Melatonin modulates the severity of taurocholate-induced acute pancreatitis in the rat.

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The aim of this study was to investigate the effects of melatonin on serum amylase, tumor necrosis factor-alpha (TNF-alpha) and histological changes in rats with taurocholate-induced acute pancreatitis. Thirty male Wistar rats were randomly divided into three groups; group 1, group 2 and group 3 were enrolled as melatonin, control and sham groups, respectively (n=10 per group). Acute pancreatitis was induced by 1 mL/kg body weight using 5% taurocholate injection into the biliopancreatic duct in groups 1 and 2 after clamping the hepatic duct. Those in group 1 received 50 mg/kg body weight melatonin by intraperitoneal (i.p.) injection. Group 2 received physiological saline i.p. at the same dose. Group 3 solely underwent laparotomy with cannulation of the biliopancreatic duct. Twenty-four hours after the intervention, the rats were killed, and serum samples were collected to measure amylase and TNF-alpha levels. Simultaneously, pancreatic tissues were removed, stained with hematoxylin-eosin and examined under a light microscope. Serum amylase and TNF-alpha levels were significantly lower in the melatonin group compared to the controls (P<0.001). The total histological score, including edema, inflammation, perivascular infiltrate, acinar necrosis, fat necrosis and hemorrhage, was also significantly lower in the melatonin group as compared to the control (P<0.0001). In conclusion, melatonin is potentially capable of reducing pancreatic damage by decreasing serum TNF-alpha levels in taurocholate-induced acute pancreatitis in rats. This result supports the idea that melatonin might be beneficial in ameliorating the severity of acute pancreatitis.
conditioned media from BxPC-3 significantly enhanced both proliferation of and tube formation by human umbilical vein endothelial cells (HUVECs) and these enhancements were significantly inhibited by the proteasome inhibitor MG132 treatment. Collectively, MG132 blocked PaCa-derived VEGF and IL-8 production through inhibition of NF-kappaB activity. Thus, proteasome inhibitors may prove beneficial as anti-angiogenic therapy for PaCa. The study shows that MG132, a proteasome inhibitor, significantly blocked pancreatic-cancer-associated angiogenesis through inhibition of NF-kappaB and NF-kappaB-dependent proangiogenic gene products VEGF and IL-8.


Determinants of accelerated small intestinal transit in alcohol-related chronic pancreatitis.


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Patients with chronic pancreatitis may have abnormal gastrointestinal transit, but the factors underlying these abnormalities are poorly understood. Gastrointestinal transit was assessed, in 40 male outpatients with alcohol-related chronic pancreatitis and 18 controls, by scintigraphy after a liquid meal labeled with 99mTc-technetium-phytate. Blood and urinary glucose, fecal fat excretion, nutritional status, and cardiovascular autonomic function were determined in all patients. The influence of diabetes mellitus, malabsorption, malnutrition, and autonomic neuropathy on abnormal gastrointestinal transit was assessed by univariate analysis and Bayesian multiple regression analysis. Accelerated gastrointestinal transit was found in 11 patients who showed abnormally rapid arrival of the meal marker to the cecum. Univariate and Bayesian analysis showed that diabetes mellitus and autonomic neuropathy on abnormal gastrointestinal transit was assessed by univariate analysis and Bayesian multiple regression analysis. Accelerated gastrointestinal transit was found in 11 patients who showed abnormally rapid arrival of the meal marker to the cecum. Univariate and Bayesian analysis showed that diabetes mellitus and autonomic neuropathy had significant influences on rapid transit, which was not associated with either malabsorption or malnutrition. In conclusion, rapid gastrointestinal transit in patients with alcohol-related chronic pancreatitis is related to diabetes mellitus and autonomic neuropathy.

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EUS-guided FNA of solid pancreatic masses: high yield of 2 passes with combined histologic-cytologic analysis.


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EUS-guided FNA (EUS-FNA) is an established tissue-acquisition technique, with most studies concentrating on cytologic analyses of specimens, with only few data existing on histologic assessment. To assess the sensitivity of a combined analysis of histologic followed by cytologic tissue diagnosis. A retrospective 3-center study was made. In consecutive patients undergoing FNA of solid pancreatic masses, core specimens were harvested for histology; residual tissue was examined cytologically. Only unequivocally positive results were regarded as malignant. Criterion standards were positive results from EUS-FNA or other histologic findings, or, if negative, clinical follow-up data (minimum 12 months). Among 192 patients (110 men; mean age 63 years) with mostly pancreatic-head masses (72.4%), overall, adequate tissue was obtained in 98.9% of all cases, with a mean of 1.88 needle passes and an overall sensitivity of 82.9% (95% CI, 76.0-88.5%). Histology and subsequent cytology provided adequate tissue and sensitivities of 86.5% and 60%, and 92.7% and 68.1%, respectively. Excluding cases with inadequate specimens, sensitivities rose by 4% to 10%. Histology showed a trend for superiority over cytology only in characterizing nonadenocarcinoma tumor types. No differences in sensitivity were found between the centers involved. At EUS-FNA in pancreatic masses, combined histologic-cytologic analysis achieved a sensitivity of more than 80%, despite a low number of needle passes and may thus save time. Histology alone did not reach higher sensitivity than cytology. In particular situations, eg, rare tumors, histology may still be required.

