Efficacy of ivermectin administration to growing pigs after a virulent porcine reproductive and respiratory syndrome virus 1-4-4 L1C challenge

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Summary

Objective: To conduct a pilot study, under noncommercial conditions, to assess the potential efficacy of ivermectin administered subcutaneously to pigs following a porcine reproductive and respiratory syndrome virus (PRRSV) 1-4-4 L1C challenge.

Materials and methods: A total of 50 feeder pigs were enrolled and allocated into 2 groups. On day 0, all pigs were challenged with PRRSV 1-4-4 L1C. Animals in group 1 received an ivermectin dose of approximately 500 µg/kg administered subcutaneously at 1 and 3 days post challenge (DPC). Group 2 animals remained untreated. Serum was collected from each animal on DPC 1, 3, 5, 7, 10, and 14 and tested individually to assess PRRSV viremia levels via quantitative polymerase chain reaction (qPCR). On DPC 14, pigs were weighed, euthanized, necropsied, and lungs were scored for lung lesions. Bronchoalveolar lavage (BAL) was performed on each set of lungs and the corresponding level of viremia was measured via qPCR. Any animal that died prior to necropsy was weighed, received a lung score, and BAL collected.

Results: There was no significant difference in viremia levels between treatment groups. There was a trend toward significance between treatment groups in lung lesion scores with the ivermectin-treated pigs exhibiting less lung pathology compared to the control group ($P = .05$).

Implications: Ivermectin administered to pigs post virulent PRRS 1-4-4 L1C challenge did not reduce the level of viremia in serum or BAL fluid but may have reduced lung lesions.

Keywords: swine, ivermectin, porcine reproductive and respiratory syndrome

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Resumen - Eficacia de la administración de ivermectina a cerdos en crecimiento después de un reto del virus virulento del síndrome reproductivo y respiratorio porcino 1-4-4 L1C

Objetivo: Realizar un estudio piloto, en condiciones no comerciales, para evaluar la eficacia potencial de la ivermectina administrada por vía subcutánea a cerdos después del reto con la cepa 1-4-4 L1C del virus del síndrome reproductivo y respiratorio porcino (PRRSV).

Materiales y métodos: Se incluyeron un total de 50 cerdos de engorda y se distribuyeron en 2 grupos. En el día 0, todos los cerdos fueron desafiados con PRRSV 1-4-4 L1C. Los animales del grupo 1 recibieron una dosis de ivermectina de aproximadamente 500 µg kg administrada por vía subcutánea los días 1 y 3 días post reto (DPR). Los animales del grupo 2 no recibieron tratamiento. Se recolectó suero de cada animal en DPR 1, 3, 5, 7, 10, y 14 y se analizó individualmente para evaluar los niveles de viremia del PRRSV mediante la reacción en cadena de la polimerasa cuantitativa (qPCR). En el DPR 14, los cerdos fueron pesados, sacrificados, se hizo la necropsia, y los pulmones fueron evaluados para detectar lesiones pulmonares. Se realizó lavado broncoalveolar (LBA) en cada conjunto de pulmones y se midió el nivel correspondiente de viremia mediante qPCR. Todos los animales que murieron antes de la necropsia fueron pesados, recibieron una puntuación pulmonar y se recolectó el LBA.

Resultados: No hubo diferencias significativas en los niveles de viremia entre los grupos de tratamiento. Hubo una tendencia a la significación entre los grupos de tratamiento en las puntuaciones de las lesiones pulmonares, ya que los cerdos tratados con ivermectina mostraron menos patología pulmonar en comparación con el grupo control ($P = .05$).

Implicaciones: La ivermectina administrada a cerdos después de una exposición virulenta con PRRS 1-4-4 L1C no redujo el nivel de viremia en el suero o en el líquido LBA, pero puede haber reducido las lesiones pulmonares.

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Résumé - Efficacité de l'administration d'ivermectin à des porcs en croissance après une infection défi avec le virus virulent 1-4-4 L1C du syndrome reproducteur et respiratoire porcin

Objectif: Mener une étude pilote, dans des conditions non-commerciales, pour évaluer l'efficacité potentielle de l'administration d'ivermectin par voie sous-cutanée à des porcs à la suite d'une infection défi avec le virus du syndrome reproducteur et respiratoire porcin (VSRRP) 1-4-4 L1C.

