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Original Article
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About the necessity of including HoBi-like pestiviruses in bovine respiratory and reproductive viral vaccines[1]

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ABSTRACT.- Hümmelgen Silva P.H., Weiblen R. & Flores E.F. 2021. **About the necessity of including HoBi-like pestiviruses in bovine respiratory and reproductive viral vaccines**. *Pesquisa Veterinária Basileira 41:e06914, 2021*. Setor de Virologia, Centro de Eventos, Universidade Federal de Santa Maria, Av. Roraima 1000, Santa Maria, RS 97105-900, Brazil. E-mail: eduardofurtadoflores@gmail.com

HoBi-like pestiviruses (HoBiPeV) constitute a novel group of bovine pestiviruses, genetically and antigenically related to bovine viral diarrhea virus 1 (BVDV-1) and BVDV-2. Recent data shows that HoBiPeV are endemic among Brazilian cattle, yet bovine reproductive/respiratory vaccines contain only BVDV-1 and BVDV-2 strains. The present study investigated the neutralizing antibody response against these pestiviruses induced by two commercial vaccines (VA = attenuated, VI = inactivated) and by three experimental, replicative, vaccine formulations (VAC1 = monovalent, BVDV-1; VAC2 = bivalent, BVDV-1 + BVDV-2; VAC3 = trivalent, BVDV-1 + BVDV-2 and HoBiPeV). Seronegative beef calves were immunized once (replicative vaccines) or twice (inactivated vaccine) and serum samples were tested by virus-neutralization (VN) 30 days after vaccination (dpv) (replicative vaccines) or 30 days after the second dose (VI). We considered a threshold VN titer of ≥60 indicative of protection against clinical disease. At 30 dpv, VA induced protective titers against BVDV-2 in 7/7 animals (GMT=289.8) and against BVDV-1 and HoBiPeV in 5/7 animals (GMTs=97.5 and 80, respectively). VI induced protective titers against BVDV-1 in 1/7 animal (GMT=16.4), 2/7 animals against BVDV-2 (GMT=53.8) and in none of the calves against HoBiPeV (GMT=12.2). When a pool of sera of each vaccine group was tested against individual Brazilian isolates, VA induced protective titers against 3/7 BVDV-1 isolates, to 9/10 (BVDV-2) and 1/8 (HoBiPeV); VI induced protective titers against 1/7 (BVDV-1), 1/10 (BVDV-2) and none (0/8) HoBiPeV isolates. The experimental vaccine VAC1 induced protective titers against BVDV-1 in 9/9 animals (GMT=320) but in no animal against BVDV-2 or HoBiPeV (GMT<10). VAC2 induced protective titers to BVDV-1 and BVDV-2 in 9/9 animals (GMTs=160 and 640, respectively), and against HoBiPeV in 7/9 animals (GMT=108.5). Finally, VAC3 induced protective titers in all animals against BVDV-1 (GMT=234.3), BVDV-2 (294.9) and HoBiPeV (201.1). Testing the pool of sera against pestivirus isolates, VAC1 induced titers ≥ 60 against 4/7 BVDV-1 but to none BVDV-2/HoBiPeV isolate; VAC2 induced protective titers against 4/7 BVDV-1; 10/10 BVDV-2 and 2/8 HoBiPeV; VAC3 induced protective titers against all BVDV-1, BVDV-2 and HoBiPeV isolates. These results indicate that vaccines composed by BVDV-1+BVDV-2, especially those containing inactivated virus, may not induce serological response against a variety of HoBiPeV isolates. Thus, the need of inclusion of HoBiPeV in vaccine formulations should be considered.

INDEX TERMS: HoBi-like, pestivirus, bovine, BVDV, antigenic diversity, diagnosis, vaccines.

RESUMO.- [Sobre a necessidade de incluir pestivírus HoBi-like em vacinas virais respiratórias e reprodutivas para bovinos.] Os pestivírus HoBi-like (HoBiPeV) compõe um grupo novo de pestivírus de bovinos, genética e antigenicamente relacionados com os vírus da diarreia viral bovina 1 e 2 (BVDV-1, BVDV2). Dados recentes indicam que os HoBiPeV são endêmicos na população bovina do Brasil, mas as vacinas respiratórias e reprodutivas bovinas contêm apenas cepas de BVDV-1 e BVDV-2. O presente estudo investigou a atividade neutralizante contra estes pestivírus induzidas por duas vacinas comerciais (VA = atenuada, VI = inativada) e por três vacinas experimentais replicativas (VAC1 = monovalente, BVDV-1; VAC2 = bivalente, BVDV-1 + BVDV-2; VAC3 = trivalente, BVDV-1 +

