Colonic function in cirrhosis of liver & in healthy controls

A. Chacko

*Department of Gastrointestinal Sciences, Christian Medical College & Hospital, Vellore*

Accepted March 13, 1997

Total and segmental colonic transit time (radio-opaque marker method), daily stool weight, stool water and stool frequency were estimated in 10 decompensated nonalcoholic male cirrhotics and 10 male controls. Total and left colonic transit times were significantly shorter \((P < 0.05)\) in cirrhotics as compared to controls. Stool frequency was significantly higher in cirrhosis \((P < 0.01)\) and showed a significantly negative correlation \((r = -0.73, P < 0.02)\) with total colonic transit time. Stool wet weight and water content were significantly higher in cirrhosis \((P < 0.01)\) as compared to controls. Colonic transit was accelerated in cirrhosis and may be an important hitherto unrecognised factor in the etiopathogenesis of diarrhoea observed in patients with cirrhosis.

**Key words** Cirrhosis - colonic transit - diarrhoea

An increase in the stool frequency, with the passage of soft or loose stools is common with all major causes of liver disease1. In the absence of obvious causes, this increased stool frequency has been attributed to fat malabsorption which occurs in cirrhosis1. We have recently shown that gastric and small intestinal transit are normal, while whole gut transit is faster in patients of cirrhosis of the liver as compared to normal subjects2. This suggests that colon transit may be accelerated in cirrhosis of the liver and may play a role in the etiopathogenesis of diarrhoea seen in cirrhosis. The aim of the present study, therefore was to measure colon transit in patients with cirrhosis and evaluate the role of transit in diarrhoea observed in these patients.

**Material & Methods**

**Subjects** : Ten patients with cirrhosis aged 33-71 yr (median age 48 yr) were studied. Diagnosis of cirrhosis was based on standard criteria3. Patients were excluded from the study if they had \((i)\) grade II-IV hepatic encephalopathy; \((ii)\) alcoholic liver disease; \((iii)\) diseases that affect gut transit like infective diarrhoea and diabetes; or \((iv)\) gave a history of taking drugs which affect transit such as prokinetic or antispasmodic drugs during the preceding 2 wk.

Viral hepatitis was responsible for cirrhosis in six patients \((3 \text{ HBsAg positive and 3 anti HCV positive})\) while in four patients the cause of cirrhosis was unknown. The severity of liver disease graded according to Pugh's modification of Childs criteria4 ranged from 7-10 with 8 patients graded as Child B and 2 as Child C.

Ten healthy, asymptomatic adults aged 28-56 yr (median age 37 yr) formed the control group.

Only male subjects were included in the present study. Women were excluded because of the radia-
tion exposure involved.

Design: The study lasted five days during which time, the subjects lived in a metabolic ward. During the first four days, whole gut, and total and segmental colonic transit were measured by radio-opaque marker techniques. Stool collections were carried out during this period and stool weights (wet/dry) and stool frequency were assessed. Stool culture and stool for parasites were also tested. Diet assessment was carried out on days 1 and 2 of the study. On day 5, all subjects underwent a colonoscopy during which segmental colonic mucosal biopsies were obtained.

Whole gut, total and segmental colon transit: Whole gut transit (mean transit time - single) was measured by the radio-opaque marker technique method described by Cummings et al. Total and segmental colonic transit times (TCTT/SCTT) were estimated by a modification of the method described by Arhan et al. In Arhan's method, radiographs were taken serially at 24 h intervals. This was reduced to 8 h in the present study, to adjust for the accelerated gastrointestinal transit in Indian subjects. Briefly, 20 radio-opaque markers of specific shape (large ring: 4 × 1 mm; small ring: 2.5 × 1.0 mm) were given randomly at 8 h interval (0600 h, 1400 h) on day 1 of the study. Anteroposterior supine abdominal radiographs were taken at 8 hourly intervals after ingestion of the first type marker and continued until all markers were expelled in the faeces. Abdominal radiographs were obtained by High kilovoltage, fast film technique which reduced the radiation dose delivered to a fraction of that of a routine abdominal X-ray. Right, left and rectosigmoid colon segments were demarcated on the films using the method of Martelli et al. Each type of marker was then counted in the whole colon and in individual segments of the colon. Total colonic transit time (TCTT) and segmental colonic transit time (SCTT) for each marker were then calculated from the formula:

\[
\frac{TCTT}{SCTT} (h) = \frac{1}{20} \left( \sum X_i \right) 8 \quad i=1
\]

\[
= 0.4 \sum X_i \quad i=1
\]

where 20 = number of markers ingested; 8 = time interval in hours between X-rays; \(X_i\) = number of markers in whole colon (TCTT) or in colonic segment of interest (SCTT); n = total number of X-rays taken. Mean values for two markers was taken as mean TCTT and mean SCTT.

Both cirrhotic and control subjects were allowed regular diet ad lib. However, salt and fluid restriction of 2g/day and 1.5 l/d respectively were imposed on cirrhotic patients. During the period of study, each diet item in every meal was weighed before the meal. Left overs, if any, were also weighed after the meal to quantitate the exact amount of each dietary item consumed. Raw ingredients used in the preparation of each dietary item were then estimated and the fibre content of the diet was then calculated from standard food tables. The mean daily dietary fibre intake in cirrhotic patients (15.19±1.01g/d) was similar to controls (15.7±1.12g/d).

Colonoscopy: All subjects underwent colonoscopy (Olympus Fiberoptic colonoscope CF1T20L, Tokyo, Japan). The colonoscopic findings, based on previous studies included the following: (i) number and location of lesions suggestive of vascular ectasias, (ii) presence of inflammatory changes such as oedema, erythema, friability and granularity; and (iii) presence of colonic and rectal varices. To evaluate correlation of colonoscopic findings with total and segmental colonic transit, an arbitrary score of 'one' was given to each of the above findings. The scores were then totalled, giving a total individual colonoscopy score for each subject.

Biopsies were taken from the right, left and rectosigmoid colonic segments. In order to evaluate the correlation between mucosal biopsy findings and colonic transit times, the biopsy findings were scored according to well defined criteria: (i) Mucosal oedema was scored '0' when absent and '1' when present; (ii) 'Acute colitis like inflammation' (more than 3 neutrophils in the lamina propria per section) as '0' when absent and '1' when present; (iii) 'Chronic colitis like inflammation' (increase in round cells in the lamina propria) was scored '0' when there were normal number of round cells and 1, 2 and 3 when there were mild, moderate and marked increases in round cells; and (iv) The number of vessels in the
lamina propria was graded '0' when there were no vessels, as '1' when there were 1-2 vessels, '2' when there were 3-5 vessels and '3' when there were more than 5 vessels per section of tissue. Total colonic mucosal biopsy score was then obtained by totalling each of the above scores for each individual subject.

Written, informed consent was obtained from all subjects enrolled in the study. The study protocol was approved by the Research and Ethics Committee of Christian Medical College and Hospital, Vellore.

Statistical analysis: Results were expressed as mean ± SEM. Comparison of different parameters between the 2 groups was carried out by the Mann-Whitney U test. Differences in proportion were assessed by Chi-square test. Correlation between variables was calculated by Pearson's Correlation Coefficient. Statistical analysis was carried out using the Minitab Statistical software package running on a PC 80286 computer\textsuperscript{14}.

Results

The results of transit time studies in controls and cirrhotic patients are shown in Table I. Total and segmental colonic transit times were shorter in patients with cirrhosis as compared to controls. These differences were significant ($P < 0.05$) for total colonic and left colonic transit time. The whole gut transit time was also shorter in patients with cirrhosis as compared to controls. The calculated orocecal transit time, however, was similar in the 2 groups.

