Rev. Bras. Saúde Prod. Anim., Salvador, v.19, n.3, p.268-276 jul./set., 2018 **ISSN 1519 9940**
http://dx.doi.org/10.1590/S1519-99402018000300004

Sheep infection by caprine lentivirus

Infecção de ovinos pelo lentivírus caprino

SOUZA, Thiago Sampaio de[1*]; PINHEIRO, Raymundo Rizaldo[2]; LIMA, Carla Caroline Valença de[3]; BRITO, Roberta Lomonte Lemos de[4]; AZEVEDO, Dalva Alana Aragão de[5]; DIAS, Ronaldo Pereira[5]; SANTOS, Vanderlan Warlington Souza dos[6]; ANDRIOLI, Alice[2]; COSTA, Joselito Nunes[7]

[1]Universidade Federal do Recôncavo da Bahia, Hospital Universitário de Medicina Veterinária, Cruz das Almas, Bahia, Brasil.
[2]Empresa Brasileira de Pesquisa Agropecuária, Centro Nacional de Pesquisa de Caprinos e Ovinos, Sobral, Ceará, Brasil.
[3]Universidade Federal do Recôncavo da Bahia, Centro de Ciências da Saúde, Santo Antônio de Jesus, Bahia, Brasil.
[4]Centro Universitário Uninta, Sobral, Ceará, Brasil.
[5]Universidade Estadual do Ceará, Programa de Pós-Graduação em Ciências Veterinárias, Fortaleza, Ceará, Brasil.
[6]Universidade Federal Rural do Semi-Árido, Programa de Pós-Graduação em Ciência Animal, Mossoró, Rio Grande do Norte, Brasil.
[7]Universidade Federal do Recôncavo da Bahia, Centro de Ciências Agrárias, Ambientais e Biológicas, Cruz das Almas, Bahia, Brasil.
*Endereço para correspondência: thiago_sampaio@hotmail.com

SUMMARY

The objective of this study was to demonstrate iatrogenic transmission of small ruminant lentivirus (SRLV) from goats to sheep and horizontal transmission between sheep. The study was conducted on a farm with separate goat and sheep rearing, and animals were monitored for lentivirus occurrence by clinical examination and testing by immunoblotting (IB), agar gel immunodiffusion (AGID), and nested polymerase chain reaction (nPCR). Positive results had not been observed in the sheep flock until this study. Conversely, virus positive dairy goats were known. For this reason, the farm performed the caprine arthritis-encephalitis (CAE) control program. The study was designed with a sheep group that presented positive animals for SRLV by nPCR. It was verified that three newborn animals in this group were rejected by their mothers and consequently received milk from the goat herd. These three animals remained with another 20 sheep of the same age, totaling 23 animals. After one year, during monitoring, 11 of the 23 animals in the group presented positive results in the nPCR and three demonstrated seroconversion by IB. Of the animals that had received goat milk, two had positive results in the nPCR and IB. The 11 animals positive in the nPCR were followed and it was verified that five animals did not present further positive results in the nPCR, nor seroconversion; two continued presenting positive results in the nPCR but were negative in the IB and AGID and four were positive in the nPCR, IB, and AGID. Thus, it was possible to demonstrate iatrogenic interspecific infection and the occurrence of horizontal caprine lentivirus transmission among sheep.

Keywords: CAE, Maedi-Visna, SRLV, transmission

RESUMO

O objetivo foi demonstrar a transmissão iatrogênica de lentivírus de pequenos ruminantes (LVPR) de caprinos para ovinos e a transmissão horizontal entre ovinos. O estudo foi conduzido em propriedade com criação não consorciada de caprinos e ovinos, monitorada para ocorrência de lentiviroses, a partir de acompanhamento clínico e testes de *immunoblotting* (IB), imunodifusão em gel de agarose (IDGA) e reação em cadeia da

