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Therapeutic Efficacy of *Boerhaavia diffusa* and *Tribulus terrestris* on Acute Kidney Disease in Dogs

Pooja Dawar[1], Brejesh Singh[1], Shashi Pradhan[1], Pushpendra Maravi[1], Srashty Singh[1], Salil Kumar Pathak[1]

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ABSTRACT

Background: A total of 24 dogs confirmed with acute kidney disease were randomly divided into four treatment groups each comprising 6 dogs. Additionally, six healthy dogs were selected as the healthy control group.

Method: A total of 24 dogs confirmed for acute kidney disease were divided randomly into four treatment groups *i.e.*, G_2, G_3, G_4, and G_5 each comprising of 6 dogs. Six healthy dogs were selected as the healthy control group (G1). Dogs of group G2 were treated with Enalapril, G_3 were treated with Pulv. *Boerhaavia diffusa*, G4 were treated with Pulv. *Tribulus terrestris* and G_5 with the combination of Pulv. *Boerhaavia diffusa* and Pulv. *Tribulus terrestris*. Supportive treatment was given as per the requirement in all the treatment groups.

Result: Haematological parameters showed a significant decrease in Hb, TEC and PCV on day 0 (pre-treatment) in all dogs. Biochemical parameters revealed a significant increase in the values of serum creatinine, BUN, ALP, and AST levels while serum sodium concentration decreased. Proteinuria was observed on urinalysis. However, on day 30 (post-treatment) significant improvement was observed in the values of haemato-biochemical and urinary parameters.

Key words: Acute kidney disease, *Boerhaavia diffusa,* Gokhru, Punarnava, Treatment, *Tribulus terrestris.*

INTRODUCTION

Acute kidney disease is defined as a sudden onset of potentially life-threatening kidney dysfunction, related to sudden damage to the renal parenchyma. It is characterized by an increase in serum creatinine with oliguria or anuria. Acute kidney disease has 4 stages. The initiation phase occurs immediately when pathological damage to the kidney is initiated. The second stage is the extension phase during which ischemia, hypoxia, inflammation and cellular injury occur. The third or maintenance phase is characterized by azotemia, uremia or both can be seen, oliguria or anuria may occur during this stage. The fourth stage is recovery, during which azotemia improves and renal tubules undergo repair, marked polyuria may occur during this stage (Ross, 2011). Common clinical signs include anorexia, vomiting, lethargy, diarrhea, polydipsia, polyuria, anuria, ataxia, dyspnoea, dehydration and pyrexia (Mugford *et al.* 2013). Diagnosis is based on clinical signs, alteration in serum creatinine, BUN, electrolyte imbalance and urinalysis.

Boerhaavia diffusa is a flowering plant belonging to the family *Nyctaginaceae*, commonly known as raktapushpa, varshaketu, punarnava (Oburai *et al.,* 2015). It is one of the oldest Asian medicines listed in Ayurveda, rich in glycosides, steroids, flavonoids, and contains various polyphenolic compounds. The therapeutic properties of *Boerhaavia diffusa* include cardioprotective, analgesic,anti-inflammatory,hepatoprotective, immunomodulatory, antibacterial and diuretic (Sani *et al.,* 2020). *Tribulus terrestris* also known as gokhru, gokshura, belongs to the family *Zygophyllaceae*. It possesses antibacterial, antifungal, anti-inflammatory, anti-urolithiasis, diuretic, hypotensive and immunomodulatory activity, aphrodisiac, antidiabetic and hepatoprotective activity (Chhatre *et al.,* 2014). *Tribulus terrestris* contains steroids, saponin, flavonoids, alkaloids, glycosides and unsaturated acids (Manhas *et al.,* 2022).

[1]College of Veterinary Science and Animal Husbandry, Nanaji Deshmukh Veterinary Science University, Jabalpur-482 001, Madhya Pradesh, India.

Corresponding Author: Pooja Dawar, College of Veterinary Science and Animal Husbandry, Nanaji Deshmukh Veterinary Science University, Jabalpur-482 001, Madhya Pradesh, India. Email: pujadawar57@gmail.com

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MATERIALS AND METHODS

This study was conducted at the Veterinary Clinical Complex, College of Veterinary Science and A.H., Jabalpur (M.P.).Dogs were screened for the presence of clinical symptoms *viz.* anorexia, vomiting, polydipsia, polyuria, anuria, duration of illness *etc*. After confirmatory diagnosis, 24 positive cases were selected to determine the plant's therapeutic efficacy.

Collection and processing of plants

Roots of *Boerhaavia diffusa* (Punarnava) and fruits of *Tribulus terrestris* (Gokhru) were procured from the Department of Plant Physiology, Agriculture College, J.N.K.V.V., Jabalpur, M.P. The collected material was cleaned manually to remove coarse impurities and then air and shade dried at a well-ventilated place. Further drying was accomplished in the incubator at 40°C to remove moisture. The dried roots and fruits were grounded in an electric mixer grinder to form a crude powder and were stored in airtight containers (Patel, 2017).

