

Equine asthma in Brazil – a scoping review

Asma equina no Brasil – revisão de escopo

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Abstract

Asthma is a chronic respiratory disease that can occur in horses of different breeds and ages. While its occurrence has been reported in many countries, its occurrence across Brazil is unclear. This review aimed to gather information about equine asthma from studies performed in Brazil by different groups and investigate a variety of horse populations. Articles published in peer-reviewed scientific journals, as well as information contained in dissertations and theses, were searched on PubMed, SciELO, Google Scholar, and the Brazilian government catalog of dissertations and theses. Fifteen studies were included in this review, and according to the published information, the authors identified equine asthma using clinical signs, endoscopic findings, and/or cytological examination of tracheal wash and/or bronchoalveolar lavage fluid. Studies have investigated horses of different breeds and activities (racehorses, police horses, riding horses, Crioulos horses, and others) and were performed in different regions with diverse climatic conditions. On the previous observed studies, the occurrence varied from 14.0% to 60.0%, with a mean occurrence of 24% for severe asthma. Other studies must be performed to further understand the occurrence of equine asthma in Brazil, according to different climatic regions.

Keywords: Endoscopy; Horses; Neutrophils; Recurrent airway obstruction; Inflammatory airway disease.

Resumo

Asma é uma doença respiratória crônica que pode ocorrer em cavalos de diferentes raças e idades. Enquanto a prevalência tem sido reportada em muitos países, no Brasil é desconhecida. Essa revisão tem como objetivo trazer informações sobre a Asma equina de estudos realizados no Brasil por diferentes grupos e investigar a população acometida. Artigos publicados em revistas científicas, assim como informações contidas em dissertações e teses, foram pesquisados no PubMed, SciELO, Google Scholar, e no Catálogo do Governo Brasileiro de dissertações e teses. Quinze estudos foram incluídos nessa revisão, e de acordo com as informações publicadas, os autores identificaram a Asma equina por meio dos sinais clínicos, achados endoscópicos e/ou exame citológico do lavado traqueal ou broncoalveolar. Esses estudos investigaram cavalos de diferentes raças e atividades (cavalos de corrida, cavalos de patrulhamento policial, animais de montaria, cavalos Crioulos, entre outros) e foram realizados em diferentes regiões do país com diversas condições climáticas. Nos estudos avaliados, a prevalência variou de 14.0% a 60.0%, com uma prevalência média de 24% para a asma severa. Outros estudos devem ser conduzidos para melhor compreensão da prevalência da asma equina no Brasil, de acordo com os diferentes climas em cada região.

Palavras-chave: Endoscopia; Cavalos; Neutrófilos; Obstrução recorrente de vias aéreas, Doença inflamatória de vias aéreas.

Resumen

El asma es una enfermedad respiratoria crónica que puede presentarse en caballos de diferentes razas y edades. La prevalencia se ha informado en muchos países, en Brasil se desconoce. Esa revisión tiene como objetivo traer informaciones sobre el asma equina de estudios realizados en Brasil por distintos grupos y investigar la población

afectada. Se buscaron artículos publicados en periódicos científicos, así como informaciones contenidas en disertaciones y tesis, en PubMed, SciELO, Google Scholar y en el Catálogo de disertaciones y tesis del Gobierno Brasileño. En esta revisión se incluye quince estudios y, según la información publicada, los autores identificaron el asma equina por medio de señales clínicas, hallazgos endoscópicos y/o exámenes citológicos del lavado traqueal o broncoalveolar. Estos estudios investigaron caballos de distintas razas y actividades (caballos de carrera, patrulleros, animales de monta, caballos criollos, y otros) como también se realizaron en distintas regiones del país con condiciones climáticas distintas. Los estudios evaluados, la prevalencia varió de 14,0% a 60,0%, con la prevalencia promedio de 24% para asma grave. Otros estudios deben ser reslizados para comprender mejor la prevalencia del asma equina en Brasil, conforme las distintas variaciones de zonas climáticas.