polimerase do tipo *nested* (nPCR). Resultados positivos no rebanho ovino não haviam sido observados até então. Por outro lado, sabia-se que o rebanho caprino leiteiro era positivo. Por este motivo, a propriedade realizava programa de controle da artrite-encefalite caprina (CAE). O estudo foi delineado em um lote de ovinos que apresentou animais positivos para LVPR na nPCR. Verificou-se que três animais neonatos deste lote foram rejeitados por suas mães e por isso receberam leite do rebanho caprino. Estes três animais permaneceram com outros 20 ovinos de mesma faixa etária, totalizando 23 animais. Após um ano, durante a realização do monitoramento, dos 23 animais do lote, 11 apresentaram resultados positivos na nPCR e três demonstraram soroconversão por IB. Dos animais que haviam recebido leite do rebanho caprino, dois tiveram resultados positivos na nPCR e no IB. Os 11 animais positivos na nPCR foram acompanhados, verificando-se que cinco animais não apresentaram mais resultados positivos na nPCR, nem soroconverteram; dois continuaram apresentando resultados positivos na nPCR, mas negativos no IB e IDGA e quatro apresentaram-se positivos na nPCR, no IB e no IDGA. Dessa forma, foi possível demonstrar a infecção interespecífica de forma iatrogênica e a ocorrência de transmissão horizontal do lentivírus caprino entre ovinos.

Palavras-chave: CAE, Maedi-Visna, LVPR, transmissão

INTRODUCTION

The genus *Lentivirus* consists of pathogens of relevance to human and animal health, such as the human immunodeficiency virus (HIV), feline immunodeficiency virus (FIV), equine infectious anemia virus (EIAV), caprine arthritis encephalitis virus (CAEV), and maedi-visna virus (MVV). These last two viruses are grouped as the small ruminant lentivirus (SRLV) (BLACKLAWS & HARKISS, 2010; LEROUX et al., 2010).
The SRLV causes caprine arthritis encephalitis (CAE) in goats and maedi-visna (MV) in sheep. These are chronic, degenerative, and multi-systemic diseases, characterized by progressive immune-mediated lesions, including five pathological conditions: arthritis, pneumonia, mastitis, encephalitis, and weight loss (LARA et al., 2005; BENAVIDES et al., 2007; GREGORY et al., 2009a; PÉREZ et al., 2015).
Goats and sheep are infected through the mucosa, especially the gastrointestinal and the respiratory tracts. The monocyte-phagocyte line cells are the main targets (BLACKLAWS, 2012). Thus, ingesting milk and colostrum contaminated by the virus is an important form of transmission (PREZIUSO et al., 2004; RAVAZZOLO et al., 2006; GREGORY et al., 2009b; SOUZA et al., 2015), as is prolonged contact between infected and susceptible animals (VILLORIA et al., 2013; SOUZA et al., 2015).
Many SRLV genotypes and subtypes have been characterized and the viruses displayed heterogeneity and the possibility of transmission between goats and sheep (SHAH et al., 2004; SOUZA et al., 2012; SOUZA et al., 2015). The genetic variability occurred because of genetic mutations and recombination (PISONI et al., 2007; LEROUX & MORNEX, 2008; OLECH et al., 2012; FRAS et al., 2013), giving rise to viral *quasispecies* (PASICK, 1998) and making the SRLV skilled in adapting to its hosts (GJERSET et al., 2007; GREGO et al., 2007; PISONI et al., 2007).
Thus, based on the above, the objectives of the present study was to confirm iatrogenic lentivirus transmission from goats to sheep and demonstrate seroconversion of animals and viral circulation among sheep.

MATERIAL AND METHODS

The study was approved by the Commission of Ethics in the use of animals of the State University of Vale do Acaraú, State of Ceará, Brazil,

number 001/12. The research was conducted on a sheep- and goat-rearing farm and animals were monitored for lentivirus occurrence by observing clinical signs and conducting the following tests: immunoblotting (IB), agar gel immunodiffusion (AGID), and nested polymerase chain reaction (nPCR). The farm was formed by different properties, which had specific animal shelters and workers. Thus, goats and sheep were raised separately on the different properties.

