BACTERIAL NEPHRITIS IN DOGS AND ITS MANAGEMENT

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Kidneys are the most vital organs of the dogs which helps to excrete the metabolic waste products from the body and to maintain the electrolyte, water and other solute balances. These kidneys time to time suffer from the bacterial infections causing bacterial nephritis due to the infections of *Escherichia coli, Staphylococcus spp., Streptococcus spp., Enterococcus, Proteus spp., Klebsiella spp.* and *Pseudomonas spp.* etc. causing 'uremia' in dogs (Osborne *et.al.,* 1972) and ultimately leading to coma and subsequent death. To detect the main bacteriological agents causing bacterial nephritis and to observe the blood-biochemical changes of nephritis before and after therapy, this study was carried out for a period of 16 weeks in the clinical cases of bacterial nephritis in dogs.

Materials and Methods

For this study twenty four clinical cases of dogs with nephritis showing symptoms of depression, fatigue, weakness, oliguria or anuria, anorexia, nausea, vomition and hind quarter weakness were selected. These dogs were of both the sexes, age Gr of 4-8 years and body weight between 10-25 Kg and of both descriptive and non-descriptive breeds. Another 6 healthy dogs of different age, sex and breeds were kept as healthy control Gror Gr- I and were maintained under normal diet without any medicines. The other 24 clinical cases of dogs with nephritis were randomly divided in 4 equal Groups i.e. Gr- II, III, IV and V.

The dogs of Gr-II were not given any treatment for nephritis and was considered as untreated control. The dogs of Gr-3 and 4 were treated with Alkasol @ 1/2 to 1 t.s.f. twice daily orally for 4 weeks, Shelsun syrup containing Calcium and Vitamin D_3 @ 5ml twice daily orally for 12 weeks, Sharkoferrol pet liquid (Iron tonic) @ 5-10 ml twice daily orally for 12 weeks and Sufate (Sucralfate) @ 5 ml twice daily orally for 8 weeks. The dogs of Gr-3 were also given a broad spectrum antibiotic Intacef Tazo @ 15-25 mg/Kg b wt. intravenously twice daily for 7 daysandGr-4 dogs were treated with the antibiotic Taxim @ 25-50 mg/Kg b.wt. intravenously in divided doses daily for 7 days. Beside these, all the dogs of Gr- 3 and 4 were given a herbal preparation, Nefrotec DSa product of M/S The Himalaya Drug Company, Bangalore@ 1 tab twice daily orally for 16 weeks. The dogs of Gr-V were only given with the herbal medicine Nefrotec DS @ 1 tab twice daily orally for 16 weeks. All the dogs of Gr-II, III, IV and V were maintained under the protein restricted diet. Other supportive therapies like DNS I/Vly, Ringer's lactate I/Vly, Reglan I/Mly, Ranitidine I/Mly and Lasix I/Mly were also given to the dogs at the recommended dosage of Gr-III, IV and Vtime to time as required.

The blood and urine samples from all these 30 dogs were collected time to time from the 0 day of the experiment and on 2^{nd}, 6^{th}, 10^{th} and 16^{th} weeks.

The urine samples were also collected by catheterization asceptically for cultural examination and were grown in Nutrient broth and Nutrient agar media. For isolation of *E.coli* and *Staphylococcus spp.* from these cultures specific growth medias like EMB agar for *E.coli* and Mannitol salt agar media for *Staphylococcus spp.* were used. Biochemical screening for confirmatory identification of *E.coli* and *Staphylococcus spp.* were also done by performing the Indole, Methyl red, Voges-Proskauer, Citrate utilisation, Urease, Catalase, tests.

The blood samples were analysed for serum total protein, albumin, urea, creatinine, calcium, phosphorus, sodium, potassium and gamma-glutamyl transferase using the standard reagent kits andthe statistical analysis was done as described by Snedecor and Cochran(1994).

Results and Discussion

The dogs of the healthy control Gr i.e. Gr-I, were active, good physical condition and had normal appetite throughout the experimental period. Their visible mucous membranes were also pink.

The dogs of Gr-II gradually developed some nervous signs like ataxia, tremor, incoordination, stupor, syncope etc. which gradually became more severe. Progressive deterioration of health and anuria also developed in these animals as they did not receive any medicinal or fluid therapy. The body condition observed in these animals could be attributed due to protein loosing nephropathy, gastrointestinal bleeding and nephropathic toxaemia (Chew and Dibartola, 1989). Two dogs of this Gr died on 5th week

and another on 7th week of the study whilethe remaining dogs survived up to the end of the trial.

