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Protective efficacy of an inactivated bivalent swine influenza vaccine

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Abstract

Swine influenza virus (SIV) is an important pathogen. Vaccination is the most effective way to prevent the disease. The objective of this study was to evaluate the protective efficacy of a commercial inactivated bivalent swine influenza vaccine (H1N1/H3N2). Vaccinated pigs with the three batches (# 201604, #201605, and #201606) had no clinical signs of disease, no viral shedding, and any lung lesions after the wild-type SIV-H1N1 LN and SIV-H3N2 HLJ challenge, and the unvaccinated pigs showed clinical signs of disease, had viral shedding, and severe lung lesions. Our results clearly demonstrate that three batches of vaccine products provided complete protection against the wild-type SIV-H1N1 LN and SIV-H3N2 HLJ challenge.

Introduction

Swine Influenza Virus (SIV) belongs to the family Orthomyxoviridae, infuenza a virus, negative, single-strand RNA virus whose genome consists of eight segments and it causes swine respiratory disease. The H1N1, H1N2 and H3N2 are main subtypes in world wild swine population [1]. Sivas an important swine pathogen involved in porcine respiratory disease. SIV infection is common throughout pig populations worldwide. Several outbreaks of swine influenza viruses within pig populations over the past years have resulted in global efforts to develop vaccines which will serve as important control measures for epidemic management [2]. Swine influenza has the following clinical symptoms: fever, lethargy, sneezing, coughing, breathing problems and decreased appetite [3]. Vaccination is the most effective measure to prevent swine influenza. Currently, swine influenza vaccines are composed of killed viruses containing both H1N1 and H3N2 subtypes. Thereby, we studied the protective efficacy of a swine influenza bivalent vaccine, inactivated (strain H1N1 LN and H3N2 HLJ).

Materials and methods

Forty healthy pigs, 4-week-age, were free from the infection of SIV and were randomly divided into eight groups (n=5). The pigs in groups 1 and 5 were vaccinated with # 201604. The pigs

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in groups 2 and 6 were vaccinated with # 201605. The pigs in groups 3 and 7 were vaccinated with # 201606. Each pig was vaccinated with 2ml of intramuscularly. All pigs were secondary vaccinated after 14 days. The three different batches of swine influenza bivalent inactivated vaccine (H1N1 LN strain and H3N2 HLJ strain), trade name "HUA-GAN-JIAN" manufactured by Sinovet biopharmaceutical Inc., China. Groups 4 and 8 were unvaccinated controls. The challenge was carried out 14 days after the second vaccination. Animals were transferred from the vaccination facility to the negative pressure animal facility three days before the challenge study. 1-4 groups were challenged with wild-type SIV-H1N1 LN, lot 001-067, (106.0TCID50/ml), 5-8 groups were challenged with wild-type SIV-H3N2 HLJ F13, lot 001-066 (106.1TCID50/ml). Each pig was injected 4 ml of wild virus via Intratracheal [4]. The clinical signs of illness included fever, loss of appetite, labored breathing and coughing. These symptoms were monitored closely, and body temperature was measured daily. Nasal swabs samples were collected for virus isolation. All pigs were sacrificed 5 days post-challenge and lungs were collected. The sections of lung were routinely stained with hematoxylin and eosin (H&E) and examined microscopically for histopathological changes. SIV-specific antigen was detected in lung tissues using a previously described immunohistochemistry (IHC) method [5,6]. (**Table 1**).

Results

Clinical evaluation

The groups 1-3 were a symptomatic after challenged with wild-type SIV-H1N1 LN, The group 4 demonstrated severe respiratory signs such as nasal discharge, coughing, asthma, and fever (Body temperature is not lower than 40.2 °C, at least 2 days) after challenged with wild-type SIV-H1N1 LN. The groups 5-7 were asymptomatic after challenged with wild-type SIV-H3N2 HLJ, The group 8 demonstrated severe respiratory signs such as nasal discharge, coughing, asthma, and fever (Body temperature is not lower than 40.2 °C, at least 2 days) after challenged with wild-type SIV-H3N2 HLJ. (**Figure 1**, **Figure 2**).

