after vaccination. Hundred percent (100%) seroconversion was observed in the treatment group at 30th day. The investigational vaccine was found to be safe as it showed no serious or adverse events following vaccination.

Keywords: Classical Swine Fever, Field Trial, Immunogenicity, Safety, Vaccine

Introduction

Classical Swine Fever (CSF) is one of the most contagious viral diseases of pigs causing huge financial losses to the pig farming industry worldwide. The high seroprevalence of CSF in India (63.3%) suggests that the disease is endemic in the country (Nandi *et al.,* 2011) conducted an epidemiological survey for studying the prevalence of CSF in pigs in India through meta-analysis and they claimed 37% seropositive pigs out of 6158 sample size from 18 states of India (Patil *et al.,* 2018), All India Animal Disease database (NADRES) reported 611 outbreaks of CSF cases between the years 2001-2015. Pig farmers suffered great economic losses due to mortality, reproductive losses, and losses due to restrictions imposed over pork and pork products resulting from classical swine fever disease outbreaks. In a study conducted by Singh et al (2016), total losses incurred each year due to the CSF outbreak were around 9.085 million INR.

Live attenuated classical swine fever vaccine provides a long term, effective and solid immunity. This can be used as the most effective tool in controlling disease outbreaks and eradicating the disease. With the objective of evaluation of live attenuated classical swine fever vaccine manufactured by Indian Immunologicals Limited (IIL), field trials were undertaken at two centers in India, *viz.* Hyderabad Veterinary College and Bangalore Veterinary College with the primary objective of assessment of safety in pigs and the secondary objective of evaluation of immunogenicity. The technology for the manufacture and testing of the CSF vaccine was obtained from Indian Veterinary Research Institute (IVRI).

Materials and Methods

Vaccine Manufacturing Technology

The technology for the manufacture and testing of the CSF vaccine was obtained from Indian Veterinary Research Institute (IVRI), Izzatnagar.

Study Design

To evaluate the immunogenicity and safety of classical swine fever vaccine the present study was conducted. The study was conducted in 80 seronegative pigs aged 3 months and above. The study design and protocol was approved by Drugs Controller General (India), New Delhi, in consultation with Department of Animal Husbandry Dairying & Fisheries (DADF). The study was undertaken after obtaining ethical approval from the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) for each trial site. The study followed Good Clinical Practices and was performed as per Veterinary International Conference on Harmonization (VICH) guidelines. Work flow and rules and regulations were followed taking guidance from Schedule Y. The study was performed at two investigational sites, College of Veterinary Science, PVNRTVU, Rajendranagar, Hyderabad, Telangana and Veterinary College, Bangalore, KVAFSU, Karnataka. Written informed consent was obtained from the farm in-charge for agreeing to comply with the study requirements before the study related procedures were performed.

Study Animals and Groups

Each center enrolled 40 pigs above 3 months age for the assessment of immunogenicity and safety of CSF Vaccine. Before enrollment of pigs in the trial, at baseline visit i.e. 10 days prior to commencement of the study, general physical health checkup was performed. Only healthy pigs with no reported medical abnormalities were enrolled in the study. All animals were screened for presence of Classical swine fever virus antibodies by ELISA and only the seronegative animals were enrolled in the study. Exclusion criteria for the animals to be enrolled in the study included participation in another trial /study 4 weeks preceding the trial vaccination, planned participation in another clinical trial during the present trial period, previous vaccination or evidence of infection with classical swine fever virus, history of allergic disease or reaction likely to be exacerbated by any component of the study vaccine including allergy to antibiotics, animal having any intercurrent illness, known or suspected primary or acquired disease of the immune system, any unstable significant underlying chronic disease, any condition which in the opinion of the investigator would pose a health risk to the animals or interfere with the evaluation of the vaccine.

