Evaluation of the patients admitted with laminitis to the Ambulatory Clinic of Utrecht University

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Content

Abstract

Laminitis is a disease of the laminae in the hoof. Various predisposing factors can play a part in the development of laminitis. For example laminitis can be caused by carbohydrate overload, endotoxemia due to colitis or retained placenta, excessive unilateral weight-bearing due to lameness on the contralateral leg, PPID and EMS. The purpose of this study is to evaluate the patients admitted to the ambulatory clinic of Utrecht University between 2003 and 2013. This evaluation provides more information about the risk factors and underlying causes of laminitis in an ambulatory clinic.

Data was collected by analysing the case histories of the patients diagnosed with laminitis (n=365) and all patients of the Ambulatory Clinic of Utrecht University (n=10143). Data used in this study consist of: age, gender, breed, species and reported underlying cause.

Ponies and mares were at significantly higher risk of developing laminitis (P<0,05) compared to the total admitted population. 41% of the patients admitted with laminitis were diagnosed with an underlying endocrinopathy. 25% of these diagnoses were confirmed by blood tests. Equine Metabolic Syndrome (EMS) was most commonly differentially diagnosed in young horses (peak at category 11 up to 15 years) and Pituitary Pars Intermedia Dysfunction (PPID) in older horses (peak at category 21+ years).

Blood testing for PPID and EMS should be encouraged. From the 59% of the laminitic patients with unknown underlying cause, probably some patients do suffer from PPID or EMS and therefore these groups can be underestimated.

Introduction

Pathology

Laminitis is a disease of the laminae in the hoof. Beside the painfulness for the horse, laminitis has a large economic impact. Of the equine operations in the USA, 13% have one or more horses affected with laminitis annually.[1] The costs for the diagnosis and treatment amount to about 8 million dollars a year. Of the horses affected with laminitis, 75 % is in such condition that they must be euthanized. The loss of these horses costs 5 million dollars annually.[2]

The pathology of laminitis is characterised by the changes of the lamellae. The hoof wall is connected to the dermis with the dermal and epidermal lamellae. The lamellae are made up of a longer primary lamella with shorter secondary lamellae attached to it like a feather structure. In experimentally induced laminitis changes to the structure of the basement membrane are found with 48 hours after administration of carbohydrate overload. It is interrupted and no longer attached to the epidermal lamellae. The collagen of the basement membrane is damaged.[3] After seven days, the remaining epidermal basal cells can reconstruct a large part of the basement membrane.[4]

However, other changes in the lamellae can't be repaired that easily. After the first episode laminitis the orientation of the primary (PEL's) and secondary epidermal lamellae (SEL's) are no longer symmetrical, the SEL's have been stretched and many of them are no longer attached to the PEL's. Eventually the primary dermal and epidermal lamellae are separated

from each other. This weakening of the lamellae can contribute to the sinking of the distal phalanx, caused by the decreased suspension in the hoof capsule. As a reaction to these alterations, neutrophils can migrate to the lamellae. Thus inflammation is not the cause of the pathology. [3],[4],[5]

Predisposing factors

In the development of laminitis, various predisposing factors can play a part. For example laminitis can be caused by carbohydrate overload, endotoxemia due to colitis or retained placenta, excessive unilateral weight-bearing due to lameness on the contralateral leg, PPID and EMS.

Pass et al suggest that laminitis occurring after acute diseases like sepsis and maybe carbohydrate overload is caused by the unavailability of glucose for the metabolism in the hooves. This change in glucose metabolism activates metalloproteinase, which can separate epithelial cells from their basement membrane. Because of the mechanical forces, the epithelia in the hooves are more affected by such conditions.[6]

Laminitis can be caused by endotoxemia. Endotoxemia can be induced by colitis, retention of fetal membranes and acute carbohydrate overload.
Another theory for the development of acute laminitis due to carbohydrate overload is a shift in gut flora. By fermenting of the carbohydrates by the bacteria, lactic acid is produced. Some bacteria die due to the low PH, giving the acid-resistant bacteria the opportunity to overgrow. In the study of Onishi et al, increased levels of *Enterobacteriaceae* and *Salmonella spp.* were found in corn starch and oligofructose infused horses. Components of this bacteria are able to disseminate hematogenously and cause inflammatory responses in other tissues.[7]