Virus isolation

The groups 1-3 were no SIV shedding after challenged with wild-type SIV-H1N1 LN, and the group 4 were SIV positive. The groups 5-7 were no SIV shedding with wild-type SIV-H3N2 HLJ, and the group 8 were SIV positive.

Pathological evaluation

Lungs of the groups 1-3 had not macroscopic consolidated lesions after challenged with wild-type SIV-H1N1 LN, the lungs had not abnormal lesions by H&E stain, the lungs had not the SIV-positive by IHC, and the group 4 had macroscopic consolidated lesions, the lungs showed thickening of bronchial walls by H&E stain, the brown staining cells of the SIV-positive were observed by IHC. Lungs of the groups 5-7 had not macroscopic consolidated lesions after challenged with wild-type SIV-H3N2 HLJ, the lungs had not abnormal lesions by H&E stain, the lungs had not the SIV-positive by IHC, and the group 8 had macroscopic consolidated lesions, the lungs showed thickening of bronchial walls by H&E stain, the brown staining cells of the SIV-positive were observed by IHC. (**Figure 3**, **Figure 4**).

Discussion

The Swine Influenza Virus (SIV) with type A, B, C, the type A swine flu virus the dangers of the most serious, can cause swine fever, anorexia, fatigue, cough, angular and breathing difficulties, etc [5]. The epidemic of the disease is characterized by sudden, short incubation period, quickly spread to the whole group, the infection rate of 100%, but the mortality is usually not more than 1%, all kinds of age, gender, varieties of pigs can be infected with type A SIV [6], this disease with more blue-ear disease, pig infectious pleuropneumonia, pig streptococcus disease, such as concurrent or secondary infection, complicating disease, severe, causing the mortality rate has risen sharply [7]. Pigs may also be of avian, swine and human influenza viruses common susceptible hosts, is a reservoir of influenza viruses and gene rearrangement "mixer" [8,9], in the spread between the evolution of the influenza virus and plays an important role. Therefore, it is necessary to develop safe and effective swine influenza vaccine, reduce the economic loss caused by SIV, avoid the recombination of influenza virus, and block the transmission of SIV cross-species barrier. Our results demonstrated that the vaccinated pigs were no systemic reactions and virus shedding, no pathologic lung lesion following challenge and no histological changes by pathological sections and IHC staining. The three batches of commercial swine influenza bivalent vaccine inactivated (strain H1N1 LN and H3N2 HLJ) could provide effective protection against wild-type (H1N1 LN and H3N2 HLJ) SIV strain challenges. In conclusion, the results of this study suggest that vaccinating for SIV is of no questionable value in pig herds to prevent SIV outbreak.

Tables

Table 1: Test design and grouping of animals

Group	Pig number	Vaccine batches	Inoculation dose/pig	Challenge virus	Challenge dose/pig
1	5	201604	2ml	wild-type SIV-H1N1 LN	4ml
2	5	201605	2ml	wild-type SIV-H1N1 LN	4ml
3	5	201606	2ml	wild-type SIV-H1N1 LN	4ml
4	5	-	-	wild-type SIV-H1N1 LN	4ml
5	5	201604	2ml	wild-type SIV-H3N2 HLJ	4ml
6	5	201605	2ml	wild-type SIV-H3N2 HLJ	4ml
7	5	201606	2ml	wild-type SIV-H3N2 HLJ	4ml
8	5	-	-	wild-type SIV-H3N2 HLJ	4ml

