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VET **HEPATIC** FORUM

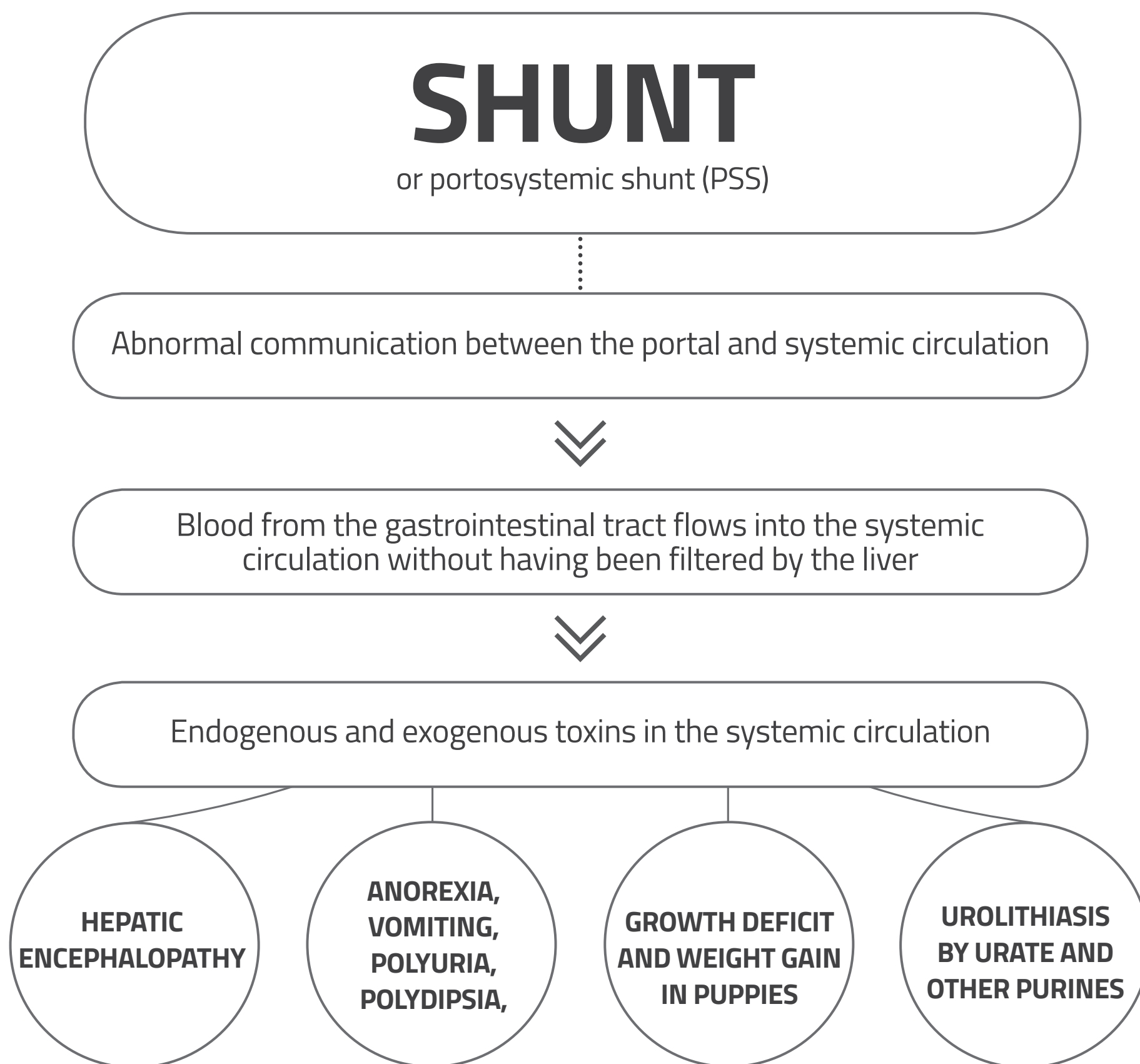


EQUILÍBRIO VETERINARY HEPATIC DIET IS EFFECTIVE IN PREVENTING THE PROGRESSION OF CLINICAL MANIFESTATIONS FROM PORTOSYSTEMIC SHUNT

