



## THERAPEUTIC EVALUATION OF HYDROXY ETHYL STARCH AND AMINO ACID INFUSION IN MANAGEMENT OF HYPOALBUMINEMIA IN DOGS WITH HEPATIC DISORDERS

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### ABSTRACT

Hypoalbuminemia in dogs is one of the common biochemical finding in day to day small animal canine practice though the causes of hypoalbuminemia are very many, hepatic disorders is one of the most common cause. In view of this twelve dogs with hepatic disorders selected based on history, clinical signs, hematology, biochemistry, urinalysis, faecal sample examination and ultrasonography. Clinical cases with an albumin concentration of less than 2g/dl were selected for the study and were divided into Group I and Group II each comprising of six animals and they were treated with Hetastarch 6% (Hestar-450®) and amino acid infusion (Hermin®) respectively for three days. The therapeutic efficacy was assessed by recording clinical improvement, albumin and total protein concentrations. There was an increase in both total serum protein and serum albumin value on 7<sup>th</sup> day when compared to day zero in Group I and Group II but the increase was significant only in Group II. Group II responded better based on the fact that percent increase in total protein and serum albumin was more when compared to Group I and it was also evidenced by the resolution of clinical signs namely ascites, hind leg edema and anorexia.

**KEY WORDS:** Hetastarch, hypoalbuminemia, amino acid infusion.

### INTRODUCTION

Liver disorders are encountered in dogs of all age groups accounting for three per cent of all diseases (Hardy, 1983). As the cellular guardian of gastrointestinal tract, the liver is pivotal in its regulation, digestion and metabolism. Liver plays a central role in diverse array of processes, including metabolism, detoxification, storage of trace minerals and immunogenic surveillance. Hypoalbuminemia is often a consequence of critical illnesses, sepsis, systemic inflammatory response syndrome (SIRS), burns and end stage hepatic failure. However, serum hypoalbuminemia is most often seen in chronic hepatic disorders (Mazzafarro *et al.*, 2002). Although colloids are now being used more commonly for the treatment of shock in veterinary medicine, their use in hypoalbuminemia due to hepatic disorders has not been investigated. Hetastarch is extremely effective in increasing plasma volume and colloid oncotic pressure in people and dogs. However, hetastarch has been shown to be equal to or superior to albumin in its ability to increase colloid oncotic pressure in hypoalbuminemic people and dogs (Rackow *et al.*, 1983). The use of amino acid infusion in hypoalbuminemia due to hepatic disorder in dogs has not been documented.

### MATERIALS & METHODS

Clinical cases presented to Veterinary college hospital, Bangalore were used for the study. Twelve dogs with non

infectious hepatic disorders selected based on history, clinical signs hematology, biochemistry, ultrasonography and with an albumin concentration of less than 2g/dl were selected for the study.

**Hematology:** Blood collected in EDTA vacutainers were analyzed within 30 min of collection. Hemoglobin, packed cell volume, total erythrocyte count, total leucocyte count, differential leucocyte count and platelet count was determined using automated blood cell analyser and the values were recorded.

**Biochemical analysis:** Blood collected in plain clot activator tubes was used for separation of serum. Serum was analyzed for biochemical parameters namely Creatinine, ALT, AST, ALP, GGT, Total protein, Total bilirubin, Albumin and Globulin within six hours.

**Urinalysis:** Urine sample was collected by catheterization of bladder and was analyzed using urinalysis reagent strips for glucose, bilirubin, ketone bodies, specific gravity, blood, pH, protein, urobilinogen, nitrites and leukocytes.

**Faecal sample examination:** Faecal swab was examined for parasitic ova after application of coverslip under low power (10X) of microscope.

**Grading of ascites:** The "Simple Descriptive Scale" method for grading ascites was used and the dogs were categorized into four groups as mentioned below (Moore *et al.*, 2003) (Table 1).

