INDUCED HEPATOPATHY IN DOGS AND ITS MANAGEMENT

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Introduction

Dog is a wonderful companion of man and is loved for its obedience, loyalty and devotion. But these dogs generally suffer from several infectious and non-infectious diseases of the vital organs like liver, kidney, lungs, heart and brain etc. Liver, is the most important vital organ and is the largest gland of the body and is responsible for many metabolic functions of the body. But this liver oftenly exposed to many infectious agents, chemicals, toxins and drugs like paracetamol etc. (Gupta, 1989) and develops hepatopathy. The present study was undertaken to study the changes in induced hepatopathy in dogs and its response to therapeutic management.

Materials & Methods

For this study a total 24 nos. of apparently healthy adult mongrel dogs of either sex and of the age group of 2 to 4 years and body weight between 12 -16 kg were selected. All the dogs were kept in identical environment under closed observations for 3 weeks for clinical observations and for laboratory examinations of blood like TC, DC, Hb and some serum biochemical profiles like glucose, protein etc. & some enzymes like AST, ALP, ALT, and GGT etc. Blood was collected on 0, 4, 8, 11 & 18th days of the experimental study.

All the dogs were dewormed with Drontal plus and vaccinated against common infectious diseases. These dogs were divided in four groups comprising 6 in each. The first group (Gr. I) was kept as healthy control group while in the dogs of Gr. II, Gr. III & Gr. IV, temporary reversible liver damage was induced with S/C injection of paracetamol @ 600 mg/kg, 200 mg/kg and 200 mg/kg at 0, 9th and 24th hours interval respectively. The dogs of Gr. II were kept as untreated control while the dogs of Gr. III, were treated with Meboliv, a herbal liver tonic of M/S Indian Herbs, Saharanpur, U.P. @ 5ml twice daily orally before meal for 15 days and the dogs of Gr. IV were treated with conventional therapies like inj. Bivinal forte, (Alembic Chemical works Ltd.) @ 1ml I/Mly on alternate days, Sharkoferol Pet liquid (Alembic Chemical works Ltd.) @ 10ml twice daily orally for 15 days and Inj., Ampilox (Boichem Pharmaceuticals) @ 500 mg I/Mly daily for 7 days and 5% Dextrose 250 ml I/Vly daily for 5days.

Besides the dogs of Gr. II, III & IV were also treated with some additional drugs like Inj. Reglan and Inj. Rantac etc. as per necessity.

All the dogs under experimental study were fed with protein restricted diet and mainly based on carbohydrate diet. The experimental pattern was approved by the University ethical committee.

All the data obtained were statistically analysed by as per Snedecor and Cochran (1994).

Table – 1: Haematological values, TLC and Clotting time of different groups of experimentally induced hepatitis in dogs.

Parameters	Groups	0 day	4th day	8th day	11th day	18th day
Hb (gm %)	Gr. I	12.34	12.45^{a}	12.41^{a}	12.32^{a}	12.47^{a}
	Gr. II	12.37	9.07^{b}	9.13^{b}	9.28^{b}	9.74^{b}
	Gr. III	12.31	9.35^{b}	10.58^{ab}	11.19^{ab}	12.28^{a}+
	Gr. IV	12.43	9.33^{b}	10.62^{ab}	11.28^{ab}	12.51^{a}+
TEC (million/mm^3)	Gr. I	7.71	7.68^{a}	7.71^{a}	7.69^{a}	7.71^{a}
	Gr. II	7.75	5.28^{b}	5.45^{c}	5.69^{c}	6.19^{b}
	Gr. III	7.48	5.14^{b}	6.08^{bc}+	6.45^{bc}+	7.35^{a}+
	Gr. IV	7.70	5.24^{b}	6.45^{b}	6.79^{b}+	7.63^{a}+
PCV (%)	Gr. I	37.50	36.50^{a}	37.83^{a}	36.67^{a}	36.67^{a}
	Gr. II	35.50	21.50^{b}	23.00^{c}	25.25^{c}	29.75^{b}+
	Gr. III	37.66	22.17^{b}	27.83^{bc}	30.83^{b}+	36.83^{a}+