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Standard steroid therapy for autoimmune pancreatitis.


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The authors aimed to establish appropriate steroid therapy regimen for autoimmune pancreatitis (AIP). Retrospective survey of AIP treatment was conducted in 17 centers in Japan in patients with AIP treated with steroid therapy. Rate of remission and relapse. Of 563 AIP patients, 459 (82%) received steroid therapy. Remission rate of steroid-treated AIP was 98%, which was significantly higher than that of patients without steroid therapy (74%, 77/104; P<0.001). Steroid therapy was given for obstructive jaundice (60%), abdominal pain (11%), associated extrapancreatic lesions except the biliary duct (11%), and diffuse
enlargement of the pancreas (10%). There was no relationship between the period necessary to achieve remission and the initial dose (30 mg/day vs 40 mg/day) of prednisolone. Maintenance steroid therapy was performed in 377 (82%) of 459 steroid-treated patients, and steroid therapy was stopped in 104 patients. The relapse rate of AIP patients on maintenance therapy was 23% (63/273), which was significantly lower than that of patients who stopped maintenance therapy (34%, 35/104; P=0.048). From the start of steroid therapy, 56% (55/99) relapsed within 1 year, and 92% (91/99) relapsed within 3 years. Of the 89 relapsed patients, 83 (93%) received steroid re-treatment, and steroid re-treatment was effective in 97% of them. The major indication for steroid therapy in AIP is the presence of symptoms. The authors recommend an initial prednisolone dose of 0.6 mg/kg/day, which is then reduced to a maintenance dose over a period of 3-6 months. Maintenance therapy with low-dose steroid reduces but does not eliminate relapses.

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**Long-term outcome of autoimmune pancreatitis.**


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Autoimmune pancreatitis (AIP) is a unique form of pancreatitis and can be complicated with various extrapancreatic lesions. Little is known about the long-term clinical course of AIP. For this study, the authors recruited 21 patients, averaging 66.5 years in age (range, 19-84 years) and observed them at a mean interval of 40.8 months (range, 18-130 months). Three of the patients were also diagnosed with retroperitoneal fibrosis, 3 had sialoadenitis, 2 had chronic thyroiditis, 1 had interstitial nephritis, and 1 had interstitial pneumonia. Three of the patients underwent surgical therapy, 12 patients received methylprednisolone (PSL) treatment, and the 6 remaining patients received no treatment. Enlargement of the pancreas was attenuated in all the PSL-treated patients. Seven of the 21 patients showed pancreatic atrophy, of whom 2 were non-PSL-treated patients. Three patients developed chronic pancreatitis. One patient was diagnosed with pancreatic cancer after 50 months of PSL therapy. As with chronic pancreatitis patients, AIP patients should be observed closely for abnormality in pancreatic function.

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**Ischemia-reperfusion of the pancreas induced hyperresponsiveness of the airways in rats.**

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Ischemia-reperfusion (I/R) of the rat pancreas induced acute pancreatitis with systemic inflammatory response syndrome. Activated inflammatory cells sequestered in the lung and the proteases released from the inflammatory pancreas both could induce lung inflammation and lung injury. Ischemia of the pancreas was induced by clamping the gastroduodenal and the splenic artery for 2 hours followed by reperfusion for 6 hours. The authors observed airway reactivity to methacholine. The pulmonary function test of Penh was used to reflect the airway responses. mRNA expression of iNOS and tumor necrosis factor-alpha (TNFalpha) in the lung tissue were measured by real time polymerase chain reactions. This protocol resulted in significant elevations of the blood concentrations of nitric oxide, hydroxyl radical, amylase, TNFalpha, and white cells among the I/R group. The mRNA expressions of iNOS and of TNFalpha in the lung tissues were significantly increased after I/R. Pulmonary function data showed that I/R of the pancreas induced significant increases in the responses to methacholine challenge: Penh was significantly increased in the I/R group compared with the sham group. Lavage white cells were significantly increased in the I/R group. I/R of the pancreas induced systemic inflammatory responses and increased white cell sequestration in the lung. Hyperresponsive responses in the airways of the reperfusion group may be due to airways inflammation, which increased white cell sequestration in the lung and the expressions iNOS and TNFalpha inflammatory mediators in lung tissues.