Though endotoxemia caused by gastrointestinal disease, retention of fetal membranes or carbohydrate overloading, can be a risk factor for laminitis. The endotoxin which can be found in the blood of horses in such conditions is LPS (Lipopolysaccharide). In studies horses where administrated with LPS, for example by the study of Tadros et al. However the administration of LPS didn't cause laminitis in these experimental conditions. Tadros et al suggested that in clinical disease horses are exposed to endotoxin over a longer period of time. They used LPS from one single strain of bacteria, in clinical disease the endotoxemia consists of different kinds of bacteria.[8]

Interestingly, the study of Karikoski et al, with horses diagnosed in first opinion equine hospital, showed that almost 90 percent of the horses diagnosed with laminitis had an underlying endocrinopathy. Of these horses, one-third was confirmed with PPID. In 84 percent of the laminitic horses, they found hyperinsulinemia. These horses also showed signs of EMS.[9]

EMS (Equine Metabolic Syndrome) is a hormonal disorder of horses. Horses suffering from EMS are overweight, the body fat is mostly placed on the neck and the rump. Other clinical signs are glucose intolerance, infertility, elevated plasma lipids and circulating insulin and an increased risk for laminitis. EMS is currently diagnosed by the clinical symptoms and a blood test for insulin and glucose. The cause of higher risk for laminitis by horses suffering from EMS is still debated upon. One theory is that the disordered glucose regulation and the

vascular changes in the lamellae are the link between EMS and laminitis. Probably the increased weight causes more tension to the deep digital flexor tendon and sets more tension to the connection of the hoof with the lamellae.[10] In the study of Carter et al, hyperinsulinaemia turned out to be a predictor for laminitis. However a better predictor for development of laminitis is the response of insulin to a challenge with oral insulin, i.m. dexamthasone or i.v. glucose.[11] Horses affected with EMS are benefit with a diet of hay, and a supplement to provide daily vitamins and minerals. When the hay is soaked in water it contains less digestible energy and non-structural carbohydrates. With this diet, insulin sensitivity in horses affected with EMS can be improved.[12]

PPID (Pituitary Pars Intermedia Dysfunction) is a disease which affects mostly older horses. Affected horses can show abnormal fat distribution, bulging supraorbital fossa, hypertrichosis, hyperhidrosis, polyuria-polydipsia, dermatophilosis, lethargy and laminitis. The diagnosis for PPID can be based on high baseline plasma ACTH concentration. In the study of Donaldson et al, it has been shown that 70% of the laminitic horses are expected to suffer from PPID. [13]

Treatment

Utrecht University Equine Clinic uses a standardized protocol for treating laminitis. Since this protocol has been introduced, horses affected with acute laminitis have recovered better. Less horses were euthanized and more horses can function again as riding horse without lameness. [14] This protocol consists of medical treatment and measurements to change management. Medical treatment consists of acepromazine (Relaquine ®), meloxicam (Metacam ®) and acetylsalicylic acid(Carbasalaat calcium sachets 600mg ®). Measurements taken to change management are: cooling the hooves, changing the diet, and in a more chronic cases special shoeing. Cooling the hooves can be done with cold water, wet sand/coco or wet bandages. The sand/coco does not only cool the hoof but it also provides comfort and support to the hoof. The horses should not be forced to walk, so it is recommended to keep the horses in a stable or small paddock. The nourishment must consist of hay and water, food like carrots, apples and concentrates must be avoided. In case of acute laminitis, if it is possible shoes should be removed and the toe should be shortened. Later in chronic cases special shoes can be used to support the hoof. In all cases of laminitis it is important to find the underlying cause. If the horse is diagnosed with PPID, IR or EMS, the horse should be treated for these diseases.[14]

Aim of this study

The purpose of this study is to evaluate the patients with laminitis that were presented to the Ambulatory Clinic of Utrecht University between 2003 and 2013. This evaluation provides more information about the risk factors for laminitis in horses, ponies and donkeys.

The hypotheses made for this study are:
-The group of patients diagnosed with laminitis by the Ambulatory Clinic of Utrecht University consists of more ponies than horses, more donkeys than horses/ponies, more female than male and more older than younger animals.
- Amongst the group of patients diagnosed with laminitis by the Ambulatory Clinic of Utrecht University PPID (older animals) and EMS (younger animals) are the most occurring underlying causes.