1. INTRODUCTION CLINICAL VALUE

Among the main changes found in the clinical routine of the veterinarian, those that involve the malfunction of metabolically active organs such as the liver are the most challenging. The liver performs many functions essential to life and plays a major role in the metabolism of proteins, carbohydrates, and fats, making **nutritional management** one of the key points in the treatment of these patients.¹ »

» Portosystemic shunt (PSS) is characterized by abnormal communication between the portal and systemic circulation, causing blood from the gastrointestinal tract to flow into the systemic circulation without having been filtered by the liver. Thus, the systemic circulation receives endogenous and exogenous toxins, which can reach the central nervous system and cause hepatic encephalopathy (HE), besides anorexia, vomiting, polyuria, polydipsia, growth deficit and weight gain in puppies and urolithiasis by urate and other purines.^{1,2,3}



PSS **treatment** can be either surgical to correct shunt or conservative clinical^{1,4}. For both treatments (if not conservative, in pre- and post-surgical), the main point is the **patient's food management**, which aims to **prevent the occurrence of hepatic encephalopathy manifestations**.^{1,3} Nutritional treatment aims to decrease the production and absorption of toxins by the intestine (ammonia, mercaptans, short-chain fatty acids, indoles, biogenic amines), preventing them from reaching the systemic circulation. The main nutritional strategies employed focus on decreasing or modifying dietary protein, modulating the intestinal microbiota, and reducing intestinal transit time.^{3,5} Knowing the amino acid profile of the diet offered to animals with PSS also seems to be the key for a successful treatment, because the reduction in liver functions can be associated with increases in plasma concentrations of aromatic amino acids (phenylalanine, tyrosine, and tryptophan) that would not be properly removed from the portal circulation and metabolized by the liver, as well as a decrease in branched-chain amino acids (leucine, isoleucine, and valine) that would be used more by muscle and fat tissue.³

2. PURPOSE

To evaluate the effects of using a low-protein food on the amino acid profile of dogs with congenital portosystemic shunt. To evaluate the efficiency of the diet in increasing the branched-chain amino acids instead of the aromatic amino acids in the circulation. To evaluate the effects of diet on the control of clinical manifestations and biochemical variables of dogs with congenital portosystemic shunt.

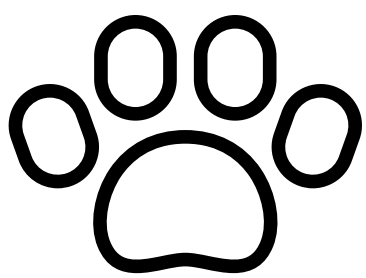


3. MATERIAL AND METHODS



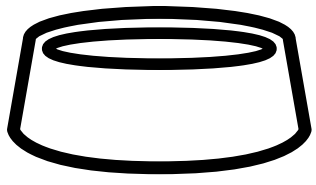
a. Study site

The study was conducted in the routine of the Medical Clinic Service of the Veterinary Hospital from the School of Veterinary Medicine and Animal Sciences of the University of São Paulo and of the Gastrovet team's Canine and Feline Gastroenterology Service, both located in the city of São Paulo - SP.



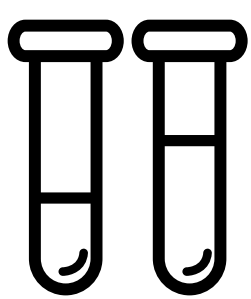
b. Selection of animals

Nine dogs of different breeds with clinical diagnosis of portosystemic shunt and nine healthy Yorkshire dogs were selected, from the Medical Clinic Service from the Veterinary Hospital of the School of Veterinary Medicine and Animal Sciences of the University of São Paulo and the Gastrovet's Canine and Feline Gastroenterology Service. For sick dogs, the criteria for inclusion in the study were having a diagnosis of portosystemic shunt, with no other concomitant conditions, being small and the owners being able to follow the protocol set for conducting the study (shunt group). The criteria for inclusion in the control group were: healthy dogs, Yorkshire breed, body condition score between 4 and 5⁶, that they accepted commercial food, and the possibility of the owners to follow the protocol set by the study.