The goat herd was positive for SRLV and tests were performed two or three times a year. Conversely, the sheep flock was tested annually and positive results for SRLV were not observed until this study. This study was conducted with a herd of 23 sheep, of which 11 presented positive results for SRLV in the nPCR.

These 11 animals were the study subjects and were monitored for six years on the farm to determine the source of the infection and assess the occurrence of clinical signs and seroconversion of the animals. In addition, the herd history was searched.

To investigate the presence of seropositive animals, 10mL blood was collected in a sterile vacuum tube without anticoagulant, by puncturing the jugular vein, after antisepsia. The blood serum was then obtained by centrifuging at 1.500g for 10 minutes, and the serum was packed in micro-tubes and stored at -20°C. The AGID and IB tests were performed following the methodology described by Pinheiro et al. (2010) and Rodrigues et al. (2014), respectively. Antigens used were produced from the secondary cultivation of goat synovial membrane (GSM), inoculated with goat standard strain CAEV-Cork (PINHEIRO et al., 2006; PINHEIRO et al., 2010).

To determine the occurrence of proviral DNA in the animals, 10mL blood was collected in tubes with ethylenediaminetetraacetic acid (EDTA). Next, the leukocyte layer was obtained by treating the total blood with ammonium chloride solution at 0.84% (FEITOSA et al., 2011). The leukocyte DNA was extracted using the protocol described by Grimberg et al. (1989) and the nPCR technique was performed following the method of Barlough et al. (1994) modified by Andrioli et al. (2006).

Two rounds of PCR amplification were used to detect the 187bp proviral DNA fragment, corresponding to the leader *gag* sequence of the caprine lentivirus genome. Two pairs of primers were selected based on the published sequence of the CAEV-Cork strain (SALTARELLI et al., 1990). The primers P_1 (5′-CAAGCAGCAGGAGGGAGAAGCTG-3′) and P_2 (5′-TCCTACCCCCATAATTTGATCCAC-3′) were used for the first amplification (BARLOUGH et al., 1994) and the primers P_3 (5′-GTTCCAGCAACTGCAAACAGTAGC AATG-3′) and P_4 (5′-ACCTTTCTGCTTCTTCATTTAATTT CCC-3′) were used for the second amplification (RIMSTAD et al., 1993). A negative control was used, constituted by autoclaved ultrapure water and a positive control came from the culture of cells from the GSM-infected with the CAEV-Cork strain.

To compare three positive DNA fragments from the nPCR with the sequences of the goat standard strain CAEV-Cork and sheep standard strain MVV-K1514, available in GenBank under accession numbers M33677 and M60610, respectively, the samples were sequenced in a platform with an Applied Biosystems® 3500 Genetic Analyzer. The sequences were aligned using Clustal W (THOMPSON et al., 1994) with the BioEdit Sequence

Alignment Editor® (HALL, 1999) and BLASTN 2.8.0 (ZHANG et al., 2000).

RESULTS AND DISCUSSION

The history of the sheep flock showed that three newborn animals had been rejected by their mothers and consequently had received milk from the dairy goats known to be CAE positive. Artificial feeding was ad libitum.

It is emphasized that the handlers did not know about the possibility of interspecies SRLV transmission, because the MV and CAE etiological agents were considered species-specific for a long time. Only recent phylogenetic analysis of viral isolates has confirmed the existence of different SRLV genotypes and subtypes that can infect both goats and sheep (SHAH et al. 2004; LEROUX et al., 2010; SOUZA et al., 2012).

The three animals that received goat milk remained with another 20 sheep in the same age group, totaling a group of 23 animals. After one year, while conducting the annual monitoring of the farm, 11 of the 23 animals presented positive results in the nPCR and three showed seroconversion detected by IB. Of the three animals that had received goat milk, only two (animals 26 and 35) had positive results in the nPCR and IB. Thus, these two animals showed iatrogenic infection resulting from suckling and became sources of infection for the other nine animals.