Figures

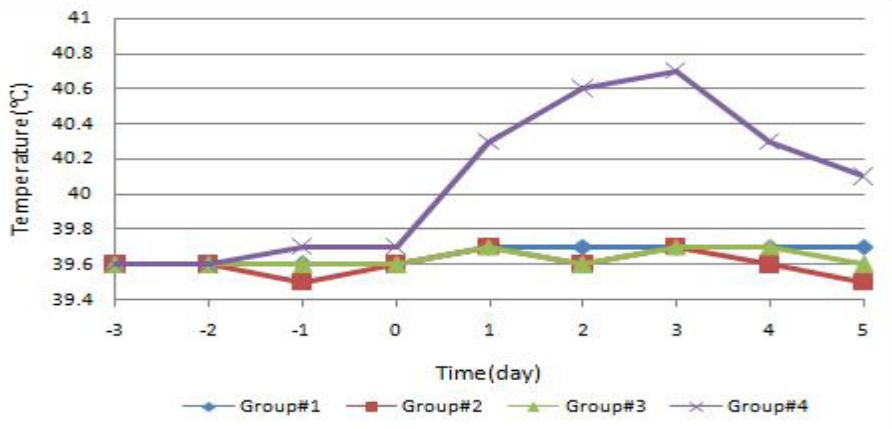


Figure 1: Pig body temperature changes after wild-type SIV H1N1 challenge

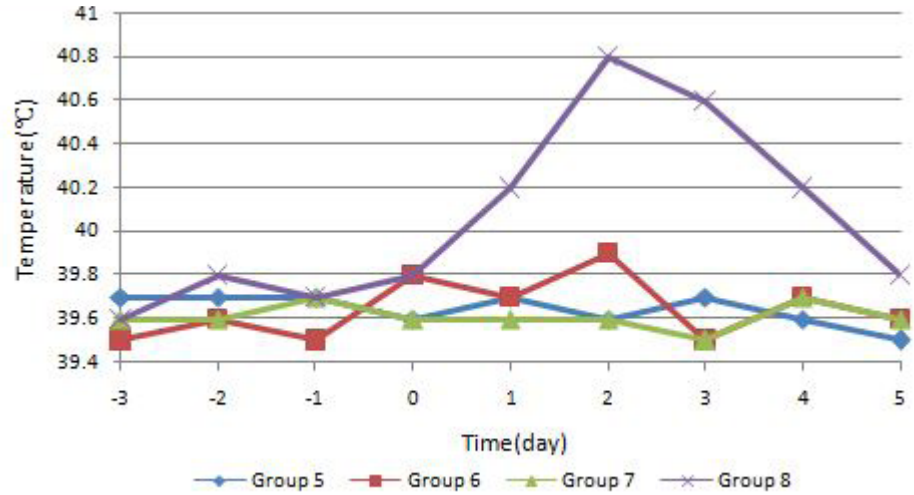
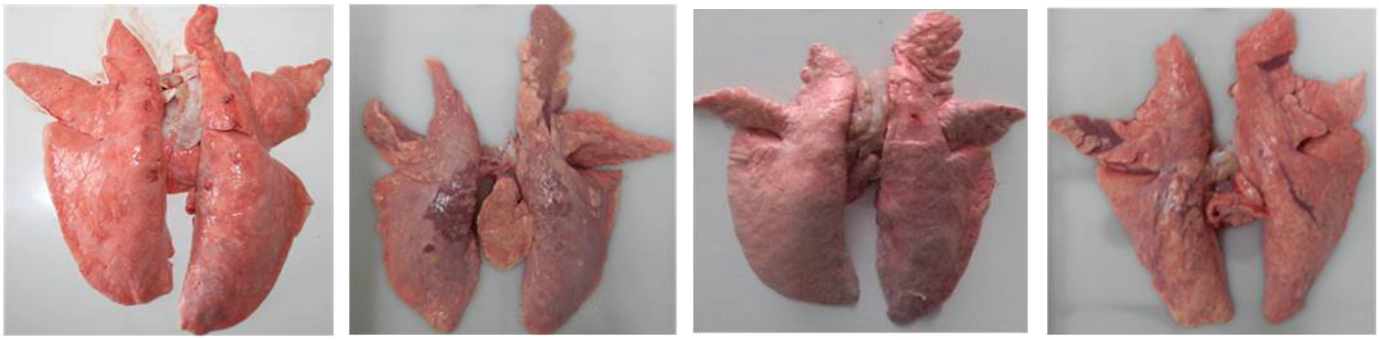


Figure 2: Pig body temperature changes after wild-type SIV H3N2 challenge



(A) (B) (C) (D)

Figure 3: Macroscopic lung lesions after the SIV challenge.

