

Clinical Findings and Blood Parameters in Extrahepatic Portosystemic Shunt in Dogs

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Abstract: This study was performed to evaluate the clinical findings, haematological and biochemical changes in experimentally induced extrahepatic portosystemic shunts in dogs. Six, different aged, weighing 20-25 kg, cross-bred dogs from both sexes were used in the study. Before the operation, the dogs were premedicated with 0.04 mg kg⁻¹ of atropine sulphate and 2 mg kg⁻¹ of xylazine hydrochloride (Rompun, 23.32 mg mL⁻¹, Bayer) then anaesthesia was induced with 15 mg kg⁻¹ of ketamine hydrochloride (Ketalar 50 mg mL⁻¹, Eczacıbaşı). A 4-6 cm graft obtained from the V. jugularis was anastomosed between the V. cava caudalis and the V. porta with a 7/0 propylene suture. The dogs were observed for 3 months. Blood samples were collected for blood count and serum ALT, AST, ALP, BUN and SBA at preoperation and in 1st, 2nd and 3rd months of postoperation as well as 1 month after the ligation of the shunts. In the clinical examinations, poor coat, depression, weight loss and holding the head down were observed; microcytic anaemia was determined and ALT, AST, ALP activities and SBA concentration increased while BUN concentration decreased. The biochemical parameters except SBA were returned to the preoperative values. In conclusion, further and detailed studies are necessary to apply this study to practice.

Key words: Dog, extrahepatic portosystemic shunt

INTRODUCTION

Portosystemic Shunts (PSS), carrying portal blood into systemic circulation bypassing the liver, are vascular connections that are located between the portal and systemic vein. In the presence of PSS, Hepatic Encephalopathy (HE) is seen due to enteric toxins (ammonia, mercaptans, short chain fatty acids and gamma-amino butyric acid) that could not be detoxified. Urolithiasis is seen in 50 % of animals due to increased excretion of ammonia and uric acid via urine especially in congenital PSS as an important complication^[1].

Portosystemic shunts can be congenital or acquired; single or multiple; intra or extrahepatic. Congenital PSS which are abnormal embryonic vessels have been reported in cats, dogs, horses, cows and humans^[2-4]. Intrahepatic or mostly extrahepatic PSS are single and they do not cause portal hypertension^[2,3,5]. Congenital PSS are usually seen in animals younger than 1-2 year-old^[6-8]. It has also been reported in older animals (4, 7, 10 years old). Genetic sources of congenital PSS are unknown^[1].

Acquired PPS are typically formed as multiple extrahepatic shunts providing connection between portal system and V. cava caudalis due to portal hypertension which results from chronic hepatitis, cirrhosis, idiopathic fibrosis. They are rudimentary, non-functional microvascular structures^[3,9].

Significant changes in haematological and biochemical parameters may not be observed in the dogs with congenital PPS. However, slight changes may occur and signs of hepatocellular dysfunction can be individually observed. In haematological examinations, microcytosis and non-regenerative anaemia can be observed^[1,3,7,10,11].

If PPS is suspected according to history, physical examination, laboratory and radiological results, detailed radiographic examination or experimental laparotomy can be performed for the diagnosis^[12-17]. However, it is not always possible to detect PPS due to difference between pressure in shunts vessels and portal circulation by angiography performed during experimental laparotomy^[7].

Medical therapies of PSS are symptomatic and direct to controlling HE symptoms. Fluid therapy is used to

remove the dehydration, maintain electrolyte and acid-base balance and blood glucose level. Enema was used for removing enteric toxins as well as low protein diet, lactose, neomycin or metronidazole therapy^[1]. The response to this therapy is positive in a short time and animals become clinically normal. If surgical therapies of PSS were not possible due to economical reasons or not preferred by the owners, animals can be medically controlled for 2 to 4 years. In long-term, animals clinically become abnormal. Some neurological symptoms occur; liver atrophy and changes in metabolism of carbohydrate, lipid and protein are permanent^[1,2].

Portosystemic shunts can be surgically cured by ligation of vessels. Ligation of extrahepatic PSS is easier than intrahepatic PSS. Medical support is necessary before the surgery. PSS can be ligated totally or partially^[2,3,18,19]. Some authors indicated that partial ligation of PSS does not make any change in clinical and laboratory results compared to those of preoperative; therefore, postoperative recurrence rate is high and requires reoperation or additional medical therapy. On the other hand, total ligation of PSS resulted in high success^[19,21]. Many authors indicated that it should be decided during the operation to choose the method according to pressure of portal vessel; while total ligation can be preferred in single cases, partial ligation can be chosen for portal hypertension, thus risk of complications could be reduced^[3,21,22].

Some authors indicated that epileptic seizure can be progressed in some animals after ligation of PSS and these epileptic seizures are not related to hyperammonemia, hypoxia, or hypoglycaemia^[23,24].