The mean 48 h stool frequency in patients with cirrhosis was significantly higher than controls (cirrhosis vs controls: $6.8 \pm 3.85$ vs $3.0 \pm 1.25$; $P < 0.01$). There was a significant negative correlation between stool frequency (SF) and total/segmental colonic transit in cirrhotic subjects (SF vs total colonic transit time: $r = 0.73$, $P < 0.02$; SF vs right colonic transit time: $r = 0.67$, $P < 0.05$; SF vs left colonic transit time: $r = 0.71$, $P < 0.05$; SF vs rectosigmoid transit time: $r = 0.62$, $P < 0.05$).

Table II shows the stool weights in cirrhosis patients and in controls. Stool wet weight and water content were significantly higher ($P < 0.01$) in the cirrhosis group. However, mean daily stool solids were similar in the two groups. There was no correlation between stool weights (wet, stool water and dry) and total and segmental colonic transit times in cirrhotic subjects.

Total colonoscopy scores were significantly higher in cirrhosis patients as compared to controls (cirrhosis vs controls: $2.9 \pm 0.4$ vs $0.5 \pm 0.2$; $P < 0.01$). Eight of the ten cirrhotic subjects exhibited erythema and friability of mucosa while only one of the control subjects showed these colonoscopic features. Mucosal oedema was seen in 8 cirrhotic subjects and 3 controls. Five of the cirrhotic subjects had colonic varices while none of the controls had colonic varices. Vascular ectasia were not observed either in cirrhosis patients or in controls. There was no correlation between colonoscopic findings and total and

<table>
<thead>
<tr>
<th>Table I. Transit times in patients with cirrhosis and controls</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Transit times (h)</strong></td>
</tr>
<tr>
<td>Cirrhosis ($n = 10$)</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Total colon</td>
</tr>
<tr>
<td>Right colon</td>
</tr>
<tr>
<td>Left colon</td>
</tr>
<tr>
<td>Rectosigmoid</td>
</tr>
<tr>
<td>Whole gut</td>
</tr>
<tr>
<td>Orocecal</td>
</tr>
<tr>
<td>Results are mean ± SEM; * $P &lt; 0.05$</td>
</tr>
<tr>
<td>Figures in parentheses are the ranges</td>
</tr>
</tbody>
</table>


Table II. Stool weights in patients of cirrhosis and controls

<table>
<thead>
<tr>
<th></th>
<th>Cirrhosis (n = 10)</th>
<th>Controls (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wet weight (g/d)</td>
<td>317.7±36.8* (163.2-601.5)</td>
<td>182.5±31.8 (24.5-309)</td>
</tr>
<tr>
<td>Water content (g/d)</td>
<td>272.8±34.5* (143.4-548.2)</td>
<td>145.7±26.3 (17.0-260.6)</td>
</tr>
<tr>
<td>Dry weight (g/d)</td>
<td>44.83±3.55 (19.82-55.29)</td>
<td>36.76±5.86 (7.52-61.27)</td>
</tr>
</tbody>
</table>

Results are mean ± SEM. * P < 0.01
Figures in parentheses are the ranges

segmental colonic transit times.

Total mucosal biopsy scores were similar in cirrhotics and controls (cirrhosis vs controls : 7.3 ± 0.7 vs 7.4 ± 0.9). Mucosal oedema and ‘acute colitis like inflammation’ were not observed in cirrhotics or in controls. ‘Chronic colitis like inflammation’ scores (cirrhosis vs controls : 2.11 ± 0.54 vs 2.9 ± 0.67) and vessel number scores (cirrhosis vs controls : 5.22 ± 0.49 vs 4.5 ± 0.52) were similar in both groups studied. There was no correlation between colonic mucosal biopsy scores and colonic transit times.