Matériels et méthodes: Cinquante porcs a été sélectionnés et répartis en 2 groupes. Au jour 0, tous les porcs ont été infectés avec le VSRRP 1-4-4 L1C. Les animaux du groupe 1 ont reçu une dose d'ivermectin d'environ 500 µg/kg par voie sous-cutanée aux jours 1 et 3 post-infection (JPI). Les animaux du groupe 2 sont demeurés non-traités. Du sérum a été prélevé de chaque animal aux JPI 1, 3, 5, 7, 10, et 14 et testé individuellement pour évaluer le degré de virémie VSRRP par réaction d'amplification en chaîne par la polymérase quantitative (qPCR). À 14 JPI, les porcs ont été pesés, euthanasiés et soumis à une nécropsie, et les poumons ont été notés pour les lésions pulmonaires. Un lavage bronchoalvéolaire (LBA) a été réalisé sur chaque paire de poumons et les niveaux de virémie correspondants mesurés par qPCR. Tout animal qui mourait avant la date prévue de nécropsie était pesé, recevait un pointage des lésions pulmonaires, et du LBA prélevé.

Résultats: Il n'y avait pas de différence significative dans les degrés de virémie entre les groupes de traitement. Il y avait une tendance vers un seuil significatif entre les groupes de traitement dans les pointages de lésions pulmonaires chez les porcs traités avec de l'ivermectin, ceux-ci montrant moins de pathologies pulmonaires que le groupe témoin ($P = .05$).

Implications: L'ivermectin administré à des porcs à la suite d'une infection défi avec la souche virulente du VSRRP 1-4-4 L1C n'a pas réduit la virémie dans le sérum ou un LBA, mais pourrait avoir réduit les lésions pulmonaires.

Porcine reproductive and respiratory syndrome virus (PRRSV) continues to devastate the US swine industry, costing producers millions of dollars of lost revenue annually due to high mortality rates and decreased production performance.[1,2] Although several vaccines exist for PRRSV, none provide sterilizing immunity. The combination of the ever-changing nature of the virus and the lack of understanding of what elicits specific immunity to PRRSV make it difficult to create a cross-protective vaccine.[3-5] There are no antiviral treatments labelled for use in swine to treat common viral diseases found in the US swine industry, including PRRSV. Field reports suggest the use of nonsteroidal anti-inflammatory drugs to reduce morbidity, however their efficacy remains questionable and may lead to gastrointestinal ulceration.[6]

Ivermectin (IVM), derived from avermectin, a macrocyclic lactone, is a parasiticide labelled for the treatment of several parasitic infections in both veterinary and human medicine. The antiparasitic labelled dose of IVM in swine is 300 µg/kg administered subcutaneously. The antiparasitic properties of IVM are generated by its apparent agonism of the gamma-aminobutyric acid receptor resulting in cell hyperpolarization and ultimately cell paralysis and death.[7] In addition to antiparasitic properties, IVM has also shown to have anticancer, antiviral, antifungal, and antibacterial effects in biological systems.[8] The antiviral effects of IVM were measured against several human flaviviruses such as West Nile and yellow fever virus. The antiviral mechanism of action is suggested to inhibit viral replication by targeting the nonstructural protein 3 helicase domain.[9] Lee and Lee[10] showed the ability of IVM to significantly reduce the viral replication of PRRSV in porcine alveolar macrophages *in vitro*. Furthermore, a 2021 case report suggested that the administration of IVM to sows and gilts in the face of a concurrent PRRSV outbreak may have reduced the severity of the outbreak, allowing production parameters to return to baseline more quickly.[11] The pharmacokinetic profile of IVM in swine suggests that, when delivered at a dose of 300 µg/kg, it can be detected in plasma for up to 20 days post administration.[12] The combination of the proposed mechanism of action and relatively slow clearance of IVM in pigs may make this molecule a suitable antiviral candidate. It is critical for the swine industry to understand if there are potential antiviral capabilities of IVM against PRRSV.

Animal care and use

This study was conducted at VRI and was reviewed and approved by VRI's Institutional Animal Care and Use Committee.