c. Experimental diet and dietary management of animals

The animals received for **8 weeks** the supporting food **Equilíbrio Veterinary Hepatic (HE) for Dogs**, recommended for dogs with liver diseases. This food is formulated with nutritional contents that meet the recommendations of the NRC (2006)⁷ and AAFCO (2012)⁸ for adult dogs, except for the protein content, aiming at the management of liver diseases. The diet was provided free of charge to the owners of the selected animals and they were instructed to follow the recommendations of the experimental protocol. The amount of food was calculated according to the individual maintenance energy requirement (NEM) of each patient. The owners were instructed to feed the animal three times a day. The food management re-evaluations were carried out at 15-day intervals.



d. Material collection, tests performed, and statistics

Animals were assessed on day 1 (T0) and after 60 days (T60) of intake of Equilíbrio Veterinary HE Dogs diet. At both times, blood samples were collected for blood count, white blood cell count, serum biochemistry, determination of serum amino acids and ammonia. The statistical analysis of the results regarding blood counts and biochemical tests was based on a mixed model that considered standard effects of group, time and interaction and, for amino acids, only standard effects of group ($p < 0.05$).



4 RESULTS & DISCUSSION



During the 60 days of study, most of the participating animals showed **good acceptance of HE food** and maintained the muscle mass score. Regarding body weight, only one animal of the shunt group had a reduction of 200g after 60 days of treatment, whereas the **body condition score (BSC)** and the **muscle mass score (MMS) remained constant**. It is important to note that **no animal had convulsive episodes** during the experimental period.

The results of blood count, hematocrit, platelets, total protein, plasma urea, creatinine, albumin, globulin from all animals in the shunt group were within the reference values for adult dogs both at timepoint 0 and 60, with no statistical difference in time evaluation within this group.

The animals in the shunt group had serum activity of the alanine aminotransferase (ALT) enzyme greater than the reference range and the values differed from those observed in the Control group ($p=0.0253$). Likewise, the alkaline phosphatase (AP) enzyme in animals in the shunt group had higher concentrations when compared to the Control group ($p=0.0004$). It is important to highlight that although both enzymes are above the reference range for adult dogs, their concentrations did not differ between timepoints 0 and 60, showing that **there was no progression of hepatic change in the diet feeding period**.

In this study, the fasting and postprandial ammonia concentrations of the animals show that the dogs in the Control group had values within the reference range for the species, while the animals in the shunt group had hyperammonemia in both fasting and post-feeding, both values differing from the Control group ($p=0.0083$; $p=0.0036$). However, both **fasting** and »



» **postprandial ammonia values did not differ between timepoints 0 and 60** among dogs with PSS. In addition, although there was no reduction in ammonia concentrations, the **clinical manifestations of hepatic encephalopathy have been controlled.**

Regarding the serum amino acids, the shunt group had higher serum concentrations of the amino acids phenylalanine (p=0.0054), glutamate (p=0.0066), serine (p=0.0054) and tyrosine (p=0.0106) when compared to the Control group; on the other hand, the amino acid alanine (p=0.0280), the Fischer ratio (p=0.0093) and the serum concentration ratio of branched-chain amino acids and tyrosine (p=0.0243) were higher in the Control group.

Brunetto and colleagues⁹ pointed out that the increase in aromatic amino acids (phenylalanine, tyrosine, and tryptophan) in relation to branched-chain amino acids (leucine, isoleucine, and valine) can be one of the factors triggering the development of hepatic encephalopathy. Additionally, in 1976, Soeters and colleagues¹⁰ reported that the molar ratio between the branched-chain amino acids and aromatic amino acids is important for evaluating liver functions, the severity of their dysfunctions and protein nutrition status, and that Fischer ratio decreases as chronic hepatitis progress to cirrhosis.

$$\text{FISCHER'S RATIO} = \frac{(\text{Leucine} + \text{Isoleucine} + \text{Valine})}{(\text{Phenylalanine} + \text{Tyrrosine})}$$

In this study, Fischer ratio was calculated and the animals in the shunt group had lower values (p=0.0093) when compared to the Control group. However, **the Fischer ratio of animals with PSS did not differ between timepoints 0 and 60, which means that the disease may not have progressed in that period with the intake of the diet.**



5. CONCLUSIONS

Based on the results found in this study: with the maintenance of the serum concentrations of the amino acid, the Fischer ratio as well as the ratio of branched-chain amino acid ratio and tyrosine, we can conclude that the nutritional management of dogs with portosystemic shunt in the **Equilíbrio Veterinary HE diet** was efficient in preventing disease progression and controlling clinical manifestations.



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