Dogs hepatic disorders associated with hypoalbuminemia

Category	Description	Score
Grade 1	Mild ; only visible on ultrasound and computed tomography	+
Grade 2	Detectable with flank bulging and shifting dullness	++
Grade 3	Directly visible, confirmed by fluid wave/thrill	+++
Grade 4	Directly visible with prominent abdominal veins, mild degree of respiratory distress	++++

**Grading of hind leg edema:** Grading of hind leg edema was done based on the dent depth and rebound time and categorized into four groups as mentioned below (Hogan, 2007) (Table 2) .

Category	Description	Score
Grade 1	Slight pitting, no visible distortion, disappears rapidly	+
Grade 2	Somewhat deeper pit, no readably detectable distortion, disappears in 10-25 seconds	++
Grade 3	Pit is noticeably deep. May last more than a minute. Dependent extremity looks swollen and fuller.	+++
Grade 4	Pit is very deep. Lasts for 2-5 minutes. Dependent extremity is grossly distorted.	++++

**Grading of anorexia:** The Simple Descriptive Scale method for grading anorexia was used and the dogs were categorized into five groups as mentioned below (Hatcher *et al.*, 2010) (Table 3).

Category	Description	Score
Grade 1	Loss of appetite with alteration in eating habits	+
Grade 2	Loss of appetite without alteration in eating habits	++
Grade 3	Oral intake altered without weight loss or malnutrition, fluid intake normal	+++
Grade 4	Associated with weight loss or malnutrition, inadequate fluid intake.	++++
Grade 5	Life threatening consequences; urgent intervention indicated	+++++

**Therapeutic trials:** Twelve dogs with hepatic disorders selected based on history, clinical signs, hematology, biochemistry, ultrasonography with an albumin concentration of less than 2g/dl were selected for the study and was divided into Group I and Group II of 6 animals each. The efficacy of the treatment regimens was assessed by recording clinical improvement albumin, and total protein concentrations.

**GROUP I:** Animals of Group I were treated with Hetastarch 6% (Hestar-450®) at 10ml/kg BW/day for 3 days (Smiley and Garvey, 1994).

**GROUP II:** Animals of Group II were treated with amino acid infusion (Hermin®) at 720mg amino acids/kg BW/day for 3 days (Ferrannini *et al.*, 1988).

Albumin, Globulin and Total protein concentrations were determined at 1<sup>st</sup> day, 2<sup>nd</sup> day, 3<sup>rd</sup> day, and 7<sup>th</sup> day in all treatment groups.

**Statistical analysis:** Descriptive statistics for the different data were analysed as per Snedecor and Cochran procedures (1989).

**RESULTS**

**Hematology:** Decrease in hemoglobin, packed cell volume, total erythrocyte count and platelet count were noticed in dogs with hepatic disorder associated with hypoalbuminemia whereas total leukocyte count was in the normal range.

**Serum biochemistry:** In the present study, increase in the activities of enzymes like ALT, AST, ALP and GGT were noticed whereas decrease in the levels of total protein and albumin were observed. All the dogs had blood urea nitrogen and creatinine values were well within the normal range.



Fig 1



Fig 2

**FIGURE 1–2.** 1. Grade 4 ascites: Directly visible with prominent abdominal veins, mild degree of respiratory distress. 2. Grade 3 hind leg edema: Pit is noticeably deep. May last more than a minute. Dependent extremity looks swollen and fuller.

**Urinalysis:** Out of the twelve cases none of the urine sample was positive for glucose, bilirubin, ketone bodies, blood protein, nitrites and leucocytes.

**Fecal sample examination:** Fecal examination of the twelve cases diagnosed with hepatic disorders associated with hypoalbuminemia did not show any ova/cyst.

#### THERAPEUTIC TRIALS

**Group I :** Total serum protein (g/dl) and serum albumin (g/dl) value were recorded on the day before treatment and on 1<sup>st</sup> day, 2<sup>nd</sup> day, 3<sup>rd</sup> day and 7<sup>th</sup> day of the therapeutic trial.