Ingestion of milk and colostrum from infected goats by sheep is an important transmission pathway of the SRLV, enabling the occurrence of interspecific infection (PÉREZ et al., 2015; SOUZA et al., 2015; LIMA et al., 2017). Additionally, the contact between the animals also facilitated horizontal transmission (PETERHANS et al., 2004; SOUZA et al., 2015) from virus dissemination by secretion (VILLORIA et al., 2013).

During observations, three periods were established according to the results obtained in the IDGA, IB, and nPCR tests (Table 1). Five of the 11 animals that had positive results in the nPCR did not present further positive results in the nPCR and did not seroconvert (animals 01, 05, 14, 42, and 48). Regarding the other six animals, two continued to present positive results in the nPCR but were negative according to the IB and AGID (animals 52 and 53), and four were positive in the nPCR, IB, and AGID (animals 26, 35, 51, and 54). Three DNA samples sequenced (animals 26, 51, and 53) showed 98 to 100% identity to the CAEV-Cork sequence and 90% identity to the MVV-K1514 sequence.

Absence of seroconversion may have occurred because of the viral pathogen itself that involves a period of latency during which it hides the infectious agent from the immune system (BLACKLAWS & HARKISS et al., 2010; BLACKLAWS, 2012; RAVAZZOLO et al., 2006; BRELLOU et al., 2007; LEROUX & MORNEX, 2008). Regarding the animals that no longer presented positive results in the nPCR, this may have occurred because of the absence of proviral DNA in monocytes of the peripheral circulation (BLACKLAWS, 2012; RAVAZZOLO et al., 2006; SOUZA et al., 2015). Furthermore, some authors have also suggested the possibility of transient infection occurring, when the virus, for reasons unknown, does not persist in the organism (HERRMANN-HOESING et al., 2007; BARQUERO et al., 2013).

Rev. Bras. Saúde Prod. Anim., Salvador, v.19, n.3, p.268-276 jul./set., 2018 **ISSN 1519 9940**
http://dx.doi.org/10.1590/S1519-99402018000300004

Table 1. Results obtained by agar gel immunodiffusion (AGID), immunoblotting (IB), and nested polymerase chain reaction (nPCR) for 11 sheep infected with small ruminant lentivirus

Periods[a]	Tests	Animals										
		01	05	14	26[b]	35[b]	42	48	51	52	53	54
I	AGID	-	-	-	-	-	-	-	-	-	-	-
	IB	-	-	-	+	+	-	-	+	-	-	-
	nPCR	+	+	+	+	+	+	+	+	+	+	+
II	AGID	-	-	-	+	+	-	-	-	-	-	-
	IB	-	-	-	+	+	-	-	+	-	-	-
	nPCR	-	-	-	+	+	-	-	+	+	+	+
III	AGID	-	-	-	+	+	-	-	+	-	-	+
	IB	-	-	-	+	+	-	-	+	-	-	+
	nPCR	-	-	-	+	+	-	-	+	+	+	+

[a] Period I: 2008 to 2009; Period II: 2009 to 2012; Period III: as of 2012.
[b] Two of the three animals that received milk from positive goats.

Clinical signs of infection were not observed in sheep, although the goat flock contained sick animals, including those with arthritis, mastitis, weight loss, paresis, and paralysis. This may have occurred because some strains are more adapted to goats and others to sheep (REINA et al., 2006; GLARIA et al., 2009; PEREZ et al., 2015). The heterogeneity of the SRLV implies variation in pathogenicity, with different responses to the infection that occurs upon the clinical manifestation presented by the animals and also on the results of serological and molecular tests (RACHID et al., 2013; SOUZA et al., 2015).

Thus, it was possible to show interspecific iatrogenic infection and the occurrence of horizontal goat lentivirus transmission among sheep. Because of this and considering that many small ruminant rearing systems in the Brazilian Northeast are integrated, proposals for sanitary measures to control or even prevent SRLV should be researched and applied, including the producers in the knowledge chain. The universities have a decisive role in this process, constructing continued discussion environments and provoking the development of technical and scientific knowledge.