The dogs of Gr-III, IV and Vwhich were under different therapies for 16 weeks showed gradual improvements. Their visible mucous membranes became slightly pink in colour and the animals showed gradual improvements of appetite, alertness and health which corroborated with the findings of Nagode *et.al.,* (1996) and Andress, (2005). Alkasol given in GrIII and IVcontaining di-sodium hydrogen citrate (1.4 mg/ml), acted as urinary alkalizer. Shelsun syrup contains elemental calcium 250 mg and vit-D_3 125 mg.As in nephritis, the calcium level drops due to less production of calcitrol from the damaged kidneys, prolonged vit-D_3 therapy helped to increase the calcium level. Sufate suspension containing sucralfate, acted as intestinal phosphate binding agent, helped to reduce the phosphorus level which became high in nephritis (Doherty, 1992). Sharkoferrol pet, the haematinic preparation (4.25g) helped to improve the blood haemoglobin level of these dogs (Kohn *et al.,* 2004).

The broad spectrum antibiotic, Intacef Tazo (Ceftriaxone 500mg and Tazobactam 62.5 mg) helped to reduce the bacterial infections of dogs of Gr-III which is a potent inhibitor of beta-lactamase enzyme produced by Gram positive and Gram negative bacteria. Another antibiotic Taxim (Cefotaxime sodium 500 mg) helped also to combat the bacterial infections of Gr-IV dogs by interfering with the bacterial cell wall synthesis.

Offering protein restricted diet in these dogs also helped to check the severity of ureamia by lowering the production of metabolic nitrogenous waste products in the blood (Plozin and Osborne, 1992).

In the treated Groups, better results were noted in GrIII and IV than in the Gr-V. In Gr-III, IV and Vdogs, Nefrotec DS, the herbal nephroprotective drug was also given, which helped to check the further renal damage. Kirtikar and Basu (1975) described *Cyperus scariosus, Rubia cordifolia* and *Mimosa pudica,* the ingredients of Nefrotec DS as useful in the urinary tract infections and inflammations. Ambasta (1994) described *Ocimum bacilicum, Saxifraga ligulata, Tectona grandis* and *Dolichos biflorus,* the other ingredients as effective diuretics and are useful in the renal infections, while Kaur (2007) described *Didymocarpus pedicellata* another ingredient has the nephroprotective effect by correcting proliferation of the renal tissues. Singh (1999) opined the anti-inflammatory, analgesic and diuretic properties of *Saxifraga ligulata* whilethe immuno-modulatory and anti-inflammatory effects of *Rubia cordifolia* on kidney have been remarked by Lodi (2007).

Among the supportive therapies given to dogs of Gr- III, IV and V, Dextrose with normal saline solution, Ringer's lactate helped to rehydrate the dogs. Reglan containing metoclopramide acted as anti-emetic drug while Ranitidine acted as H2 receptor blocker to reduce gastritis. Eldervit containing Vit-B complex helped to improve the general health condition of these dogs.

Results of blood-biochemical tests and urine culture of the healthy dogs of Gr-1 were found normal throughout the experimental period.

After culture of the urine samples of these 24 dogs, *E.coli* was detected from the urine of 8 dogs, *Staphylococcus spp.* from 7 dogs and a mixed infection of both *E.coli* and *Staphylococcus spp.* were detected from the urine samples of the rest clinical cases of nephritis.

The results of the blood-biochemical tests have been presented in table 1 which shows that amongst the 0 days values, there was significant ($P<0.01$) declination of the Total Protein values in the clinical cases of Nephritis in GrIII, IV and V(5.29±0.88gm/dl, 5.26±0.23gm/dl, 5.28±0.18gm/dl, 5.39±0.22gm /dl respectively) than the 0 day value of GrI (6.80±0.20gm/dl).In the dogs of GrII, there was further reduction of mean serum total protein levels which was even significantly ($P<0.01$) lower at 16th week (4.41±0.37gm/dl) as compared to its 0 day value,which might be due to more loss of blood through gastrointestinal bleeding and proteinuria which develop in Nephritic patients (Kaneko, 1989; Devaux *et al.,* 1996). Following conventional treatment with antibiotics, haematinics and calcium etc., the mean serum total protein values of GrIII and IV increased gradually and significantly ($P<0.05$) from the 6th week onwards in GrIII and IVand on 16th week the values recorded were 6.61±0.79gm/dl and 6.82±0.13gm/dl respectively. However, in GrV, gradual

improvements were also noted but significant (P<0.01) improvements was noted from 10th week onwards.

