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Evolution of cattle intoxications in southern Rio Grande do Sul: Spatial distribution and trends over 42 years¹

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ABSTRACT.- Scheid H.V., Ribeiro L.S., Venâncio F.R., Bohm B.C., Engelmann T.M., Brum F.R.P., Sallis E.S.V. & Schild A.L. 2023. **Evolution of cattle intoxications in southern Rio Grande do Sul: Spatial distribution and trends over 42 years.** *Pesquisa Veterinária Brasileira 43:e07395, 2023*. Laboratório Regional de Diagnóstico, Faculdade de Veterinária, Universidade Federal de Pelotas, Campus Capão do Leão, Capão do Leão, RS 96010-900, Brazil. E-mail: alschild@terra.com.br

Several toxic diseases cause mortality in cattle in southern Rio Grande do Sul State, Brazil. The aim of this study was to carry out a comparative analysis to determine the evolution of the main intoxications that occurred in cattle in southern Rio Grande do Sul from 1979 to 1999 and from 2000 to 2020. The spatial distribution and trend of occurrence of these intoxications over the 42 years in southern Rio Grande do Sul were determined using data from the Regional Diagnostic Laboratory of the Faculty of Veterinary Medicine at the Federal University of Pelotas (LRD-UFPel), which will make it possible to predict their occurrence in the coming years. From January 1979 to December 1999, 3,753 bovine materials were received for diagnosis at LRD-UFPel, and 3,653 cases were received from 2000 to 2020. Of the total number of materials received, 394 were diagnosed as intoxications, with 140 cases from 1979 to 1999 and 252 cases from 2000 to 2020. Out of 140 cases diagnosed in the first 21 years of operation of the LRD-UFPel, 113 (80.7%) were poisoning by plants, 22 (15.7%) by fungi outbreaks, and five (3.57%) by chemical substances. From 2000 to 2020, of the 252 diagnosed outbreaks 224 (88.8%) were caused by toxic plants. 10 (3.96%) by fungi, 12 (4.76%) by chemical substances, and six (2.38%) by insects. In the temporal trend analysis, a significant linear trend was observed with values of p=0.03 and an annual percentage change (APC) of 2.5 for the increase in the number of diagnoses of poisoning in general over the 42 years of the study. When analyzing the temporal trend of poisoning by Senecio spp., there was an increase in the occurrence of the diagnosis, with different characteristics and inflection points over time, with an annual growth rate of 9% in diagnoses during the first 21 years. There was a decrease in the occurrence of poisoning by Solanum fastigiatum, Echium plantagineum, and Claviceps paspali. Furthermore, poisoning by Ramaria flavo-brunnescens and *Baccharis coridifolia* maintained a similar percentage throughout the study period. It is concluded that toxic diseases will likely remain important causes of cattle death in the region.

INDEX TERMS: Toxic diseases, epidemiology, spatial analysis, temporal trend analysis, cattle.

