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Authors
Chigerwe, M
Aleman, M

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Seizure Disorders in Goats and Sheep

M. Chigerwe and M. Aleman

Background: Goats and sheep are more likely to be presented for examination for seizures than are cattle, possibly as a consequence of their relatively smaller body size. Currently, no reports describing seizure disorders in goats and sheep are available.

Objectives: To describe clinical features and treatment outcomes of sheep and goats presented for seizures.

Animals: A total of 59 goats and 21 sheep presented for seizures.

Methods: Retrospective study. Medical records from 1994 to 2014 at the Veterinary Medical Teaching Hospital, University of California, Davis, were reviewed. Descriptive statistics were used to summarize data. Logistic regression was performed to determine whether variables were associated with mortality.

Results: The majority of seizures in goats and sheep had structural or metabolic causes. Polioencephalomalacia (PEM) secondary to ruminal lactic acidosis or PEM of undetermined cause was the most frequently diagnosed cause of seizures in goats and sheep. The proportions of mortality in goats and sheep were 49.2 and 42.9%, respectively. Age increased the odds mortality (odds ratio [OR], 1.51; 95% confidence interval [CI], 1.07, 2.14) in goats. Goats with structural or metabolic causes of seizures had higher odds for mortality (OR, 37.48; 95% CI, 1.12, 99.10) than those with unknown causes. Age and etiological diagnosis were not significant (P > .05) predictors of mortality in affected sheep.

Conclusions and Clinical Relevance: Seizure disorders in goats and sheep are associated with high mortality, despite treatment. Current treatment in goats and sheep with seizures warrants further investigation to determine whether treatments are beneficial or detrimental to survival.

Key words: Caprine; Forebrain; Neuron; Ovine.

A seizure is defined as a transient occurrence of physical signs with a finite duration, a tendency to begin and end abruptly, and caused by abnormal excessive or synchronous neuronal activity in the brain. These neuronal paroxysmal discharges can be detected by clinical manifestations, electroencephalographic recording, or both. Epilepsy is a complex chronic disorder of the brain characterized by recurrent seizures caused by a variety of pathological processes. According to the International League Against Epilepsy (ILAE), seizures are classified as genetic, structural or metabolic, and unknown, based on etiology. Further classification of epilepsy has been determined through clinical manifestations and electroencephalographic (EEG) recordings. Seizures can manifest as localized, generalized, or non-motor (psychic or behavioral, autonomic). Recently, a consensus report on epilepsy definition, classification, and terminology was published in veterinary medicine.

In a retrospective study of 43 beef cattle, most seizures were classified as reactive (70%), and the underlying cause was identified in the majority of cases. Causes of seizures in cattle included metabolic disorders, cerebral cortical necrosis, inflammatory or infectious, and intoxications. In ruminants, muscle contractions during a seizure episode can cause the animal to fall down, compromising the safety of the handler during examination or transportation. Sheep and goats are relatively smaller in size compared to cattle; thus, on-farm examination or transportation to a veterinary clinic is more feasible. Consequently, it is anticipated that sheep and goats experiencing seizures are more likely to be presented for examination compared to cattle.

Currently, studies describing seizure disorders in goats and sheep are not available. The objective of our retrospective study was to describe the clinical features and treatment outcomes of sheep and goats presented for seizures.
Materials and Methods

Medical records of goats and sheep presented to the William P. Pritchard Veterinary Medical Teaching Hospital (VMTH), University of California, Davis, from 1994 to 2014 were reviewed. Inclusion criteria included goats and sheep with seizures based on evaluation by a VMTH clinician or a referring veterinarian. Data collected included signalment, physical examination findings, neurological examination findings, diagnostic test findings, clinical or definitive diagnosis, medical treatments, and treatment outcomes. Goat breeds were classified as meat or dairy (Alpine, Boer, Cashmere, Kiko, Lamancha, Nubian, Oberhasli, San Clemente, Spanish, and Toggenburg), dwarf (pygmy or dwarf Nigerian), or other (Tennessee fainting). Sheep breeds were classified as meat or dairy breeds (Barbados, Hampshire, Jacob, Shetland, Shropshire, Suffolk) or other (Bighorn).

