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Reproductive, productivity, and mortality outcomes in late-gestation gilts and their litters following simulation of inadvertent exposure to a modified-live vaccine strain of porcine reproductive and respiratory syndrome (PRRS) virus

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ABSTRACT

The study evaluated the safety of a modified live-virus (MLV) porcine reproductive and respiratory syndrome (PRRS) vaccine in susceptible, pregnant gilts. To simulate inadvertent exposure secondary to postvaccination shedding of PRRS-MLV, seronegative gilts ($n=51$) were exposed by IM vaccination at 90 days of gestation. Vaccinated and nonvaccinated, seronegative control gilts ($n=25$) were maintained in separate facilities. The PRRS-MLV vaccine was given in a 2 mL dose on day 0. On day 7 all vaccinated gilts were PRRSV-PCR-positive for PRRSV and had responded serologically as determined by an ELISA. All control gilts remained PRRSV-PCR- and ELISA-negative throughout the study. Abortions did not occur in gilts from either group. The difference between vaccinated and control gilts in average number of piglets per litter (12.43 and 12.16, respectively), number of live births per litter (11.21 and 11.54), and mean piglet birth weight (3.22 and 3.26 lbs) were not significantly different. Piglets in the control group had significantly greater average daily gain versus piglets from vaccinated gilts (0.52 vs. 0.46 lbs, $P<0.0001$). Preweaning mortality was significantly greater ($P=0.0023$) in piglets from the vaccinated gilts (19.7% vs. 10.9%). A single gilt accounted for 18.2% of stillbirths in the vaccinated group. Air samples were borderline PRRSV-PCR-positive for PRRSV on days 29 and 32, after more than 98% of gilts had farrowed. Results demonstrated that vaccination of pregnant gilts at the time of peak fetal susceptibility was nonabortigenic and that the PRRS-MLV agent did not significantly affect reproductive outcomes. Lower ADG in piglets from vaccinated gilts may be due to PRRS-MLV viremia following transplacental or post-farrowing exposure. Air sampling results indicated that environmental contamination with PRRS-MLV shed from vaccinated gilts was minimal.

1. Introduction

Since porcine reproductive and respiratory and syndrome (PRRS) was first described and the PRRS virus (PRRSV) was identified as being the causative agent more than two decades ago, the disease continues to be clinically relevant and economically significant [1,2]. By some recent estimates, PRRS is the most costly disease affecting the swine industry [3–6]. Elimination of PRRSV from a production site or maintaining a PRRSV-free herd is sometimes attempted [4,7–9]. However, PRRSV is readily shed by infected swine and has an affinity for transmission via fomites and in aerosols, creating a tenacious presence in the environment [3,10–17]. Studies have shown that airborne transmission of PRRSV can occur over distances as great as 4.7 km, with the virus still remaining infectious [12]. Thus, without intensive biosecurity, reinfection occurs on a high percentage of PRRSV-free farms, often within a matter of months [7,9].

Because PRRS is endemic in most swine-producing countries and has a substantial adverse economic impact, vaccination is a key component of most PRRS disease control strategies [3,4]. Modified live-virus (MLV) vaccines have important advantages over

Abbreviations: ELISA, enzyme linked immunosorbent assay; LSM, least squares mean; PCR, polymerase chain reaction; PRRS, porcine reproductive and respiratory syndrome; PRRSV, PRRS virus.

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inactivated vaccines for immunizing swine against PRRSV. These include a stronger and more complete immune response, including cell mediated immunity [4,18–20]; immunogenicity in previously unexposed swine [13,18,21,22]; PRRSV neutralization, resulting in the ability to limit postchallenge viremia, transplacental infection and viral shedding [4,8,13,19,21]; protection against clinical disease following a single vaccine dose [4,18,23]; and some degree of cross-protection against heterologous strains of PRRSV [18,22].

Growing and finishing pigs are the principal target population for vaccination with PRRS-MLV agents, which are generally contraindicated in pregnant swine as a safety precaution. The MLV vaccine virus replicates in the host, which allows shedding of attenuated PRRSV and creates the potential for exposure of immunologically naïve swine to the vaccine virus [19,22,24]. The safety implications of PRRS-MLV replication in vivo include the possibility of genetic recombination and reversion to virulence following horizontal transmission to a second host [4,6,19]. Pregnant sows infected with PRRS-MLV, either by vaccination or inadvertent exposure, and their transplacentally infected litters may shed vaccine virus and expose susceptible pigs [19]. Because field strains of PRRSV affect productivity of growing swine and reproductive performance in pregnant sows, it has been theorized that PRRS-MLV vaccine strains have the potential to mimic these effects following in vivo replication in susceptible host animals. To illustrate, European investigators have isolated genetically-confirmed modified-live PRRS vaccine virus from stillborn and non-viable fetuses from non-vaccinated sows [25]. While the study involved only one commercial PRRS-MLV vaccine and a cause-and-effect etiology was not confirmed, it suggests that fetal mummification and stillbirths following in utero replication of PRRS-MLV in pregnant sows can occur [19,25]. While various studies have shown that vaccination of pigs with PRRS-MLV results in positive productivity outcomes in endemic herds [4,19,21,27], a negative effect on performance of growing swine due to in vivo replication of PRRS-MLV in the respiratory tract or lymphatic system has also been proposed [19,23,26].