There were significant (P<0.01) reductions of the serum albumin levels in GrII,III, IV and V, the clinical cases of dogs with Nephritis on 0 day (Table 1) as compared to the healthy control dogs of GrI and it might be due to the loss of blood through gastrointestinal bleeding in uremic conditions, increased filtration of albumin through damaged glomeruli as also opined by Osborne *et al*. (1972) and Cook and Cowgill (1996) in nephriticdogs.Thereafter the mean albumin levels gradually increased and significant (P<0.5) increase was noted in GrIII, IV and Vfrom the 6th week onwards and almostnormal serum albumin values were recorded on 16th week.

Table 1. Serum total protein, Albumin, Calcium, Phosphorus, Sodium and Pottasium levels in nephritic dogs before and after treatment:

Parameters	Days/ Weeks	Gr I	Gr II	Gr III	Gr IV	Gr V
Serum Total Protein (gm./dl)	0 day	6.80 ±0.20	5.29 ±0.88 β	5.26 ±0.23 β	5.28 ±0.18 β	5.39 ±0.22 β
	2nd week	6.86 ±0.70	5.21 ±0.33	5.21 ±0.27	5.23 ±0.88	5.32 ±0.53
	6th week	6.85 ±0.79	5.15 ±0.15	5.89 ±0.82*	6.21 ±0.60*	5.37 ±0.94
	10th week	6.87 ±0.76	4.67 ±0.36	6.33 ±0.14*	6.42 ±0.63*	6.21 ±0.70**
	16th week	6.87 ±0.73	4.41 ±0.37**	6.61 ±0.79**	6.82 ±0.13**	6.77 ±0.45**
Serum Albumin (gm./dl)	0 day	3.25 ±0.10	2.13 ±0.32 β	2.14 ±0.77 β	2.22 ±0.13 β	2.36 ±0.47 β
	2nd week	3.24 ±0.14	2.00 ±0.74	2.11 ±0.30	2.08 ±0.44	2.32 ±0.65
	6th week	3.28 ±0.18	1.96 ±0.62	2.82 ±0.49*	2.86 ±0.82*	2.67 ±0.27*
	10th week	3.31 ±0.13	1.78 ±0.31	2.98 ±0.24*	3.12 ±0.85**	2.86 ±0.13*
	16th week	3.28 ±0.52	1.76 ±0.68	3.14 ±0.52**	3.18 ±0.96**	3.02 ±0.37**
Serum Calcium (mg/dl)	0 day	9.97 ±0.10	8.14 ±0.13 β	8.06 ±0.31 β	8.00 ±0.15 β	8.26 ±0.46 β
	2nd week	10.32±0.75	7.92 ±0.26	8.02 ±0.14	8.04 ±0.52	8.21 ±0.47
	6th week	10.33±0.57	7.66 ±0.20*	8.94 ±0.32*	9.27 ±0.60*	8.94 ±0.52*
	10th week	10.24±0.64	7.55 ±0.58	10.33±0.15**	10.56±0.21**	9.67 ±0.46*
	16th week	10.36±0.15	7.10 ±0.42	11.27±0.96**	11.32 ±0.25**	10.21±0.44**
Serum Phosphorus (mg/dl)	0 day	4.21 ±0.53	9.43 ±0.68 β	9.77 ±0.16 β	9.82 ±0.42 β	8.76 ±0.49 β
	2nd week	4.26 ±0.26	9.79 ±0.19	9.01 ±0.33	9.31 ±0.50	7.87 ±0.30
	6th week	4.29 ±0.26	10.32 ±0.15	7.62 ±0.20	7.31 ±0.33	6.87 ±0.64
	10th week	4.30 ±0.57	10.58 ±0.14	6.23 ±0.32*	6.67 ±0.35*	5.01 ±0.75*
	16th week	4.36 ±0.97	10.82±0.68**	5.32 ±0.14**	5.29 ±0.73**	4.89 ±0.35*
Serum Sodium (mEq/L)	0 day	143.82±0.16	154.02±0.26 β	158.02±0.12 β	158.33±0.10 β	159.37±0.16 β
	2nd week	144.37±0.32	156.89±0.96	151.62±0.25*	150.97±0.73*	155.32±0.48
	6th week	145.77±0.26	162.38±0.52*	152.37±0.50*	146.92±0.38*	149.97±0.64*
	10th week	146.33±0.97	165.92±0.38*	149.96±0.55*	146.21±0.24*	148.67±0.74*
	16th week	146.72±0.22	169.69±0.36**	144.33±0.96**	145.24±0.27*	146.39±0.63*
Serum Potassium (mEq/L) Serum	0 day	4.45 ±0.57	5.48 ±0.14 β	5.63 ±0.32 β	5.64 ±0.76 β	5.47 ±0.80 β
	2nd week	4.41 ±0.34	5.52 ±0.76	4.97 ±0.26	5.62 ±0.43	5.39 ±0.35
	6th week	4.37 ±0.99	5.67 ±0.31	4.82 ±0.55*	4.87 ±0.35*	4.96 ±0.85*
	10th week	4.39 ±0.64	5.93 ±0.17	4.46 ±0.14*	4.67 ±0.24*	4.77 ±0.53*
	16th week	4.42 ±0.97	6.17 ±0.26	4.39 ±0.53**	4.41 ±0.86**	4.44 ±0.53**