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RESUMO.- [Evolução das enfermidades tóxicas em bovinos na região sul do Rio Grande do Sul: distribuição espacial e tendência em 42 anos.] Na região sul do Rio Grande do Sul, dentre as principais enfermidades que causam mortalidade em bovinos estão diversas doenças tóxicas, destacando-se as intoxicações por plantas e micotoxicoses. O objetivo deste trabalho foi realizar um estudo comparativo para determinar a evolução das principais intoxicações que ocorreram em bovinos na região sul do Rio Grande do Sul de 1979 a 1999 e de 2000 a 2020, estabelecendo a distribuição espacial e a tendência de ocorrência dessas intoxicações nos 42 anos de atividades do Laboratório Regional de Diagnóstico da Faculdade de Veterinária da Universidade Federal de Pelotas (LRD-UFPel), possibilitando prever sua ocorrência nas próximas décadas. Foram recebidos no laboratório de janeiro de 1979 a dezembro de 1999 e de janeiro de 2000 a dezembro de 2020, 3.753 e 3.653 materiais de bovinos para diagnóstico, respectivamente. Do total de materiais recebidos, 392 foram diagnosticados como intoxicações, sendo 140 entre os anos de 1979 a 1999 e 252 casos de 2000 a 2020. Dos 140 casos diagnosticados nos primeiros 21 anos de funcionamento do LRD-UFPel, 113 (80,7%) foram intoxicações por plantas, 22 (15,7%) intoxicações por fungos e cinco (3.6%) intoxicações por substâncias químicas. Entre os anos de 2000 e 2020 dos 252 casos diagnosticados 224 (88,8%) foram por plantas tóxicas, 10 (3,9%) por fungos, 12 (4,8%) por substâncias químicas e seis (2,4%) foram por insetos. Na análise de tendência temporal foi observada uma tendência linear significativa com valores de p=0,003 e mudança percentual anual (APC) de 2,5 no crescimento do número de diagnósticos de intoxicações em geral ao longo de todo o período de funcionamento do LRD-UFPel. Quando analisada a tendência temporal da intoxicação por Senecio spp. houve aumento na ocorrência do diagnóstico, com características e pontos de inflexão diferentes ao longo do tempo, sendo observado crescimento anual de 9% nos diagnósticos durante os primeiros 21 anos. Conclui-se que houve queda na ocorrência das intoxicações por Solanum fastigiatum, Echium plantagineum e Claviceps paspali e que as intoxicações por Ramaria flavo-brunnescens e Baccharis coridifolia mantiveram um percentual semelhante em todo o período. Além disso, as doenças tóxicas provavelmente permanecerão como importantes causas de morte de bovinos na região apesar de bem conhecidas, devido em parte, às dificuldades em fazer o controle das mesmas.

TERMOS DE INDEXAÇÃO: Doenças tóxicas, epidemiologia, análise espacial, análise de tendência temporal, bovinos.

INTRODUCTION

In Brazil, a country of continental dimensions with five different biomes, there are countless different plant genera and species that cause disease and death in cattle. Due to extensive breeding, plant poisoning is one of the main causes of cattle mortality and economic losses throughout the country. These poisonings have been frequently studied in recent decades, and some toxic plant species and genera are well-known in their regions of occurrence (Rissi et al. 2007, Pessoa et al. 2013). However, some poisonings by plants or fungi do not occur every year due to climatic conditions or other factors and end up being neglected in terms of diagnosis by farmers and veterinarians, which can lead to considerable economic losses when they occur again after a period of time (Riet-Correa & Medeiros 2001, Rissi et al. 2007, Lucena et al. 2010). Poisoning by *Baccharis coridifolia*, known since the colonization of South America (Cobo 1964, Almeida et al. 2013), and *Ramaria flavo-brunnescens*, known since the 1950s (Barros 1958, Freitas et al. 1966), are clear examples of the importance of identifying these etiological agents, knowing their toxic principles and/or modes of action to prevent outbreaks.

Despite the vast literature and studies related to intoxications in cattle in Brazil (Tokarnia et al. 1979, 2000, 2012, Riet-Correa et al. 1983, Rissi et al. 2007, Pessoa et al. 2013), research on the evolution of these intoxications and the trend of occurrence and spatial distribution in a particular region is needed to establish the biological behavior of toxic agents in order to predict and prevent these intoxications. It is possible that changes in and/or the emergence of large soybean fields or transgenic crops may also influence the expansion of toxic species (Monquero 2005).

The objective of the study was to carry out a comparative analysis to determine the evolution of the main cattle intoxications occurring in southern Rio Grande do Sul State from 1979 to 1999 and from 2000 to 2020. Our aim was to establish the spatial distribution and occurrence trend of these intoxications in the 42 years of activities of the "Laboratório Regional de Diagnóstico" (Regional Diagnostic Laboratory) of the "Faculdade de Veterinária" (Faculty of Veterinary Medicine) at "Universidade Federal de Pelotas" (LRD-UFPel) to predict their occurrence in the coming decades.

MATERIALS AND METHODS

A retrospective study of cattle poisonings diagnosed at the "Laboratório Regional de Diagnóstico" of the "Faculdade de Veterinária" at "Universidade Federal de Pelotas" (LRD-UFPel) was carried out. For this study, cattle necropsies or organ protocols sent for histopathological analysis from January 1979 to December 1999 and from January 2000 to December 2020 were reviewed. The various diagnoses were divided according to the etiological agent into poisoning by plants, fungi/mushrooms, insects, and chemical substances. The different intoxications were grouped in each study period, and data on morbidity, mortality, lethality, time of year of occurrence, animal age, and number of outbreaks/cases were extracted.