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BVDV-2 e HoBiPeV). Bezerros soronegativos foram imunizados uma vez (vacinas replicativas) ou duas (vacina inativada) e amostras de soro foram testadas por vírus-neutralização (VN) 30 dias após a vacinação (dpv) (vacinas replicativas) ou 30 dias após a segunda dose (VI). Títulos neutralizantes ≥60 foram considerados indicativos de proteção contra doença clínica. Nesta data, a VA induziu títulos protetivos contra o BVDV-2 em 7/7 animais (GMT=289,8) e contra BVDV-1 e HoBiPeV em 5/7 animals (GMTs=97,5 e 80, respectivamente). VI induziu títulos protetores contra BVDV-1 em 1/7 animal (GMT=16,4), em 2/7 animais contra BVDV-2 (GMT=53,8) e em nenhum contra HoBiPeV (GMT=12,2). Quando um *pool* de soro de cada grupo vacinal foi testado frente a isolados Brasileiros, a VA induziu títulos protetores contra 3/7 isolados de BVDV-1, 9/10 (BVDV-2) e 1/8 (HoBiPeV); VI induziu títulos protetores em 1/7 contra BVDV-1, 1/10 (BVDV-2) e em nenhum (0/8) contra isolados de HoBiPeV. A VAC1 induziu títulos protetores contra BVDV-1 em 9/9 animais (GMT=320) mas em nenhum animal contra BVDV-2 ou HoBiPeV (GMT<10). VAC2 induziu títulos protetores contra BVDV-1e BVDV-2 em 9/9 animais (GMTs=160 e 640, respectivamente),e contra HoBiPeV em 7/9 animais (GMT=108,5). Finalmente, VAC3 induziu títulos protetores em todos os animais contra BVDV-1 (GMT=234,3), BVDV-2 (294,9) e HoBiPeV (201,1). No teste de *pool* de soro contra isolados de pestivírus, VAC1 induziu títulos ≥60 contra 4/7 BVDV-1 mas contra nenhum isolado de BVDV-2/HoBiPeV; VAC2 induziu títulos protetores contra 4/7 BVDV-1; 10/10 BVDV-2 e 2/8 HoBiPeV; VAC3 induziu títulos protetores contra todos BVDV-1, BVDV-2 e HoBiPeV. Esses resultados indicam que vacinas contendo apenas BVDV-1 BVDV-2, especialmente aquelas inativadas, podem não conferir resposta sorológica protetora contra vários isolados de HoBiPeV. Portanto, a necessidade de se incluir cepas de HoBiPeV nas vacinas deve ser considerada.

TERMOS DE INDEXAÇÃO: HoBi-like, pestivírus, bovinos, BVDV, diversidade antigênica, diagnóstico, vacinas.

INTRODUCTION

Bovine pestiviruses include the prototype Bovine viral diarrhea virus 1 (BVDV-1), BVDV-2 and HoBi-like (HoBiPeV) (ICTV 2020). BVDV-1 and BVDV-2 are distributed worldwide and have been historically associated with a variety of clinical manifestations and reproductive failure in cattle (Baker 1995). HobiPeV viruses were initially identified in 2004 (Schirrmeier et al. 2004) and have already been detected in several continents (Liu et al. 2009, Decaro et al. 2011, Bauermann et al. 2013, Mishra et al. 2014, Haider et al. 2014).

Pestiviruses are enveloped (~50nm in diameter), single stranded RNA viruses with a genome 12,3 kb in length. The RNA genome contains a long open reading frame (ORF) flanked by two untranslated regions (5' and 3' UTRs). The ORF is translated into a polyprotein of approximately 3988 aminoacids (aa) which is co- and post-translationally processed into 11-12 mature structural and non-structural proteins (Tautz et al. 2015). The pestiviruses are classified in species and subtypes according to the identity of the highly conserved 5'UTR and the genes encoding the proteins N^{pro}, NS3 and E2 (Becher et al. 1997). Nonetheless, other viral genes have been proposed to properly subtype BVDV isolates, in addition to analysis of the whole genome (Oliveira et al. 2021). BVDV-1 and BVDV-2 isolates present a high antigenic diversity, mainly to the high variable envelope glycoprotein E2 (Ridpath 2013).