The purpose of this study was to diagnose the PSS and HE cases due to PSS by clinical, haematological and biochemical findings, to gain experience in surgical therapy of PSS and to apply these experiences in clinical practice.

MATERIALS AND METHODS

Materials of this experimental study consisted of 6 cross-breed dogs with different ages, sexes and weights (ranged from 20 to 25 kg). This study was approved by Ethics Committee of University of Ankara, Faculty of Veterinary Medicine.

Premedication was performed by subcutaneous injection of atropine sulphate (0.04 mg kg⁻¹) and then intravenous xylazine hydrochloride (2 mg kg⁻¹) injection following 12 h fasting. Electrocardiography was monitored and an arterial catheter was introduced to A. femoralis to monitor blood pressure. Moreover, an intra-catheter was introduced to V. cephalica for serum infusion and anaesthetic application. Then, anaesthesia was induced by ketamin hydrochloride (15 mg kg⁻¹).

The dogs in lateral recumbency underwent surgical procedure; V. jugularis was dissected by two parallel skin incisions of 6 to 8 cm in length and subcutaneous mucosa was dissected. A 4-6 cm blood vessel section was removed after ligation of V. jugularis at proximal and distal sides with silk suture material (No. 0). Then the incision was closed up and the patient was positioned in dorsal recumbency for cranial laparotomy.

Resected V. jugularis (graft) was kept in serum physiologic after cleaning of conjunctive tissue until performing the anastomosis procedure.

First the portal vein, then V. cava caudalis was dissected in 4 to 5 cm length following intravenous heparin injection of 100 IU kg⁻¹ to prevent thrombosis during the anastomosis procedure. One end of the graft that prepared previously was anastomosed into V. porta by 7/0 propylene suture. The open end of graft was clamped and blood flow from V. porta into graft was observed. The other open end of graft was anastomosed into V. cava caudalis by 7/0 propylene suture.

Portal vein at distal part was occluded by vessel pens, then 15 to 20 mL contrast agent, urografin, was injected into the proximal part of occlusion. Then X-ray of this region was taken to confirm whether the anastomosis is working or not. Postoperative medication was performed.

The dogs were observed for 3 months. Blood samples were collected for haematological and biochemical analysis at monthly intervals. Sera were separated and stored at -20°C until analysis. Serum alanine aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline Phosphatase (ALP), Blood Urea Nitrogen (BUN) and Bile Acids (SBA) levels were determined by a spectrophotometer using commercial kits. Patients were followed clinically for HE symptoms.

At the end of 3 months, patients underwent laparotomy, then the shunt was totally ligated by silk suture (No. 0). After ligation portal pressure was observed. Animals were observed for a month during post operative care and at the end of the month blood samples were collected for the haematological and biochemical analysis that mentioned above. Then the animals were sent to a dog care house belonging to the municipality.

Data were analysed by SPSS 9.0 version for Windows. The differences with regard to time were determined with paired t test. Data were expressed as means±SEMs

RESULTS

The dogs in the study tolerated the anaesthetic and surgical protocols very well. V. jugularis as graft material was contracted just after resection of it.

Table 1: Haematological changes in experimentally induced portosystemic shunts in dogs

Parameters	Sampling times (months)				
	Preoperative		Postoperative		Following shunt ligation
	0	1	2	3	1
RBC ($10^6 \mu\text{L}^{-1}$)	6.16±0.31	5.62±0.12	3.71±0.43	3.14±0.41	5.92±0.55
MCV (μm^3)	66.83±2.39	61.20±1.47	47.66±6.15	35.05±6.93	62.00±1.81
HCT (%)	41.95±1.36	38.45±1.18	24.26±2.97	17.46±1.50	38.88±4.14
WBC ($10^3 \mu\text{L}^{-1}$)	13.94±0.94	13.72±1.46	9.38±1.30	9.20±1.08	8.87±1.00
HB (g dL^{-1})	14.28±0.63	12.48±0.68	7.45±0.68	6.40±0.29	11.80±2.47

RBC: (1-2), (2-4), (3-4): $p < 0.05$; (0-2), (1-3): $p < 0.01$; (0-3): $p < 0.001$, MCV: (3-4): $p < 0.05$; (0-1), (0-3), (1-3): $p < 0.01$, HCT: (0-1), (2-3): $p < 0.05$; (1-2), (3-4): $p < 0.01$; (0-2), (0-3) (1-3): $p < 0.001$, WBC: (0-2), (0-3), (0-4): $p < 0.05$, HB: (1-2), (1-3): $p < 0.01$; (0-2), (0-3): $p < 0.001$

Table 2: Biochemical changes in experimentally induced portosystemic shunts in dogs