The purpose of this study was to vaccinate PRRSV-naive, pregnant gilts with a PRRS-MLV to simulate inadvertent exposure, and then compare reproductive, productivity, and mortality outcomes in the vaccinated gilts and their litters with the same parameters for a non-vaccinated control group. Results would determine the relative safety of the PRRS-MLV vaccine in production settings where inadvertent exposure to susceptible breeding stock could occur. It should be noted that vaccination of pregnant swine was a non-label application of the test vaccine.

2. Materials and methods

2.1. Test animals, facilities, and animal management

Healthy, pregnant Yorkshire-Landrace crossbred gilts ($n = 76$) purchased from a PRRSV-negative source and with no history of PRRSV vaccination were used as test animals. Pre-enrollment PCR testing confirmed that serum samples from all gilts were negative for PRRSV (VetMax, Life Technologies, Grand Island, NY) and porcine circovirus type-2 (Iowa State University Veterinary Diagnostic Laboratory [ISU-VDL] assay). Gilts were serologically positive for *Mycoplasma hyopneumoniae* antibodies as determined by an ELISA (ISU-VDL assay). The least squares mean (LSM) *M. hyopneumoniae* ELISA titers were not significantly different ($P = 0.758$) between vaccinated and control gilts (Table 1).

Gilts were housed throughout the study in farrowing crates in a commercial farrowing building. The farrowing building was divided into two adjacent sections that were sealed off from each other but with a common pit, creating separate air spaces for each section. Vaccinated and control gilts and their litters were maintained separately in their respective sections. Air-exchange tests confirmed that there was no detectable transfer of ambient air between the two sections.

Table 1
Serologic response in PRRS-MLV vaccinated pregnant gilts and non-vaccinated controls (Serology data was transformed by the log10 (titer + 1) transformation).

ELISA assay	Study day	LSM titer in vaccinates (n)	LSM titer in controls (n)
M. hyopneumoniae	−7	0.209[a] (51)	0.217[a] (25)
PRRSV	−7	0.010[a] (51)	0.010[a] (25)
PRRSV	0*	0.011[a] (51)	0.013[a] (25)
PRRSV	7	0.017[a] (50)	0.009[b] (25)
PRRSV	48	0.417[c] (49)	0.006[d] (22)

LSM, least squares mean; PRRS-MLV, porcine reproductive and respiratory syndrome modified live-virus. Values with different superscripts (a and b) in the same row are significantly different ($P = 0.0075$). Values with different superscripts (c and d) in the same row are significantly different ($P = 0.0001$).

Gilts and their litters were cared for in compliance with the Institutional Animal Care and Use Committee guidelines of the American Association of Laboratory Animal Care. All pigs were observed daily for signs of clinical disease or non-viability throughout the trial. Biosecurity protocols required personnel performing husbandry or administrative tasks to first visit the section where control animals were housed before entering the section where vaccinated pigs were housed. Personnel changed their outerwear whenever they moved between the two sections of the test facility.

2.2. Study design

A randomized block design was used to allocate gilts to a block of three animals each. Within blocks each gilt was randomly assigned to either the vaccinated or control group in a 2:1 ratio. Vaccinated gilts ($n = 51$) were given modified live-virus PRRSV vaccine (Fostera PRRS, Zoetis, Florham Park, NJ) and controls ($n = 25$) were given sterile diluent. Both treatments were administered in a 2 mL IM dose at approximately 90 days of gestation on day 0 of the study.

On days −7, 0, 7, and 48, serum samples were obtained from each gilt for PRRSV and *M. hyopneumoniae* ELISA testing and for PCR analysis for PRRSV. A commercial ELISA (PRRS X3, Idexx, Westbrook, ME) was used to determine PRRSV serologic response. Quantitative PCR (PRRSV-PCR) results were expressed either as genomic copies or as a cycle time (CT) value. CT values are inversely proportional to genetic copies of the target analyte, so that CT values $\geq$40, 37–40, and $\leq$36 were considered negative, suspect, and positive, respectively [5].

Piglet birth weights and weaning weights were determined as the basis for calculating total weight gain (TWG) and average daily gain (ADG). Piglet mortality and cause of death were noted. Blood samples for serologic and PCR testing were obtained from the piglets from litters of vaccinated and control gilts ($n = 25$ and 13, respectively) determined by a random number generator on the day of farrowing prior to suckling and on the day of weaning.

Air samples were obtained daily from both sections of the farrowing barn throughout the study. Air samples were quantitatively analyzed for PRRSV by means of PCR. A liquid cyclonic air collector (Midwest MicroTek, Brookings, SD) with a capacity of 400 L min^{-1} was used to obtain aerosol-borne PRRSV samples for preparation as a diagnostic analyte, as previously described [15,16,28]. The analytic sensitivity for detecting PRRSV in aerosols had previously been determined to be 1×10^1 $TCID_{50}$/mL [15]. Separate collector machines were used for the vaccinated and control sections of the barn, with the collectors positioned 1 m from an exhaust fan. Three 30-min air samples were obtained daily.