Experimental design

A total of 24 dogs were selected for the study. These dogs were randomly divided into 4 groups each comprising 6 dogs. Six healthy dogs served as the control group (Table 1).

Statistical analysis

The data pertaining to the quantitative haemato-biochemical and vital clinical parameters were analyzed according to standard procedures (Snedecor and Cochran, 1994).

RESULTS AND DISCUSSION

Hematological profile

The mean values of hemoglobin in between the groups were found to be significant described in Table 2. These findings are in agreement with Pareta *et al.* (2011), Kulkarni *et al.*(2012), Oburai *et al.*(2015) and Athaley (2018). However, these observations are in contrast with those of Cowgill and Francey (2005) who reported with pre-renal azotemia, normal hemoglobin levels were seen. The decline in the Haemoglobin level in the study could be attributed to the impaired function of the kidney to stimulate erythropoiesis with the hormone Erythropoietin. Less erythropoiesis fails to stimulate the bone marrow for enough production of red blood cells effectively causing a decrease in the haemoglobin levels.

The mean values of total erythrocyte count in between groups *i.e.* G_2 and G_5 were found to be significant. These findings were consistent with Mrudula *et al.* (2005) and Srivastava *et al.* (2011). These findings are suggestive of anemia in affected dogs. Anemia could be due to reduced erythropoietin formation (Table 2).

The difference in mean total leukocyte count values between the groups was non-significant (Table 2). These findings were in accordance with Cowgill and Francy (2005), Manu and Kuttan (2009), Rajpoot and Mishra (2011), Oladele *et al.* (2011), Bhowmik *et al.* (2012) and Kumari (2013). However, the findings were partially in accordance with the findings of Lew *et al.* (2006) and Mugford *et al.* (2013). In acute kidney disease, infection or massive tissue damage can lead to an increase in leukocytes. Hence, indicates the presence of inflammation, having either infectious or non-infectious origin.

The difference in mean packed cell volume (%) between the groups was found significant (Table 2). These observations are in agreement with the earlier published reports of Oburai *et al.* (2015) and Athaley (2018). The low packed cell volume before treatment might be due to the decreased hemoglobin value as directly correlated with hemoglobin value.

Biochemical profile

The difference in mean serum creatinine between the groups was found significant.(Table 3). These observations are similar of Yadav *et al.* (2011), Pareta *et al.* (2011), Kulkarni *et al.* (2012), Kumari (2013), Athaley (2018) and Thade (2019). An increase in creatinine levels could be

Table 1: Treatment protocol for acute kidney disease in dogs.

Group	Number of animals	Drugs and dosages
G_1	06	Healthy control group
G_2	06	Enalapril @ 0.5 mg/kg body weight PO, OD for 28 days
G_3	06	Pulv. *Boerhaavia diffusa* @40 mg/kg body weight PO, OD for 28 days
G_4	06	Pulv. *Tribulus terrestris* @ 20 mg/kg body weight PO, OD for 28 days
G_5	06	Pulv. *Boerhaavia diffusa* @ 20 mg/kg body a *Tribulus terrestris* @10 mg/kg body weight PO, OD for 28 days

Table 2: Haematological findings.

	Haemoglobin (g/dl)		Total erythrocyte count ($\times10^6$/µl)		Total leukocyte count ($\times10^3$/µl)		Packed cell volume (%)	
Group (n=6)	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment
G_1	14.08^{aA}±0.47	14.15^{aA}±0.46	6.50^{aA}±0.25	6.54^{aA}±0.24	11.53±1.30	11.52±1.32	42.25^{aA}±1.44	45.15^{aA}±1.09
G_2	08.25^{bB}±1.25	13.07^{abA}±0.54	4.19^{bc}±0.30	6.67^{aA}±0.16	17.81±2.53	15.34±1.86	24.75^{bB}±2.86	37.62^{bA}±1.16
G_3	07.83^{bC}±0.32	11.86^{bA}±0.17	3.62^{bB}±0.11	5.6^{aA}±0.51	17.33±2.76	15.33±1.70	25.73^{bB}±3.01	36.38^{bcA}±2.04
G_4	08.73^{bB}±1.07	10.92^{bA}±0.21	4.92^{bA}±0.72	5.28^{aA}±0.66	15.33±2.90	13.50±1.69	26.33^{bA}±3.07	33.62^{cA}±1.68
G_5	08.38^{bB}±0.83	12.20^{abA}±0.58	4.29^{bA}±0.73	6.05^{aA}±0.38	16.44±3.17	16.53±3.23	25.98^{bA}±2.32	36.67^{bA}±2.40

Table 3 : Biochemical findings.