Palabras clave: Endoscopia; Caballos; Neutrófilos; Obstrucción recurrente de las vías aéreas, Enfermedad inflamatoria de las vías aéreas.

1. Introduction

By definition, asthma in humans is a chronic respiratory disease characterized by non-septic airway inflammation, followed by a history of chronic episodes of coughing, wheezing, shortness of breath, and chest tightness, which vary in different episodes, and are accompanied by bronchoconstriction and changes in lung tissue remodeling (Gina, 2018). In horses, the terminology had chanced along the years to identify a chronic inflammatory lower airway disease, such as heaves, recurrent airway obstruction, inflammatory airway disease (IAD), tracheal IAD, bronchial IAD, chronic bronchitis, summer pasture-associated obstructive pulmonary disease, summer pasture-associated obstructive airway disease, summer heaves, and summer recurrent airway obstruction (RAO) (Bond et al., 2018). Chronic obstructive pulmonary disease (COPD), heaves, bronchitis, and chronic bronchiolitis have been reported in older horses and are associated with the environment, especially stable bed material and hay dust (Tremblay et al., 1993; Woods et al., 1993; Tesarowsky et al., 1996).

More recently, the term equine asthma was proposed for chronic inflammation of the small airways, encompassing IAD and RAO, to improve owners' and veterinarians' understanding of these conditions (Lavoie, 2015; Couetil et al., 2016). The main findings of asthma in people, like clinical findings (cough, changes in pulmonary auscultation, and recurrent respiratory distress), inflammatory infiltrate demonstrated in the assessment of bronchoalveolar lavage (BAL) fluid, and changes related to bronchoconstriction and remodeling of lung tissue have also been observed in horses (Bond et al., 2018; Ter Woort et al., 2018).

IAD, now considered mild to moderate asthma, is reported as occurring in 11% to 50% of racehorses in training and affecting up to 80% over their lifetime (Christley & Rush, 2007). Many of them are presented with pulmonary inflammation in the first few weeks after being stabled and starting training (Malkides et al., 2003; Ivester et al., 2014), and can go subclinical, showing non-specific signs such as cough and poor performance. According to Christley et al (2001), cough is observed in only 38% of the patients and can't be relied only on this clinical sign. Tracheal mucus and presence of increased amounts of inflammatory cells (neutrophils, eosinophils, and/or mast cells) in BAL fluid, with no clinical signs of respiratory effort at rest or infection is also observed (Couetil et al., 2016), although tracheal mucus and BAL cytology association haven't been reported yet (Couetil et al., 2020).

RAO, a severe asthma, affects horses over seven years old. It differs from mild/moderate asthma specifically because it causes respiratory difficulty at rest, bronchoconstriction, and neutrophilic inflammatory infiltrate above 25% in the BAL fluid (Hotchkiss et al., 2007). When RAO occurs in horses grazing pasture, the condition is described as pasture-related asthma but is also known as summer pasture-associated obstructive pulmonary disease, summer pasture-associated obstructive airway disease, summer heaves, and summer RAO, usually because of hot humid climates on north hemisphere. It shows neutrophilic airway inflammation, airway hyperresponsiveness and airway remodeling. (Bond et al., 2018) (Couetil et al., 2020).

In Brazil, a large country with different climatic conditions, several studies have described chronic lung conditions related to the different stages of equine asthma. However, there are no approximate numbers on the occurrence of these

conditions in Brazil as a whole. Therefore, this scoping review aimed to classify the nomenclature and standardize it for better understanding and to gather information about equine asthma from studies performed in Brazil to understand its occurrence in the country.

