Assessing the Efficacy of Urosdeoxycholic Acid in Different Therapeutic Approaches for Canine Hepatic Dysfunction: A Comparative Study

Comment [AL1]: Evaluating the Effectiveness of Urosdeoxycholic Acid in Various Treatment Approaches for Canine Liver Dysfunction: A Comparative Study

Abstract

Comment [AL2]: Need grammatical correction

Liver dysfunction in dogs presents significant challenges to veterinary practice, with clinical symptoms ranging from modest to severe. For the development of optimize treatment strategies, this study was conducted atCollege of Veterinary and Animal Sciences, G.B.P.U.A. & T, Pantnagar U.S. Nagar (Uttarakhand) from September 2021 to April 2022. in dogs diagnosed with hepatic dysfunctionThis study involved a therapeutic trial on dogs with liver impairment, 18 dogs diagnosed with hepatic dysfunction were dividedinto three groups i.e. B, C, and D. Each group received different therapeutic protocols, and changes in hematobiochemical profiles were observed and ~~were~~compared before and after treatment.Dogs in Group B received Urosdeoxycholic acid, Group C received Urosdeoxycholic acid + Silymarin, and Group D received Ursodeoxycholic acid + L Ornithine L Aspartate. Haematological and biochemical parameters were evaluated at presentation and after 21 days of treatment. Urosdeoxycholic acid demonstrated efficacy in improving biochemical parameters, with additional benefits observed when combined with L-Ornithine L-Aspartate or Silymarin. Group D exhibited the most significant improvement, suggesting the effectiveness of combination therapy. These findings underline the importance of regular monitoring and appropriate therapeutics in managing hepatic dysfunction in dogs, with combination therapies offering enhanced recovery through hepatoprotective, antioxidant, and anti-inflammatory mechanisms.

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1. Introduction

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Liver is a prime organ in the body that is involved in several functions, including metabolism, purification, vitamin, trace mineral storage and immunogenic regulation but because of dual blood supply and high blood flow liver is more susceptible to disease than other systems and organs**[1][2]**Hepatic dysfunction was first defined in humans as a potentially reversible disorder resulting from severe liver injury and including signs of encephalopathy shortly after the onset of symptoms in patients with no prior history of liver disease **[3].** It was then further defined as an altered alanine aminotransferase (ALT) plasma concentration and a progressively increasing serum bilirubin concentration **[3][4].**Hepatic disorders include hepatocellular

reversible and irreversible injury (necrosis), porto systemic shunt, neoplsia (primary hepatic and secondary) and hepatic fibrosis or cirrhosis **[5].** Endocrine diseases such as Diabetes mellitus, hyperadrenocorticism (Cushing's disease), and hyperthyroidism can all cause impaired liver function because of their effects on the organ **[6].** Hepatic dysfunction often results due to various etiological agents such as bacteria, virus, fungi, toxins and drugs**[7].**It was estimated that disease of liver had a prevalence of about 1.06 % among all disease of dogs presented to veterinary clinics **[8].**Clinical manifestations of hepatic disorders are frequently nonspecific. Dogs with hepatic dysfunction may be present for a number of causes, including anxious symptoms such as polydipsia, polyuria, lethargy, ascites, jaundice and nervous disorders. Thus, hepatic illness always doubtful until a blood biochemical test is performed**[9].**Extensive hepatobiliary screening comprises a hematobiochemical profile, analysis of urine, measurement of clotting time, liver function tests, ultrasonography, radiography, bile cytology and histopathology[**10].**It has been reported that after a 70 % partial hepatectomy, the liver returns to its normal size and function in about two weeks due to hepatocyte and cholangiocyte replication**[11] [12]**.Hence due to regenerating capacity of liver hepatic dysfunction can be managed with a good therapeutic approach. Treatment for a variety of hepatobiliary disorders usually emphasized on removing predisposing factors, reducing their impact, regenerating damaged hepatocytes, and restoring hepatic dysfunctions **[13].** Various therapies are available for proper management of liver dysfunction which includes steroids, diuretics, antioxidants, diet with appropriate protein, fluid therapies, antibiotics and hepatic protectants**[14]**. Medicine that are commonly used as therapy in canine hepatic dysfunction aims in reversal of inflammation, reducing advancement of fibrosis, shielding against hydrophobic bile acid damage, and defending from oxidative damage **[15]**Among variety of drugs exhibiting these properties some are silymarin, ursodeoxycholic acid and L-Ornitine L-Aspartate etc. Ursodeoxycholic acid was studied in therapeutic management of hepatic dysfunction in dogs by various researchers.**[16] [17].** The present research aims finding therapeutic efficacy ofdifferent drugs in combination of ursodoxycholic acid to find effective therapeutic protocol in canine hepatic dysfunction.