HoBi-like (HoBiPeV) pestiviruses were initially identified in fetal bovine serum (FBS) imported from Brazil (Schirrmeier et al. 2004) and subsequently identified in several countries, in FBS (Xia et al. 2011) and associated with a variety of clinical manifestations and reproductive failure in cattle (Liu et al. 2009, Decaro et al. 2011, 2014, Decaro 2020). In Brazil, HoBiPeV have been described in several states contaminating FBS (Monteiro et al. 2018) and associated with several pathologies (Cortez et al. 2006, Bianchi et al. 2011, Weber et al. 2016, Cruz et al. 2018, Hoppe et al. 2019). Recent data indicate that HoBiPeV are endemic and comprise from 10 to 20% of the pestiviruses circulating in Brazilian cattle (Flores et al. 2018).

HoBiPeV are genetically and antigenically closely related to BVDV-1 and BVDV-2, yet discrete and relevant antigenic differences have been demonstrated between these groups of viruses (Bauermann et al. 2012, Larska et al. 2012, Decaro et al. 2013). The low serologic reactivity between BVDV species and HoBiPeV represents a serious concern regarding immunodiagnostic and vaccine efficacy (Bauermann et al. 2012, 2013, Decaro et al. 2013).

Modified live (MLV) and inactivated vaccines have been largely used to prevent and/or to reduce the losses associated with BVDV infection worldwide (Ridpath 2013, Newcomer et al. 2017, Moennig & Becher 2018). A number of vaccines are available in Brazil, most containing adjuvanted, inactivated BVDV-1 and BVDV-2 antigens combined with other viral and bacterial agents. In the last years, two MLV vaccines containing BVDV-1 and BVDV-2 were introduced in the market. Up to the present, no commercial vaccine contains HoBiPeV strains.

As the antigenic differences between BVDV species and HoBiPeV are relevant and the efficacy of current respiratory/reproductive bovine vaccines against HoBiPeV isolates is uncertain, we sought to investigate the neutralizing activity against HoBiPeV induced by some vaccines. In addition, we investigated the serological reactivity of three experimental vaccines against HoBiPeV: a monovalent (BVDV-1); bivalent (BVDV-1, BVDV-2) and trivalent (BVDV-1, BVDV-2 and HoBiPeV).

MATERIALS AND METHODS

Experimental design. To investigate the neutralizing activity against BVDV-1, BVDV-2 and HoBiPeV present in sera of immunized cattle, groups of seronegative cattle were vaccinated with each of two commercial vaccines (VA = attenuated vaccine, single dose; VI = inactivated vaccine, two doses) and with three experimental, replicative, vaccine formulations (VAC1 = monovalent, BVDV-1; VAC2 = bivalent, BVDV-1+BVDV-2; VAC3 = trivalent, BVDV-1+BVDV-2+HoBiPeV) in a single dose. Serum samples for virus-neutralizing assays (VN) against BVDV-1, BVDV-2 and HoBiPeV were collected at day 30 post-vaccination (replicative vaccines) or 30 days after the second dose (VI). Virus neutralizing titers ≥60 were considered indicative of protection (Howard et al. 1989).

Viruses and cells. BVDV and HoBiPeV strains/isolates were amplified and quantitated in MDBK cells (Madin-Darby bovine kidney, ATCC - CCL-22). VN assays also used MDBK cells. Cells were cultured in minimum essential medium (MEM) supplemented with 10% horse serum, penicillin (10.000UI/mL), streptomycin (10mg/mL), ciprofloxacin (10mg/mL) and amphotericin B (250µg/mL) at 37°C in a 5% CO_2 atmosphere. The BVDV-1, BVDV-2 and HoBiPeV

strains or isolates used herein were previously described, Cortez et al. 2006, Bianchi et al. 2011, Silveira et al. 2017, Dias et al. 2017).

Commercial vaccines. Two commercial vaccines containing BVDV-1 and BVDV-2 strains were used: VA (attenuated) and VI (inactivated). VA contains replicative BVDV-1 and BVDV-2 strains, whereas VI contains adjuvanted, inactivated BVDV-1 and BVDV-2 antigens combined with antigens of other viral and bacterial agents. Fourteen seronegative heifers were divided in two groups and vaccinated either with VA (single dose) or VI (two doses, 30 days apart) by the intramuscular (IM) route. Serum samples were collected at day 30 post-vaccination (D30, VA) and 30 days after the second dose (VI, D60) for VN testing.