Diagnostic tests performed included CBC, serum biochemical analysis, blood culture, cerebrospinal fluid (CSF) analysis, toxicological analysis, rumen fluid analysis, fecal examination, immunological analysis, radiographic examination, ultrasonographic examination, computed tomography (CT), magnetic resonance imaging (MRI), electroencephalography (EEG), and necropsy.

Etiological diagnosis of seizures was classified as genetic, structural or metabolic, and unknown. This seizure classification was considered more applicable to goats and sheep compared to the companion animal classification. Treatment outcome was considered as discharged alive, euthanized, or died. Animals that received treatment before presentation to the VMTH or had seizures observed by the client only were excluded from the study.

Statistical Analysis

Descriptive statistics were used to summarize the data. Portions of occurrence of seizures among goat breeds were assessed using a chi-square or Fisher exact test. Logistic regression predicting mortality (death or euthanasia) was performed for goats with age, breed, medical treatments, and etiological diagnosis of the seizures as independent variables. In the logistic regression model for sheep, age and etiological diagnosis of the seizures were considered as independent variables. Breed was excluded as a variable because only 2 sheep were classified as other breeds. Genetic etiological diagnosis was excluded because none of the goats or sheep were diagnosed with genetic cause of seizures. Effect of treatment in the logistic regression analysis for sheep was excluded because all were medically treated. A variable was considered to be significantly associated with mortality if the OR was >1 with a corresponding P < .05. Model assessment was performed using the Hosmer and Lemeshow goodness-of-fit test. For all statistical analysis, a commercial statistical software was used. P < .05 was considered significant.

Results

Fifty-nine goats and 21 sheep met the inclusion criteria representing 1.9% of sheep and goats presented to the VMTH during the same time period. Median (range) age for goats was 1 year (1 day – 12 years) and 1 year for sheep (7 days – 10 years). Age was not indicated in the medical record for 7 goats and 2 sheep. Forty-three (72.9%) goats were of the meat or dairy breed, 14 (23.7%) were pygmy or dwarf Nigerian, and 2 (3.4%) were classified as other breed. In goats, proportion of meat or dairy breeds was overrepresented (P < .0001) compared to pygmy or dwarf Nigerian or other breeds. Nineteen (90.5%) of sheep included were of the meat or dairy breed and 2 (9.5%) were classified as other breed. The proportion of sheep meat or dairy breeds was overrepresented (P < .0001) compared to other breeds.

Diagnostic tests performed singly or in combination for diagnosis of the cause of seizures in goats and sheep after physical and neurological examination are summarized in Table 1. Polioencephalomalacia (PEM, cerebrocortical necrosis) of undetermined cause was considered a tentative diagnosis in goats and sheep that presented with (1) neurological signs consistent with forebrain disease, (2) response to therapeutic doses of thiamine hydrochloride, and, when available, (3) an unremarkable or mild mononuclear pleocytosis with increased in protein concentration on CSF analysis. The etiological diagnoses of seizures are summarized in Table 2. Seizures due to hypoglycemia in goats were diagnosed in neonates (<6 weeks old) with hypoglycemia secondary failure to nurse during the first 48 hours after birth (3 cases) and severe diarrhea caused by helminthiasis (2 cases). Seizures secondary to hypoglycemia in the single sheep case was a 7-day-old lamb that failed to nurse because of recumbency. Diagnosis was made at necropsy for goats and sheep diagnosed with meningitis, brain abscesses, leukoencephalomalacia, meningoepithelial hyperplasia, systemic sarcosporidiosis, and hereditary myelopathy. Trueperella pyogenes, Corynebacterium pseudotuberculosis (2 cases), Streptococcus sp (1 case), and Actinomyces sp (1 case) were cultured from brain abscesses in goats. Leukoencephalomalacia of the cerebral cortex associated with vasculitis secondary to sepsis caused by Escherichia coli metritis (1 case) and vasculitis of undetermined cause (1 case) were reported in 2 cases (Table 2).