Despite of the many other risk factors found in other studies, this study will focus on the underlying causes, gender, age, and the differences between horses versus ponies and horses/ponies versus donkeys. Other risk factors will not be evaluated in this study, because of the limited information available from the participating patients.

Materials and methods

Collecting data

To collect the data, a computer with the veterinary software program Vetware installed on it was used. The Ambulatory Clinic of Utrecht University has stored information about owners, patients and treatments in Vetware over the past ten years. To collect data about patients diagnosed with laminitis, the following searching terms were used: 'hoefbevangen', 'bevangen', 'laminitis'. During the study other search terms were used to gain more understanding about the underlying causes. The used terms for this were: 'nageboorte', 'ret sec', 'toxinemie' and 'overbelasting'. The specified period was from 01-01-2003 to 20-11-2013. All collected information was sorted and analysed to determine the relevance of the data. Some patients could be excluded after the first view. Some dossiers contained the searching terms just to exclude laminitis as possible diagnose and the searching term 'bevangen' could also be used for patients with exertional rhabdomyolysis instead of laminitis. Automatically some important information was enclosed in the Excel files, for example gender, breed, species and birthdates. Other information had to be collect by filling in all patient numbers.
The numbers of the relevant patients were typed one by one in Vetware to extract all available information for each selected patient. The Excel file was extended with the information required for this study. In the Excel file the following information was collected:

- Recidive after the first diagnosis of laminitis
- X-rays of the third phalanx
- Information about underlying causes for laminitis found by a blood test (for example PPID or EMS)
- Clinical signs for PPID or EMS
  The clinical signs of PPID which were looked for are hypertrichosis, abnormal fat deposits, or just the notation of the suspicion of PPID.
  The clinical signs of EMS which were looked for are excessive condition, cresty neck or just the notation of the suspicion of EMS.
- Treatment

Vetware could also make a list of all patients admitted to the Ambulatory Clinic in the same period of time. Of all patients the following information was collected: species, breed an gender.

The data was exported to Excel 2010. Graphs were made in Excel. For the statistical analysis the program IBM SPSS Statics 20 was used.

Animals

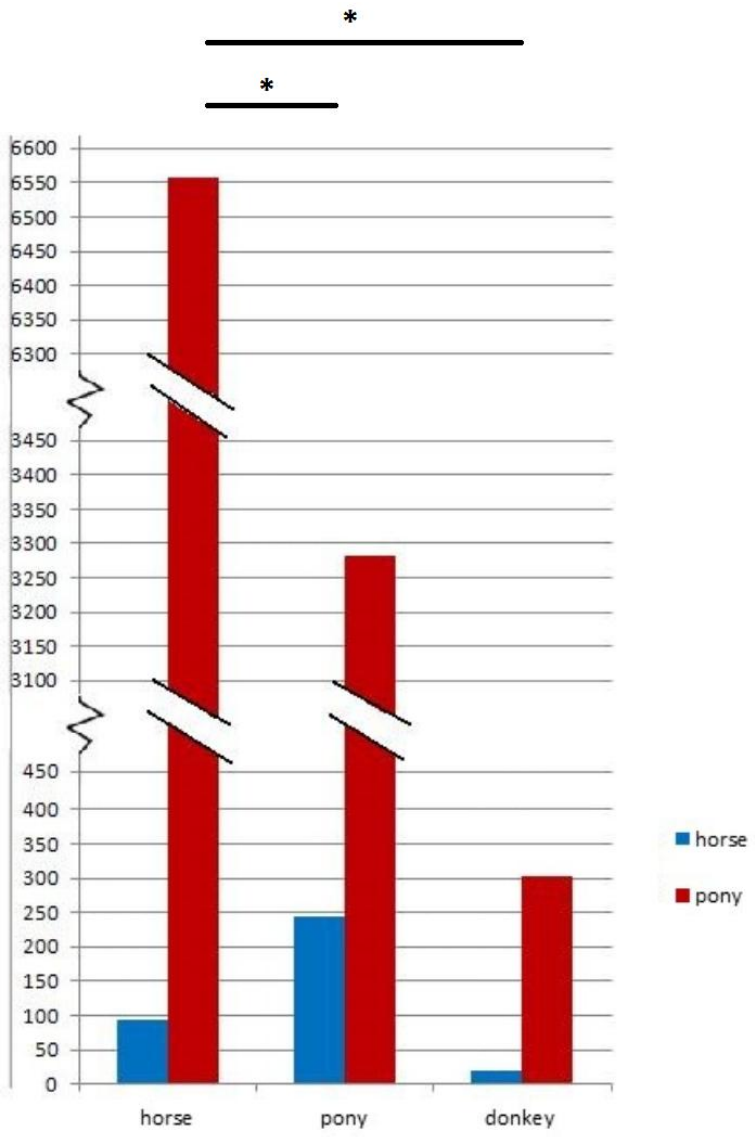
The total amount of patients visited/examined by the Ambulatory Clinic of Utrecht University from 2003 to 2013 consisted of 6557 horses, 3282 ponies and 304 donkeys. From these patients, 94 horses, 244 ponies and 19 donkeys were found with a diagnosis of laminitis. From the laminitic patients 138 were male and 227 were female.