Materials and methods

Experimental design

All pigs were sourced from colostrum-deprived caesarean-derived (CDCD) dams inseminated with commercial Duroc boar semen, housed in a biosafety level-1 barn during gestation. Prior to transport to the biosafety level-2 isolation facility, PRRSV-naïve status was confirmed via enzyme-linked immunosorbent assay and quantitative polymerase chain reaction (qPCR). At arrival, pigs were weighed, blocked by litter, and randomly allocated into 2 treatment groups, each containing 25 pigs. The animals were allowed to acclimate for 2 days prior to challenge. At 0 days post challenge (DPC), study animals were approximately 8 weeks of age and the mean weight was 24.9 kgs (range, 14.9-34.4 kgs). Beginning on DPC-1 through the end of the study (DPC 14), all pigs were observed for clinical signs associated with PRRSV infection or IVM toxicity. A numerical value was assigned to each pig for a respiratory, depression, and body condition score (normal = 0, mild = 1, moderate = 2, severe = 3). On DPC 0, all pigs were challenged with PRRSV restriction fragment length polymorphism (RFLP) 1-4-4 L1C variant isolate ISU21-1775 with a target dose of 4-5 log median tissue culture infectious dose/mL.[13] Challenge material was delivered intranasally (1 mL/nare) followed by a 1 mL intramuscular injection for a total of 3 mL of challenge material administered to each animal. On DPC 1, using the mean weight of the group 1 animals, IVM (Boehringer Ingelheim) was administered subcutaneously to each animal at a dose of approximately 500 µg/kg (1.2 mL). The group 2 pigs remained untreated. The group 1 pigs were retreated on DPC 3 at the same dose, while the group 2 pigs remained untreated. Blood was collected from each pig via jugular venipuncture using individual needles (20 gauge × 3.8 cm) and vacutainers on DPC 0, 1, 3, 5, 7, 10, and 14. Blood was centrifuged at 3000*g* for approximately 10 minutes; the serum

was harvested and submitted to the Iowa State University Veterinary Diagnostic Laboratory (ISU VDL) to determine PRRSV viremia levels by qPCR. Any pig that died prior to the end of study was weighed, a lung lesion score was recorded, and a bronchoalveolar lavage (BAL) was performed. Fourteen days post challenge, body weights were recorded for all remaining pigs and necropsies performed to determine percentage of observed lung lesions. Total lung lesions for each pig were scored by the primary investigator and calculated using the following formula[14]: Total lung lesions = Right apical % × 0.11 + right cardiac% × 0.10 + right diaphragmatic% × 0.34 + left apical% × 0.05 + left cardiac% × 0.06 + left diaphragmatic% × 0.29 + intermediate% × 0.05. Bronchoalveolar lavage fluid was collected from each set of lungs and the corresponding level of viremia was measured via PRRSV qPCR by the ISU VDL.

Dose determination

The IVM dose regimen used in this study was arbitrarily selected to reflect the *in vitro* exposures presented to various viral targets in studies previously described and represents an off-label dose.[10] It was selected at a higher range within the dose spectrum to maximize the potential to detect dose dependent effects on PRRSV. Additional studies requiring dose refinement and establishment of a sufficient withdrawal period to protect food safety would be warranted prior to implementation as a routine practice. These components were deemed premature, especially considering the ethical obligation to minimize animals impacted with research, considering that no *in vivo* evidence of efficacy at any level has been discovered in the peer-reviewed literature. The potential side effects of IVM toxicity have been described to be neurologic in several species, including pigs and humans.[15,16] Presence or absence of clinical neurologic signs of IVM toxicity were included in daily observations. The pigs in this study were excluded from the human and animal food supply.

Statistical analysis

The primary outcome variable was the level of viremia (copies of target DNA per mililiter) in serum and BAL. These outcomes were evaluated using a generalized linear mixed model as appropriate (the MIXED procedure in SAS [SAS Institute; version 9.4]). The BAL viremia values were subject to analysis of variance (ANOVA), with treatment group as a fixed effect and litter as a random effect. Serum viremia values were evaluated using repeated measures ANOVA, with treatment group, day post challenge, and day × group interaction as fixed effects and litter as a random effect. A compound symmetric structure was assumed for the covariance matrix. The PRRSV copy numbers were $\log_{10}$ transformed prior to statistical analysis.

Secondary outcome variables included average daily gain and lung scores. These outcomes were subject to ANOVA as previously described. Lung lesion scores were arcsine transformed prior to statistical analysis.

Clinical scores associated with body condition, depression, and respiratory observations were subject to analysis using the Kruskal-Wallis test (the NPAR1WAY procedure in SAS) for each day.

Results

There was not a statistically significant difference detected between treatment groups in the viremia level in BAL or serum (Tables 1 and 2). In addition to the primary outcome variables, there was no significant difference noted in average daily gain between treatment groups (Table 3). Only 3 animals gained weight over the course of the 14-day study. All 3 animals belonged to the IVM-treated group (data not shown). On DPC 14, the percentage of lung lesions in the IVM-treated group was less than the control group, although not statistically significant ($P = .05$; Table 3).