Discussion

The present study was carried out on a fairly homogenous group of cirrhotic patients with hepatic decompensation. A modification of the radiopaque marker method described by Arhan et al6 was used to measure total and segmental colonic transit. The radiopaque markers used in the present study have been validated earlier15 and it was shown that transit time estimation was not significantly influenced by variation in marker size and shape as long as the markers conformed to the specifications described in this study. As intestinal transit times are faster in Indian subjects7 and as whole gut transit in Indian cirrhotics in an earlier study2 was found to be 18.0 ± 1.3 h, the time interval between radiographs in the present study was reduced to 8 h. This reduction in time interval between radiographs is also in conformity with the recommendations for radiopaque marker studies of colonic transit in patients expected to have fast transit times16. The formula used for calculating total and segmental colon transit in the present study is valid as the time interval between radiographs was constant6.

Our results show that total and segmental colonic transit in cirrhosis is faster than in controls, the accelerated colon transit being predominantly due to rapid transit through the left and rectosigmoid colonic segments. Faecal bulk is an important factor in regulating transit. The mean daily stool weight in cirrhotic subjects (318 g) in the present study, was significantly higher than controls (183 g). However, the absence of correlation between stool weights and total and segmental colonic transit times suggests that faecal bulk is not responsible for accelerated colonic transit in cirrhosis. These findings are in agreement with those of Burkitt et al17 who showed that there was no correlation between stool weights and transit times, when stool weight exceeded 200g/day. Increase in dietary fibre intake can accelerate intestinal transit5,18. In the present study, mean dietary fibre intake in cirrhotics was similar to controls, suggesting that dietary fibre was not involved in accelerated colonic transit in cirrhosis.

Can malabsorption known to occur in cirrhosis be responsible for accelerated colon transit? In an earlier study we have shown that malabsorption is mild in cirrhosis of liver2. Further, Jeyanthi et al7 in a study of intestinal transit in patients with tropical sprue found that despite severe malabsorption and a striking increase in stool weights in tropical sprue, there was no change in whole gut transit as compared to controls. This suggests that accelerated colon transit seen in the present study is not due to malabsorption of cirrhosis. The influence of portal colopathy on colon transit was also evaluated in the present study. There was no correlation between colonoscopy or colonic biopsy scores and colonic transit times suggesting that portal colopathy may not be responsible for accelerated colonic transit in cirrhosis. It should however be noted, that portal colopathy and portal hypertension are not synonymous11. The role
of portal hypertension in accelerated colon transit in cirrhosis is yet to be resolved. The elderly as a group, frequently complain of constipation which suggests that transit may be slowed in the older age group. In the present study however, the cirrhotic subjects though older than controls (mean age of cirrhosis vs controls: 48.6 vs 38.4 yr) had a faster colon transit showing that age was not responsible for the rapid colon transit in cirrhosis. Stress stimulates colonic motility and may play a role in accelerated colon transit in cirrhosis. The effect of stress on colonic transit was not examined in this study because of the nonavailability of techniques, validated in Indian population, for evaluating stress.

Stool frequency in cirrhosis is significantly higher than in controls. The significant negative correlation between stool frequency and total and segmental colonic transit, suggests that accelerated colon transit is one of the factors responsible for increased stool frequency in cirrhosis. Water content of stool was significantly higher in cirrhosis as compared to controls. There was no correlation between stool weights (wet, stool water, dry) and total and segmental colonic transit times in patients of cirrhosis suggesting that increase in stool water in cirrhosis was not due to accelerated colon transit.

In conclusion, this study has demonstrated accelerated colonic transit, increased stool frequency and increased stool water content in cirrhosis patients. The significant correlation between colonic transit and stool frequency suggests that accelerated colon transit may contribute to increased stool frequency. The increased stool frequency and stool water seen in cirrhosis in this study suggests that they may be contributory factors to diarrhoea observed in patients with cirrhosis.

References


*Reprint requests:* Dr A. Chacko, Professor of Gastroenterology, Department of Gastrointestinal Sciences, Christian Medical College and Hospital, Vellore 632004