	Gr. IV	37.33	23.00 ^{b}	28.67 ^{b}	31.83 ^{ab}+	37.17 ^{a}+
TLC (thousand/mm^3)	Gr. I	12.98	12.97 ^{b}	12.95 ^{b}	13.28 ^{b}	12.84 ^{b}
	Gr. II	13.08	15.99 ^{a}	15.79 ^{a}	15.52 ^{a}	14.71 ^{a}
	Gr. III	12.92	15.70 ^{a}	14.67 ^{a}	13.87 ^{b}+	13.05 ^{b}+
	Gr. IV	13.13	15.49 ^{a}	14.57 ^{a}	13.77 ^{b}+	12.91 ^{b}+
Clotting Time (min.)	Gr. I	4.33	4.33 ^{b}	4.50 ^{b}	4.42 ^{b}	4.21 ^{b}
	Gr. II	4.46	6.25 ^{a}	5.81 ^{a}	5.69 ^{a}	5.44 ^{a}
	Gr. III	4.33	6.08 ^{a}	5.50 ^{a}	5.20 ^{a}	4.54 ^{b}+
	Gr. IV	4.58	6.08 ^{a}	5.58 ^{a}	5.33 ^{a}+	4.54 ^{b}+

Value bearing at least one common superscript with the same column do not differ significantly (P> 0.05). +Significant at 5% level (P < 0.05) in comparison to its lowest value in the same group.

Table – 2: Serum biochemical values of the different groups of experimentally induced hepatitis in dogs:

Parameters	Groups	0 day	4th day	8th day	11th day	18th day
Serum Glucose (mg/dl)	Gr. I	77.59	81.33 ^{a}	78.85 ^{a}	79.45 ^{a}	77.43 ^{a}
	Gr. II	79.40	50.47 ^{b}	48.45^{c}	51.95^{c}	61.11 ^{b}+
	Gr. III	78.28	54.11 ^{b}	64.22 ^{b}+	72.37 ^{b}+	78.76 ^{a}+
	Gr. IV	79.49	54.75 ^{b}	67.36 ^{b}+	74.26 ^{ab}+	79.68 ^{a}+
Total Bilirubin (mg/dl)	Gr. I	0.42	0.49 ^{b}	0.41^{c}	0.43^{c}	0.45 ^{b}
	Gr. II	0.45	1.69 ^{a}	1.45 ^{a}	1.27 ^{a}+	0.83 ^{a}+
	Gr. III	0.42	1.45 ^{a}	1.14 ^{ab}	0.87 ^{b}+	0.48 ^{b}+
	Gr. IV	0.44	1.48 ^{a}	1.12 ^{b}+	0.83 ^{b}+	0.44 ^{b}+
Total Protein (gm/dl)	Gr. I	7.05	7.03 ^{a}	7.02 ^{a}	6.95 ^{a}	7.04 ^{a}
	Gr. II	7.03	4.93 ^{b}	4.81 ^{c}	5.02 ^{c}	5.92 ^{b}+
	Gr. III	6.98	5.03 ^{b}	5.59 ^{b}+	6.16 ^{b}+	6.93 ^{a}+
	Gr. IV	6.89	4.98 ^{b}	5.77 ^{b}+	6.21 ^{b}+	6.99 ^{a}+

Value bearing at least one common superscript with the same column do not differ significantly (P> 0.05). +Significant at 5% level (P < 0.05) in comparison to its lowest value in the same group.

Table – 3: Serum enzymatic values of different groups of experimentally induced hepatitis in dogs:

Parameters	Groups	0 day	4th day	8th day	11th day	18th day
ALT (IU/L)	Gr. I	24.50	24.17 ^{b}	24.50 ^{b}	25.83 ^{b}	24.67 ^{b}
	Gr. II	25.17	203.75 ^{a}	197.25 ^{a}	175.75 ^{a}	121.50 ^{a}
	Gr. III	26.33	192.67 ^{a}	124.67 ^{a}+	89.33 ^{b}+	35.83 ^{b}+
	Gr. IV	25.83	188.17 ^{a}	132.83 ^{a}	86.33 ^{b}+	32.33 ^{b}+
AST (IU/L)	Gr. I	21.50	21.83 ^{c}	21.33 ^{c}	22.50 ^{c}	21.50 ^{b}
	Gr. II	21.66	198.75 ^{a}	164.75 ^{a}+	140.75 ^{a}+	98.75 ^{a}+
	Gr. III	20.33	159.17 ^{ab}	109.00 ^{b}+	77.00 ^{b}+	26.33 ^{b}+
	Gr. IV	21.00	155.00 ^{b}	99.17 ^{b}+	71.67 ^{b}+	22.67 ^{b}+
ALP (IU/L)	Gr. I	24.64	25.28 ^{b}	24.93 ^{c}	24.07 ^{c}	24.28 ^{b}
	Gr. II	24.92	202.28 ^{a}	199.48 ^{a}	181.54 ^{a}	133.59 ^{a}
	Gr. III	26.16	200.09 ^{a}	121.06 ^{b}+	80.62 ^{b}+	30.65 ^{b}+
	Gr. IV	25.97	195.97^{a}	118.22 ^{b}+	71.13 ^{bc}+	26.97 ^{b}+
GGT (IU/L)	Gr. I	5.88	5.84 ^{b}	5.91 ^{c}	5.90 ^{c}	5.89 ^{b}
	Gr. II	5.89	14.65 ^{a}	12.88 ^{a}	11.89 ^{a}	10.51 ^{a}+
	Gr. III	6.37	13.83 ^{a}	10.28 ^{b}+	8.80 ^{b}+	6.41 ^{b}+
	Gr. IV	6.56	13.74 ^{a}	10.23 ^{b}+	8.61 ^{b}+	6.24 ^{b}+

Value bearing at least one common superscript with the same column do not differ significantly (P> 0.05). +Significant at 5% level (P < 0.05) in comparison to its lowest value in the same group.