All the enrolled animals were randomly divided into two groups in the ration of 3:1, treatment group with 30 animals

and control group with 10 animals, at each center. On the first day of the study (Day 0), venous blood sample was collected in plain vacutainer tubes aseptically from all enrolled animals. Blood sample was withdrawn from all animals to determine the antibody titre for Classical swine fever virus. After withdrawal of blood sample from the treatment group animals, they were vaccinated with Classical Swine Fever vaccine at the dose rate of 1ml per animal intramuscularly. Each animal in the control group was injected with1ml of normal saline intramuscularly. The animals were observed for local and systemic side effects during vaccination and in the follow-up period of 21 days post-vaccination.

Post-Vaccination Evaluation of Safety

Safety evaluation was performed by identifying number of pigs experiencing local and/or systemic reactions and serious adverse events occurring during vaccination and in the follow up period of the study. Post-vaccination, animals were closely monitored for any possible serious adverse events. Other non-serious adverse events occurring after vaccination were also recorded. Local adverse events monitored included local pain, swelling, rashes, skin eruption, sloughing of mucous membrane while the systemic adverse events included fever, irritability, anorexia, restlessness, and diarrhoea. All the enrolled animals were followed up for local and systemic adverse events up to 21 days after vaccination. All the reported adverse events were assessed for their causal relationship with the vaccine and for their seriousness and severity.

Evaluation of Immunogenicity

Enzyme-linked immunosorbent assay (ELISA) was employed for evaluation of post vaccination immunogenicity by determining the humoral immune response against Classical Swine Fever vaccine. Detection of antibodies against the CSF vaccine antigen in serum was performed by ELISA using IDEXX classical swine fever virus Antibody (CSFV Ab) ELISA Kit following manufacturer's instructions. Seroconversion rate of the vaccine was determined at 30 days after the vaccination. Seroconversion was defined as any rise in antibody titer post-vaccination in comparison with pre-vaccination.

Statistical Analysis: Student's t-test was performed to compare the results.

Results and Discussion

Immunogenicity

Immunogenicity of the vaccine was compared by seroconversion rate of animals between the two groups. The animals were considered seronegative to classical swine fever virus antibodies when it gave a blocking percentage value less than or equal to 30%; and seropositive when the test sample gave a blocking percentage value greater than or equal to 40%. At 30 days post-vaccination, there was 100% seroconversion in animals of the treatment group while in the control group at 30 days post-vaccination, none of the animals were found positive for CSFV antibodies at both the centers. The seroconversion rate on day 0 and day 30 has been compared and represented in Table 1 and Figure1 and 2 for both the study center.

Table 1: Seroconversion on 0th day and 30th DPV in vaccinated pigs at both the study centers

Trial Site	Group	0^{th} DPV (n=30)	30^{th} DPV (n=30)	T value	P value
Bangalore Veterinary College	Treatment group pigs	9.03±14.26	58.40 ±9.13	17.77	<0.0001*
Hyderabad Veterinary College	Treatment group pigs	13.24±9.92	80.71 ±14.42	23.49	<0.0001*

**Indicates significant difference ($P \leq 0.05$) between seroconversion on 0^{th} day and 30^{th} DPV.*

In the vaccinated group (n=30), there was 100% seroconversion on day 30 compared to day 0. The 30^{th} DPV seroconversion rate in vaccinated group of animals was found to be significantly different ($P \leq 0.05$) when compared to 0^{th} day as determined by Student "t" test. The control group remained unresponsive throughout the study period.

Safety

None of the animals showed serious and non-serious adverse events during the observation and follow-up period of the study after vaccination. The safety and immunogenicity study of classical swine fever vaccine in pigs revealed

that it is safe after intramuscular administration without any local or systemic adverse events immediately after the vaccine administration and during the follow-up period of 30 days.