Statistical analyses

For the graph about gender and the graph about species, the data was statistically analysed. The program used to make the calculations was IBM SPSS Statistics 20. For this data it was important to know if the differences between laminitic or non-laminitic patients of different genders and species were significant. To analyse this, the Chi square Cross tabs test has been used. When looking at the different genders, only male versus female had to be compared, however when looking at the different species, calculations had been made between horse versus pony, pony versus donkey and donkey versus horse.
This analysis supplies a certain P value. When this value was below 0.05, the difference for laminitic or non-laminitic patients was found to be significant.

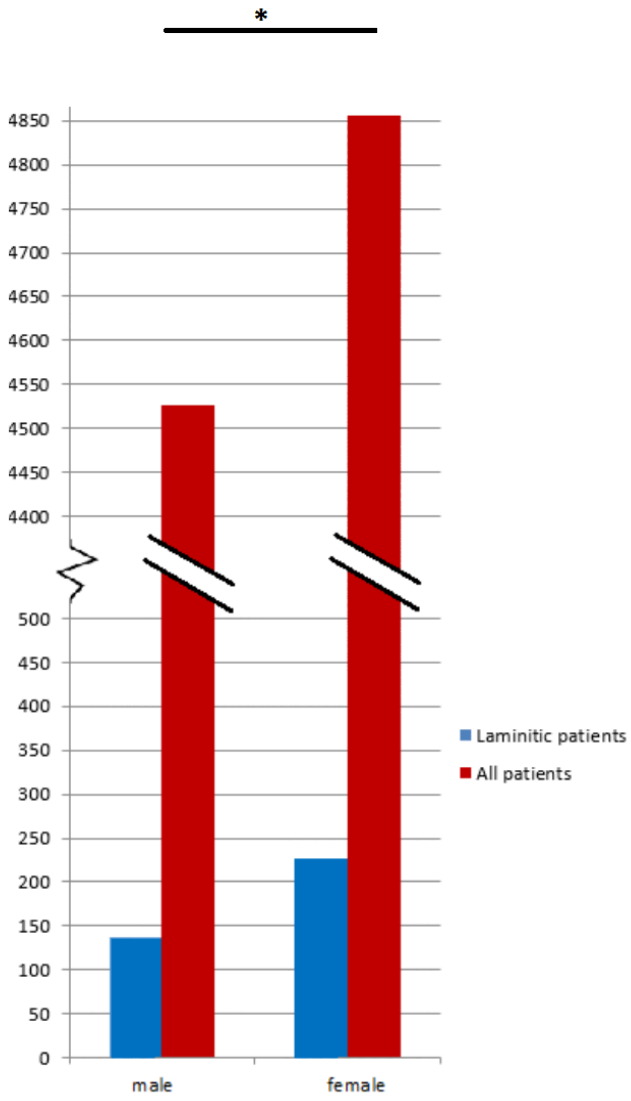
Results

Between 2003 and 2013 10,143 patients were admitted to the Ambulatory Clinic of the Utrecht University. 365 of these patients were diagnosed with laminitis. Amongst the patients diagnosed with laminitis there were 102 horses, 244 ponies and 19 donkeys. From all patients admitted to the Ambulatory Clinic 6,557 were horses, 3,282 ponies and 304 donkeys. The percentage of the total admitted patients which were diagnosed with laminitis is 1,56% of the horses, 7,43% of the ponies and 6,25% of the donkeys. (Graph 1) The difference between horses versus ponies and between horses and donkeys is significant (Chi Square cross tabs X^2= 223,94 and 36,84 P=0,00). However the difference between donkeys and ponies is not significant (Chi Square Cross tabs X^2=0,60 P=0,44)