Group (n=6)	Creatinine (mg/dl)		BUN (mg/dl)		ALP (U/L)		AST (U/L)		Sodium (mEq/L)		Potassium (mEq/L)	
	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment	Pre-Treatment	Post-Treatment
G_1	0.68^{aA}± 0.07	0.65^{aA}± 0.04	12.20^{bA}±0.29	12.30^{bA}±0.23	48.00^{bA}±3.68	48.50^{bA}±3.43	36.00^{bA}±1.39	36.40^{bA}±1.48	146.33^{aA}±1.56	147.12^{bA}±1.57	4.37±0.37	4.37±0.33
G_2	5.18^{aA}± 0.99	1.65^{bB}± 0.12	78.91^{aA}±1.38	28.83^{bB}±1.07	125.17^{aA}±4.13	53.50^{bC}±4.15	86.30^{aA}±5.00	39.95^{bC}±2.16	133.02^{bA}±4.13	137.68^{bA}±1.81	4.72±0.37	4.50±0.31
G_3	6.90^{aA}± 0.82	2.25^{abB}± 0.43	83.53^{aA}±2.32	29.07^{bB}±0.23	105.96^{aA}±5.50	77.83^{aB}±4.45	79.23^{aA}±7.99	62.67^{aA}±6.16	125.50^{bA}±4.73	135.33^{bA}±2.46	4.75±0.39	4.69±0.32
G_4	6.89^{aA}± 1.46	3.05^{aA}± 1.00	83.82^{aA}±1.13	36.52^{aB}±1.09	111.88^{aA}±7.75	81.17^{aB}±4.81	91.20^{aA}±1.79	57.13^{aA}±4.60	130.33^{bA}±3.79	133.67^{bA}±3.36	3.90±0.57	4.12±0.37
G_5	6.83^{aA}± 0.87	2.20^{bB}± 0.11	81.64^{aA}±2.46	29.55^{bB}±0.68	108.37^{aA}±5.37	72.00^{aB}±4.13	86.90^{aA}±7.87	52.65^{abB}±6.34	131.58^{bA}±3.38	139.63^{bA}±1.18	4.15±0.34	4.23±0.30

due to decreased kidney function. The reduction in the creatinine levels (post-treatment) can be explained due to the diuretic effect of the herbal plants and their phytoconstituents.

The difference in mean blood urea nitrogen between the groups was found significant (Table 3). These findings are similar to Banjare *et al.* (2012), Kumari (2013), Nigamand *et al.* (2016) and Athaley (2018). The property of herbal plants has been attributed to their free radical scavenging activity and nephroprotective activity which may account for a reduction of blood urea nitrogen levels.

The difference in mean alkaline phosphatase between the groups was found significant (Table 3). These findings are corroborated by the earlier reports by Eubig *et al.* (2005), Puri *et al.* (2015), Sumit *et al.* (2018) and Rimer *et al.* (2022). It may be due to the plasma alkaline phosphatase activity originating from the liver, bone and intestine.

The difference in mean serum aspartate aminotransferase values between the groups was found significant (Table 3). The results of the present study were similar to Eubig *et al.* (2005), Puri *et al.* (2015), Sumit *et al.* (2018) and Rimer *et al.* (2022). This could be indicative of the severity of the disease manifested by extra-renal complications such as pancreatitis, liver injury, *etc*.

Urinary parameters

The difference in mean urine pH between the groups was non-significant. A similar finding by Rani (2004), Kumar (2009), Kumari (2013) and (Thade 2019). It may be due to the reason that urine pH tends to vary throughout the day because it is influenced by diet and digestion. Changes in urine pH at any time may be masked by retained urine with a different pH.

The difference in mean urine protein values between the groups was found significant. These findings correlate with Graner (2007), Kumar *et al.* (2011), Srivastava *et al.* (2011), Kumari (2013), Puri *et al.* (2015) and Athaley (2018). It may be due to severe glomerular injury with nephrotic syndrome, tubule-interstitial inflammation and endothelial dysfunction.

The difference in mean urine specific gravity between the groups was non-significant. These observations are consistent with Labato (2000), Stanley and Langston (2008), Pareta *et al.* (2011), and Kumari (2013). Suggestive reason for the unchanged specific gravity of urine in renal failure dogs is acute nephritis, oliguric phase of renal failure, protein-losing nephrotoxic nephrosis and early renal dysfunction.

CONCLUSION

The hematological findings revealed a significant decrease in hemoglobin, total erythrocyte count and packed cell volume. However, the values returned to normal (post-treatment) in G_2 and G_5 and close to normal in G_3 and lastly G_4. The biochemical analysis revealed a significant increase in serum creatinine, BUN, ALP and AST levels,

while a decrease in sodium concentration which returned to near normalcy post-treatment. Based on percent recovery in dogs in all four treatment groups *i.e.* G_2-G_5 , the best therapeutic response was elicited by treatment group G_2 followed by G_5 and G_3 in sequence on day 14 (post-treatment). In treatment group G_4 similar bio-response was of lesser magnitude.

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Conflict of interest

The authors declare that they have no conflict of interest.

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