

IGF-I does not improve fat malabsorption in cirrhotic rats

Impaired digestion and/or absorption of nutrients has been considered one of the pathological mechanisms involved in the nutritional disturbance of cirrhosis (10, 11). Moderate fat malabsorption occurs in patients with liver cirrhosis (1, 7). The severity of steatorrhea (14) has been related to decreased output of bile acids, cholestasis and advanced histological stages (6). The aim of this study was to explore whether IGF-I treatment for two weeks modified fat intestinal absorption, measured from faecal fat content, in cirrhotic and healthy rats.

Male Wistar rats (125-130 g), fed *ad libitum*, were used. Liver cirrhosis was induced by carbon tetrachloride (CCl₄) inhalation twice a week for 11 weeks (3, 4) and, to accelerate cirrhosis development, phenobarbital was also added to drinking water (400mg/L) 1 week before and during the entire period of CCl₄ exposure. Cirrhotic rats were randomly assigned to two different groups to receive the vehicle (CI, n=12) or IGF-I for 14 days (CI-IGF, n=12, 2 µg x 100g bw⁻¹ d⁻¹). Treatment with IGF-I or saline began 7 days after finishing CCl₄ exposure. Control rats were randomly assigned to two different groups to receive the vehicle (CO, n=12) or IGF-I (CO-IGF, n=12). Faeces of day 14 were obtained and animals sacrificed by decapitation day 15th. Six mL of blood were previously obtained, being serum stored at -20 °C. Faeces were dried, pulverized and extracted in a Soxhlet extractor (9). The residue was dried, mixed with 3 N HCl and re-extracted with diethyl ether to obtain the total faecal lipids, finally dried under vacuum at 60 °C to constant weight. Cholestasis parameters (bilirubin, cholesterol and alkaline phosphatase) were determined using a Hitachi 747 autoanalyzer (Boehringer Mannheim, Germany)

The results (Table I) show that faeces weight referred to 100g of body weight in CO-IGF group is significantly lower than in CO (p=0.05) and cirrhotic groups. Faecal lipid content in cirrhotic animals increases (p<0.05) as compared to control groups, and no differences were found between untreated and IGF-treated cirrhotic animals (Table I). A clear cholestasis, expressed by increased serum levels of bilirubin, alkaline phosphatase and cholesterol, is observed in untreated cirrhotic animals and reduced after treatment with IGF-I.

The present study shows that a moderated steatorrhea is present in CCl₄-induced cirrhosis. However, IGF-I-treatment, that was able to normalise sugar and amino acid intestinal transport (3, 4, 13), does not improve lipid absorption in this experimental model. Steatorrhea is a common feature in cirrhotic patients and it is above all related to the diminution of both hepatic bile salt and pancreatic exocrine secretion (1, 7). In patients with mild cholestasis, the faecal fat is either normal or only modestly elevated (7,10). Cirrhotic animals included in this work show a moderated increase of faecal fat content associated with cholestasis. In cirrhotic rats treated with IGF-I serum level of cholestasis markers diminish but the treatment does not increase fat absorption. This finding suggests that others factors (apart of cholestasis) are involved in the pathogenesis of fat malabsorption in cirrhosis.

The major consequence of steatorrhea is the malabsorption of fat-soluble vitamins, especially vitamin D and vitamin A (12). Vitamin D deficiency is frequently associated with calcium malabsorption (8) and eventually affects bone metabolism. In fact, hepatic osteodystrophy occurs frequently in cirrhotic patients with steator-

Table I. Faecal weight (g/100 g bw x day) and fat content (%) and serum levels of alkaline phosphatase (U/l), bilirubin (mg/dl) and cholesterol (mg/dl) in the four experimental groups.

	CO	CO-IGF	CI	CI-IGF
Faecal weight	0.66 ± 0.17	0.59 ± 0.1	0.74 ± 0.01*	0.96 ± 0.16*
Faecal fat	113 ± 8	93 ± 6	136 ± 9*	136 ± 9*
Alkaline phosp.	283 ± 17	263 ± 14	489 ± 66***	398 ± 30*\$
Bilirubin	0.40 ± 0.08	0.31±0.04	0.99 ± 0.28*	0.56 ± 0.14
Cholesterol	82.6 ± 4.1	74.3 ± 4.8	147.1 ± 32*	114.1 ± 6.9

Values are mean ± SEM. n = 12 (each group): *p < 0.05. **p < 0.01 and ***p < 0.001 vs. CO groups. \$p < 0.05 vs. CI group.

rhea. Animals with CCl₄-induced cirrhosis showed osteopenia that improved with treatment with IGF-I for three weeks (2). In the present study, the treatment lasts only two weeks in animals with a similar stage of liver cirrhosis, without ascites. Since fat absorption is not modulated by treatment with IGF-I, the beneficial effect on bone could be due to a direct action of this growth factor (2).

In summary, animals with early liver cirrhosis show a deficient intestinal fat absorption with increased faecal fat content. This malabsorption is not corrected by treatment with IGF-I.

Key words: Liver cirrhosis, Fat absorption, Steatorrea, Faecal fat content.

Palabras clave: Cirrosis, Absorción lipídica, Esteatorrea, Grasa fecal.

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