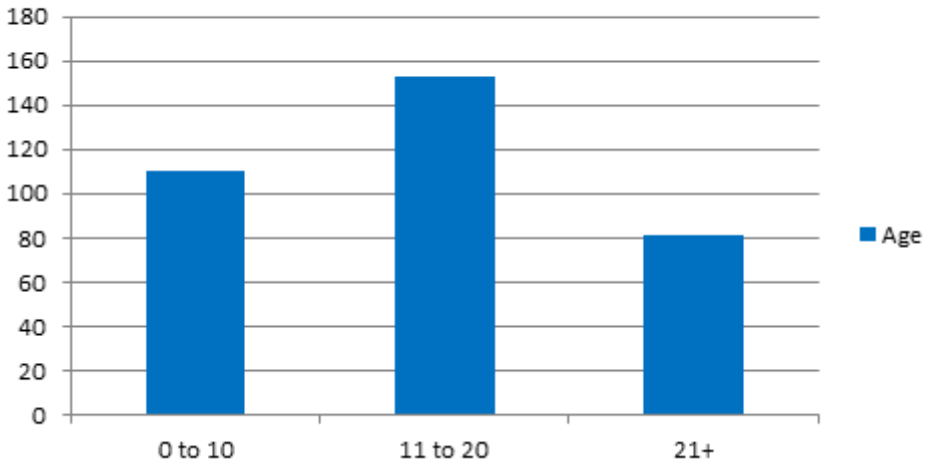
Graph 1, This bar chart shows the percentage of horses, ponies and donkeys that were diagnosed with laminitis between 2003-2013 by the Ambulatory Clinic of Utrecht University. The difference between horses versus ponies and donkeys versus horses was significant (X^2=223,94 and 36,84 P=0,00)

4,527 of all patients were male and 4,856 patients were female. 138 males and 227 females were diagnosed with laminitis. Thus 3,04% of the males and 4,67% of the females were diagnosed with laminitis. (Graph 2) This difference between males and females is significant (Chi Square Cross tabs X^2= 17,58 P=0,00)



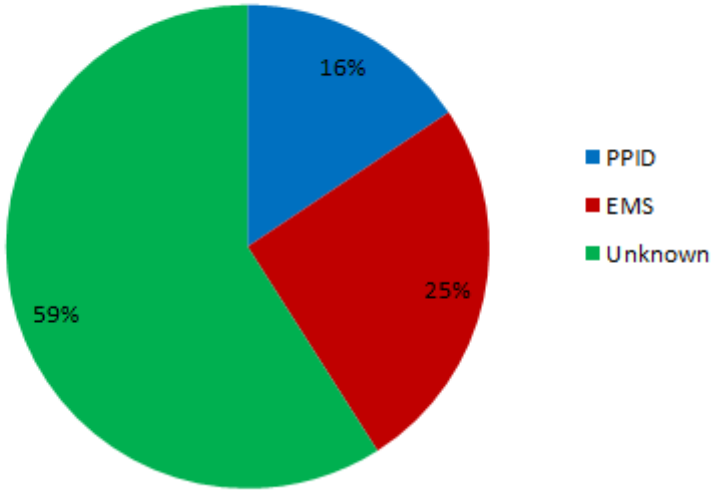
Graph 2, This bar chart shows the percentage of male and female patients diagnosed with laminitis between 2003 and 2013 by the Ambulatory Clinic of Utrecht University. The difference between male and female was significant (X^2*= 17,58 P=0,00)*

The laminitic patients in this study have an age in a range from 2 to 35 years at the moment of the first diagnosis of laminitis, with an average of 15 years. 110 patients are aged between 0 and 10, 153 are aged between 11 and 20 and 81 patients were 21 years or older. (Graph 3)