2. Methodology

The present study is a scoping review to gather research and reports concerning equine asthma in Brazil. The inclusion criteria were: studies on equine asthma performed only in Brazil and published in peer-reviewed journals, found in PubMed, SciELO, or Google Scholar, written in English or Portuguese. Results from dissertations and theses were also considered, found using Google Scholar and the Brazilian government catalog of dissertations and theses (<https://catalogodeteses.capes.gov.br/catalogo-teses/#!/>). The search terms used included horse, COPD, IAD, RAO, asthma, cough, and respiratory system. Fifteen articles were included in this review, published from 1999 to 2021. Six of them were published in English and nine in Portuguese, with an abstract in English.

3. Results and Discussion

3.1 Distribution

Equine asthma was identified in different Brazilian states (Rio Grande do Norte, Paraná, Rio de Janeiro, Rio Grande do Sul, São Paulo, and Distrito Federal), in all seasons of the year, in different horse breeds, and various sports disciplines. In addition, it has been reported in mules (Melo et al., 2007).

Fifteen studies on mild to moderate asthma included information on the clinical signs, endoscopic examination, tracheal wash (TW), or BAL fluid. In one study, 25 police horses in Rio de Janeiro were reviewed using physical examinations, ventigraphy (to measure interpleural pressure), airway endoscopy, and BAL fluid cytology. Asthma was present when at least two of the parameters were abnormal. They reported a occurrence of 60% of asthmatic horses, with all investigated animals presenting BAL fluid neutrophils above 10% (Amaral et al., 1999). In a similar population, also in Rio de Janeiro, the occurrence of mild to moderate asthma was found to be 43.4% of the horses evaluated, with all animals without clinical manifestations of asthma (Sad et al., 2012), while in riding horses, the occurrence of mild asthma was 17.4% and severe asthma was 4.3% (Lessa et al., 2005). In the state of Rio Grande do Norte, in the northern region of the country, a occurrence of 8% of horses with severe asthma and 6.7% of horses with mild asthma was identified in the military police squad (Rocha et al., 2014).

3.2 Endoscopic findings

Studies completed the diagnosis by endoscopic examination having characterized equine asthma using endoscopic findings. Gerber et al. (2004) and Holcombe (2005) through the reporting of the amount of mucus in the tracheal lumen.

In the study by Sad et al. (2013), endoscopic examination was used to identify horses with asymptomatic airway inflammatory disease in a population of horses considered clinically healthy. Thirty-two adult horses of mixed breeds underwent endoscopic examination, and 53.12% of them presented tracheal mucus scores of II to IV, which is considered a sign of asymptomatic mild/ moderate asthma. (Sad et al., 2013).

Another study described information from endoscopic files of 1,030 Thoroughbred (TB) racehorses, in which the authors identified 126 that were examined because they presented with a cough. Tracheal mucus was detected in 88.1% (111 out of 126), scored as grade 1 in 6.3% (8 out of 126), grade 2 in 11.9% (15 out of 126), grade 3 in 23.0% (29 out of 126), grade

4 in 19.0% (24 out of 126), and grade 5 in 27.8% (35 out of 126). The study demonstrated that 83.7% of horses were examined due to a cough presenting grade 2 or higher of tracheal mucus (Silva et al., 2011).

A positive correlation between cough and increased amounts of secretion in the trachea in horses with asthma has been previously described (Couetil et al., 2007, 2016; Benedice et al., 2008). Moreover, endoscopic findings of increased amounts of tracheal mucus are among the main clinical findings of horses with asthma (Couetil et al., 2016). They are reported to be the basis for the diagnosis of equine asthma, most of the time in association with TW cytology, performed by veterinarians working in the horse racing industry in the United Kingdom (Kinninson & Cardwell, 2020).