2.Material methods

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In this study, a therapeutic trail was conducted in clinical cases of dogsexhibiting clinical signs of liver impairment presented to Veterinary Clinical Complex College of Veterinary

Comment [AL10]: Dog condition like age, sex,bodyweight, physiological condition

and Animal Sciences, G.B.P.U.A. & T, Pantnagar U.S. Nagar (Uttarakhand). 18 dogs that were diagnosed with hepatic dysfunction wererandomlydivided into 3 groups irrespective of their age breed and sex with 6 animals in each group namely Group B. Group C, Group D. The dogs in each group were subjected to different therapeutic protocol and changes in their hematobiochemical profile was noticed.Dogs in group B were given Urosdeoxycholic acid @15mg/kg b.w./ day od orally and dogs in group B were Urosdeoxycholic acid (15mg/kg b.w./ day od orally) + Silymarin (Sylibon syrup,2 tsp BID orally) while dogs in group D were given Ursodeoxycholic acid +L Ornithine L Aspartate (Hepamerz syrup, 2tsp TID orally) as a therapeutic protocol. Dogs in group A were selected as a healthy control. The changes in hematobiochemical parameters were compared on the day of presentation and at the end of trail i.e day 21to assess the efficacy of various therapeutic protocol.

Comment [AL11]: Procedure before x ray or ultrasound

2.1.Haematological parameter

Comment [AL12]: Specification of machine

Approximately 2 mL of blood was taken from a cephalic or saphenous vein using dry disposable syringe vials containing EDTA (ethylene diamine tetra-acetic acid) and antiseptic procedures with performing appropriate safety protocols. The sample so acquired was labelled, and blood parameters of freshly collected samples were analysed for evaluation of various blood parameters as per standard protocol mentioned by Jain, 1986.

2.2.Biochemical parameter

Comment [AL13]: Specification of machine

A sterile syringe was used to collect 3 ml of blood, which was then immediately transferred to a test tube without any anticoagulant. The blood was then allowed to coagulate for roughly 1 hour in a slant posture before being centrifuged for 10 minutes at 2,000 to 3,000 rpm to get the serum. The separated serum was then placed into a dry Eppendorf tube with a micropipette for measurement of different serum parameters on a spectrophotometer using an Erba diagnostics kit. The values of several serum parameters were calculated manually.

2.3. Statistical Analysis

The data was expressed as Mean±SE. Standard error of mean and p-values were used to determine whether there was any significant difference among different treatment groups using unpaired t test with the help of SPSS software version 22.0

3. Result and discussion

Comment [AL14]: Need grammatical correction

Dogs affected with liver ailment usually display a spectrum of clinical signs which includes depression, weakness, nervous signs, jaundice, anorexia, vomiting, change in spleen size, diarrhea, emaciation, dark brown urine, pyrexia, polydipsia, polyuria, epigastric pain, ascites, coma, change in liver size, dark or light-colored stools, hemorrhage, and urticaria**[19].** Similar clinical manifestations were documented in the present study, with predominant signs being dullness, inappetence, vomiting, polydipsia, fever and emaciation observed in 74.46%, 57.44%, 53.01%,51.06%,46.80%,31.91%,42.56% of cases, respectively.Other signs such as icterus, ascites, epigastric pain and neurological disorder was seen sporadic in occurrence. Dogs with hepatic dysfunction exhibits major alterations in hematological and biochemical parameters **[20].** Similar findings were observed in this study.Hepatic dysfunction has predictable prognosis with a good therapeutic approach. Meyer et al., 1997studied effect of urosdeoxycholic acid in chronic hepatitis of a dogs and found decrease in biochemical prameters such as ALT, AST, ALP, Cholesterol and bilirubin thereby improving hepatic ailment. Urosdeoxycholic acid has a number of different methods of action, one of which is increasing the quantity of hydrophilic bile acid while decreasing the harmful endogenous hydrophobic bile acids in cholestatic liver disease by a dilutional action moreover it also protects hepatocytes from bile acid-induced apoptosis and increases hepatobiliary secretion **[21].**