From Table 4 it can be observed that the total protein value increased from 4.317±0.193 g/dl to 4.517±0.151 g/dl by the end of 7<sup>th</sup> day. From Table 5 it is evident that serum albumin value increased from 1.433±0.102 g/dl to 1.617±0.116 g/dl by the end of 7<sup>th</sup> day. It is evident from Table 7 that the percent increase in the total protein and serum albumin value in Group I was 4.63% and 12 % respectively. From Table 6 it is evident that the mean scores of ascites, anorexia, and hind leg edema in dogs with hepatic disorders associated with hypoalbuminemia on day zero in Group I were 3, 1.6, and 1.6 respectively and that of 7<sup>th</sup> day was 2, 1.16, and 1.16 respectively.

**TABLE 4:** Mean total serum protein (g/dl) value in dogs with hepatic disorders associated with hypoalbuminemia in the treatment groups Group I and Group II

Days	Treatment Regimen	
	Group I	Group II
0	4.317±0.193 <sup>aA</sup>	5.10±0.212 <sup>aB</sup>
1	4.333±0.197 <sup>aA</sup>	5.70±0.357 <sup>abB</sup>
2	4.367±0.174 <sup>aA</sup>	5.783±0.390 <sup>abB</sup>
3	4.433±0.166 <sup>aA</sup>	5.967±0.390 <sup>abB</sup>
7	4.517±0.151 <sup>aA</sup>	6.167±0.424 <sup>abB</sup>

Note: Means bearing same superscripts (small letters row-wise and Capital letters column wise) are not significantly different ( $P < 0.05$ ).

**TABLE 5:** Mean serum albumin (g/dl) value in dogs with hepatic disorders associated with hypoalbuminemia in the treatment groups Group I and Group II

Days	Treatment Regimen	
	Group I	Group II
0	1.433±0.102 <sup>aA</sup>	1.15±0.117 <sup>aA</sup>
1	1.483±0.101 <sup>aA</sup>	1.30±0.121 <sup>aA</sup>
2	1.500±0.112 <sup>aAB</sup>	1.41±0.135 <sup>abA</sup>
3	1.592±0.108 <sup>aA</sup>	1.65±0.156 <sup>abA</sup>
7	1.617±0.116 <sup>aA</sup>	2.05±0.152 <sup>abB</sup>

Note: Means bearing same superscripts (small letters row-wise and Capital letters column wise) are not significantly different ( $P < 0.05$ ).

**TABLE 6:** Mean scores of Ascites, Anorexia, and Hind leg edema in dogs with hepatic disorders associated with hypoalbuminemia in the treatment groups of Group I and Group II

Clinical sign	Zero day		3 <sup>rd</sup> day		7 <sup>th</sup> day	
	Group I	Group II	Group I	Group II	Group I	Group II
Ascites	3	3	2.16	1.6	2	1.3
Anorexia	1.6	1.83	1.5	1.16	1.16	1.0
Hind leg edema	1.6	1.6	1.3	1.0	1.16	0.83

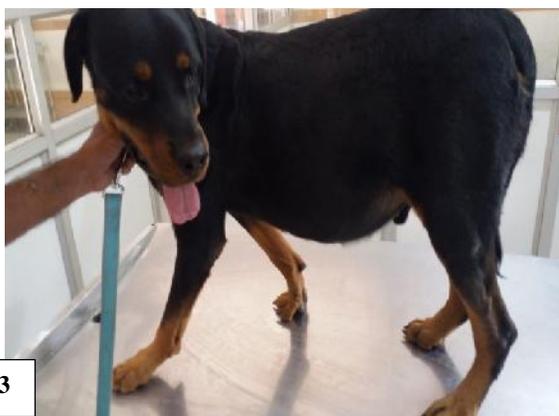
**TABLE 7:** Per cent increase in values of total serum protein and serum albumin in different treatment groups

Category	Total protein	Albumin
Group I	4.63%	12%
Group II	20.9%	78.2%

**Group II :** By the end of 7<sup>th</sup> day the mean ± SE total serum protein and serum albumin value was recorded to be 6.167±0.424 g/dl and 2.05±0.152 g/dl respectively which indicated that there is an increase when compared to zero day and was statistically significant ( $P < 0.05$ ) (Table 4 and 5).