Table 1. Diagnostic tests performed singly, or in combination, as part of the diagnosis of the cause of seizures in goats and sheep (N = 59 goats; N = 21 sheep). CSF = cerebrospinal fluid, CT = computed tomography, EEG = electroencephalography, MRI = magnetic resonance imaging.

| Diagnostic Test Performed | Goats | Sheep |
|---------------------------|-------|-------|
| Proportion of Patients with Diagnostic Test Performed % (N) | | |
| CBC | 37.2 (22/59) | 42.9 (9/21) |
| Chemistry | 94.9 (56/59) | 23.8 (5/21) |
| Fecal flotation | 16.9 (10/59) | 4.8 (1/21) |
| Radiographs | 10.2 (6/59) | 9.5 (2/21) |
| Ultrasound | 5.1 (3/59) | 0 (0/21) |
| CSF analysis | 10.2 (6/59) | 14.3 (3/21) |
| Rumen fluid analysis | 3.4 (2/59) | 0 (0/21) |
| Toxicology | 3.4 (2/59) | 9.5 (2/21) |
| CT Scan | 0 (0/59) | 4.8 (1/21) |
| MRI | 3.4 (2/59) | 0 (0/21) |
| EEG | 10.6 (6/59) | 0 (0/21) |
| Blood culture | 0 (0/59) | 4.8 (1/21) |
| Viral isolation | 0 (0/59) | 4.8 (1/21) |
| Necropsy | 44.1 (26/59) | 42.9 (9/21) |
| No test performed | 1.7 (1/59) | 0 (0/21) |
Table 2. Causes of seizures in goats and sheep (N = 59 goats; N = 21 sheep). PEM = polioencephalomalacia, CNS = central nervous system.

| General Etiological Diagnosis | Specific Etiology | Goats % (N) | Sheep % (N) |
|-------------------------------|-------------------|-------------|------------|
| Structural/metabolic          | PEM secondary to  | 22.0 (13/59)| 1.7 (1/21) |
| Structural/metabolic          | ruminal lactic acidosis | 18.6 (11/59)| 57.1 (12/21) |
| Genetic                       | Hypoglycemia      | 8.5 (5/59)  | 4.8 (1/21) |
| Genetic                       | Hypernatremia     | 3.4 (2/59)  | 4.8 (1/21) |
| Genetic                       | Meningitis        | 8.5 (5/59)  | 9.5 (2/21) |
| Genetic                       | Trauma            | 1.7 (1/59)  | 4.8 (1/21) |
| Genetic                       | Cortical thermal  | 1.7 (1/59)  | 0 (0/21)   |
| Genetic                       | Necrosis secondary to disbudding | 3.4 (2/59)  | 0 (0/21)   |
| Genetic                       | Nervous coccidiosis | 10.2 (6/59)| 0 (0/21)   |
| Genetic                       | Brain abscess     | 1.7 (1/59)  | 9.5 (2/21) |
| Genetic                       | Copper intoxication| 1.7 (1/59)  | 0 (0/21)   |
| Genetic                       | Bronchopneumonia  | 1.7 (1/59)  | 0 (0/21)   |
| Genetic                       | Leukoencephalomalacia | 3.4 (2/59)  | 0 (0/21)   |
| Genetic                       | Meningoepithelial | 1.7 (1/59)  | 0 (0/21)   |
| Genetic                       | Hyperplasia       | 1.7 (1/59)  | 0 (0/21)   |
| Genetic                       | Systemic          | 1.7 (1/59)  | 0 (0/21)   |
| Genetic                       | Sarcosporidiosis  | 1.7 (1/59)  | 0 (0/21)   |
| Genetic                       | Suspected hereditary | 1.7 (1/59)  | 0 (0/21)   |
| Genetic                       | CNS spongiform myelinopathy | 10.2 (6/59)| 9.5 (1/21) |

*Unknown causes of seizures consisted of cases in which the diagnosis was not made from ante-mortem and or postmortem diagnostic tests.