(A) Lung of unvaccinated pig had macroscopic consolidated lesions after challenged with wild-type SIV-H1N1 LN
(B) Lung of vaccinated pig had not macroscopic consolidated lesions after challenged with wild-type SIV-H1N1 LN
(C) Lung of unvaccinated pig had macroscopic consolidated lesions after challenged with wild-type SIV-H3N2 HLJ
(D) Lung of vaccinated pig had not macroscopic consolidated lesions after challenged with wild-type SIV-H3N2 HLJ

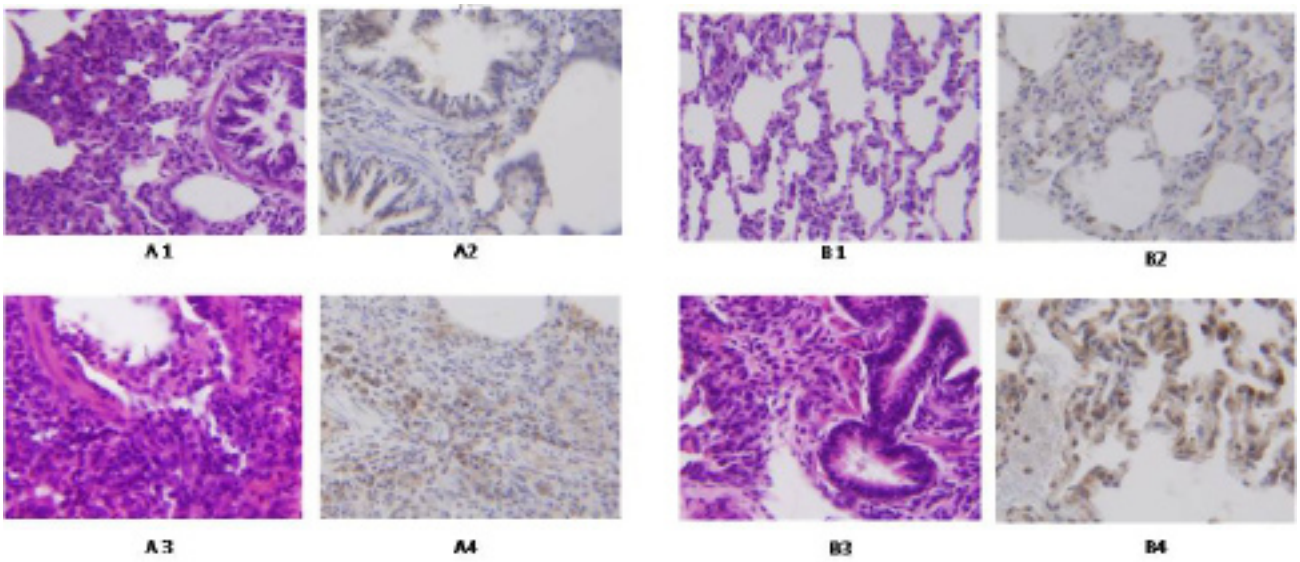


Figure 4: (A1) The lung of unvaccinated pig challenged with wild-type SIV H1N1 LN showed thickening of bronchial walls and lymphocytes invasion by H&E staining(200×).
(A2) The lung of unvaccinated pig challenged with wild-type SIV H1N1 LN ,the brown staining cells of the SIV-positive were observed by IHC(200×).
(B1) The lung of vaccinated pig challenged with wild-type SIV H1N1 LN had not abnormal lesions by H&E stain(200×).
(B2)The lung of vaccinated pig challenged with wild-type SIV H1N1 LN had not the SIV-positive by IHC(200×).
(C1) The lung of unvaccinated pig challenged with wild-type SIV H3N2 HLJ showed thickening of bronchial walls and lymphocytes invasion by H&E staining(200×).
(C2) The lung of unvaccinated pig challenged with wild-type SIV H3N2 HLJ,the brown staining cells of the SIV-positive were observed by IHC(200×).
(D1) The lung of vaccinated pig challenged with wild-type SIV H3N2 HLJ had not abnormal lesions by H&E stain(200×).
(D2)The lung of vaccinated pig challenged with wild-type SIV H3N2 HLJ had not the SIV-positive by IHC(200×).

Acknowledgments

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Authors' contributions

Weiwei Su,Wei Lu, Xiuhua Zhang, Ying Wu, Qin Sun, Wei Wang, Shucheng Zhang, Hua Wu performed the study and wrote the manuscript. He wei Zhang and Hua Wu participated in revision the manuscript, Hua Wu is the leader of the project. All authors read and approved the final manuscript.

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