Experimental vaccines. The experimental, replicative vaccines, were composed by the supernatant of MDBK cells inoculated with the respective viruses. The cell supernatants were harvested after 24-36 hours of inoculation, cleared by low-speed centrifugation and stored at -80ºC until use. Viral suspensions were quantitated by limiting dilution. VAC1 contained BVDV-1 IBSP-4 strain ($10^{5,98}TCID_{50}$/mL); VAC2 contained IBSP-4 (BVDV-1) and BVDV-2 SV323/04 ($10^{6,1}TCID_{50}$/mL); VAC3 contained BVDV-1 (IBSP-4) + BVDV-2 (SV323/04) + HoBiPeV (SV757/15 -$10^{6,04}TCID_{50}$/mL). Each vaccine dose contained a total of 3 x $10^{6,0}TCID_{50}$. Twenty-seven seronegative calves were divided in three groups and immunized once by the IM route with VAC1, VAC2 or VAC3. Serum samples were collected 30 days after vaccination (D30) for VN tests.

Virus-neutralization (VN). VN assays were performed in microtiter 96-well plates, incubating two-fold dilutions of serum (starting at 1:10) against approximately 100-200 $TCID_{50}$ of the respective virus. VN assays for BVDV antibodies have been described elsewhere (Dias et al. 2017). VN titers were converted in geometric mean titers (GMT) (Thrusfield 1986). Individual serum samples were tested against IBSP-4 (BVDV-1), SV323/04 (BVDV-2) and SV757/15 (HoBiPeV); whereas *pools* of samples were tested against seven BVDV-1, ten BVDV-2 and seven HoBiPeV Brazilian isolates, belonging to the SV/UFSM virus bank (Fig.1-5). Each pool was composed by an equivalent amount of the individual samples. The VN titers of the respective *pools* represent an approximate mean titer of the vaccine group against each viral isolate.

Statistics. Geometric mean titers (GMT) were calculated according to Thrusfield (1986) and compared using the Friedmann-Dunn test (Bauermann et al. 2013) in the GraphPad Prism® software. Differences among GMTs were considered significant when $p<0.05$ (95% confidence interval).

Committee on Animal Welfare and Use. The animal work has been approved by an Institutional Committee on Animal Use and Welfare (CEUA-UFSM approval # 9888201017).

RESULTS

The virus-neutralizing (VN) titers induced by the immunizations against BVDV-1, BVDV-2 and HoBiPeV strains are presented in Table 1 and 2. Additionally, *pools* of sera from each vaccine group were tested against seven BVDV-1 isolates, 10 BVDV-2 and 8 HoBiPeV (Fig.1-5). At 30 dpv, VA induced protective titers (≥60) against BVDV-2 in 7/7 animals (GMT=289.8); against BVDV-1 and HoBiPeV in 5/7 animals (GMTs=97.5 and 80, respectively). VI induced titers ≥60 to BVDV-1 in only one animal (GMT=16.4), in 2/7 animals against BVDV-2 (GMT=53.8) and in none of the calves against HoBiPeV (GMT=12.2). When a "pool" of sera of each vaccine group was tested against Brazilian isolates, VA induced titers ≥60 against 3/7 BVDV-1 isolates, to 9/10 (BVDV-2) and 1/8 (HoBiPeV); VI induced protective titers against 1/7 (BVDV-1), 1/10 (BVDV-2) and none HoBiPeV isolates (0/8). The experimental vaccine VAC1 induced protective titers against BVDV-1 in 9/9 animals (GMT=320) but in no animal against BVDV-2 or HoBiPeV (GMT<10). VAC2 induced protective titers to BVDV-1 and BVDV-2 in 9/9 animals (GMTs=160 and 640, respectively), and against HoBiPeV in 7/9 animals (GMT=108.5). Finally, VAC3 induced protective titers in all animals against BVDV-1 (GMT=234.3), BVDV-2 (294.9) and HoBiPeV (201.1). Testing the pool of sera against pestivirus isolates, VAC1 induced titers ≥60 against 4/7 BVDV-1 but to none BVDV-2/HoBiPeV isolate; VAC2 induced protective titers against 4/7 BVDV-1; 10/10 BVDV-2 and 2/8 HoBiPeV; VAC3 induced protective titers against all BVDV-1, BVDV-2 and HoBiPeV isolates.

DISCUSSION

Bovine pestiviruses are closely related yet present antigenic differences that may compromise immunodiagnostic and vaccine efficacy (Bauermann et al. 2012, 2013, Decaro et al. 2013, Dias et al. 2017). Our group has been long investigating the immune response induced by experimental and commercial BVDV-containing vaccines (Vogel et al. 2001, 2002, Lima et al. 2005, Anziliero et al. 2015, Dotto 2020). The emergence and wide distribution of HoBiPeV among Brazilian cattle prompted us to investigate the serologic response against these novel viruses induced by two commercial and three experimental vaccines.