A temporal analysis of the occurrence trend of poisoning by *Senecio* spp. and other poisonings was conducted to assess their patterns with regard to the number of outbreaks over time. Temporal trends were calculated based on animal incidence rates using joinpoint regression models (Joinpoint Regression Program version 4.8.0.1). Temporal trends were examined by segmented linear regression, based on the calculation of annual percentage changes (APCs) and average annual percentage changes (AAPCs), with their respective 95% confidence intervals (95% CIs). APCs and AAPCs were considered significant when p<0.05 and their 95% CIs did not include zero. The results were interpreted as follows: positive and significant APCs/AAPCs were considered increasing trends in the occurrence of intoxications, negative and significant APCs/AAPCs were considered decreasing trends in the occurrence of intoxications, and in cases lacking significance, the trend was considered stable.

For the statistical analysis of the spatial distribution of intoxications in general and intoxications by *Senecio* spp. in particular, a geographic coordinate system was used considering the 25 municipalities that are currently served by the LRD-UFPel (Fig.1). Maps were prepared with an interval of 21 years, referring to the incidence rates by municipality of intoxications in general and intoxications by *Senecio* spp. in particular, as this was the only intoxication type with a sufficient number of cases for this analysis. Municipalities that were emancipated after 1990 were not allocated in the comparative map of the first 21 years of the study. The maps were obtained based on data provided by the "Instituto Brasileiro de Geografia e Estatística" (Brazilian Institute of Geography and Statistics) (IBGE 2021) in shapefile format (.shp) and subsequently analyzed in QGIS 3.4.7 software.

RESULTS

From January 1979 to December 2020, 7,406 bovine materials were received at the LRD-UFPel for diagnosis, with 3,753 cases received from 1979 to 1999 and 3,653 cases from 2000 to 2020, with an average of 176.3 cases being forwarded per year. Of these, 392 were diagnosed with poisoning, with 141 cases between 1979 and 1999 and 252 cases between 2000 and 2020. Out of 140 cases diagnosed in the first 21 years of activities of the LRD-UFPel, 113 (80.1%) were plant poisonings, 22 (15.6%) were fungi/mushroom poisonings and six (4.3%) were chemical poisonings (Table 1). From 2000 to 2020, of the 252 cases diagnosed (Table 2), 224 (88.88%) were caused

by toxic plants, 10 (3.9%) by fungi/mushrooms, 12 (4.76%) by chemical substances and six (2.38%) by insects. The epidemiological data of each intoxication type, age interval between the youngest and oldest cattle affected, and time of occurrence are shown in Table 1 and 2.

In the temporal trend analysis, a significant linear trend was observed with values of p=0.003 and APC of 2.5 for the increase in the number of diagnoses of intoxications in general throughout the entire period of operation of the LRD, with no subtrends being observed (Fig.2). When the trends of intoxications, in general, were analyzed over periods of 21 years, no statistically significant values were found. When analyzing the temporal trend of poisoning by Senecio spp., there was an increase in the occurrence of this diagnosis, with different characteristics and turning points over time. From 1979 to 1999 and from 2000 to 2001, there was a significant increase in the number of poisonings by the *Senecio* spp., with *p* values < 0.001 and APC of 9.1 and an annual increase of 9% in diagnoses during the first 21 years of operation of the LRD-UFPel. Over the other years (2002-2020), the APC values were not significant (Fig.3).

Incidence rates of poisoning, in general, increased in the municipalities served by the LRD-UFPel between the compared periods (Fig.4). Cases of poisoning by *Senecio* spp. also showed



Fig.1. Map of the region served by the "Laboratório Regional de Diagnóstico" of the "Faculdade de Veterinária" at "Universidade Federal de Pelotas" (LRD-UFPel) included in the spatial analysis of the occurrence of poisonings in general and by *Senecio* spp.