Results and Discussion

The dogs of the healthy control group (Gr.I) were very active, alert, healthy and had good appetite & physical condition and also had pink mucous membranes and normal temperature, respiration and pulse rates.

After administration of paracetamol in all the dogs of Gr. II, III, & IV, they developed depression, loss of appetite, weight loss, vomition, diarrhoea, polydipsia, pale to yellow mucous membranes, constipation, polypnoea, jaundice, brown colour urine, anaemia and in-coordination etc. and similated with the observations of Schlesinger (1995) and Vijaya Kumar *et al.* (2004) in dogs with hepatic disorders.

The dogs of Gr. II, which were kept as untrated control showed marked symptoms and very mild improvements were noticed throughout the experimental study and 1 dog died on 4th day.

However the dogs of Gr. III & IV responded well to the treatment and almost all the dogs became normal at the end of the study. The improvements of Gr. IV were in accordance with the findings of Kadvekar and Murkibhai (1971) and Blood *et al.* (1983) who also treated dogs with vit. B. complex and liver extract, glucose and calcium with hepatic disorder. Similarly, the improvements in Gr. III with herbal hepatotonic treatment were in conformity with the observations of Dwivedi & Sharma (1989) and Pattnaik (2004) with different herbal hepatotonic treatments in dogs.

The main ingredients of Meboliv like Andrographis paniculata is very effective in protecting liver as remarked by Dwivedi *et al.* (1986) and *Eclipta alba* the other ingredient is an anti hepatotoxic drug (Mehra and Handa, 1968).

From the table–1, it is evident that, there is marked deterioration of the haematological values like Hb, TEC on PCV on 4th day of the experiment in Gr, II, III & IV. Thereafter in the untreated control group II, no or mild improvements were noted which corroborated with the observations of Bhattacharya *et al.* (1998) and Vijaya Kumar *et al.* (2004) in dogs with hepatic dysfunctions, but following treatments with vit. B complex with liver extract, iron, calcium etc. in Gr. IV, there were significant ($P<0.05$) improvements of the values from 8th day onwards and became normal on 11th day and simulated with the findings of Roy Chowdhury (1981) in bovines and Pradhan (1991) in goats. In Gr. III, with treatment of herbal hepatonic, there was gradual & slow improvements in comparison to Gr. IV & became normal on day 18 and simulated with the observations of Dwivedi & Sharma (1989) in dogs and Pradhan & Misra (1994) in goats with treatments of herbal hepatotonics. It is postulated that the herbal ingredients helped to decrease the cell destruction and to increase the cell production and ultimately helped to increase the Hb, TEC & PCV values.

It is also evident from the table-1 that, there is leucocytosis from 4th day onwards in all the experimental groups which simulated with the findings of Voros *et al.* (1991) and Sevelius (1995) in dogs & is probably due to stress reactions and acute inflammatory changes of the liver due to paracetamol toxicity. But following treatments in Gr. III & IV, gradually the TLC values became normal from day 11 onwards and claimed improvements with the herbal & other treatments.

The clotting time in Gr. II, III & IV was found to increase markedly on day 4 and confirmed improper synthesis of proteins by liver required for clotting mechanisms as opined by Rowsel (1969). However in Gr. III it became normal on day 18 while in Gr. IV, it became normal on day 14.

The results of the serum biochemical changes have been presented in table – 2 and it is evident from the table that there is significant ($P<0.05$) reduction of glucose level on day 4 in all the experimental groups which corroborated with the finding of Varshney and Hoque (2002) in dogs with hepatic dysfunctions. Mullen (1976) opined, liver is the important organ for maintenance of blood sugar level and paracetamol toxicity depletes the liver glycogen and caused marked reduction of free glucose level. Thereafter the levels increased significantly ($P < 0.05$) from 8th day onwards in both Gr. III & IV and rapidly became normal in Gr. IV than Gr. III. Meboliv the herbal hepatotonic, might have stimulated the liver for carbohydrate metabolism and induced gluconeogenesis in Gr. III, while in Gr. IV, the vit. B. complex with liver extract and Dextrose therapy helped to improve the hepatic functions more effectively.