ACKNOWLEDGEMENTS

We acknowledge the Bahia State Research Support Foundation (FAPESB) for the promotion of the project, the National Council for Scientific and Technological Development (CNPq) for research funding, the Coordination for the Improvement of Higher Education Personnel (CAPES) for scholarships, and the Brazilian Agricultural Research Corporation - Goats and Sheep for supporting the implementation of the experiment.

REFERENCES

ANDRIOLI, A.; GOUVEIA, A.M.G.; MARTINS, A.S.; PINHEIRO, R.R.; SANTOS, D.O. Fatores de risco na transmissão do lentivírus caprino pelo sêmen. **Pesquisa Agropecuária Brasileira**, v.41, n.8, p.1313-1319, 2006.

BARLOUGH, J.; EAST, N.; ROWE, J.D.; HOOSEAR, K.V.; DEROCK, E.; BIGORNIA, L.; RIMSTAD, E. Double-nested polymerase chain reaction for detection of caprine arthritis-encephalitis virus proviral DNA in blood, milk, and tissues of infected goats. **Journal of Virological Methods**, v.50, n.1-3, p.101-113, 1994.

BARQUERO, N.; GOMEZ-LUCIA, E.; ARJONA, A.; TOURAL, C.; LAS HERAS, A.; FERNÁNDEZ-GARAYZABAL, J.F.; DOMENECH, A. Evolution of specific antibodies and proviral DNA in milk of small ruminants infected by small ruminant lentivírus. **Viruses**, v.5, n.10, p.2614-2623, 2013.

BENAVIDES, J.; GARCÍA-PARIENTE, C.; FERRERAS, M. C.; FUERTES, M.; GARCÍA-MARÍN, J.F.; PÉREZ, V. Diagnosis of clinical cases of the nervous form of Maedi-Visna in 4- and 6- month old lambs. **The Veterinary Journal**, v.174, n.3, p.655-658, 2007.

BLACKLAWS, B.A. Small ruminant lentiviruses: Immunopathogenesis of visna-maedi and caprine arthritis and encephalitis virus. **Comparative Immunology, Microbiology and Infectious Diseases**, v.35, n.3, p.259-269, 2012.

BLACKLAWS, B.A.; HARKISS, G.D. Small Ruminant Lentiviruses and Human Immunodeficiency Virus: Cousins that Take a Long View. **Current HIV Research**, v.8, n.1, p.26-52, 2010.

BRELLOU, G.D.; ANGELOPOULOU, K.; POUTAHIDIS, T.; VLEMMAS, I. Detection of Maedi-Visna Virus in the liver and heart of naturally infected sheep. **Journal of Comparative Pathology**, v.136, n.1, p.27-35, 2007.

FEITOSA, A.L.V.L.; TEIXEIRA, M.F.S.; PINHEIRO, R.R.; PINHEIRO, A.A.; AZEVEDO, D.A.A.; ALVES, S.M. Primeiro isolamento de lentivírus de pequenos ruminantes em caprino naturalmente infectado em rebanho do Rio Grande do Norte, Brasil. **Arquivos do Instituto Biológico**, v.78, n.4, p.501-505, 2011.

FRAS, M.; LEBOEUF, A.; LABRIE, F.M.; LAURIN, M.A.; SOHAL, J.S.; L'HOMME, Y. Phylogenetic analysis of small ruminant lentiviruses in mixed flocks: Multiple evidence of dual infection and natural transmission of types A2 and B1 between sheep and goats. **Infection, Genetics and Evolution**, v.19, p.97-104, 2013.

GJERSET, B.; JONASSEN, C.M.; RIMSTAD, E. Natural transmission and comparative analysis of small ruminant lentiviruses in the Norwegian sheep and goat populations. **Virus Research**, v.125, n.2, p.153-161, 2007.

