Evidence for oxidant stress in chronic pancreatitis

C GANESH PAI, SREEJAYAN,* M N A RAO*

Gastroenterology Unit, Kasturba Medical College, Manipal 576 119 and
*College of Pharmaceutical Sciences, Manipal, Karnataka

Background: Oxidant stress leading to lipid peroxidation is reported to be the common link in the pathogenesis of chronic pancreatitis irrespective of etiology. Aim: To look for evidence of lipid peroxidation in duodenal juice in patients with chronic pancreatitis. Methods: 19 patients with chronic pancreatitis (14 tropical, 5 alcoholic) and 19 age- and sex-matched subjects with abdominal pain without any cause were studied. Contents were aspirated from the second part of the duodenum during gastro-duodenoscopy. Malonyl dialdehyde (MDA) levels were measured in duodenal juice by the thiobarbituric acid method. Results: MDA levels were higher in patients than in the control group (mean [SD] 42.6 [17.0] vs 29.2 [11.7] nmol/mL; p <0.05). On linear and multiple regression analysis, none of the disease factors correlated with duodenal juice MDA levels. Conclusions: Lipid peroxidation products are increased in patients with chronic tropical and alcoholic pancreatitis. [Indian J Gastroenterol 1999;18:156-157]

Key words: Duodenal Juice, lipid peroxidation

While excessive alcohol intake is a cause of chronic pancreatitis (CP), no etiological factors are known in tropical and idiopathic forms of the disease. The exact pathophysiological mechanisms involved in CP are unknown. The proposed mechanisms include changes in the constitution of pancreatic juice, ductal obstruction and repeated episodes of acute inflammation.

Recent reports suggest that the central abnormality is oxidant stress leading to lipid peroxidation in alcoholic and idiopathic pancreatitis. However, little data exist on lipid peroxidation in tropical pancreatitis. The present study was designed to look for evidence of lipid peroxidation in patients with tropical or alcoholic pancreatitis.

Methods

Nineteen consecutive patients with chronic pancreatitis (14 men; mean age 33.4 y, range 14-69) were studied. Nineteen age- and sex-matched patients with abdominal pain, without any cause detected for the pain and without history of alcohol abuse, acted as controls. Pancreatitis was excluded in the control subjects by serum amylase and lipase estimation, abdominal radiographs, ultrasonography and CT scan, where appropriate. Endoscopic cholangiopancreatography was done in patients and controls if clinically indicated. Those with concomitant diabetes were excluded. Written informed consent was obtained from all and the study was approved by the ethics committee of the institution.

Duodenal juice analysis

Duodenal content was aspirated from the second part close to the papilla using a dry syringe and a dry cannula passed through the suction channel of a gastroscope. Care was taken to minimize contamination by gastric content; gastric contents were aspirated completely before the duodenum was entered. Flushings with water was avoided while the endoscope was in the duodenum; 0.5 to 2 mL of juice was collected per patient. Drugs to stimulate pancreaticobiliary secretion were not used prior to collection. Malonyl dialdehyde (MDA) was measured in the duodenal juice by the thiobarbituric acid method.

Statistical analysis

MDA levels were compared between the two groups using the Mann Whitney U test. Clinical data from the patients were correlated with MDA levels by linear and multiple regression analysis. Statistical significance was set at <0.05.

Results

Fourteen patients (mean age 29 y) had tropical pancreatitis and 5 (mean age 45.7 y) had disease due to alcohol abuse. The patient characteristics are shown in Table 1.

Lipid peroxidation levels

The mean (SD) duodenal juice MDA level was 42.6 (17.0) nmol/mL in the patient group and 29.2 (11.7) nmol/mL in the control group (p<0.05). There was no difference in MDA levels between male and female patients, between those with and without diabetes, and between those with alcoholic and tropical pancreatitis (Table 2).

On linear regression analysis, none of the variables correlated with MDA levels. Age, sex, duration of pain, its frequency and severity, etiology of pancreatitis, diabetes

Table 1: Characteristics of patients with chronic pancreatitis

<table>
<thead>
<tr>
<th></th>
<th>Tropical pancreatitis (n = 14)</th>
<th>Alcoholic pancreatitis (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>9/5</td>
<td>4/1</td>
</tr>
<tr>
<td>Duration of pain in months (range)</td>
<td>1-60</td>
<td>0-36</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Pseudocysts</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Severity of pain: mild/moderate/severe</td>
<td>0/2/58</td>
<td>1/1/12</td>
</tr>
</tbody>
</table>

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Table 2: MDA levels in subgroups of patients with chronic pancreatitis

<table>
<thead>
<tr>
<th>Group</th>
<th>MDA levels (mmol/mL) Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>46.6 (15.7)</td>
</tr>
<tr>
<td>Women</td>
<td>27.7 (14.8)</td>
</tr>
<tr>
<td>Tropical pancreatitis</td>
<td>39.7 (15.4)</td>
</tr>
<tr>
<td>Alcoholic pancreatitis</td>
<td>49.1 (13.9)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>49.6 (16.4)</td>
</tr>
<tr>
<td>Non-diabetes</td>
<td>36.4 (15.9)</td>
</tr>
</tbody>
</table>

Discussion

Previous studies have shown evidence for lipid peroxidation in the duodenal juice of patients with chronic pancreatitis. However, duodenal juice was collected after secretin stimulation to obtain samples rich in lipid fractions from the liver. Lipid peroxidation products in the bile were considered to be the result of oxidant stress consequent to induction of hepatic cytochrome P-450. Subsequent studies have shown such enzyme induction in the pancreas of patients with CP. Bile diversion in patients with CP was not associated with improvement in the clinical course, suggesting that hepatic changes could be just a marker of pathophysiological changes in the pancreas or elsewhere.

We have shown that lipid peroxidation products can be demonstrated even in unstimulated duodenal juice of patients with CP. This may suggest that bile is not the exclusive source of lipid peroxides in these patients. Low serum levels of antioxidants were found in a study from Macraes, as also evidence for induction of hepatic cytochrome P-450. Thus, lipid peroxidation combined with low dietary intake of antioxidants might be important in the pathogenesis of CP.

There are limitations in the present study. We studied only one parameter as evidence for lipid peroxidation. While MDA levels in plasma, tissue, and cell membranes have been shown to be good indicators of lipid peroxidation, this has not been done on duodenal juice samples. We did not measure the coefficient of variation of this test on the same sample. Future studies will also have to measure other parameters such as serum MDA, thiols and glutathione reductase. The lack of correlation between MDA levels and clinical parameters could be due to the small numbers in the study. Finally, demonstration of lipid peroxidation does not necessarily prove its role in pathogenesis — it could as well be the result or accompaniment of the disease. However, the results of this study as well as those of others taken together suggest that lipid peroxidation is important in pathogenesis.

The relative role of oxidant stress in the causation of the clinical and pathophysiological changes of CP is yet to be defined. This abnormality however appears to be central to the pain of CP since micronutrient antioxidant supplements have been shown to ameliorate it. The role of antioxidant supplements in tropical pancreatitis and their effect on other manifestations of the disease await evaluation.

References


Correspondence to: Dr Ganesh Pai

Received December 18, 1998. Received in final revised form May 21, 1999. Accepted June 1, 1999