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Hepatic Connective Tissue Changes After Surgical Treatment of Portal Hypertension

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Abstract

The study was done on twenty patients, they were classified into two groups one group with no evidence of liver disease or portal hypertension, the other group was admitted for surgical treatment of oesophageal varices and portal hypertension (elective splenectomy and devascularization). Blood samples were collected from both groups pre and post operatively and were divided into 3 parts: a part for routine investigations, another for detection of serum procollagen III and the third part for estimation of plasma fibronectin by radioimmunoassay. Liver biopsy was taken for histopathological examination and estimation of total collagen.

Introduction

THE excessive deposition of collagen in the extracellular space is the main feature of hepatic fibrosis and involves two structurally distinct forms of interstitial collagens, namely type I and type II. The increase of collagen with progression of hepatic fibrosis is the main phenomenon in liver cirrhosis. Recent studies suggest that serum level of type III procollagen could be valuable, non invasive monitor of hepatic fibrogenesis as there is a close correlation between its level and the degree of fibrosis in portal tracts.

The liver was found to be the main source of plasma fibronectin and hepatocytes are the major source for circulating fibronectin. So, it may reflect the degree and severity of liver damage resulting from fibrosis and cirrhosis.

The relationship between the degree of hepatic fibrosis and plasma fibronectin and serum procollagen III is helpful in the detection of the degree of fibrosis and may reflect the beneficial effect of surgical correction of portal hypertension (splenectomy and devascularization) on the progress of hepatic fibrosis.

Patients and Methods

This study was conducted on 20 patients, they were classified into 2 groups: The first group (control group), consists of 10 patients who were admitted to the Department of Surgery, Al Hussain Hospital. They had chronic calcular cholecystitis. No evidence of hepatic disease or portal hypertension was present in this group as investigated clinically, by laboratory, ultrasonographically and endoscopically.

The second group consists of 10 patients who were to be operated upon for the treatment of oesophageal varices and portal hypertension (3 patients gave history of hematemesis). They gave previous history of bilharziasis and were treated medically. All of them have undergone elective splenectomy and devascularization.

Blood samples were collected from both groups preoperatively and postoperatively (3 weeks, 3 months and six months) and were divided into 3 parts; part for routine investigations, another for detection of serum procollagen III and the third part for estimation of plasma fibronectin by radioimmunoassay.

Liver biopsy (1-2 grams) was taken from the anterior margin of the liver during the operation and was divided into two parts, one for histopathological examination (stained with hematoxylin - eosin and Masson's trichrome stain) and the other for estimation of the total collagen by estimation of hydroxyprolene.

Results

The total collagen contents of the liver in the control group ranged from 1.8 mg/gm to 5.3 mg/gm in comparison to higher levels found in the seconed group (from 15 mg/gm to 40 mg/gm), while the collagen fibres deposited in the control group ranged from zero to 2 (+) with marked elevation of collagen fibres deposition in the second group (from 2 (+) to 3 (+). This is summarized in table (I).

Table (II) represents the level of serum procollagen III in the control group in comparison to the second group after 3 weeks, 3 months and 6 months after surgery. The highest levels in the second group showed marked decrease after surgery while that of the control group

Table (I): Comparison between the Two Groups as Regards to Collagen Level.

		Min.	Max.	Mean	SD	PD	*p*
Total collagen	GI	1.8	5.3	4.432		0.799	< 0.001
	GII	15	40	29.85	7.931		
Collagen fibres	GI	0.0	2 (+)	0.382 (+)	0.713 (+)		< 0.05
	GII	2 (+)	3 (+)	2.450 (+)	0.563 (+)		

Table (II): Comparison between the Two Groups as Regards the Procollagen III Level.