GLARIA, I.; REINA, R.; CRESPO, H.; DE ANDRÉS, X.; RAMÍREZ, H.; BIESCAS, E.; PÉREZ, M.M.; BADIOLA, J.; LUJÁN, L.; AMORENA, B.; DE ANDRÉS, D. Phylogenetic analysis of SRLV sequences from an arthritic sheep outbreak demonstrates the introduction of CAEV-like viruses among Spanish sheep. **Veterinary Microbiology**, v.138, n.1-2, p.156-162, 2009.

GREGO, E.; BERTOLOTTI, L.; QUASSO, A.; PROFITI, M.; LACERENZA, D.; MUZ, D.; ROSATI, S. Genetic characterization of small ruminant lentivirus in italian mixed flocks: evidence for a novel genotype circulating in a local goat population. **Journal of General Virology**, v.88, n.12, p.3423-3427, 2007.

GREGORY, L.; BIRGEL JÚNIOR, E.H.; LARA, M.C.C.S.H.; ANGELINI, M.; ARAÚJO, W.P.; RIZZO, H.; MAIORKA, P.C.; CASTRO, R.S.; KIRALY, A.C.M.; BENESI, F.J.; BIRGEL, E.H. Clinical features of indurative mastitis caused by caprine arthritis encephalitis virus. **Brazilian Journal of Veterinary Pathology**, v.2, n.2, p.64-68, 2009a.

GREGORY, L.; LARA, M.C.C.S.H.; VILLALOBOS, E.M.C.; HASEGAWA, M.Y.; CASTRO, R.S.; RODRIGUES, J.N.M.; ARAÚJO, J.; KELLER, L.W.; DURIGON, E.L. Detecção do vírus da artrite encefalite caprina em amostras de leite de cabras pela reação em cadeia da polimerase (PCR) e nested-PCR. **ARS Veterinária**, v.25, n.3, p.142-146, 2009b.

GRIMBERG, J.; NOWOSCHIK, S.; BELLUSCIO, L.; MCKEE, R.; TURCK, A.; EISENBERG, A. A simple and efficient non-organic procedure for the isolation of genomic DNA from blood. **Nucleic Acids Research**, v.17, n.20, p.83-90, 1989.

HALL, T.A. Bioedit: a user-friendly biological sequence alignment editor and analysis program for Windows 95/98/NT. **Nucleic Acids Symposium Series**, v.41, p.95-98, 1999.

HERRMANN-HOESING, L.M.; PALMER, G.H.; KNOWLES, D.P. Evidence of proviral clearance following postpartum transmission of an ovine lentivirus. **Virology**, v.362, n.1, p.226-234, 2007.

LARA, M.C.C.S.H.; BIRGEL JÚNIOR, E.H.; GREGORY, L.; BIRGEL, E.H. Aspectos clínicos da artrite-encefalite dos caprinos. **Arquivo Brasileiro de Medicina Veterinária e Zootecnia**, v.57, n.6, p.736-740, 2005.

LEROUX, C.; CRUZ, J.C.M.; MORNEX, J.F. SRLVs: A genetic continuum of lentiviral species in sheep and goats with cumulative evidence of cross species transmission. **Current HIV Research**, v.98, n.1, p.94-100, 2010.

LEROUX, C.; MORNEX, J.F. Retroviral infections in sheep and the associated diseases. **Small Ruminant Research**, v.76, n.1-2, p.68-76, 2008.

LIMA, C.C.V.; AYRES, M.C.C; PINHEIRO, R.R.; COSTA, J.N.; ANDRIOLI, A.; SOUZA, T.S.; AZEVEDO, D.A.A.; SANTOS, V.W.S.; ARAÚJO, J.F.; SOUSA, A.L.M.; PEIXOTO, R.M.; DAMASCENO, E.M.; COSTA NETO, A.O. Caprine lentivirus in sheep milk and semen. **Arquivo Brasileiro de Medicina Veterinária e Zootecnia**, v.69, n.2, p.391-397, 2017.