Table 3. Medical therapies performed singly, or in combination, as part of management in goats and sheep with seizures (N = 59 goats; N = 21 sheep). NSAID = Nonsteroidal anti-inflammatory drugs.

| Medical Treatment | Goats % (N) | Sheep % (N) |
|-------------------|-------------|-------------|
| IV fluids         | 74.6 (44/59)| 85.7 (18/21)|
| Thiamine          | 71.2 (42/59)| 81.0 (17/21)|
| Diazepam          | 62.7 (37/59)| 52.4 (11/21)|
| Antibiotics       | 57.6 (34/59)| 61.9 (13/21)|
| Mannitol          | 20.3 (12/59)| 38.1 (8/21) |
| NSAA—flunixin meglumine | 13.6 (8/59)| 4.8 (1/21) |
| Corticosteroids   | 8.5 (5/59)  | 9.5 (2/21)  |
| Intranasal oxygen | 5.1 (3/59)  | 4.8 (1/21)  |
| Phenobarbital (oral) | 3.9 (2/59)| 0 (0/21)   |
| Furosemide        | 1.7 (1/59)  | 0 (0/21)   |
| Vitamin/selenium  | 1.7 (1/59)  | 0 (0/21)   |
| Blood transfusion  | 0 (0/59)    | 4.8 (1/21)  |
| D-penicillamine   | 1.7 (1/59)  | 4.8 (1/21)  |
| Ammonium molybdate| 0 (0/59)    | 9.5 (2/21)  |
| Clostridium tetani antitoxin | 1.7 (1/59)| 0 (0/21)   |
| Fenbendazole      | 0 (0/59)    | 4.8 (1/21)  |
| No treatment performed | 3.4 (2/59) | 0 (0/21)   |

Discussion

The majority of causes of seizures in both goats and sheep were classified as structural or metabolic. Within the structural or metabolic classification, PEM secondary to ruminal lactic acidosis or PEM of undetermined cause was the most common disease condition diagnosed. The relatively higher proportion of diagnosis of PEM of undetermined cause or secondary to ruminal

Table 4. Logistic regression predicting probability of mortality (death or euthanasia) in goats is summarized in Table 4. Age increased the odds of mortality (OR, 1.51; 95% CI, 1.07, 2.14; P = .004) in goats. Goats diagnosed with structural or metabolic causes of seizures had higher odds for mortality (OR, 37.48; 95% CI, 1.12, 99.10; P = .003) compared to those diagnosed with unknown causes. Goat breed (P = .845) and treatment (P = .273) were not significant predictors of mortality. The logistic regression model for goats was a good fit (P = .413). The logistic regression predicting mortality in sheep is summarized in Table 5. Age (P = .293) and etiological diagnosis (P = .416) were not significant predictors of mortality in sheep.

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Table 5. Logistic regression predicting mortality in goats as a function of age, breed, general etiological diagnosis, and treatment (N = 59), 95% CI—95% confidence interval.

| Variable                | Estimate (95% CI) | Odds Ratio (95% CI) | P value |
|-------------------------|------------------|---------------------|---------|
| Intercept               | 0.635 (−0.352, 1.623) | –                  | .207    |
| Age                     | −0.069 (−0.116, −0.022) | 1.51 (1.07, 2.13) | .004    |
| Breed                   | −0.030 (−0.236, 0.266) | 1.03 (0.21, 5.14) | .845    |
| Etiological diagnosis   | −0.537 (−0.894, −0.179) | 37.48 (1.12, 99.10) | .003    |
| Treatment               | 0.485 (−0.381, 1.352) | 0.01 (0.001, 9.02) | .273    |

95% CI, 1.07, 2.14; P = .004 in goats. Goats diagnosed with structural or metabolic causes of seizures had higher odds for mortality (OR, 37.48; 95% CI, 1.12, 99.10; P = .003) compared to those diagnosed with unknown causes. Goat breed (P = .845) and treatment (P = .273) were not significant predictors of mortality. The logistic regression model for goats was a good fit (P = .413). The logistic regression predicting mortality in sheep is summarized in Table 5. Age (P = .293) and etiological diagnosis (P = .416) were not significant predictors of mortality in sheep.