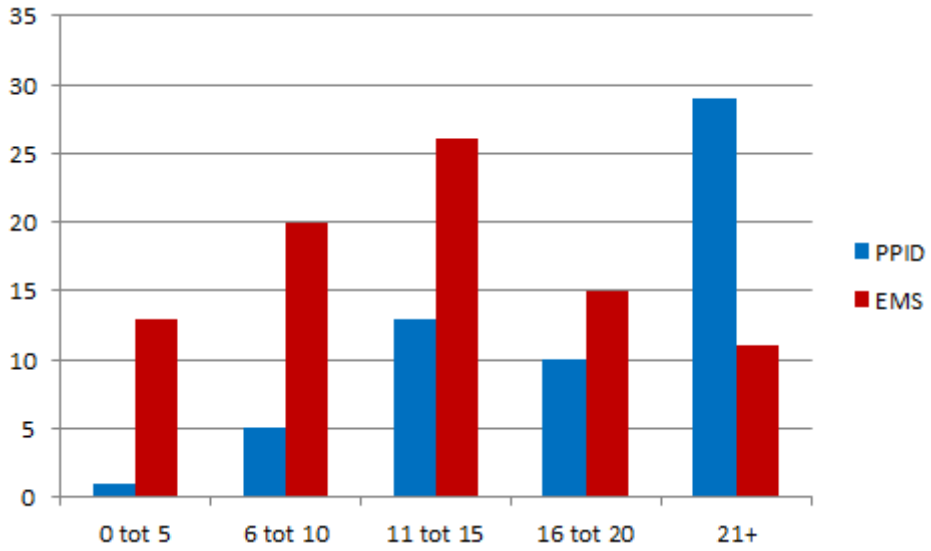
Graph 3, This bar chart shows the ages of the patients with laminitis, at the time of their first diagnosis of laminitis by the Ambulatory Clinic of Utrecht University.

For 59% of the patients diagnosed with laminitis the underlying cause for the development of laminitis is unknown. 25% of the patients were diagnosed with EMS and 16% with PPID, by blood test or by clinical signs. (Graph 4) This were respectively 219,94 and 58 horses. From the horses diagnosed with EMS, only one was diagnosed by blood test. By PPID 35 of the diagnosis were confirmed by blood test.



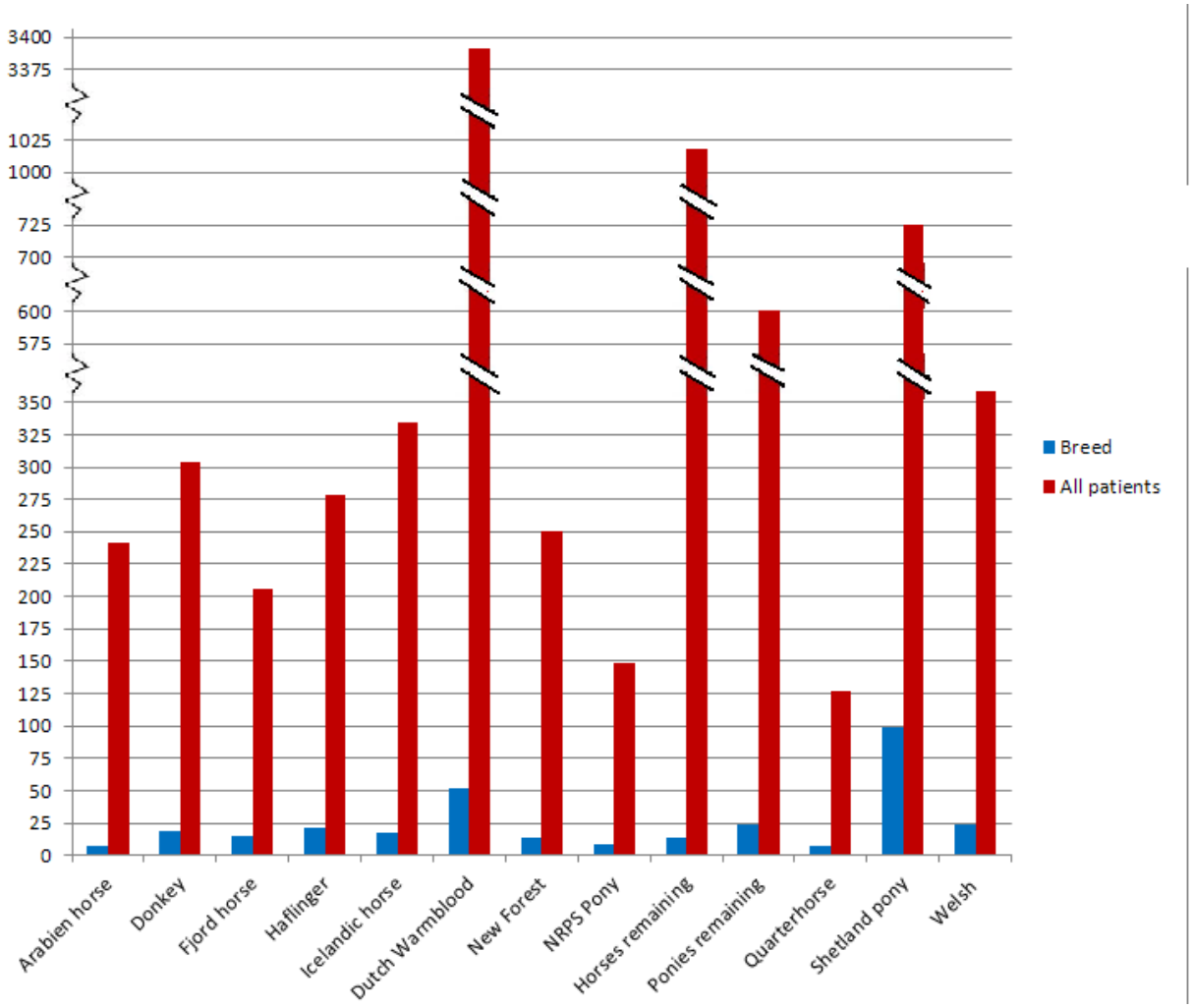
Graph 4, This pie chart shows the underlying causes (unknown or signs of PPID or EMS) for the patients diagnosed with laminitis between 2003 and 2013 by the Ambulatory Clinic of Utrecht University.