			57 57				
Diagnostic 1979-1999	No. cases/ Outbreaks	%	Age	Time of the year	Morbidity %	Mortality %	Lethality %
Plant poisoning	113	80.7					
Senecio spp.	79	56.4	1.5-9 years	All year	0.4-60	0.05-57.1	5.3-100
Solanum spp.	9	6.42	1-12 years	May-Dec	7.1-13.3	0.03-0.04	50-100
Echium spp.	7	5.0	3 months-3 years	Apr-Oct	0.5-39.1	0.5-29.7	76-100
Amaranthus spp.	5	3.57	3 months-4.5 years	Apr-Jun	1.5-37.9	1.1-22.3	20-75
Baccharis coridifolia	4	2,85	3 months-2.5 years	Mar-Sep	4.7-35.3	4.6-29.4	75-100
Xanthium spp.	3	2.14	6 months-3 years	Agu-Sep	3.1-80.6	3.1-80.6	100
Cestrum parqui	2	1.42	6 months-3 years	Jan-Aug	15-81.8	15-27.3	33.3-100
Ammi majus	1	0.7	Adults	Mar	100	NI	NI
Prunus sellowii	1	0.7	Adults	Jun	NI	NI	NI
Enterolobium contortisiliquum	1	0.7	3 years	Jun	42.8	NI	NI
Sorghum	1	0.7	2-3 years	Jun	13.3	10	75
Fungal/fungal toxins poisoning	22	15.7					
Claviceps paspali	20	14.28	6 months-4 years	Mar-May	0.3-33.3	0.1-6.2	10-100
Ramaria flavo-brunnescens	2	1.42	Adults	May	10.6-26.6	1.2-6.7	11.8-25
Chemical substances poisoning	5	3.57					
Urea	2	1.42	1 month-3 years	Aug-Sep	0.5	0.5	100
Carbolineum	1	0.7	Adults	Aug	2.7	0.7	25
Organophosphates	1	0.7	1 year	Aug	90.5	90.5	100
Sodium chloride	1	0.7	7 years	Dec	100	100	100
TOTAL	140	100					

Table 1. Cases/outbreaks of poisoning by plants, fungi, and chemical substances diagnosed in cattle at the "Laboratório Regional de Diagnóstico" of the "Faculdade de Veterinária" at UFPel from 1979 to 1999 and the relationship between age, time of year, morbidity, mortality, and lethality

NI = not informed.

Table 2. Cases/outbreaks of poisoning by plants, fungi, and chemical substances diagnosed in cattle at the "Laboratório Regional de Diagnóstico" of the "Faculdade de Veterinária" at UFPel from 2000 to 2020 and the relationship between age, time of year, morbidity, mortality, and lethality

Diagnostic 2000-2020	No. cases/ Outbreaks	%	Age	Time of the year	Morbidity %	Mortality %	Lethality %
Plant poisoning	224	88.88					
Senecio spp.	202	80.15	3 months-10 years	All year	0.1-100	0.1-100	16.6-100
Baccharis coridifolia	8	3.17	6 months-7 years	Nov-Jun	0.4-100	0.4-100	56.52-100
Xanthium spp.	6	2.38	6 months-5 years	Aug-Jan	1.16-57.14	1.16-57.14	100
Amaranthus spp.	5	1.98	1.5-8 years	Jan-May	0.54-6.92	0.54-11.29	66.66-100
Prunus sellowii	1	0.39	4.5 years	May	16.66	16.66	100
Solanum fastigiatum	1	0.39	4 years	Jun	18	8	44.44
Dodonaea viscosa	1	0.39	4 years	Apr	18.7	18.7	100
Fungal/fungal toxins poisoning	10	3.96					
Claviceps paspali	3	1.19	6-9 months	Apr-Jun	1.6-33.33	1.6-26.66	50-100
Aflatoxins	3	1.19	1-4anos	Jun-Sep	2.94-8.5	0.5-11.76	5.88-100
Ramaria flavo-brunnescens	3	1.19	1.5 years	May	2.58	34.83	100
Diplodia maydis	1	0.39	6 years	Jun	25	25	100
Chemical substances poisoning	12	4.76					
Organophosphates	7	2.77	7 days-5 years	Oct-Jan	1.4-100	0.7-86.65	16-100
Ionophore antibiotics	3	1.19	2-3 years	May-Sep	14-100	4.0-14	4-100
Abamectin	1	0.39	3-4 months	May	6	6	100
Sodium chloride	1	0.39	3 years	Jun	0.9	0.9	100
Insect poisoning	6	2.38					
Perreyia flavipes	6	2.38	1-3 years	Jul-Sep	0.8-3.70	0.8-38.70	100
TOTAL	252	100					



Fig.2. Temporal analysis of the trend of occurrence of poisonings in general from 1979 to 2020 in the area served by the "Laboratório Regional de Diagnóstico" of the "Faculdade de Veterinária" at "Universidade Federal de Pelotas" (LRD-UFPel).