**Discussion**

The majority of causes of seizures in both goats and sheep were classified as structural or metabolic. Within the structural or metabolic classification, PEM secondary to ruminal lactic acidosis or PEM of undetermined cause was the most common disease condition diagnosed. The relatively higher proportion of diagnosis of PEM of undetermined cause or secondary to ruminal
enzyme transketolase. Transketolase is the rate-decreased activity of the thiamine diphosphate-dependent zure activity. Severe bronchopneumonia can cause tissue hypoxia (including the brain), and spongy degeneration of the pons and brainstem leading to seizures. Hereditary central nervous system spongiform myelinopathy has been reported in African dwarf goats and sheep. Diagnosis of PEM, such as high-carbohydrate diets. The term PEM has been used in reference to softening of the gray matter of the brain, attributed to altered thiamine metabolism, hypotension, lead poisoning or hypernatremia. The term PEM also might be used in reference to any neurologic disease syndrome associated with an altered thiamine status. Ruminal lactic acidosis results in decreased ruminal thiamine synthesis, increased thiaminase-producing bacteria (Clostridium sporogenes and Bacillus spp), and decreased activity of the thiamine diphosphate-dependent enzyme transketolase. Transketolase is the rate-limiting enzyme in the pentose phosphate pathway, which is required for energy metabolism in nervous tissue.

The relationship between PEM and thiamine is uncertain. Although earlier studies reported sheep and cattle to be in a state of thiamine deficiency, other studies reported no alterations in blood thiamine concentrations between cattle with PEM and those with other neurologic diseases. Additionally, increased concentrations of rumen hydrogen sulfide, with no alterations in thiamine concentrations, were observed during peak PEM occurrence in steers. In our study, diagnosis of PEM secondary to ruminal lactic acidosis was based on history, physical examination findings, serum biochemical analysis, rumen fluid analysis, and necropsy. Previous reports indicate that response to therapeutic doses of thiamine in cattle or sheep with sulfur-induced PEM were variable. Hence, nonresponsiveness to thiamine treatment does not rule out an antemortem diagnosis of PEM. Consequently, cases of PEM in our study might have been misdiagnosed if they did not respond to thiamine administration.

Copper toxicosis causes intravascular hemolysis leading to tissue hypoxia (including the brain), and spongy degeneration of the pons and brainstem leading to seizures. Severe bronchopneumonia can cause tissue hypoxia, which can lead to seizures. Hereditary central nervous system spongiform myelinopathy was reported in 1 pygmy goat in our study. Spongiform myelinopathy has been reported in African dwarf goats and results in spongy changes in the white and gray matter of the cerebral cortex, leading to seizure activity. Meningoepithelial hyperplasia reported in 1 goat in our study could have caused seizure activity due to the pressure exerted on the cerebral cortex. Sarcocystis sp was identified in the brain, lungs, kidneys, rumen, and heart in 1 case (4-month-old Boer) in our study. The prevalence of intramuscular Sarcocystis in goats and sheep has been estimated at 52–79 and 18–100%, respectively. However, reports of systemic sarcosporidiosis in small ruminants are unavailable in the literature. The mechanism by which coccidiosis causes neurological signs, including seizures, is not clearly understood. Bacteria isolated from the brain abscesses in goats in our study were Gram-positive anaerobes, consistent with previous studies in cattle.