The age of the patients diagnosed with both laminitis and EMS varied from 1 up to 31 years, with a peak in the category of 11 up to 15 years. Patients diagnosed with both laminitis and EMS have an age in the range from 5 up to 31 years, with a peak in the category of 21+ years. (Graph 5)



Graph 5, This bar chart shows the ages of the patients diagnosed with laminitis between 2003 and 2013 by the Ambulatory Clinic of Utrecht University, which also were diagnosed with- or showing signs of PPID or EMS.

Of the laminitic patients 28% are Shetland ponies. This is the biggest group of laminitic patients. Compared to the total amount of admitted Shetland ponies, they are the largest group: 13.66% of the admitted Shetland ponies were diagnosed with laminitis. After the Shetland pony the largest groups are Haflinger, Fjord, Welsh pony, and Donkey with respectively 7.55%, 7.28%, 6.70% and 6.25%. The greatest part of the admitted horses to the Ambulatory Clinic were Dutch Warmbloods (36%). The Dutch Warmbloods were the second largest group of al laminitic patients (15%). When compared to the total amount of Dutch Warmbloods, the amount of Dutch Warmbloods diagnosed with laminitis is not very large, as only 1.53% of these Dutch Warmbloods have been diagnosed with laminitis. (Graph 6)



Graph 6, This bar chart shows the breeds of horses that were diagnosed with laminitis and the breed of the total number of horses admitted by the Ambulatory Clinic between 2003-2013 The breeds which have five or less horses diagnosed with laminitis were omitted.

Discussion

The data used in this study is obtained from Vetware. This means that the quality and quantity of the data depends on how much information was stored in this software program. Vetware is used to make up the invoice and information about the treatment and medication of patients can be stored. However there can be some complementary information about the condition of the patient. This study has made an attempt at finding out which underlying causes there are with the laminitis patients. Patients for whom an underlying cause could not be found were placed in the group 'Unknown'. Due to the lacking information it is possible that many horses in group 'Unknown' do suffer from either PPID or EMS, however it is not diagnosed or saved in Vetware. Therefore the groups PPID and EMS are probably underestimated.