It is evident from table – 2 that, there is significant ($P< 0.05$) increase of total bilirubin level on day 4 in Gr. II, III & IV and simulated with the findings of Vijay Kumar *et al.* (2004), but rapid declinations were noticed in Gr. III & IV, when mild declination was

noticed in the untreated control group. Hyperbilirubinaemia is the result of disturbance of the balance between rate of production of bilirubin and the rate of excretion and diminished excretion is due to failure of the liver parenchymal cells to excrete bilirubin. The treatments in Gr. III & IV, helped in regeneration of the liver parenchymal cells effectively and induced rapid excretion than in Gr. II.

The table-2 also shows that, there were significant ($P < 0.05$) reductions of the total protein values on day 4 in all the experimental groups (Gr. II, III & IV) which still declined on day 8 in the untreated group and corroborated with the findings of Vijay Kumar *et al.* (2004) in dogs with hepatic insufficiency. Mullen (1976) remarked, since albumin is synthesized in the liver, paracetamol toxicity caused decreased production of albumin and poor total protein values. However, rapid improvements were noted from 8^{th} day onwards in both Gr. III & IV showing effective treatments with herbal hepatotonic in Gr. III & vit. B. complex with liver extract in Gr. IV.

The changes in serum enzymatic levels have been recorded in table – 3.

The table – 3 shows that, there were no significant differences ($P < 0.05$) in the values of ALT on 0 day in between the different groups of dogs. But after paracetamol toxicity, the values reached marked significantly ($P<0.05$) on the 4^{th} day in all the experimental groups and confirmed the findings of Rutgers *et al.* (1993) and Sen *et al.* (2001) in dogs with hepatic damage. Transamination of amino acid is the synthetic function of hepatic cells and the enzymes. The ALT and AST catalyze these two reactions. When hepatic cells are damaged, these enzymes leak in the circulation and therefore elevation of plasma transaminase level is a highly sensitive indicator of hepatic insufficiency (Hill and Kelly, 1974).
However, there were very slow declination in the following observations of the untreated Gr.II, while rapid declinations were noted in Gr. III and Gr. IV, indicating prompt regenerations in these groups with herbal and liver tonic treatments.

Similarly, the table – 3 also shows that, there was marked increase of AST levels in all the experimental groups (Gr. II, III & IV) on day 4 which similated with the observations of Rutgers *et al.* (1993) in dogs with liver disorders. But following treatments in Gr. IV, the values rapidly declined & became normal on day18 & simulated with the observations of Pradhan (1991) in goats. There were also prompt declinations in Gr. III.

The table – 3 also shows that after induction of hepatitis in Gr. II, III & IV, there was tremendous increase of the ALP values on day 4 which corroborated with the observations of Vershney and Hoque (2002) in dogs. It is postulated that since hepatic serum ALP is mainly contributed by the hepatocytes lining the canaliculi and bile duct epithelium and as this enzyme is mainly present in the microsomal membranes of the cells therefore the paracetamol toxicity caused damage to these cells and resulted in increase of ALP activities. However, following treatments in Gr. III & IV, there were rapid declinations of the values and it became normal on day 18 in Gr. IV.

Similarly it is also evident from the table – 3 that, there was significant ($P< 0.05$) increase of the GGT values on day 4 in all the experimentally induced hepatotoxicity with paracetamol in Gr. II, III &IV and corroborated with the findings of Abdel Kader and Hauge (1986) in dogs with hepatic disorders. Thereafter there were rapid declinations in the following observations and became normal in both Gr. III & IV on day 18.

In Gr.IV, treatment with vit. B. complex with liver extract, antibiotic, calcium and dextrose etc. helped in rapid regeneration of the hepatocytes and confirmed the observations of Kadvekar and Murkibhavi (1971) in bovines. Similarly in Gr. III, Meboliv, being a hepatic stimulant restored the functions of liver and helped to reduce the GGT activities.

The different ingredients of Meboliv like *Andrographis paniculata* is a cholagogue and is effective in protecting liver damage (Dwivedi *et al.,* (1986), *Eclipta alba* is an antihepatotoxic drug (Mehra and Handa, 1968), *Phyllanthus niruri* and *Boerrhavia diffusa* are the excellent remedies for jaundice & constipation (Kirtikar & Basu, 1975). Kirtikar and Basu (loc. cit.) also opined *Amphanamixis rohituka* and *Tephrosia purpurea,* the other ingradients are very useful in remedy of liver disorders.

Therefore on the basis of the results obtained, it is concluded that, both the Meboliv, the herbal hepatotonic used in Gr. III and vit. B. complex with liver extract and Dextrose etc.

used in Gr. IV were found effective in correcting of hepatic dysfunctions in dogs.

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