Complete blood cell count and serum biochemical analysis were the 2 most commonly performed ante-mortem diagnostic tests. This finding is most likely a result of easy of collection of blood samples, fast turnaround of results, and generation of information useful as guidance for choice of supportive treatment, such as IV fluids. Interestingly, CSF collection and analysis was only performed in a small proportion of goats and sheep, despite previous reports. Rumen fluid analysis was only performed in 2 cases despite 22% (13/59) of goats diagnosed with PEM secondary to ruminal lactic acidosis. This is most likely because the history and physical examinations were sufficient to make a diagnosis of PEM secondary to ruminal lactic acidosis. Intravenous fluids, thiamine, diazepam, and antibiotics were the most commonly administered medications in this study. The higher frequency of administration of thiamine while awaiting diagnostic test results in this study might be a result of the higher frequency of differential diagnoses that cause seizures by interfering with thiamine metabolism in sheep and goats. Diazepam has been recommended to control seizures in ruminants and was the most commonly used short-term anticonvulsant treatment in our study. In 2 goats (Table 3), with undetermined cause of seizures, phenobarbital was administered PO for long-term management of seizures. Because of a lack of studies in the literature on the pharmacokinetics and pharmacodynamics of phenobarbital in goats for seizure management, the dosage and frequency of dosing of phenobarbital was based on response to treatment and assessment of blood concentrations of phenobarbital, once treatment was initiated. Furthermore, therapeutic concentrations for any anticonvulsant in ruminants are unknown.

Mannitol and furosemide were administered to decrease brain edema in our study. Hyperosmolar treatment (mannitol or hypertonic saline) has been used in human and in veterinary medicine to decrease brain edema. Evidence of effectiveness of mannitol, hypertonic saline, and sodium chloride in decreasing brain edema associated with neurologic disease causing seizures in goats and sheep is lacking. Use of an NSAID, nimesulide, decreased prostaglandin E2 concentrations in a thiamine deficiency rat model (Wernicke’s encephalopathy). However, rather than being neuroprotective, administration of nimesulide precipitated encephalopathy and exacerbated neuronal death due to

| Variable | Estimate (95% CI) | Odds Ratio (95% CI) | P value |
|----------|------------------|---------------------|---------|
| Intercept | 0.753 (0.442, 1.064) | 1.000 | .001 |
| Age | −0.046 (−0.132, 0.040) | 0.954 (0.787, 1.968) | .293 |
| Etiological diagnosis | −0.175 (−0.60, 0.246) | 0.822 (0.321, 1.548) | .416 |

Table 5. Logistic regression predicting mortality in sheep as a function of age, general etiological diagnosis, and treatment (N = 21), 95% CI—95% confidence interval.
thiamine deficiency. Reviews of the use of an NSAID in humans with neurodegenerative diseases indicated that inflammation in the brain was complex and administration of NSAID might not be beneficial. Evidence to support the benefit of NSAID use in goats and sheep with neurologic disease also is lacking. Administration of dexamethasone at 0.04 mg/kg q24h for 3 consecutive days suppressed neutrophil function in cattle. Effects of dexamethasone in inflammatory conditions leading to seizures in ruminants are unknown. Ammonium molybdate and D-penicillamine were administered as specific antidotes for copper toxicity.

Mortality reported in our study was relatively high in both goats (49.2%) and sheep (42.9%) compared to beef cattle with seizure disorders (16.3%). The odds (OR = 1.5) of mortality increased with age. Although goats diagnosed with structural or metabolic causes of seizures had higher odds for mortality (OR = 37.48), the 95% CI of the estimate was wide (1.12–99.10) suggesting that the variable estimate was not precise.

Limitations of this study include information bias because case selection was based on medical records. Although not available in this study, CSF protein analysis can be performed by the Pandy reaction whereas cell count analysis can be performed by a Fuchs-Rosenthal chamber, at a cost-effective price. Additionally, cases with historical seizures or seizures not witnessed by a veterinarian were excluded. The results of our study are from a single institution and might have limited external validity. Finances, client compliance, and clinician expertise also could have been confounding factors for mortality.

The majority of causes of seizures in goats and sheep were classified as structural or metabolic. Polioencephalomalacia secondary to ruminal lactic acidosis or PEM of undetermined cause was the most frequently diagnosed cause of seizures. Mortality associated with diseases causing seizure disorders was high in goats and sheep despite treatment.

Footnote

a SAS 9.4 Version, Cary, NC

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Conflict of Interest Declaration: Authors disclose no conflict of interest.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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