The groups 'PPID' and 'EMS' consists of patients diagnosed with PPID and EMS by a blood test and patients which were diagnosed by the clinical signs. Many of the horses have not been bloodtested for these diseases. Due to the high costs of the blood test for EMS, in practice this test has not been used very often. In this study, only 6 horses were tested for EMS. Recently a new test for PPID has been released that works by determining ACTH baseline value in blood. Before availability of this test in October 2012, testing for PPID was more difficult. PPID has to be treated during the rest of the life of the affected horses. Some owners don't want to treat their horses for so long, therefore they are not interested in a PPID test for their horses. For the cases with clinical symptoms for PPID or EMS which have not been tested, the groups 'PPID clinical' and 'EMS clinical' are used. Horses were placed in these groups when indications for clinical symptoms have been found in Vetware. So this depends on whether or not the findings suggesting clinical signs of PPID or EMS were stored in Vetware. It has been found that the clinical signs of PPID are very characteristic, therefore in this study the horses which showed clinical signs of PPID were assumed to have PPID. For some graphs and calculations, clinical PPID/EMS and bloodtested cases of PPID/EMS were put together.

The graph of the breeds displays the distribution amongst different breeds. The breeds which have five or less horses diagnosed with laminitis were omitted. For this graph, no statistical analyses have been made, because of the small groups. This graph is placed in this article to show which breeds are more at risk to develop laminitis. Therefore this is a specification of the subdivision of horses versus ponies. The graph shows that the Shetland pony has a very high risk of developing laminitis. Other breeds which have a high risk to develop laminitis are the Welsh pony, the Haflinger and donkeys.

Menzies-gow et al did not find a significantly higher risk for ponies to develop laminitis compared to horses.[16] The findings of Menzies-gow et al are in contrast to the results of this study. However Karikoski et al had observed that there were more ponies than other breeds diagnosed with laminitis, and Wylie et al find a continuous variable for increased risk of laminitis with each cm decrease in height. In this study no association has been found between the risk of laminitis and increasing age.[9,18] In the study of Polzer and Slater was no association found between age, gender, breed or seasonality and the risk on laminitis.[19]

Interpreting graph , it is important to realise that above 21 years is quite old for horses. In the group of 21+ there are less horses because not many horses reach that age.

In this study, more females than males were suffering from laminitis. Possibly this is related to the higher risk of females having PPID as suggested in previous studies.[15] The graph

showing the gender of the patients also displays the total amount of males and females treated by the Ambulatory Clinic.
Between 2003 and 2013 only a small amount of stallions were admitted by the Ambulatory Clinic, therefore all male animals are together in one group.

In the study of Menzies-gow et al, females were at greater risk of laminitis than males.[16] Alford et al mentioned the possibility for endogenous and exogenous estrogen and estrogenic compounds to be the reason why females are at greater risk to develop laminitis.[17]

Conclusion

The first hypothesis was: *The group of patients diagnosed with laminitis by the Ambulatory Clinic of Utrecht University consists of more ponies than horses, more donkeys than horses/ponies, more female than male and more older than younger animals.* This hypothesis can be partly accepted. The results showed than more ponies than horses were affected with laminitis. Donkeys admitted with laminitis are a small group, compared with horses and ponies admitted with laminitis. However when the total amount of horses, ponies and donkeys admitted to this first opinion equine hospital was taken into account, donkeys were not the largest group, but certainly an important group. Graph 6 shows that the greatest group of breeds from the horses admitted with laminitis is the Shetland pony. Another important group is the Dutch Warmblood, as 36,1% of all admitted horses are Dutch Warmbloods.

The group of females was significantly greater than the group of males affected with laminitis. It cannot be said that the horses admitted with laminitis where older. The group of horses between 11 to 20 years are slightly larger than other age groups. The group of horses with ages between 0 and 10 years was the second largest.

The second hypothesis was: *Amongst the group of patients diagnosed with laminitis by the First opinion horse practice of Utrecht University PPID (older animals) and EMS (younger animals) are the most occurring underlying causes.* When looking at the results only, this hypothesis can be rejected. The greatest part (59%) of the underlying causes was unknown. When taking the discussion into consideration, this hypothesis should not be rejected immediately. It can be assumed that the group of PPID and EMS patients is much larger than only the number of patients which were diagnosed by bloodtesting. Furthermore graph 5 shows that with horses in age category 21+, the underlying case is more often PPID than EMS.

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