All: 5 Joinpoints

Fig.3. Temporal analysis of the trend of occurrence of poisoning by *Senecio* spp. from 1979 to 2020 in the area served by the "Laboratório Regional de Diagnóstico" of the "Faculdade de Veterinária" at "Universidade Federal de Pelotas" (LRD-UFPel).

a significant increase both in the number of municipalities affected and in the incidence rates of intoxication. Poisoning by *Senecio* spp. from 1979 to 1999 had an incidence in eight municipalities of 0.01 to 5.00 cases per total number of cattle in the municipality, and in the last two decades, the incidence was greater than 5.00 in nine municipalities.

DISCUSSION

In the present study, diagnoses of intoxications increased from 141 cases/outbreaks in the first two decades of the study to 256 cases/outbreaks in the following two decades, with a significant increase in the annual percentage of intoxications (p=0.003 and APC 2.5). The number of bovine materials received from 1979 to 1999 was slightly higher than the number of materials/necropsies received from 2000 to 2020. This seems to suggest that the increase was not due to an increase in the number of bovine materials received but due to an actual increase in cases of intoxication. It was observed that the occurrence of intoxications from 1979 to 1999 represented 4% of all bovine materials/necropsies received in the laboratory and that there was a gradual increase from 2000 to 2020, reaching 7% in this animal species. The spread

of toxic plants throughout the municipalities in the region and the improvement in the efficiency of the laboratory with the dissemination of information on its activities reaching a greater number of professionals may have influenced the gradual increase in diagnoses of poisonings in the area served by the LRD-UFPel over the years. Among intoxications, cases of poisoning by plants were the most frequent, with the number of cases of poisoning by Senecio spp. being the highest, which was also observed in beef cattle in other regions of Rio Grande do Sul (Molossi et al. 2021). However, in the first 21 years of the study, the increase was significant (p < 0.001), and in the last 21 years, there was no consistency in the annual number of diagnoses. The significant increase in the first 21 years can be explained by the beginning of the activities of the LRD-UFPel and the disclosure of information to farmers and veterinarians on the different intoxications that occurred in the region, and in particular about poisoning by Senecio spp. This intoxication has been studied and recognized as a cause of great economic losses in livestock for more than four decades in Rio Grande do Sul (Méndez et al. 1987, Karam et al. 2004, Rissi et al. 2007, Lucena et al. 2010, Panziera et al. 2018). It should be noted that in the second period of the study, from 2000 to 2020, peaks of increase in the diagnosis



Fig.4. Statistical analysis of the spatial distribution of poisonings in general and by *Senecio* spp. From 1979 to 1999 and 2000 to 2020 in the area served by the "Laboratório Regional de Diagnóstico" of the "Faculdade de Veterinária" at "Universidade Federal de Pelotas" (LRD-UFPel).

of this intoxication were observed. One of them, from 2004 to 2008, probably occurred due to the severe drought in the region (Grecco et al. 2010), and the other, from 2011, possibly occurred due to the great spread of *Senecio madagascariensis*, a species with great dispersal capacity and which does not found in the region in previous years, having caused several outbreaks associated with mortality in the southern region of the state in 2013 (Stigger et al. 2014). It is noteworthy that in the first period of the study, poisoning by *Senecio* spp. was observed in cattle older than two years of age, probably due to its chronic character (Méndez et al. 1987, Driemeier et al. 1991, Barros et al. 1992), but in the last two decades, outbreaks in young cattle with less than 1.5 years of age occurred in the region, suggesting greater availability of the plant or increased concentration of pyrrolizidine alkaloids (Grecco et al. 2010).