There was no difference between the tracheal mucus scores of coughing and healthy animals in the two studies. Michelotto et al. (2011) investigated yearling TBs at farms (n = 33), after 30 days of stabling (n = 42), and after approximately five months of race training (n = 27), and found tracheal mucus scores of two or higher in 66.6%, 54.7%, and 63.0%, respectively (Michelotto et al., 2011). Almeida et al. (2015) evaluated 50 animals of different breeds and activities (36 coughing and 14 healthy). There was no difference in the median for mucus scores between the two groups (healthy: 2.0, cough: 2.8) (Almeida et al., 2015). Finally, the presence of tracheal mucus did not correlate with the clinical manifestations of asthma in the study by Sad et al. (2012), in which 43.4% of 53 horses had tracheal mucus scores of two or higher without displaying any changes in the physical examination (Sad et al., 2012).

It must be considered that for horses in training, the amount of mucus in the trachea may vary depending on the time of assessment, training level, and time of year. Thirty-eight Crioulo horses in training were evaluated by endoscopic examination of the airways within 90 min after high-intensity and short-duration exercise; 21.05% of the animals presented a history of coughing. Tracheal mucus grade 1 was observed in 42.10% of the horses and grade 2 or higher in 36.84%. There was no difference between the performance of the animals that presented with grade 2 or higher tracheal mucus than grade 1 animals. Moreover, the study also showed no difference between those with exercise-induced pulmonary hemorrhage (EIPH) and healthy ones, but horses with tracheal mucus II-IV had lower performance than animals with EIPH (p=0.0132) (Abreu, 2009).

3.3 Tracheal wash (TW)

The TW technique is well described and is widely used for diagnosing inflammation in the lower airways. It is easier to perform than collecting BAL fluid, as it is usually performed during endoscopic examination, and there is no need for sedation. TW was shown to have greater sensitivity and specificity for detecting increased quantities of neutrophils in airways than BAL (Rossi et al., 2018). However, the procedure is not indicated for the diagnosis of asthma according to the ACVIM consensus (Couetil et al., 2016). However, this is the most used technique for cytological investigation of the airways by United Kingdom equine veterinarians because of its practicality, does not affect horse training, and is useful for understanding airway conditions as well as treatment results (Kinninson & Cardwell, 2020).

Considering a cutoff of 25% of neutrophils in the TW cytology, the study of Almeida et al. (2018) investigated a group of 18 TB racehorses. Sixty days after entering training, they found that the mean neutrophil count was higher than 27%. At 90 days, the mean neutrophil count was 5.1%. The authors reinforced the need for routine airway evaluation in racehorses during training.

TW feasibility allows samples to be collected even in a competitive environment. In a study by Michelotto Jr. et al. (2007), 27 quarter horses were investigated 30 min after a three-barrel competition using endoscopic examination and TW. Endoscopic examinations revealed tracheal mucus with a score of two or higher in 33.32% of the horses. In the TW cytology, there were a mean of $23.10 \pm 35.93\%$ neutrophils and $44.09 \pm 35.68\%$ epithelial cells (Michelotto Jr et al., 2007). The presence of epithelial cells in TW samples is rarely discussed in the literature and may be associated with different causes, such as viral

infections or due to the collection procedure (Fernandes et al., 2000). A retrospective study indicated that the inclusion of epithelial cell readings significantly changed the final percentage of cells in the TW analysis. Including epithelial cells, 41% of the investigated horses were considered asthmatic because they demonstrated more than 20% neutrophils. In contrast, 62% were considered asthmatic when not including epithelial cells (Allen et al., 2019).

3.4 Bronchoalveolar lavage (BAL) fluid

Currently, the use of BAL fluid cytology is indicated for the confirmatory diagnosis of asthma in horses (Couetil et al., 2016). Together with the history, clinical signs, endoscopic findings, and BAL fluid cytology, the diagnosis of mild to moderate asthma in horses could be considered in horses with less than 5% neutrophils, 1% eosinophils, and 2% mast cells, and severe asthma in horses with more than 25% neutrophils (Couetil et al., 2016).

