SHORT COMMUNICATION

ALTERED LIPID PROFILE IN LIVER AMOEBIASIS AND ITS EMENDATION WITH METRONIDAZOLE TREATMENT*

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(Received on May 16, 1981)

Summary : Liver amoebic abscess was produced by introducing 16,000 trophozoites of *Entamoeba histolytica* directly into the livers of growing hamsters. A group of the infected animals received orally 64 *mg* metronidazole/*kg* body weight for 5 days from the day of the infection. The treated group was autopsied 7 or 14 days after the treatment.

Histologically, liquefaction of large parenchymal areas and biochemically, elevation in cholesterol, triglycerides, bile acids and decrease in phospholipids were observed in infected livers. The infected hamsters exhibited hyperlipidemia and hypocholesterolemia. With metronidazole treatment all the values tended to shift towards control levels. The magnitude of the shift was determined by the post-treatment period.

Key words : liver amoebic abscess, metronidazole treatment period, hypocholesterolemia, hyperlipidemia

INTRODUCTION

In liver amoebic abscess elevation in hepatic cholesterol (6) and decrease in serum cholesterol (5) have been observed. With metronidazole treatment, improvement has been observed in the cholesterol status of the infected hamsters; however, control levels were not attained (5). The present study was therefore planned to explore the

*This paper was presented at the XII International Congress of Nutrition held at San Diego, California, USA in August 1981.

lipid profile of *E. histolytica* infected and metronidazole-treated hamsters in relation to the duration of the treatment. In addition the hepatic tissue of the infected and treated hamsters was examined for histopathological changes.

MATERIALS AND METHODS

Fortytwo male growing hamsters were divided into 2 groups of 33 infected and 9 controls. Eighteen of the infected animals received 64 *mg* metronidazole/*kg* body weight for a period of 5 days from the day of the infection. Nine each of the infected and infected-treated were autopsied at 7 days and the remaining nine at 14 days post treatment. The inoculum administered (7) into the liver contained 16000 trophozoites/ hamster. The controls received inoculum devoid of trophozoites. The presence of motile amoeba in a smear taken from the periphery of the liver abscess confirmed amoebic nature of the abscess. The hamsters were housed individually in galvanized cages and were fed *ad libitum* for 7 days (unless otherwise stated). At autopsy blood was collected from jugular vein and the livers of infected hamsters were examined for the size of the abscess. The abscess involving 75% of the tissue was considered as large–abscess (2). One cm square piece each of the infected (area farthest from the abscess) and infected-treated livers was placed in 10% formalin solution for histological study (1). The hepatic tissues and serum were analysed for total lipids (3) (serum only) cholesterol, (17), phospholipids (16), triglycerides (15) and bile acids (14) (hepatic tissue only).

The significance of the differences between the two means was calculated. All tests were considered significant at 95% level (9).

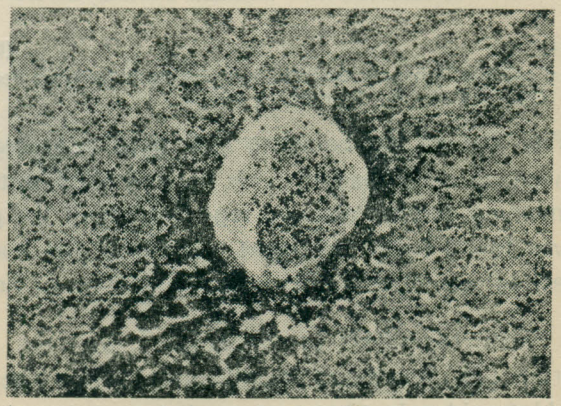
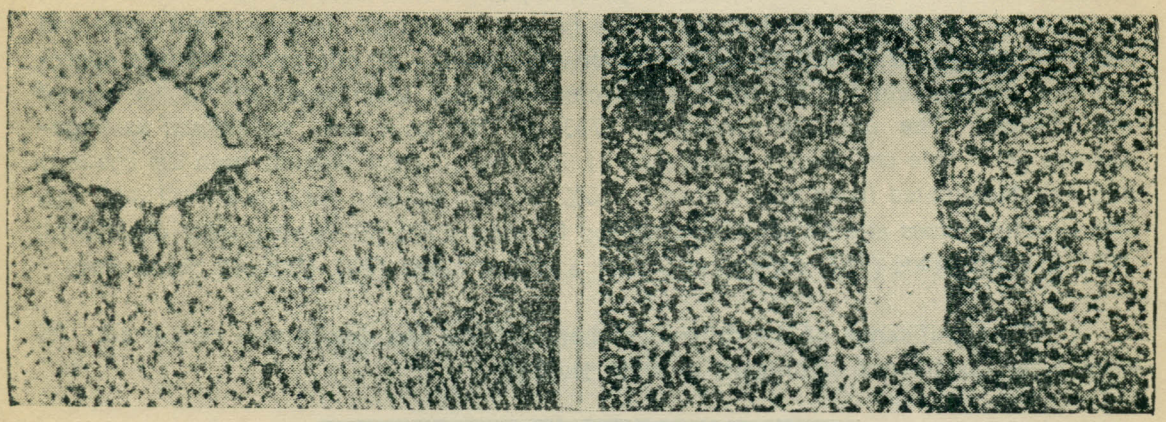


Fig. 1 : Histological changes in hepatic tissue in liver amoebiasis in hamsters (x 100)

RESULTS AND DISCUSSION

Histologically, the infected livers showed liquefaction of the entire liver parenchyma except for a few small patches (Fig. 1). The central vein and portal triad were extremely enlarged and infiltrated with leucocytes. There was proliferation of connective tissue which divided the parenchyma into pseudolobules. Similar changes in liver at sites distant from the abscess cavity have been reported (12).