Echium plantagineum, a toxic plant with the same active principle as *Senecio* spp., caused intoxication outbreaks only in the first 21 years of the study, representing 5% of intoxications. This is a plant whose toxicity is highly variable and it grows only in pastures in the first year of implantation (Méndez et al. 1985). The absence of outbreaks in the last 20 years reinforces the concept that there is variation in plant toxicity, since in some areas where *E. plantagineum* was found, there were no cases of intoxication. Additionally, the use of certified seeds has been adopted by many farmers to improve the quality of pastures, helping to prevent *E. plantagineum* from infesting pastures or crop fields by not planting seed mixtures that may contain this invasive species (Stigger et al. 2014).

Intoxication by *Solanum fastigiatum* occurred more frequently from 1979 to 1999, being diagnosed in 6.4% of cases, compared to the last 21 years in which it was observed only once (0.4%). The low morbidity and mortality associated with the chronic character of this intoxication may explain the considerable decrease in the number of cases, since after the identification of this plant as toxic in the first decade of this study (Riet-Correa et al. 1983), when the first clinical signs are observed, producers typically remove the animals from the areas where the plant occurs or send them to slaughter, and thus do not send materials to the laboratory.

Outbreaks of *Baccharis coridifolia* poisoning were observed in 2.8% and 3.1% of cases in the two study periods, respectively. Intoxication by this plant has been known since the time of the colonization of the Americas (Cobo 1964), and management measures to prevent its occurrence have been known and publicized for many decades. Some of these measures have been tested and shown to be effective in preventing outbreaks (Almeida et al. 2013). This is probably one of the reasons why the percentage of occurrence has remained stable. Some cases still occur because the control measures are not applied properly or because they are not effective, as when the plant is burned, which causes the animals to inhale the smoke, a measure that continues to be used and, in general, does not prevent cattle from consuming the plant (Almeida et al. 2013).

Poisoning by *Xanthium* spp. occurred in 2.1% of cases of poisoning from 1979 to 1999 and in 2.3% of cases from 2000 to 2020. The percentage of cases was similar in both study periods. It is noteworthy that in all outbreaks, poisoning occurred by ingesting the cotyledons of the budding plant after heavy rains from late winter to early summer. The southern region of the Rio Grande do Sul State is characterized by flat

and swampy fields, and outbreaks occurred on properties located on the banks of rivers or streams (Riet-Correa et al. 1983, 1984, Alberti et al. 2020), where the ideal environmental conditions for plant growth occur (Alberti et al. 2020). Poisoning by *Xanthium* spp. through ingestion of food contaminated by seeds is unlikely to occur in the region because cattle are commonly raised in pastures and are not fed crop residues (Driemeier et al. 1999). This was also observed in cattle confined in the region where the only poisoning diagnosed was by *Senecio* spp., having no relation to the ingestion of contaminated food (Estima-Silva et al. 2020).

Outbreaks of poisoning by Amaranthus spp. represented 3.5% of diagnoses of toxic diseases in the first 21 years and 2% in the subsequent 21 years, with no significant variation in the percentage of diagnoses in the two studied periods. Despite not being an important toxic plant from the point of view of the number of outbreaks, it is associated with high lethality that can reach 100% (Stigger et al. 2013). This plant can grow on fertilized land, and outbreaks can occur when cattle are grazed on crop stubbles that have not been completely harvested, especially when there is drought and lack of fodder in summer and autumn (Ferreira et al. 1991. Lemos et al. 1993, Torres et al. 1997). From 2000 to 2020, two outbreaks were described on a farm where Amaranthus spp. invaded pastures of *Brachiaria* sp. and, therefore, there was no shortage of forage, indicating that this intoxication can also occur in situations of adequate food quantity but with a large infestation by the plant that is palatable for cattle (Riet-Correa et al. 1983, Ferreira et al. 1991, Stigger et al. 2013).

Among the cases of mycotoxicosis diagnosed in Rio Grande do Sul, poisoning by *Claviceps paspali* was the most frequent, accounting for 14.5% of the diagnoses of poisoning made in the first 21 years of the study and only 1.2% since the 2000s. This sharp decrease in the number of diagnoses probably occurred for two reasons: first, intoxication became known to veterinarians and farmers after diagnosis in the first decades of operation of the LRD-UFPel; second, it is a disease with pronounced neurological clinical signs but with low mortality and high animal recovery (Rissi et al. 2007, Riet-Correa et al. 2013). Cases may not have been reported for this last reason. It is likely that a greater number of outbreaks have occurred in the last 20 years and they were often reported but not registered in the LRD-UFPel due to the lack of material for necropsy and/or histopathology.