Body condition scores were more likely to be lower in the IVM-treated pigs as compared to the control pigs at 8 and 9 DPC (Table 4). Depression scores were more likely to be lower in IVM-treated pigs as compared to the control pigs at 6, 8, 12, and 13 DPC (Table 5). Respiratory scores were more likely to be lower in IVM-treated pigs as compared to control pigs at 6 DPC; at 9 DPC, scores were more likely to be higher in IVM-treated pigs as compared to the control pigs (Table 6).

At scheduled necropsy (14 DPC), 16 of 25 animals (64%) in the IVM-group and 14 of 25 animals (56%) in the control group completed the study (Table 7).

Discussion

The results of this study suggest that IVM, when administered subcutaneously to pigs at a dose of approximately 500 µg/kg at 24 and 72 hours post virulent PRRSV RFLP 1-4-4 L1C variant strain challenge, does not reduce the level of viremia in serum or BAL. However, IVM administered at this dose and time may reduce the presence of lung lesions and may lessen the clinical impact post challenge. Several factors could contribute to this conclusion including overall study design, PRRSV strain virulence, IVM dosage, timing of administration relative to challenge, the effect of an immunosuppressive virus on the pharmacokinetic profile and bioavailability of IVM, and genetic susceptibility of the experimental pigs used in this study.

During October 2020, the PRRSV 1-4-4 L1C variant strain emerged in the United States and devastated the swine industry with unprecedented production losses.[17] A presentation at the 2022 Iowa State University James D. McKean Swine Disease Conference showed that the challenge virus used in this study has potentially higher transmissibility and pathogenicity compared to other PRRSV strains, even of the same lineage.[13] Although IVM did not appear to mitigate the infectivity and shedding of PRRSV in this study, it may show efficacy when challenged with a less virulent PRRSV strain. Further studies are needed to explore this hypothesis.

A label claim for IVM as an antiviral therapeutic has not been approved by the US Food and Drug Administration, therefore the dosing regimen used in this study was estimated based on the *in vitro* PRRSV work done by Lee and Lee[10] and the limited information known about the pharmacokinetic behavior of IVM in swine.[12] Although IVM's half-life is relatively long, the level of active ingredient may not have reached therapeutic levels to have an antiviral effect on the PRRSV challenge used in this study.[12] Ivermectin's proposed antiviral mechanism of action as a viral helicase inhibitor prevents viral replication by altering the trafficking of viral proteins between the cytoplasm and nucleus of the host cell.[7] A study by Mastrangelo et al,[9] assessed the efficacy of IVM *in vitro* against the flavivirus yellow fever virus. Like PRRSV, the yellow fever virus is a single-stranded RNA virus that relies on

Table 1: Summary of BAL viremia outcomes

Variable	LSMeans (SEM)		*P* value*
	Group 1	Group 2	
PRRSV Ct	19.04 (.039)	19.57 (.39)	.25
PRRSV copies/mL†	8.29 (.12)	8.13 (.12)	.26

* The BAL viremia values were subject to ANOVA, with treatment group as a fixed effect and litter as a random effect.

† PRRS copies/mL were log10 transformed prior to analysis to stabilize the residuals. Log10 LSMeans are presented.

BAL = bronchoalveolar lavage; PRRSV = porcine reproductive and respiratory syndrome virus; Ct = cycle threshold.

Table 2: Summary of serum viremia outcomes

Variable	Days post challenge	LSMeans (SEM)		*P* values*		
		Group 1	Group 2	Group	Day	Group × Day
PRRSV Ct†	0	36.9894 (.4586)	36.9787 (.4599)	.96	< .001	.85
	1	20.2094 (.4586)	20.8147 (.4599)			
	3	18.5734 (.4586)	18.8547 (.4599)			
	5	17.4694 (.4586)	17.3947 (.4599)			
	7	17.5934 (.4586)	17.3747 (.4599)			
	10	17.3141 (.4702)	17.1766 (.4712)			
	14	20.3964 (.5267)	20.0854 (.5527)			
PRRSV copies/mL‡	0	0.0032 (.1397)	0.0064 (.1401)	.96	< .001	.83
	1	7.9376 (.1397)	7.7516 (.1401)			
	3	8.4387 (.1397)	8.3470 (.1401)			
	5	8.7707 (.1397)	8.7930 (.1401)			
	7	8.7327 (.1397)	8.8026 (.1401)			
	10	8.8193 (.1433)	8.8606 (.1436)			
	14	7.8766 (.1605)	7.9750 (.1684)			

* Serum viremia values were evaluated using repeated measures ANOVA, with treatment group, day post challenge, and day × group interaction as fixed effects and litter as a random effect.