Attenuated (modified live virus, MLV) and inactivated, adjuvanted vaccines have been used for BVDV prevention and control worldwide. Inactivated vaccines are safe, yet generally induce lower levels of antibodies; require multiple doses and induce a predominantly humoral response. In contrast, MLV vaccines usually stimulate higher levels of antibodies and cell-mediated immunity as well (Ridpath 2013, Newcomer et al. 2017, Moennig & Becher 2018). Nonetheless, the use of MLV vaccines in pregnant cows has been limited due to safety concerns (Newcomer et al. 2017, Moennig & Becher 2018). Historically, a number of inactivated BVDV-containing vaccines have been available in Brazil; only recently two MLV vaccines were introduced in the market.

Both humoral and cellular immune responses contribute for protection against BVDV infection. Nevertheless, virus-neutralizing (VN) antibodies are easier to measure and provide a reliable indicator of the immune response (Ridpath 2013). The VN titers that correlate with protection, however, are difficult to ascertain since protection depends upon a variety of viral and host factors. As a whole, Howard et al. (1989) estimated that VN titers of ≥60 of passively acquired neutralizing antibodies would be able to confer protection from clinical disease. As the response induced by inactivated vaccines is predominantly humoral, VN titers would approximately reflect the magnitude of the immune response. On the other hand, MLV vaccines induce both cellular (cytotoxic T-cell response) and humoral immune response (Newcomer et al. 2017). Thus, for these vaccines, VN titers would be only a partial indicator of the immune response. Anyways, we used the VN value of 60 proposed by Howard et al. (1989) as the threshold to evaluate the serological response to vaccination.

Our results demonstrated that, considering titers ≥60, vaccine formulations containing only BVDV-1 or a combination

of BVDV-1 and 2, especially those inactivated, would not induce protective titers against a number of HoBiPeV isolates. Although a limited number of isolates are available to date, significant antigenic variability has been observed among field HoBiPeV isolates (Dias et al. 2017). The failure to neutralize these viruses may be overcomed by addition of a HoBiPeV strain to the vaccine formulation, as demonstrated in animals immunized with VAC3. In the United States (US), commercial vaccines contain a combination of BVDV-1 and BVDV-2 strains and, in some cases, addition of more than one BVDV-1 or BVDV-2 subtypes has been recommended (Ridpath 2013). To date, there is no evidence of circulation of HoBiPeV in the US (Bauermann, FV personal communication). In Brazil, most