In this study recovery was evaluated on the basis of resolution of clinical signs and improvement in hematobiochemical parameters. The average duration of disappearance of clinical signs was least in group D (6 -14 days) followed by group C (8 -16 days) and group B (6- 19) days.In hematological study, it was observed that there was significant increase in hemoglobin, packed cell volume, total erythrocyte count ingroup C and D and significant changes in neutrophils, lymphocytes in all therapeutic group post treatment as compared to day of presentation while total leucocyte count, platelets improved non-significantly in all treatment groups post treatment.(table1). There was improvement in all treatment groups but better values were seen in group D followed by group C and group B respectively. Improvement in mean values of hematological parameter during therapeutic study in all treatment group was due toimproved liver function due to effect of hepatoprotectives in impaired liver.This improvement might be due to effect of improved liver function due to effect of hepatoprotectives in impaired liver and use of ancillary treatment including

antipyretics, antacids, antibiotic and other supportive and hematinic which was similarly observed by Singh *et al..*, 2019.

Findings of biochemical parameter revealed significant decrease in total bilirubin ALT, AST, GGT, ALP, blood glucose and there was significant increase in total protein, albumin, while parameters such as globulin, A:G ratio, blood urea nitrogen, serum creatinine, cholesterol differ non-significantly in all treatment group post treatment as compared to day of presentation (Table 2) Improvement was seen in all therapeutic groups due to hepatoprotective drugs but there was more improvement in groups D followed by group C where urosdeoxycholic acid was used in combination with L- Ornithine L – Aspartate and Silymarin respectively. L-ornithine L-aspartate dissociates into its constituent ornithine and aspartate that are readily absorbed by active transport. L-ornithine serves as an intermediary in the urea cycle in periportal hepatocytes in the liver and as an activator of carbamoyl phosphate synthetase and L-aspartate, by transamination to glutamate via glutamine synthetase in perivenous hepatocytes as well as by skeletal muscle and brain by which ammonia is detoxified**[23].**L-ornithine L-aspartate was also found effective in canine hepatic dysfunction by Hudyma and Slivinska,(2015)when used in combination with phospholipids. **S**ilymarin has hepatoprotective nature and manifests anti-fibrotic, anti-inflammatory, immunomodulating, hepatocytes regenerating quality, anti-oxidant and anti-lipid peroxidative property**[25].** Hepatoprotective nature of silymarin was also observed byKumar et al., 2013 in dogs with hepatic dysfunction. Various treatments, including S-adenosylmethionine, zinc, and D-penicillamine, have demonstrated efficacy in addressing hepatic dysfunction in canines across diverse research studies**[27] [28]**In this study combination of urosdeoxycholic acid and L- Ornithine L – Aspartate was found more effective as a therapeutic agent in canine hepatic dysfunction followed by combination of urosdeoxycholic acid and silymarin and urosdeoxycholic acid as an individual therapeutic agent.

4. Conclusion

From the present research work it is concluded thatregular monitoring with proper therapeutics indogs affected with hepatic dysfunction can contribute towards good prognosis. It was established better improvement in clinical signs and hematobiochemical in group D is combination of urosdeoxycholic acid + L-Ornithine L-Aspartate had better improvements in dogs with hepatic dysfunction These drugs with the help of their hepatoprotective antioxidant, anti-inflammatory property enhances recovery in dogs with hepatic dysfunction.

The findings of present study can contribute to the selection of good therapeutic medicines which can be used in combination with urosdeoxycholic acid in dogs with hepatic dysfunction.