† Where Ct values were > 37 a value of 37 was reported.

‡ PRRSV copies/mL were $\log_{10}$ (copy + 1) transformed prior to analysis to stabilize the residuals. Log_{10} LSMeans are presented.

PRRSV = porcine reproductive and respiratory syndrome virus; Ct = cycle threshold.

Table 3: Summary of average daily gain and lung lesion scores outcomes

Variable	LSMeans (SEM)		*P* value*
	Group 1	Group 2	
Lung lesion scores†	36.06%	57.76%	.05
Average daily gain	-0.47 (.075)	-0.50 (.079)	.82

* These outcomes were subject to ANOVA, with treatment group as a fixed effect and litter as a random effect.

† Lung lesion scores were arcsine transformed prior to analysis to stabilize the residuals. Back transformed LSMeans are presented.

Table 4: Summary of body condition scores

Day post challenge	Group	Body condition score					
		0		1		2	
		n	%	n	%	n	%
0	1	25	100.00	0	0	0	0
	2	25	100.00	0	0	0	0
1	1	25	100.00	0	0	0	0
	2	25	100.00	0	0	0	0
2	1	25	100.00	0	0	0	0
	2	25	100.00	0	0	0	0
3	1	25	100.00	0	0	0	0
	2	25	100.00	0	0	0	0
4	1	24	96.00	1	4.00	0	0
	2	21	84.00	4	16.00	0	0
5	1	20	80.00	5	20.00	0	0
	2	21	84.00	4	16.00	0	0
6	1	15	60.00	10	40.00	0	0
	2	19	76.00	6	24.00	0	0
7	1	19	76.00	6	24.00	0	0
	2	15	60.00	10	40.00	0	0
8	1	12	48.00	13	52.00	0	0
	2*	5	20.00	13	52.00	7	28.00
9	1	10	40.00	14	56.00	1	4.00
	2*	5	20.83	13	54.17	6	25.00
10	1	4	17.39	19	82.61	0	0
	2	7	30.43	13	56.52	3	13.04
11	1	2	9.09	20	90.91	0	0
	2	0	0	21	100.00	0	0
12	1	1	5.26	18	94.74	0	0
	2	0	0	18	85.71	3	14.29
13	1	0	0	18	100.00	0	0
	2	0	0	15	93.75	1	6.25
14	1	0	0	15	93.75	1	6.25
	2	0	0	12	85.71	2	14.29

* Group 1 significantly different from group 2 at $P < .05$.

Table 5: Summary of depression scores

Day post challenge	Group	Depression scores							
		0		1		2		3	
		n	%	n	%	n	%	n	%
0	1	25	100.00	0	0	0	0	0	0
	2	25	100.00	0	0	0	0	0	0
1	1	25	100.00	0	0	0	0	0	0
	2	25	100.00	0	0	0	0	0	0
2	1	25	100.00	0	0	0	0	0	0
	2	25	100.00	0	0	0	0	0	0
3	1	25	100.00	0	0	0	0	0	0
	2	25	100.00	0	0	0	0	0	0
4	1	24	96.00	1	4.00	0	0	0	0
	2	24	96.00	1	4.00	0	0	0	0
5	1	22	88.00	3	12.00	0	0	0	0
	2	18	72.00	7	28.00	0	0	0	0
6	1	22	88.00	3	12.00	0	0	0	0
	2*	16	64.00	9	36.00	0	0	0	0
7	1	22	88.00	3	12.00	0	0	0	0
	2	17	68.00	6	24.00	2	8.00	0	0
8	1	19	76.00	6	24.00	0	0	0	0
	2*	1	4.00	17	68.00	7	28.00	0	0
9	1	1	4.00	23	92.00	0	0	1	4.00
	2	0	0	19	79.17	5	20.83	0	0
10	1	2	8.70	21	91.30	0	0	0	0
	2	2	8.70	19	82.61	0	0	2	8.70
11	1	0	0	20	90.91	0	0	2	9.09
	2	0	0	21	100.00	0	0	0	0
12	1	0	0	18	94.74	1	5.26	0	0
	2*	0	0	8	38.10	13	61.90	0	0
13	1	0	0	18	100.00	0	0	0	0
	2*	0	0	6	37.50	10	62.50	0	0
14	1	0	0	15	93.75	0	0	1	6.25
	2	0	0	14	100.00	0	0	0	0

* Group 1 significantly different from group 2 at $P < .05$.