Parameters	Sampling times (months)				
	Preoperative		Postoperative		Following shunt ligation
	0	1	2	3	1
ALT (IU L^{-1})	38.70±8.80	115.48±12.46	192.78±14.96	264.78±15.28	77.32±17.49
AST (IU L^{-1})	30.53±12.48	113.45±12.02	203.05±25.66	239.85±11.59	96.63±23.77
ALP (IU L^{-1})	64.61±8.01	158.05±30.29	243.52±31.97	338.03±103.28	140.57±24.28
BUN (mg dL^{-1})	60.57±11.66	48.08±8.24	36.53±6.54	25.39±4.18	26.85±2.03
SBA ($\mu\text{mol L}^{-1}$)	4.95±0.58	25.65±7.81	70.08±27.84	94.75±26.49	16.73±5.23

ALT: (2-3) : $p < 0.05$; (1-2): $p < 0.01$; (0-1,2,3), (1-3), (3-4): $p < 0.001$, AST: (0-4) : $p < 0.05$; (0-1), (1-2), (2-4): $p < 0.01$; (0-2,3), (1-3), (3-4): $p < 0.001$, ALP: (0-1,3,4) : $p < 0.05$; (0-2), (1-2), (2-4): $p < 0.01$, BUN: (0-1,4), (1-2), (1-4), (2-3) : $p < 0.05$; (0-2,3,4), (1-3): $p < 0.01$, SBA: (0-3), (2-3) : $p < 0.05$

Therefore, it caused problems during the anastomosis. When grafts were shorter (dogs 1 and 4) or longer (dog 6), blood flow was affected negatively. There was no complication in the sections of V. jugularis that graft materials had been taken.

During the anastomosis between V. cava caudalis and V. porta, there was no bleeding, vessel rupture, or leaking in anastomosis line. There was also no post operative complication.

The dogs clinically followed up for HE symptoms and atypical symptoms like depression, weight loss, head down and hair abnormalities were observed.

During the shunt ligation, graft material decreased in all cases. Portal pressure was between 8.5-10.5 mmHg before ligation and 9-11.5 mmHg after total ligation of the shunts which were the reference range for dogs.

Statistically significant differences were determined between preoperative and post operative measurements conducted in the 2nd and the 3rd months while no statistically significant differences were observed between the preoperative measurements and the measurements after the 1st month of shunt ligation in haematological parameters (Table 1). Statistically significant differences were determined in biochemical parameters between preoperative and all of the post operative measurements as well as the measurements after the 1st month of shunt ligation (Table 2).

DISCUSSION

Atypical clinical symptoms such as abnormal hair coat, depression, lethargy, weight loss, head down^[1-9] were observed in the dogs in the middle of the 2nd month during 3 months of post operative period. Symptoms related to neurological system were not observed as indicated earlier^[1].

Johnson et al.^[1] reported that haematological and biochemical findings of dogs with congenital PPS are usually insignificant, however, haematological microcytosis and non-regenerative anaemia as well as slight changes in biochemical parameters as the signs of hepatocellular dysfunctions can be observed individually. In the present study, blood index reduced gradually with the time thus microcytic and hypochromic anaemia occurred.

In general, if the activities of aminotransferases are not two fold higher than the reference value, the increases in the activity of these enzymes are not accepted as significant^[12,13]. In the present study, ALT, AST and ALP activities were within the reference range in the preoperative period; however, their activity were increased almost double in the first month of post operative period and continued to increase in the second and third months. After shunt ligation, activity of these enzymes decreased, but they were still higher than the

normal levels. The increases in the activity of these enzymes in serum may result from the liver damage. It was reported that the increased enzyme activities due to the liver damage returned to normal levels within 2-3 weeks following the removal of the reason of the damage^[13].

Fasting SBA levels were significantly increased in post operative period; therefore, post prandial SBA level was not determined. After shunt ligation, SBA level was decreased but it was still higher than normal. Serum bile acids measurement in human and animals is a very reliable test for liver function and an indicator test when ALT and AST activities are high^[12,13,15].

Surgical therapies of PSS include ligation of shunt vessels. Shunts can be ligated partially or totally^[2,3,18,19,22,24]. Hunt^[24] reported that the success was high in total ligation. In this study, shunts were ligated totally and no complication after ligation procedure was observed. Although liver enzymes were increased, lack of any increase in portal pressure may show that experimental shunts in dogs for 3 months did not cause a severe damage in the liver. However, it is possible to speculate that the longer duration of the shunt may result in severe liver damage.

Radiological diagnosis of PSS requires experience and equipment; therefore, in suspicious cases laparotomy and intra operative venography can be applied directly^[6]. In this study, intra operative portography was successful in half of the cases.

As a result, experience was gained on both diagnostic methods and surgical therapy in PSS treatment that are not well known in Turkey. Since the PSS can be seen without typical symptoms, in PSS suspicious cases experimental laparotomy should be considered. Therefore, further studies may be needed to gain more experience and to apply these experience on clinical practice.

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