In contrast the hepatic tissue of metronidazole-treated (7 days post-treatment) hamsters showed somewhat smaller necrotic areas (Fig. 2a). The sinusoids and portal areas however, were still infiltrated with leucocytes, but in some parts of the section mono- and binucleated hepatocytes could be observed indicating a mitotic division of a mononucleate cell without accompanying division of the cytoplasm. On the other hand



(a) (b)

Fig. 2 : Histological changes in hepatic tissue in liver abscess in hamsters treated with metronidazole (a) for 7 days and (b) for 14 days (x 100)

the hepatic section (Fig. 2b) of the hamsters (14 days post-treatment, revealed only a few focal areas of necrosis accompanied with leucocyte infiltration of sinusoids and portal areas. The remaining section showed regeneration of the parenchyma although the hepatic structure was found to be deranged. Earlier it has been reported that 80% of cases of chronic intestinal amoebiasis show disorganization of hepatic cells (8).

In the infected livers, regardless of the abscess size, the levels of cholesterol, bile acids and triglyceride (TG) increased significantly while those of phospholipids decreased (Table I). Metronidazole treatment tended to bring these values closer to the control values. However, at the end of 14 days post-treatment, the cholesterol and

triglyceride contents of the livers still remained higher than the control levels. In normal healthy condition, the influx of cholesterol into hepatic tissue stimulates cholesterol degradative process to counteract cholesterol accumulation (11). Although similar trend was observed in this study yet the cholesterol levels in infected livers rose significantly perhaps due to decreased number of functional cells (Fig. 1). Moreover, the increases observed in bile acids might just be due to the destruction of bile ductules and consequently retention of bile. In infected livers, the cholesterol to bile acid ratio was 3 times higher than that of the controls. The ratio exhibited a shift towards the control ratio with treatment. The decrease in hepatic phospholipids in infection could be attributed to the decreased number of functional hepatocytes. As compared to the control values, the higher TG and lower phospholipids levels in infected livers indicated decreased release and/or oxidation of TG. In infected hamsters, the ratio of cholesterol to phospholipids was 5-times that of the controls and showed marked decrease with treatment.

TABLE I : Hepatic lipids in controls, infected and treated hamsters in liver amoebiasis. (Mean±S.E.)

Groups	*Cholesterol*	*Bile acids*	*P–lipids*	*T.G.*	*Chol/ bile acid*	*Chol/ phospholipid*
			mg/100g wet wt.			
Control	203±13.76	153±2.58	86.8±7.86	265±17.02	1.3	2.3
Infected (15)	682±39.86	184±1.14	60.9±3.80	679± 8.96	3.8	11.2
Abscess size :						
Large (8)	714±46.04	187±1.03	62.6±6.67	700± 3.09	3.8	11.4
Small (7)	646±68.20	181±1.64	59.0±3.43	658± 8.32	3.6	10.9
Treated :						
7 days (9)	420±13.91	168±1.33	56.0±3.22	531±23.33	2.5	7.5
14 days (9)	256±13.44	149±2.37	87.9±6.33	375±10.81	1.7	2.5

Figures in parentheses indicate the number of observations.

The infected hamsters irrespective of the size of the abscess exhibited hyperlipemia, hypocholesterolemia and hypophosphatemia (Table II). The hyper-lipemia could be either due to increased secretion of adrenocorticotropic hormone (4), leading to increased

TABLE II : Serum lipids in controls, infected and treated hamsters in liver amoebiasis. (Mean±S.E.)

Groups	*Total lipids*	*Cholesterol*		*P–lipids*	*T.G.*	*% Esterified chol.*
		Total	*Free*			
		mg/dl				
Control	622±35.81	190±11.38	89±8.22	368±13.85	35.0±1.07	53
Infected	906±45.19	110±2.52	83±2.74	285±13.03	36.4±1.36	24
Abscess size :						
Large	778±6.41	114±4.50	78±1.74	255±8.23	38.4±1.40	32
Small	1003±7.69	106±1.82	87±3.75	308±12.37	34.3±1.99	18
Treated :						
7 days	548±29.75	153±8.90	98±1.70	304±7.44	36.4±0.48	36
14 days	574±3.85	175±4.50	73±2.68	318±6.96	40.4±0.81	58

adipose tissue lipolysis or due to inhibitory effects of endotoxins on plasma lipid clearing factor (13). Hypocholesterolemia in liver amoebiasis has been reported earlier (10). The values for serum esterfied cholesterol as per cent of total cholesterol indicated impairment in esterification process in liver amoebiasis (Table II). With treatment, improvement in esterification process was observed. The serum TG levels were significantly higher in 14-day treated group when compared with those of the controls and 7-day treated group suggesting improvements in mobilization of the accumulated TG from the liver perhaps due to the increased phospholipid levels. It is evident from these data that in liver amoebiasis lipid profile of the host was altered and metronidazole treatment rectified the altered lipid profile.

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Financial assistance from UGC is gratefully acknowledged.

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