Table 6: Summary of respiratory scores

Day post challenge	Group	Respiratory scores							
		0		1		2		3	
		n	%	n	%	n	%	n	%
0	1	25	100.00	0	0	0	0	0	0
	2	25	100.00	0	0	0	0	0	0
1	1	25	100.00	0	0	0	0	0	0
	2	25	100.00	0	0	0	0	0	0
2	1	24	96.00	1	4.00	0	0	0	0
	2	25	100.00	0	0	0	0	0	0
3	1	25	100.00	0	0	0	0	0	0
	2	24	96.00	1	4.00	0	0	0	0
4	1	23	92.00	2	8.00	0	0	0	0
	2	19	76.00	6	24.00	0	0	0	0
5	1	22	88.00	3	12.00	0	0	0	0
	2	18	72.00	7	28.00	0	0	0	0
6	1	23	92.00	2	8.00	0	0	0	0
	2*	17	68.00	8	32.00	0	0	0	0
7	1	15	60.00	5	20.00	5	20.00	0	0
	2	17	68.00	6	24.00	2	8.00	0	0
8	1	4	16.00	12	48.00	9	36.00	0	0
	2	4	16.00	15	60.00	5	20.00	1	4.00
9	1	2	8.00	8	32.00	15	60.00	0	0
	2*	0	0	19	79.17	5	20.83	0	0
10	1	0	0	2	8.70	21	91.30	0	0
	2	0	0	8	34.78	14	60.87	1	4.35
11	1	0	0	0	0	22	100.00	0	0
	2	0	0	2	9.52	19	90.48	0	0
12	1	0	0	0	0	18	94.74	1	5.26
	2	0	0	2	9.52	19	90.48	0	0
13	1	0	0	2	11.11	16	88.89	0	0
	2	0	0	2	12.50	14	87.50	0	0
14	1	0	0	1	6.25	15	93.75	0	0
	2	0	0	3	21.43	9	64.29	2	14.29

* Group 1 significantly different from group 2 at $P < .05$.

Table 7: Summary of mortalities occurring prior to study completion*

Group 1			Group 2		
Pig ID	**Mortality**	**Euthanasia date**	**Pig ID**	**Mortality**	**Euthanasia date**
493	Euthanized	9 DPC	485	Found dead	14 DPC
512	Found dead	12 DPC	506	Found dead	13 DPC
525	Euthanized	11 DPC	521	Found dead	9 DPC
536	Found dead	10 DPC	534	Found dead	10 DPC
541	Found dead	13 DPC	540	Found dead	13 DPC
563	Euthanized	11 DPC	557	Found dead	13 DPC
571	Found dead	11 DPC	562	Found dead	13 DPC
575	Found dead	14 DPC	566	Euthanized	10 DPC
592	Found dead	14 DPC	568	Found dead	14 DPC
			570	Euthanized	10 DPC
			572	Found dead	13 DPC

* At study completion (14 DPC), 16 of 25 animals in group 1 and 14 of 25 animals in group 2 were euthanized and necropsied as scheduled.

a nonstructural protein for viral replication. The authors concluded that IVM exerted antiviral activity only when administered during the first 14 hours after viral cell entry. Therefore, IVM appears to be effective exclusively during the replication cycle when viral helicase is active.[8] Future studies assessing IVM efficacy on PRRSV should include a prechallenge or immediate postchallenge dosing protocol.

It has been well documented that the immunosuppressive nature of disease, specifically PRRSV, impacts the pharmacokinetic profile of parenterally administered pharmaceuticals. Pigs infected with PRRSV had a lower overall plasma concentration of intramuscularly injected ceftiofur hydrochloride.[18,19] It is unknown, however, if a PRRSV infection changes the bioavailability of IVM in swine.

The pigs used in this study were derived from CDCD dams inseminated with commercial boar semen. The genetic background of the animals used in this study may not represent the robust immunologic profile of a pig derived in a commercial setting. Future studies should include pigs sourced from a commercial setting.

Implication

Under the conditions of this study, ivermectin did not reduce the level of PRRSV 1-4-4 variant L1C in serum or BAL.

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Conflict of interest

None reported.

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