

DIETARY MANAGEMENT OF HEPATIC COPPER ACCUMULATION IN LABRADOR RETRIEVERS

Gaby Hoffmann, Paul G. Jones¹, Vincent Biourge², Ted S.G.A.M. van den Ingh, Peter Bode³, Jan Rothuizen
Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, Utrecht University, NL • 1. Waltham Center for Pet Nutrition - Masterfoods, Leics, UK • 2. Royal Canin, Centre de Recherche, Aimargues, France • 3. Interfaculty Reactor Institute, Delft University of Technology, NL.



INTRODUCTION

Copper-associated chronic hepatitis (CACH) has recently been recognized in the Labrador as an inherited disorder with a late onset of clinical signs. No studies have investigated dietary management for the long-term treatment of this disease or for its potential in delaying the onset of clinical signs in subclinical Labradors.

OBJECTIVES

To investigate the effects of a low-copper diet and zinc gluconate on hepatic copper concentrations in Labradors.

Animals: Twenty-four client-owned Labradors that were related to patients affected with CACH and that had been diagnosed with elevated hepatic copper concentrations.

Groups: The dogs were assigned to one of two groups in a randomized double-blind manner to receive a supplement of zinc gluconate or a placebo). Zinc tablets contained 25 mg elemental zinc as zinc-gluconate salt. Placebo tablets contained 160 mg lactose. Dosage of the prescription was according to the following scheme:

Bodyweight:		
<28 kg (<61.6lbs):	8 tablets BID	(200mg BID)
28 – 35kg (61.6- 77lbs):	9 tablets BID	(225mg BID)
above 35 (>77lbs):	10 tablets BID	(250mg BID)

DIET

All dog owners were provided with the same commercial canned diet (Veterinary Diet Hepatic, Royal Canin, Aimargues), which originated from a single, analyzed production batch. The diet contained 4.8 ppm copper, and 102 ppm zinc on a dry matter basis. Labradors of our study who ate between 420-840 g diet per day, received between 18-36mg zinc daily with their diet. Per kilogram bodyweight the approximate mineral ingested from the diet was 0.039 mg copper, and 0.83 mg zinc.

RESULTS

Twenty-one dogs completed the study. Hepatic copper concentrations decreased in both groups at recheck 1 (N=21, group 1, $P < 0.001$; group 2, $P = 0.001$) and at recheck 2 (N=16, group 1, $P = 0.03$; group 2, $P = 0.04$). No difference in hepatic copper concentrations was found between the two groups prior to treatment ($P = 0.65$), at recheck-1 or at recheck-2 ($P = 0.52-0.79$).

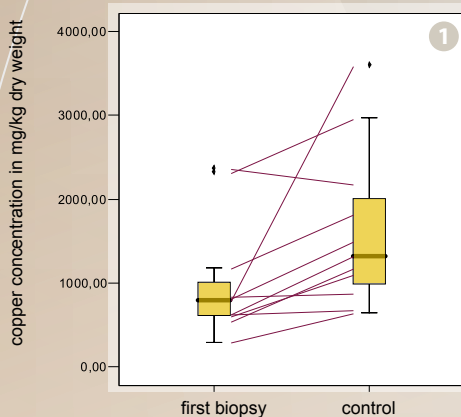
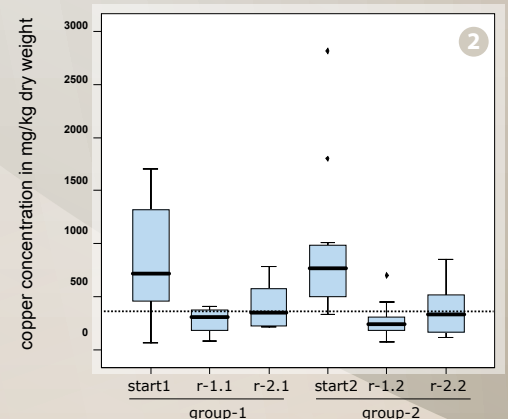


Figure 2: Hepatic copper measurements

Quantitative measurement of hepatic copper improved during treatment in both groups (group-1: diet & zinc, group-2: diet & placebo). After 8 months, at recheck-1, hepatic copper concentrations had decreased significantly in both groups of dogs, compared to the starting point (start1: group-1 at starting point, median 720 mg/kg dry weight, range 70-1700, r1.1: group-1 at recheck-1: median 328mg/kg, range 84-450, $p < 0.001$, r2.1: group-1 at recheck-2: median 340mg/kg, range 220-790, $p = 0.03$, start2: group-2 at starting point, median 770mg/kg, range 340-2810, r2.1: group-2 at recheck-1: median 236 mg/kg, range 80-700, $p = 0.001$, r2.2: group-2 at recheck-2: median 320 mg/kg, range 118-850, $p = 0.04$). There was no difference in hepatic copper concentrations between both groups at recheck-1 ($p = 0.52$), and there was no difference between groups at recheck-2 ($p = 0.79$). There was no further decrease of hepatic copper concentrations between recheck-1, and recheck-2 (group-1 $p = 0.44$, group-2 $p = 0.25$). Upper and lower horizontal borders of the boxes describe borders of upper and lower quartile of the data. The distance between these values is H-spread. Values outside 1.5 times H-spread above and below the hinges are outliers (Diamond). Outliers appear as such in the figure but these dogs were not excluded from statistical testing. Horizontal bars describe the median of the measured copper concentrations.

Figure 1: Progression of hepatic copper accumulation without treatment in 11 dogs

Measurement of hepatic copper concentrations was repeated before any treatment was given, and while the dogs were fed their usual maintenance diet. In all but one dog hepatic copper concentrations increased during the time interval of 8.7 months between both measurements from a median of 793 mg/kg dry weight (SD:702 mg/kg, range 290-2370, mean of 1000mg/kg) to a median of 1320 mg/kg dry weight (SD:954 mg/kg, range 630-3610, mean 1626 mg/kg, $p = 0.04$). Upper and lower horizontal borders of the boxes describe borders of upper and lower quartile of the data. The distance between these values is H-spread. Values outside 1.5 times H-spread above and below the hinges are outliers (Diamond). Outliers appear as such in the figure but these dogs were not excluded from statistical testing. Lines between box1 and box2 indicate individual responses of the patients.



CONCLUSIONS

Feeding of low copper diets to Labradors is effective in reducing hepatic copper concentrations. Adjunctive treatment with zinc does not appear to increase the copper-lowering effects of dietary management.