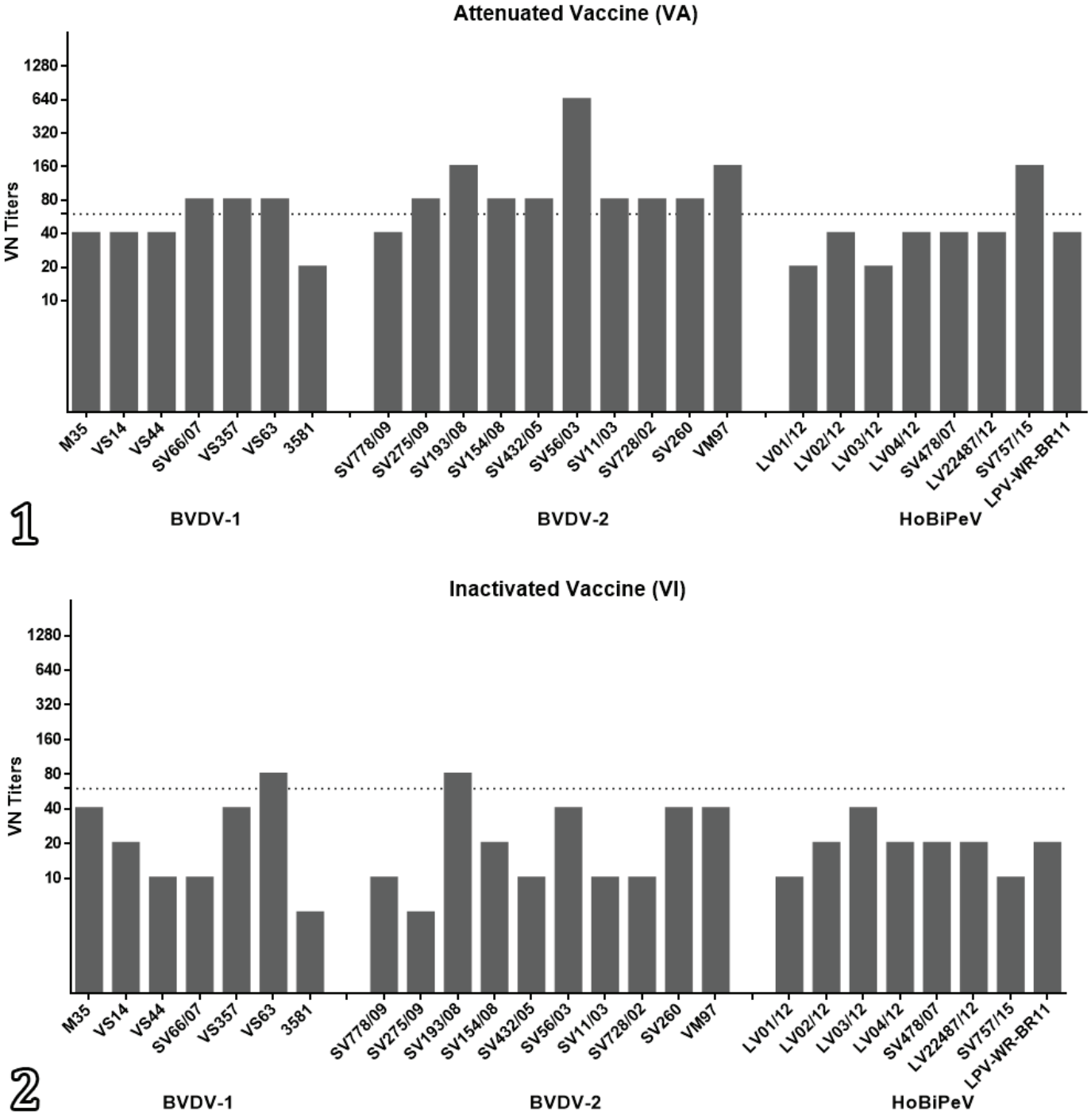
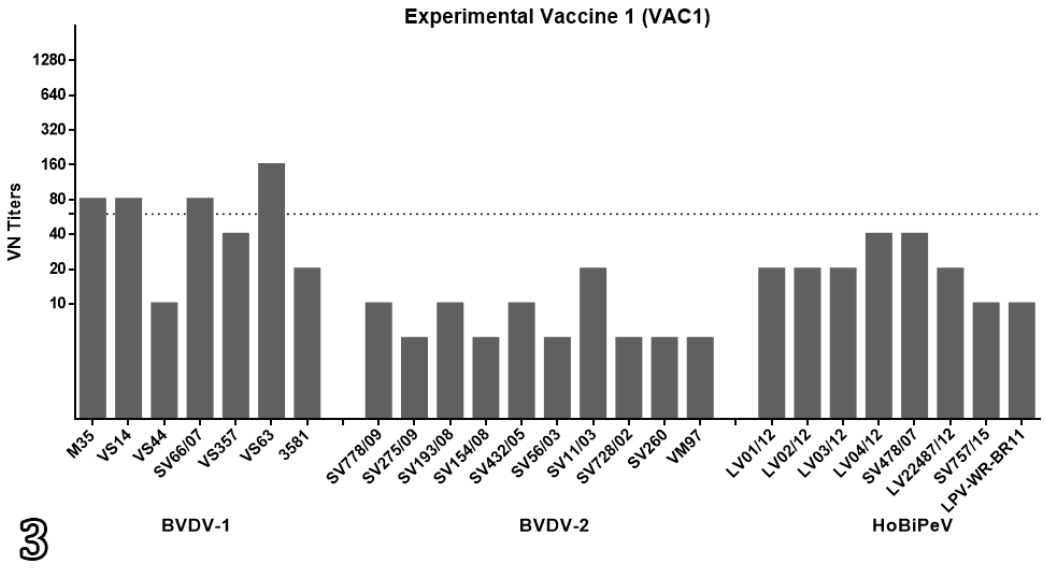
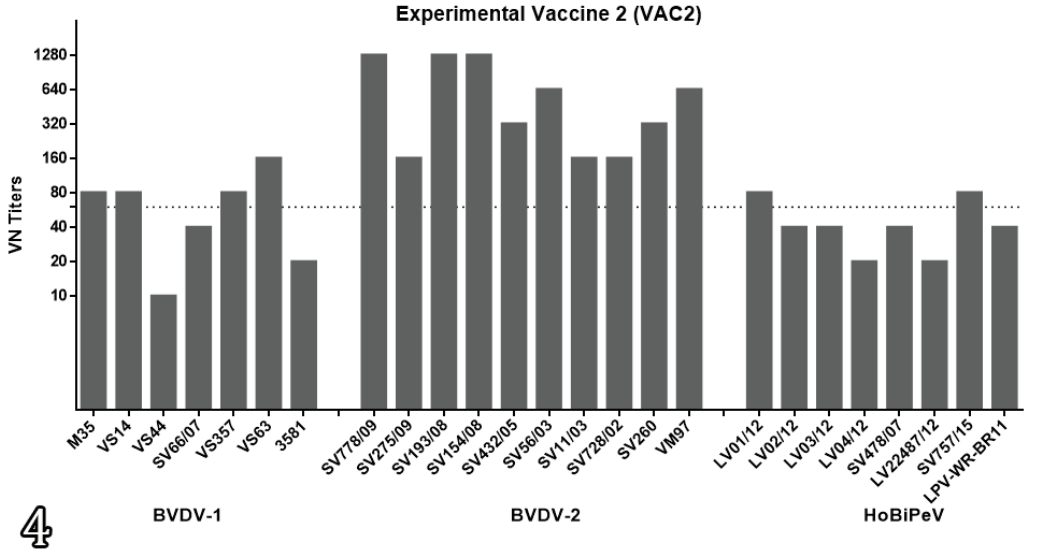