		Min	Max	Mean	SD	*p*
Pre-operative	GI	1.3	4.5	2.522	0.67	< 0.005
	GII	4.5	12	7.256	2.011	
3 Weeks after operation	GI	1.5	4	2.61	0.64	< 0.001
	GII	4.3	12.5	8.03	2.327	
3 months after operation	GI	1.6	4.3	3.11	0.66	< 0.005
	GII	2.7	13	7.90	3.055	
6 months after operation	GI	1.5	3.9	2.7	0.69	< 0.001
	GII	2.5	11.5	6.85	2.393	

remained within average after an initial postoperative rise.

The increasing level of plasma fibronectin from surgery onwards in the second group is opposed by more or less stable levels in the control group. The results are summarized in table (III).

Liver biopsy in the control group revealed fatty liver changes in 3 cases (30%), while the remaining 7 cases (70%) were normal. In the second group, 4 cases (40%) were diagnosed as pure bilharzial fibrosis, while the remaining 6 cases (60%) were diagnosed as mixed liver cirrhosis (bilharzial periportal fibrosis and post hepatic cirrhosis). There was extensive deposition of collagen fibres in these cases as proved by Masson's trichrome stain (Fig. I).

Discussion

Type I and III collagens are the two main components of normal and fibrotic liver. In normal, both type I and type III are present nearly in equal amounts [1]. In fibrosis and cirrhosis the majority of deposited collagen are that of type III [2].

Table (III): Comparison between the Two Groups as Regards to Fibronectin Level.

		Min.	Max.	Mean	SD	*p*
Pre-operative	GI	150	355	270.37	49.20	< 0.001
	GII	85	315	151.32	66.12	
3 Weeks after operation	GI	140	380	289.18	52.33	< 0.001
	GII	90	320	167.91	72.91	
3 months after operation	GI	180	350	295.79	44.32	< 0.005
	GII	110	380	194.51	62.77	
6 months after operation	GI	200	365	298.76	48.12	< 0.001
	GII	100	420	203.22	71.13	

Fig. (1): Wedge liver biopsy. Pure bilharzial fibrosis with thick portal tracts & marked collagen fibers deposition (Mason's Trichrome x 200).

We found no difference of collagen contents of the liver whether it is normal or fatty and this is in accordance with the data give by Murata et al and Fisher [3,4]. Collagen accumulation is not the primary pathological event, but rather results from inflammatory process that initially occurs in the affected organ [5].

The total hepatic collagen in group II is about seven folds more than that of group I, which is similar to the five folds increase in collagen contents of fibrotic liver group I,.which is similar to the five folds increase in collagen contents of fibrotic liver proved by Fisher and 3 to 6 folds increase observed by Hassanein et al [6].

There was no significant difference between the level of serum procollagen III in patients with normal and fatty liver which is similar to the results of Galambos et al [7]. There is 3 folds increase in its serum concentration in group II fibrotic patients compared to group I control patients. This result is comparable to that of El-Mohandes et al. [8] who found 2-3 folds increase in serum procollagen III in patients with hepatic fibrosis .

In group I, the serum procollagen III was elevated significantly after 3 months of surgery, but returned to the preoperative levels after 6 months. This temporary postoperative rise could be due to postoperative healing process as suggested by Bensten et al [9].

The level of serum procollagen III in group II was also elevated in the postoperative period, but returned after 6 months to its preoperative level which is already high if compared to that of the control group. This compares favorably with the results of Fessler and Fessler [10].

In the control group, plasma fibronectin ranged from 150-355 mg/L. which is favorable comparable to the results of Steven et al. (260 - 380 mg/L) [11] and Abdul - Rahman et al. (168 - 430 mg/L) [12]. There was marked decrease in the level of plasma fibronection in group II patients in comparison to group I patients, which is similar to that observed in different studies [12,13,14,15,16].

The level of plasma fibronectin showed no significant changes in group I in the postoperative period. In group II, there was significant increase in plasma fibronectin levels after the operation in the postoperative period. This may be explained by improved liver condition or as suggested by Angelis due to the effect of splenectomy as spleen is the major site where fibronectin is degradated [17].

So, the levels of serum procollagen III and plasma fibronectin correlate well with the degree of hepatic fibrosis or cirrhosis and also with the progress of this pathology.

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