$^{\beta}$ =p<0.01(significant at 1% level) in respect to healthy animals,
*=p<0.05(significant at 5% level) in respect to 0 day,
**=p<0.01(significant at 1% level) in respect to 0 day.

The table 1 also shows that there is significantly (P<0.01) low serum calcium levels in GrII, III, IV and Von 0 day in comparison to their healthy control Group or Gr I (9.97±0.10mg/dl) and the values recorded were 8.14±0.13mg/dl, 8.06±0.31mg/dl, 8.00±0.15mg/dl, 8.26±0.46mg/dl respectively and this reduction of serum calcium level in the clinical cases of nephritis is might be due to more loss of calcium through the gastrointestinal tract (Krawiec, 1996) and less absorption of calcium due to less production of calcitrol from the damaged kidneys (Nagode *et al.*, 1996). But following treatment, the calcium levels increased in all the treated Groups but rapid increase was noted in GrIII and IV as compared to GrV, and significant (P<0.05) improvements were recorded in GrIII, IV and Vfrom 6th week onwards. Increase in this serum calcium levels in GrIII and IV was due to calcium and sucralfate therapy. Sucralfate, the intestinal phosphate binding agent, helped to reduce the phosphate level as well as helped to increase the serum calcium level as also opined by Doherty (1992) in uremic dogs.

There was significant (P<0.01) increase of the mean serum phosphorus levels in the dogs with Nephritis before treatment (0 day) in GrII, III, IV and Vin comparison to the 0 day value of GrI (4.21±0.53mg/dl) and this hyperphosphataemia developed due to poor glomerular filtration through the damaged kidneys which simulated with the findings of Doherty (1992), Devaux *et al*. (1996) and Nandy (2004) in dogs with nephritis leading to renal failure. But following treatment in GrIII and IV, the mean serum phosphorus levels declined significantly (P<0.05) from the 10th week onwards in comparison to their 0 day values and in 16th week they reached to 5.32±0.14mg/dl and 5.29±0.73mg/dl respectively, which was postulated to be due to the prolonged use of Sucralfate which acted as the intestinal phosphate binding agent and caused less absorption of phosphorus from the gastro-intestinal tract as also opined by Doherty (1992). In the Gr V, it declined slowly and significant (P<0.05) decrease was noted from 10thand it is due to the continued therapy of Nefrotec DS which helped in gradual improvement of the kidney condition and helped in proper excretion of phosphorus.

The table 1 also showed that there was a significant (P<0.01) increase of the values of serum sodium between the clinical cases of dogs with nephritis of Gr II, III, IV and Vwith the healthy control dogs of Gr Ion 0 day and it is might be due to the oliguric condition that develops in dogs with Nephritis which causedblockage of the glomerular filtration of sodium due to the damaged glomeruli and supported the views of Forrester and Less (1994) in dogs with nephritis.In Gr III, IV and V, significant (P<0.05) decrease was noted from 2nd week in Gr III, IV and from 6th week in Gr V as compared to their 0 day values.

There was also a significant (P<0.01) increase of potassium levels in Gr II, III, IV and Vdogs as compared to the healthy control Gr (Gr I) value of on 0 day and these might also be due to the blockage of glomerular filtration of potassium due to damaged glomeruli. But following treatment in GrIII, IV and V, the serum potassium levels declined significantly (P<0.05) from 6th week in Gr III, IV and V which might be due to the fluid therapy and other therapies which helped to decrease the higher concentration of potassium.

The table 2 shows that there was a significantly (P<0.01) higher values of serum urea nitrogen in the clinical cases of nephritis in Gr II, III, IV and V respectively as compared to the healthy control Gr (Gr I) and is due to decreased filtration of NPN substances through the damaged glomeruli and simulated with the observations of Kerlin (1995) and Devaux *et al.* (1996) in dogs with nephritis. However, significant (P<0.05) decrease was noticed from the 2nd week in Gr III and IV and from 6th week onwards in Gr V, but normalization of urea level could not be done in the Gr III, IV and V since irreversible renal structural lesions persisted in Nephritis.