OLECH, M.; RACHID, A.; CROISÉ, B.; KUZMAK, J.; VALAS, S. Genetic and antigenic characterization of small ruminant lentiviruses circulating in Poland. **Virus Research**, v.163, n.2, p.528-536, 2012.

PASICK, J. Maedi-Visna Virus and Caprine Arthritis-Encephalitis Virus: Distinct species or quasispecies and its implications for laboratory diagnosis. **Canadian Journal of Veterinary Research**, n.62, p.241-244, 1998.

PÉREZ, M.; BIESCAS, E.; REINA, R.; GLARIA, I.; MARÍN, B.; MARQUINA, A.; SALAZAR, E.; ÁLVAREZ, N.; DE ANDRÉS, D.; FANTOVA, E.; BADIOLA, J.J.; AMORENA, B.; LUJÁN, L. Small ruminant lentivirus-induced arthritis: clinicopathologic findings in sheep infected by highly replicative SRLV B2 genotype. **Veterinary Pathology**, v.52, n. 1, p.132-139, 2015.

PETERHANS, E.; GREENLAND, T.; BADIOLA, J.; HARKISS, G.; BERTONI, G.; AMORENA, B.; ELIASZEWICZ, M.; JUSTE, R.; KRAßNIG, R.; LAFONT, J.; LENIHAN, P.; PÉTURSSON, G.; PRITCHARD, G.; THORLEY, J.; VITU, C.; MORNEX, J.; PÉPIN, M. Routes of transmission and consequences of small ruminant lentiviruses (SRLVs) infection and eradication schemes. **Veterinary Research**, v.35, n.3, p. 257-274, 2004.

PINHEIRO, R.R.; OLORTEGUI, C.D.C.; GOUVEIA, A.M.G.; ARAÚJO, S.C.; ANDRIOLI, A. Desenvolvimento de dot-blot para detecção de anticorpos para o vírus da artrite-encefalite caprina em caprinos. **Revista Portuguesa de Ciências Veterinárias**, v.101, n.557-558, p.51-56, 2006.

PINHEIRO, R.R.; ANDRIOLI, A.; GOUVEIA, A.M.G.; ARAGÃO, M.A.C.; MARTINEZ, P.M. Avaliação de antígenos para o diagnóstico de lentivírus em rebanho caprino sob programa de controle. **Arquivos do Instituto Biológico**, v.77, n.1, p.133-137, 2010.

PISONI, G.; BERTONI, G.; PURICELLI, M.; MACCALLI, M.; MORONI, P. Demonstration of coinfection with and recombination by caprine arthritis-encephalitis virus and maedi-visna virus in naturally infected goats. **Journal of Virology**, v.81, n.10, p.4948-4955, 2007.

PREZIUSO, S.; RENZONI, G.; ALLEN, T.E.; TACCINI, E.; ROSSI, G.; DEMARTINI, J.C.; BRACA, G. Colostral transmission of Maedi-visna virus: sites of viral entry in lambs born from experimentally infected ewes. **Veterinary Microbiology**, v.104, n.3-4, p.157-164, 2004.

RACHID, A.; CROISÉ, B.; RUSSO, P.; VIGNONI, M.; LACERENZA, D.; ROSATI, S.; KUZMAK, J.; VALAS, S. Diverse host-virus interactions following caprine arthritis-encephalitis virus infection in sheep and goats. **Journal of General Virology**, v.94, n.3, p.634-642, 2013.

RAVAZZOLO, A.P.; NENCI, C.; VOGT, H.R.; WALDVOGEL, A.; OBEXER-RUFF, G.; PETERHANS, E.; BERTONI, G. Viral load, organ distribution, histopathological lesions and cytokine mRNA expression in goats infected with a molecular clone of the caprine arthritis encephalitis virus. **Virology**, v.350, n.1, p.116-127, 2006.