It is evident from Table 7 that the percent increase in the total protein and serum albumin value in Group II was 20.9% and 78.2 % respectively.

From Table 6 it is evident that the mean scores of ascites, anorexia, and hind leg edema in dogs with hepatic disorders associated with hypoalbuminemia on day zero in Group II were 3, 1.83, and 1.6 respectively and that of 7<sup>th</sup> day was 1.3, 1.0, and 0.83 respectively.



**Fig 3**



**Fig 4**

**FIGURE 3-4.** 3. A four year old Rottweiler with hepatic disorder associated with hypoalbuminemia showing distended abdomen (ascites) and dull (Before therapy). 4. Complete reduction of ascites and active by 7<sup>th</sup> day after therapy with amino acid infusion.

### DISCUSSION

As indicated by the urinalysis, these animals did not have an apparent renal disease and further the results also indicated that there was no hepatic disorder associated with pigment metabolism. Faecal examination of the twelve cases did not show any ova/cyst which indicated that there was no parasitic infestation contributing to hypoalbuminemia. Based on all this, in the present study the twelve cases included were confirmed as hepatic disorder associated with hypoalbuminemia.

### THERAPEUTIC TRIALS

**Group I:** Dogs with hepatic disorders associated with hypoalbuminemia in Group I were treated with Hetastarch (Hestar-450®) for three days. It is evident from Table 4 and 5 that there is an apparent increase in both total serum protein and serum albumin value on 7<sup>th</sup> day, when compared to day zero. However, the increase was not statistically significant. The findings of the present study is in concurrence with the findings of Smiley and Garvey (1994) who also reported that there is no significant increase in the total serum protein and serum albumin value. Though there was resolution of ascites and hind leg edema secondary to hypoalbuminemia to some degree in all the dogs of Group I. This may be attributed to increase in colloid oncotic pressure because hetastarch is equal to or superior to albumin in its ability to increase colloid oncotic pressure in hypooncotic people and dogs (Rackow *et al.*, 1983) rather than increase in albumin level through synthesis.

**Group II:** Dogs with hepatic disorders associated with hypoalbuminemia in Group II were treated with amino acid infusion (Hermin®) for three days. By the end of 7<sup>th</sup> day the mean  $\pm$  SE total serum protein and serum albumin value was recorded to be  $6.167 \pm 0.424$  g/dl and  $2.05 \pm 0.152$  g/dl respectively which indicated that there is an increase when compared to zero days and was statistically significant ( $P < 0.05$ ). The findings of the present study is in accordance with the findings of Skillman *et al.* (1976) who reported that there is significant increase in the synthesis of albumin and total serum protein in patients given amino acid infusion. The increase in albumin synthesis may be due to the rapid response of the liver to protein deprivation and protein repletion (Kirsch *et al.*,

1968, Waterlow *et al.*, 1968, Sidransky *et al.*, 1968 and Rothschild *et al.*, 1969). In human subjects it has been hypothesized that the increase in albumin synthesis may be due the increase supply of precursor amino acids or a specific effect of one or more amino acids. However, there is paucity of information to the stimulant action of albumin synthesis after treatment with amino acid infusion in dogs with hepatic disorder associated with hypoalbuminemia.

Group II responded better based on the fact that percent increase in total protein and serum albumin was more when compared to other Group I. It was also evidenced by the mean scores of ascites, hind leg edema and anorexia.

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