5. References

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Table1: Effect of different therapeutic protocol on hematological profile of dogs with hepatic dysfunction

	GROUP A	Group B		Group C		GROUP D	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Hemoglobin	12.72±0.30	8.92±0.94[a]	11.13±0.55[a]	9.03±0.72[a]	11.57±0.35[b]	9.15±0.87[a]	12.08±0.43[b]
PCV	47.50±1.87	26.50±4.62[a]	39.17±3.93[a]	27.83±3.50[a]	43.00±2.25[b]	25.83±4.87[a]	43.67±3.41[b]
TEC	6.40±0.15	4.21±0.50[a]	5.44±0.39[a]	3.96±0.3[a]	5.59±0.21[b]	4.08±0.49[a]	5.81±0.25[b]
TLC(10^3/µl)	10.48±1.23	19.85±3.06[a]	13.15±1.15[a]	19.30±2.86[a]	12.32±0.65[a]	20.75±3.22[a]	12.40±0.72[a]
Neutrophil(%)	63.50±1.95	81.67±4.72[a]	68.17±2.69[b]	82.50±5.04[a]	65.50±2.26[b]	83.33±6.08[a]	64.67±1.86[b]
Lymphocyte(%)	29.67±0.33	13.67±3.99[a]	24.50±2.67[b]	13.00±3.78[a]	27.50±2.09[b]	12.33±4.85[a]	29.00±1.69[b]
Monocyte(%)	3.50±0.89	1.83±0.31[a]	3.00±0.31[a]	1.67±0.33[a]	2.83±0.31[a]	1.66±0.21[a]	3.00±0.37[a]
Platelets(10^6/µl)	3.32±0.20	1.63±1.02[a]	2.52±0.98[a]	1.78±1.10[a]	2.83±1.09[a]	1.68±1.16[a]	3.03±1.17[a]

Mean ±S.E. with different alphabet in superscript(a,b,c) differ significantly

Table 2: Effect of different therapeutic protocol on biochemical profile of dogs with hepatic dysfunction

	GROUP A	Group B		Group C		GROUP D	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
ALT (IU/L)	67.33±2.99	157.17±20.50[a]	92.17±7.73[b]	160.67±20.60[a]	87.17±7.25[b]	168.50±21.75[a]	84.67±6.78[b]
AST(IU/L)	43.83±3.06	109.83±17.18[a]	57.33±6.15[b]	111.50±17.54[a]	51.67±4.39[b]	117.00±19.71[a]	50.67±.3.99[b]
ALP(IU/L)	62.67±3.25	212.67±34.36[a]	99.33±13.71[b]	217.83±35.07[a]	86.33±12.12[b]	220.83±35.51[a]	79.50±10.20[b]
GGT(IU/L)	4.52±0.29	17.87±4.29[a]	7.62±0.88[b]	19.32±4.02[a]	7.17±0.91[b]	22.02±4.31[a]	6.17±0.63[b]
Total bilirubin(mg/dl)	0.25±0.02	1.86±0.37[a]	0.52±0.13[b]	1.74±0.41[a]	0.37±0.12[b]	1.89±0.44[a]	0.36±0.09[b]
Total protein(g/dl)	6.68±0.08	5.33±0.37[a]	6.12±0.23[b]	5.38±0.34[a]	6.27±0.23[b]	5.43±0.42[a]	6.37±0.22[b]
Albumin(g/dl)	3.60±0.07	2.12±0.26[a]	3.05±0.17[b]	3.22±0.19[a]	2.10±0.21[b]	2.25±0.32[a]	3.38±0.19[b]
Globulin(g/dl)	3.08±0.07	3.22±0.36[a]	3.07±0.19[a]	3.28±0.29[a]	3.05±0.16[a]	3.18±.0.27[a]	2.98±0.11[a]
A: G(g/dl)	1.17±0.04	0.72±0.13[a]	1.02±0.08[a]	0.67±0.08[a]	1.07±0.09[a]	0.70±0.11[a]	1.13±0.05[a]
BUN(mg/dl)	18.00±0.73	16.83±4.59[a]	18.67±1.31[a]	16.00±4.37[a]	19.17±1.30[a]	15.17±4.25[a]	19.67±1.15[a]
Creatinine(mg/dl)	1.20±0.12	1.10±0.28[a]	1.20±0.08[a]	1.15±0.37[a]	1.22±0.11[a]	1.13±0.34[a]	1.25±0.06[a]
Glucose (g/dl)	93.33±1.5	66.33±7.06[a]	84.00±2.83[b]	62.67±6.24[a]	86.17±2.50[b]	60.00±7.80[a]	88.17±2.57[b]
Cholesterol(mg/dl)	159.33±2.44	227.83±25.27	205.33±23.24	231.50±22.62	202.67±20.45	236.33±26.54	198.83±18.65

Mean ±S.E. with different alphabet in superscript(a,b,c) differ significantly