Almeida et al. (2015) used the association of BAL fluid and TW to investigate 36 horses of different breeds and ages in the southern region of Brazil that presented with a cough and compared them with 14 healthy horses from a control group. In this study, the coughing group presented a higher grade of mucus and a higher number of neutrophils in the BAL fluid ($30.3\% \pm 27.3\%$ vs. $5.0\% \pm 4.2\%$, $p=0.001$) and in the TW fluid ($46.4\% \pm 30.8\%$ vs. $19.5\% \pm 22.9\%$, $p=0.003$) compared to the control horses (Almeida et al., 2015). Considering the diagnosis of asthma according to the last ACVM consensus (Couetil et al., 2016), 38.9%, 47.2%, and that 13.9% of the coughing horses presented mild to moderate asthma, severe asthma, or were normal, respectively, and six horses from the control group showed cytological profiles compatible with mild asthma.

BAL fluid cytology was used to investigate police horses in the city of Rio de Janeiro, finding that animals with asymptomatic mild/ moderate asthma showed a mean of 15% neutrophils and 1.19% eosinophils (Lessa et al., 2011) and 7.1% neutrophils and 0.7% eosinophils (Sad et al., 2013). In a second study, 32 police horses were divided into healthy and asymptomatic mild/ moderate asthma groups based on their tracheal mucus scores, with the authors finding that the results were not influenced by the age of the animals. Finally, in another study, the group of police animals showed that 60% of the animals had signs of severe asthma, with more than 50% of neutrophils in the BAL fluid cytology in 36% of the horses investigated (Amaral et al., 1999).

Equine pasture asthma was recently reported in two horses. After clinical manifestations of asthma, horses underwent endoscopic examination and were found to have a tracheal mucus score of three. In the BAL fluid cytological examination, the animals presented 29.7% and 27.0% neutrophils and 1.3% and 1.5% eosinophils, respectively, in addition to Curshmann spirals in one of the animals (Gouvea et al., 2021).

3.5 Microbiologic and biochemical investigations

In a multicentric study with airway samples from three Brazilian states (Rio Grande do Sul, Paraná, and São Paulo), 32 horses were evaluated and classified as being healthy (18 horses) or having severe asthma (14 horses). Mycological analyses showed that 42.3% of the animals were positive for microscopy, with fungal conidia and hyphal fragments. Of these, 6.7% were in the healthy group and 90.9% in the group of animals with asthma. Similarly, fungal concentration in tracheal lavage samples in CFU/mL differed significantly between groups ($P < 0.001$), averaging 5 CFU/mL in healthy animals and 310 CFU/mL in animals with asthma (Xavier et al., 2014).

BAL has also been used for sample collection and other measurements, in addition to cytology. A study of two-year-old TB racehorses in the first months of race training found increased bioactivity of the pro-inflammatory molecule platelet-activating factor, higher BAL fluid concentration of protein, and evidence of oxidative stress associated with decreased phagocytosis of alveolar macrophages. These findings were associated with the presence of hemosiderophages in BAL fluid (Michelotto Jr. et al., 2011).

Finally, alkaline phosphatase was higher in the TW of horses with lower airway inflammation ($18.9 \pm 11.2 \times 103$ U/L) than in healthy horses ($10.3 \pm 5.9 \times 103$ U/L) ($P = .021$). This finding must be further studied, but the authors asserted that it was possible to identify the early stages of airway inflammation using such biochemical investigations (Viscardi et al., 2016).

4. Conclusion

The included studies indicate that the occurrence of equine asthma ranges between 14.7% and 60% in Brazil. The occurrence appears to be influenced by several diagnostic parameters. The mean occurrence of severe cases of equine asthma was 24.1% in the Brazilian horse population.

Brazil is a large country with many climatic, territorial, and cultural differences; thus, the great variation in the results obtained in the included studies is unsurprising. However, several research groups have applied diagnostic techniques worldwide that enable comparisons to be made between locations. We did not find any studies that used pulmonary function tests in cases of equine asthma syndrome. Thus, further research on this subject is required in Brazil.

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