Fig.1-2. Virus neutralizing titers against pestivirus isolates in pools of sera of cattle immunized with commercial vaccines. (**1**) Atenuatted vaccine (VA) and (**2**) inactivated vaccine (VI). The dotted line indicates the titer of 60, indicative of protection against clinical disease (Howard et al. 1989).





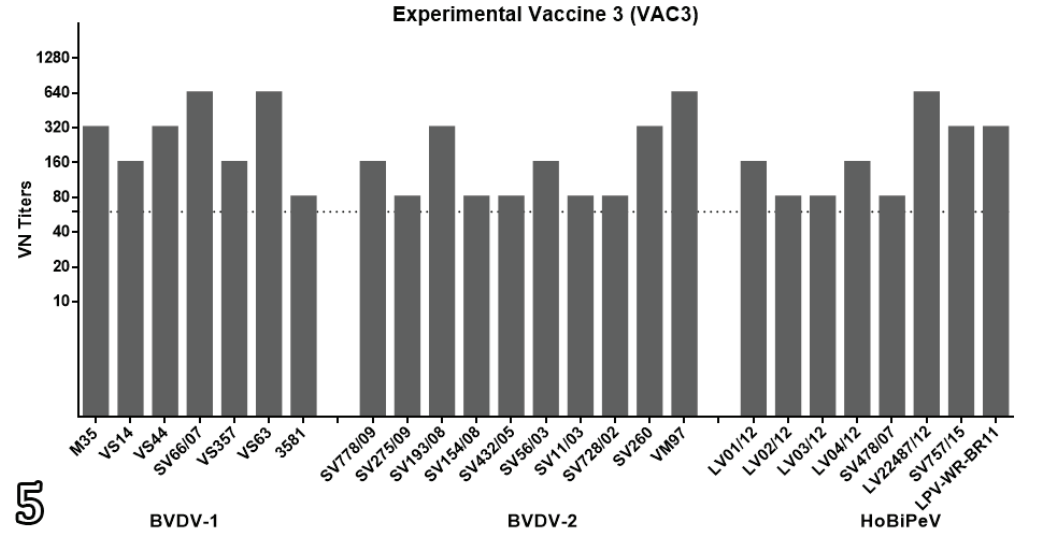


Fig.3-5. Virus neutralizing titers against pestivirus isolates in pools of sera of cattle immunized with experimental vaccines. (**3**)VAC1 = monovalent (IBSP.4-BVDV-1), (**4**) VAC2 = bivalent (IBSP.4-BVDV-1 + SV323/04-BVDV-2), (**5**) VAC3 = trivalent (IBSP.4-BVDV-1 + SV323/04-BVDV-2 + SV757/15-HoBiPeV). The dotted line indicates the titer of 60, indicative of protection against clinical disease (Howard et al. 1989).