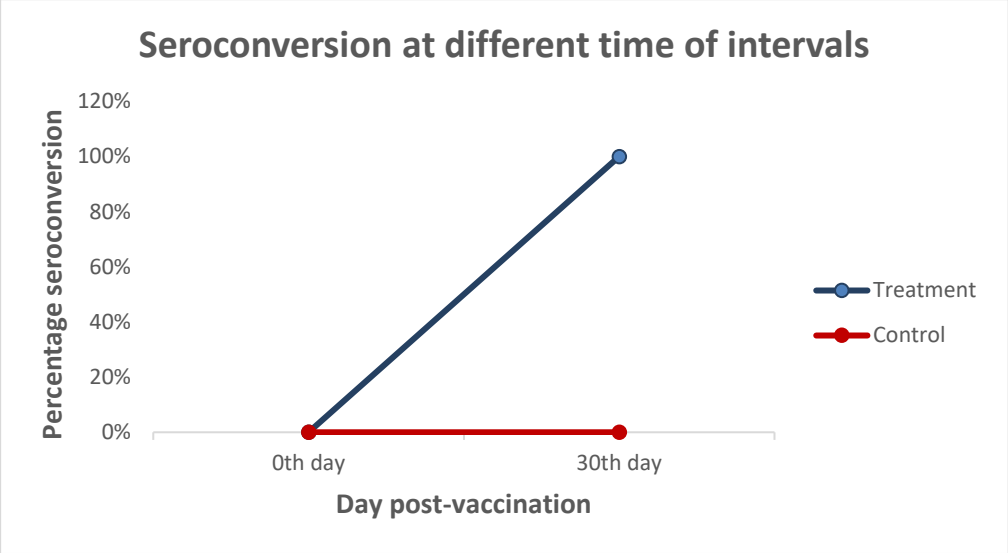

Figure 1: Percent seroconversion at different time points in animals of two groups at Bangalore center

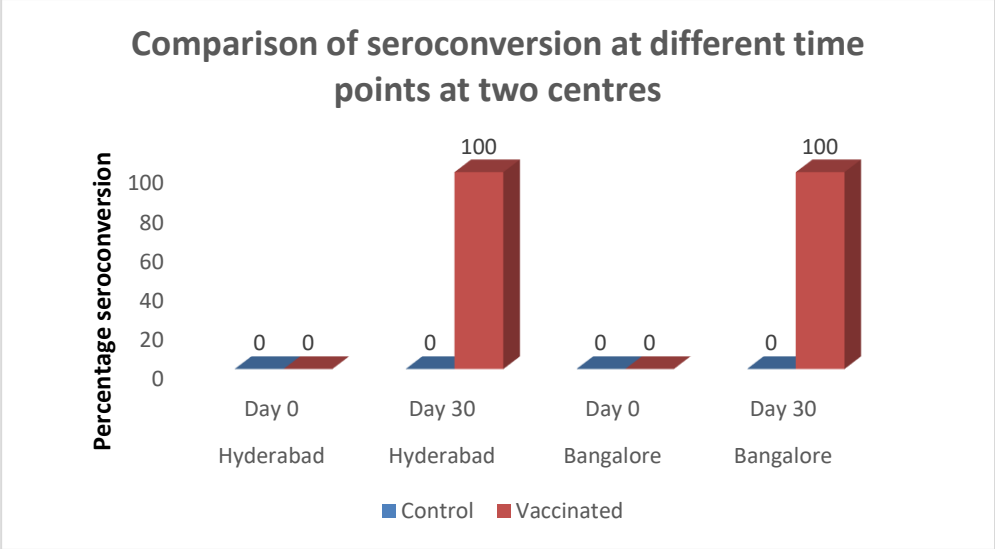

Figure 2: Comparative seroconversion in different groups of animals at different time points at two trial centers

Conclusion

The study demonstrated 100% seroconversion after vaccination in the animals. The results were statistically compared with the control group and were found to provide significantly high seroconversion in vaccinated groups. No serious side effects were found following vaccination. It is concluded that the live attenuated classical swine fever vaccine manufactured by Indian Immunologicals Limited is safe and induced immune response in pigs above three months of age when administered through intramuscular route.

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Conflict of Interests

There is no conflict of interest.

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