The low number of mycetism diagnoses involving Ramaria *flavo-brunnescens* in the two periods (1.4% and 1.2%) suggests that knowledge about the disease may have, to a large extent, prevented outbreaks through the management of areas of eucalyptus forests by fencing or by removing animals from these areas during the autumn months (Alves et al. 2014, Scheid et al. 2022). Additionally, the large annual variation in the occurrence of the mushroom and its toxicity is another factor in the reduction of intoxication outbreaks. In southern Rio Grande do Sul, in 2020 and 2021, a small occurrence of the mushroom was reported in eucalyptus forests in the municipalities of Pelotas, Capão do Leão, and Jaguarão, where the disease has been observed (Scheid et al. 2022). This is probably a consequence of the drought observed in the period and is in accordance with what was reported in several studies about the climatic influences on the occurrence of the mushroom and its toxicity (Sallis et al. 2004, Riet-Correa et al. 2004).

With regard to poisoning by chemical substances, it was observed that there was no marked change in the percentage of occurrence when comparing the first two decades with the final two decades of the study. These poisonings accounted for 4.3% and 6.2% of cases from 1979 to 1999 and from 2000 to 2020, respectively. In this group, organophosphate poisoning stands out. Intoxication by organophosphates has increased considerably in the last two decades, accounting for 0.7% to 3.5% of diagnoses of toxic diseases in cattle. This may be related to the greater availability of this active principle for use in animals, since these poisonings occur fundamentally due to human error, such as errors in dosage or route of application (Grecco et al. 2009, Santos et al. 2014). It should also be considered that the nine outbreaks that occurred in the summer of 2013-2014 were influenced by the atypical heat that occurred in relation to normal averages for the region and that excessive heat exacerbates the absorption of the active principle (Santos et al. 2014).

Poisoning by *Perreyia flavipes* was observed only in the second period of the study, representing 2.3% of cases of toxic diseases. This intoxication was diagnosed in Uruguay in the 1990s (Dutra et al. 1997), and cases in southern Rio Grande do Sul were observed in 2006 and 2011 (Soares et al. 2008). This is an intoxication that depends on suitable climatic conditions for its occurrence (Raymundo et al. 2009), and for this reason, the number of outbreaks is variable and does not occur frequently.

Other plant poisonings and mycotoxicoses occurred sporadically in the two periods of study, and their importance in the context of toxic diseases in cattle was relatively small. Some plants, such as *Cestrum* sp. and *Dodonaea viscosa*, are more important from the point of view of differential diagnosis, reinforcing the need for their identification, since they cause toxic diseases similar to those caused by *Xanthium* spp. and *P. flavipes*.

According to the spatial analysis, there was a significant increase in the incidence of poisoning in general in eight municipalities in the region served by the laboratory compared to the incidence in the same region in the first 21 years of the study. This demonstrates that there has been a real increase in cases of toxic diseases in the region, which may also be associated with the dissemination of the activities of the laboratory diagnostic service. It is noteworthy that poisoning by *Senecio* spp. from 1979 to 1999 had an incidence in eight municipalities from 0.01 to 5.00, and in the last two decades, its incidence was greater than 5.00 in nine municipalities, demonstrating the increase in cases of this intoxication in the region.

CONCLUSIONS

The results of this study allowed us to conclude that there was a significant linear temporal trend in the number of diagnoses of poisonings in the southern region of Rio Grande do Sul.

The percentage of outbreaks of poisoning by *Solanum fastigiatum, Echium plantagineum,* and *Claviceps paspali* decreased in the last 21 years of the study.

The poisonings by *Ramaria flavo-brunnescens* and *Baccharis coridifolia* occurred during the 42 years without significant variation.

In the first 21 years of the study, there was a temporal trend toward an increase of 9% per year in cases of poisoning by *Senecio* spp.

There was an increase in the absolute number of cases of poisoning by *Senecio* spp. in the comparison between the first 21 years of the study and the subsequent 21 years.

Organophosphate poisoning has increased considerably over the last two decades and is fundamentally related to errors in dosage and route of application in both periods.

The poisonings will remain an important cause of death in cattle in the region despite the wide disclosure of information on their occurrence.

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