REINA, R.; MORA, M.I.; GLARIA, I.; GARCÍA, I.; SOLANO, C.; LUJÁN, L.; BADIOLA, J.J.; CONTRERAS, A.; BERRIATUA, E.; JUSTE, R.; MAMOUN, R.Z.; ROLLAND, M.; AMORENA, B.; DE ANDRÉS, D. Molecular characterization and phylogenetic study of Maedi Visna and Caprine Arthritis Encephalitis viral sequences in sheep and goats from Spain.**Virus Research**, v.121, n.2, p.189-198, 2006.

RIMSTAD, E.; EAST, N.E.; TORTEN, M.; HIGGINS, J.; DEROCK, E.; PEDERSEN, N.C. Delayed seroconversion following naturally acquired caprine arthritis-encephalitis virus infection in goats. **American Journal of Veterinary Research**, v.54, n.11, p.1858-1862, 1993.

RODRIGUES, A.S.; BRITO, R.L.L.; PINHEIRO, R.R.; DIAS, R.P.; ALVES, S.M.; SOUZA, T.S.; SOUZA, K.C.; AZEVEDO, D.A.A.; ANDRIOLI, A.; MAGALHÃES, D.C.T.; TEIXEIRA, M.F.S. Padronização do ELISA indireto e Western Blot para o diagnóstico da artrite-encefalite caprina. **Arquivo Brasileiro de Medicina Veterinária e Zootecnia**, v.66, n.2, p.417-424, 2014.

SALTARELLI, M.; QUERAT, G.; KONINGS, D.A.M.; VIGNE, R.; CLEMENTS, J.E. Nucleotide sequence and transcriptional analysis of molecular clones of CAEV which generate infectious virus. **Virology**, v.179, n.1, p.347-364, 1990.

SHAH, C.A.; BÖNI, J.; HUDER, J.B.; VOGT, H.R.; MÜHLLHER, J.; ZANONI, R.; MISEREZ, R.; LUTZ, H.; SCHÜPBACH, J. Phylogenetic analysis and reclassification of caprine and ovine lentiviruses based on 104 new isolates: evidence for regular sheep-to-goat transmission and world-wide propagation through livestock trade. **Virology**, v.319, n.1, p.12-26, 2004.

SOUZA, T.S.; PINHEIRO, R.R.; COSTA, J.N.; LIMA, C.C.V.; ANDRIOLI, A.; AZEVEDO, D.A.A.; SANTOS, V.W.S.; ARAÚJO, J.F.; SOUSA, A.L.M.; PINHEIRO, D.N.S.; FERNANDES, F.M.C.; COSTA NETO, A.O. Interspecific transmission of small ruminant lentiviruses from goats to sheep. **Brazilian Journal of Microbiology**, v.46, n.3, p.867-874, 2015.

SOUZA, T.S.; PINHEIRO, R.R.; LIMA, C.C.V.; COSTA, J.N. Transmissão interespécie dos lentivírus de pequenos ruminantes: revisão e desafios. **Acta Veterinaria Brasilica**, v.6, n.1, p.23-34, 2012.

THOMPSON, J.D.; HIGGINS, D.G.; GIBSON, T.J. Clustal W: improving the sensitivity of progressive multiple sequence alignment through sequence weighting, position specific gap penalties and weight matrix choice. **Nucleic Acids Research**, v.22, n.22, p.4673-4680, 1994.

VILLORIA, M.; LEGINAGOIKOA, I.; LUJÁN, L.; PÉREZ, M.; SALAZAR, E.; BERRIATUA, E.; JUSTE, R.A.; MINGUIJÓN, E. Detection of Small Ruminant Lentivirus in environmental samples of air and water. **Small Ruminant Research**, v.110, n.2-3, p.155-160, 2013.

ZHANG, Z.; SCHWARTZ, S.; WAGNER, L.; MILLER, W. A greedy algorithm for aligning DNA sequences. **Journal of Computational Biology,** v.7, n.1-2, p. 203-14, 2000.

Receipt date: 22/05/2018
Approval date: 09/08/2018