Table 2. Serum Urea, Creatinine and GGT levels in nephritic dogs before and after treatment:

Parameter	Days/ Weeks	Gr I	Gr II	Gr III	Gr IV	Gr V
Serum Urea (mg/dl)	0 day	19.47±0.74	105.67 ±0.96β	106.20 ±0.24β	109.60 ±0.74β	97.44 ±0.66 β
	2nd week	19.23±0.30	115.53 ±0.15	96.72 ±0.42*	97.77 ±0.75*	95.12 ±0.13
	6th week	19.97±0.26	135.61 ±0.36	82.66 ±0.45**	80.12 ±0.82**	86.34 ±0.67*
	10th week	18.47±0.23	169.12 ±0.13	59.32 ±0.42**	58.57 ±0.55**	74.67 ±0.35**
	16th week	18.17±0.85	181.70 ±0.90	40.33 ±0.68**	42.33 ±0.45**	61.07 ±0.24**
Serum Creatinine (mg/dl)	0 day	0.84 ±0.87	7.25 ±0.90 β	7.12 ±0.57 β	7.27 ±0.53 β	6.67 ±0.77 β
	2nd week	0.92 ±0.15	8.67 ±0.61	7.28 ±0.17	6.52 ±0.51	5.72 ±0.17
	6th week	0.81 ±0.23	9.13 ±0.34	5.21 ±0.87*	5.20 ±0.38*	4.22 ±0.23*
	10th week	0.91 ±0.18	9.62 ±0.35	3.11 ±0.96*	3.53 ±0.43*	2.92 ±0.73*
	16th week	0.87 ±0.56	10.62 ±0.38	1.97 ±0.47**	2.07 ±0.48**	2.17 ±0.75*
GGT (IU/L)	0 day	3.41 ±0.47	7.37 ±0.16 β	7.46 ±0.42 β	7.57 ±0.40 β	7.21 ±0.55 β
	2nd week	3.32 ±0.18	7.99 ±0.16	7.39 ±0.22	7.27 ±0.23	7.17 ±0.54
	6th week	3.17 ±0.93	8.17 ±0.26	5.97 ±0.46*	5.97 ±0.85*	6.62 ±0.27*
	10th week	3.33 ±0.23	9.62 ±0.84	4.97 ±0.57*	4.96 ±0.43*	4.87 ±0.74*
	16th week	3.39 ±0.96	10.97 ±0.99	4.17 ±0.79*	4.27 ±0.76**	4.36 ±0.96**

β =p<0.01(significant at 1% level) in respect to healthy animals,
*=p<0.05(significant at 5% level) in respect to 0 day,
**=p<0.01(significant at 1% level) in respect to 0 day.

It is also noted from table 2 that there was a significant (P<0.01) increase of the mean serum creatinine levels in Gr II, III, IV and Von 0 day and is due to poor filtration of creatinine through the rest part of kidney tissues and damaged glomeruli and was supported by the observations of Kerlin (1995) in renal failure uremic dogs. Significant (P<0.05) declinations from its 0 day value was noted from 6th week onwards in Gr III and IV and it might be due to treatment of antibiotic, Calcium and Sucralfate in these Grs and due to reestablishment of electrolyte balance with fluid therapy and also due to normalization of urination to some extent by the application of diuretics. In Gr V, the herbal ingredients of Nefrotec DS had some anti-inflammatory, diuretic and nephroprotective effects on kidneys. Besides, dietary management with protein restricted diet also helped to reduce the uremic complications. Normalization of the level was not possible as the maximum parts of the kidney had irreversible renal structural lesions in nephritisand with the help of this therapy, it was tried to reduce the complications too some extent.

From the table 2 it also clearly evident that there is significant (P<0.01) increase of the mean serum GGT levels in the clinical cases of Nephritis in dogs of Gr II, III, IV and V, as compared to the healthy control Gr I on 0 day and simulated with the findings of Heine (1991) in dogs with nephritis and it might be due to more release of GGT from the damaged renal tubular cells. Thereafter, significant (P<0.05) declinations were noted from 6th week onwards in GrIII, IV and V when in the untreated control GrII there were further increase of GGT values as they did not receive any medicines.

From the above study, it is clearly evident that all the supportive medicines including the antibiotics used in this study in Gr III and IV, helped effectively to correct the bacterial infections and other complications of nephritis in dogs and the herbal medicine Nefrotec DS used in Gr V alone was also found moderately effective in treating bacterial nephritis in dogs.

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