Table 1. Neutralizing antibody titers against BVDV-1, BVDV-2 and HoBiPeV induced by two commercial vaccines

Vaccine	Animal #	Neutralizing titer to		
		BVDV-1 (IBSP-4)	BVDV-2 (SV323/04)	HoBiPeV (SV757/15)
Vaccine A - VA (attenuated)	7040	320	80	40
	7042	80	320	80
	7044	40	160	80
	7076	320	640	160
	7057	80	640	160
	7120	80	320	80
	7121	40	320	40
GMT		97.5 ^{AB}	289.8 ^{A}	80 ^{B}
Vaccine I - VI (inactivated)	7007	20	20	≤10
	7038	10	40	≤10
	7051	10	40	≤10
	7089	10	80	≤10
	7128	20	20	20
	7164	80	640	≤10
	7165	10	40	10
GMT		16.4 ^{AB}	53.8 ^{A}	12.2 ^{B}

GMT = Geometric mean titers; ^{A,B} Different letters indicate significant differences (^{p}<0.05) among GMTs in the Friedmann-Dunn test.

Table 2. Neutralizing antibody titers against BVDV-1, BVDV-2 and HoBiPeV induced by three experimental, replicative vaccines

Vaccine	Animal	Neutralizing titer to		
		BVDV-1 (IBSP-4)	BVDV-2 (SV323/04)	HoBiPeV (SV757/15)
Vaccine 1 (VAC1)	51	320	20	<10
	52	640	<10	10
Monovalent (BVDV-1)	53	320	<10	<10
	54	640	<10	<10
	55	160	<10	10
	56	160	<10	10
	57	320	<10	<10
	58	320	<10	<10
	59	320	<10	10
GMT		320 ^{A}	<10 ^{B}	<10 ^{B}
Vaccine 2 (VAC2)	61	160	640	160
	62	320	640	40
Bivalent (BVDV-1, BVDV-2)	63	160	320	40
	64	80	640	160
	65	160	320	320
	66	160	640	160
	67	160	1280	80
	68	320	1280	160
	69	80	640	80
GMT		160 ^{B}	640 ^{A}	108.5 ^{B}
Vaccine 3 (VAC3)	1	160	80	80
	2	640	320	320
Trivalent (BVDV-1, BVDV-2, HoBiPeV)	3	640	160	160
	4	320	80	160
	5	160	320	640
	6	160	1280	160
	7	160	1280	1280
	8	160	640	80
	10	160	160	80
GMT		234.3 ^{A}	294.5 ^{A}	201.1 ^{A}

GMT = Geometric mean titers; ^{A,B} Different letters indicate significant differences (p<0.05) among GMTs in the Friedmann-Dunn test.

commercial vaccines (inactivated or attenuated) contain BVDV-1 and BVDV-2 strains; no current vaccine contains HoBiPeV.

The antigenic relationship between HoBiPeV and BVDV species (BVDV-1 and BVDV-2) results in variable levels of cross-neutralization between members of these groups of viruses. The cross-neutralization, which reflects the level of antigenic similarity, seems to be higher between BVDV-2 and HoBiPeV than between BVDV-1 and HoBiPeV (Bauermann et al. 2012, 2013, Decaro et al. 2013, Dias et al. 2017). Thus, would the current BVDV vaccines induce moderate to high levels of neutralizing antibodies against the vaccine strains (BVDV-1/BVDV-2), cross-neutralization against HoBiPeV, at variable levels, is expected to occur. This has been demonstrated in our study, in which commercial and experimental BVDV-1/BVDV-2 vaccines showed variable levels of neutralization against HoBiPeV. Nonetheless, a number of studies from our group have shown that commercial vaccines do not usually induce such high VN levels upon the recommended protocol of two-doses (Vogel et al. 2001, 2002, Lima et al. 2005, Anziliero et al. 2015, Baccili et al. 2019, Dotto 2020). Thus, is conceivable that the response to vaccination with current BVDV-containing commercial vaccines would not result in protective cross-neutralization titers to HoBiPeV isolates. Thus, improving the quality of current vaccines and the eventual inclusion of HoBiPeV strain in their formulation will certainly contribute for a better vaccine efficacy. In addition, the inclusion of representative Brazilian BVDV strains in vaccine formulations may be advisable if they prove to be antigenically more similar to local isolates. These observations are especially important at the present, when vaccine industries are expanding their portfolios by adding bovine respiratory and reproductive viral vaccines.

CONCLUSION

The results obtained herein indicate that vaccine formulations containing only BVDV-1, or a combination of BVDV-1 and BVDV-2 may not confer protective virus-neutralizing (VN) titers against HoBiPeV isolates. Hence, inclusion of HoBiPeV strains in vaccine formulations in Brazil may be advisable.

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Conflict of interest statement.- The authors declare no conflict of interest.

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