The Journal of
Lithotripsy & Stone Disease

APRIL 1991
VOLUME 3 NUMBER 2

CONTENTS

UROLOGICAL CLASSIC ARTICLE

ISOLATION OF A POTENT CHOLESTEROL NUCLEATING-PROMOTING ACTIVITY FROM HUMAN GALLBLADDER BILE: ROLE IN THE PATHOGENESIS OF GALLSTONE DISEASE. *Groen AK, Noordam CH, Drapers JAG, et al. Hepatology 1990;11:525–533.*

Gallbladder bile contains nucleating-promoting activity that binds to concanavalin A. The activity was found in gallbladder bile from cholesterol gallstone patients but also in gallbladder bile from patients without stones and patients with pigment stones. Bile from patients with multiple cholesterol gallstones contained high concanavalin A-binding nucleation-promoting activity. The activity was much lower in bile samples from pigment stone patients, patients without stones and patients with a solitary cholesterol stone. Serum contained very little activity and no concanavalin A-binding nucleation-promoting activity could be demonstrated in gallbladder mucosa. This suggests that concanavalin A-binding nucleation promoter is produced in the liver or bile duct epithelium. The activity was fully resistant to digestion with pronase but was heat labile and could be destroyed by prolonged incubation with a mixed glycosidase preparation indicating that sugar residues are important for this activity. On a Superose 12 gel permeation column, promoting activity eluted in two major peaks at apparent molecular weights of 150 ± 30 kD (n = 5) and < 5 kD, respectively.

The mobility on the column was not influenced by pronase digestion. The factor with the higher molecular weight could be isolated further by polyacrylamide gel electrophoresis under nondenaturing conditions. On sodium dodecyl sulfate-polyacrylamide gel electrophoresis, the apparent molecular weight of the glycoprotein was 130 kD. In conclusion, gallbladder bile contains nucleating-promoting activity that binds to concanavalin A. The activity is increased in bile from patients with multiple cholesterol gallstones and could therefore play an important role in the pathogenesis of gallstone disease.

Comment

Abnormal rapid nucleation of cholesterol from supersaturated gallbladder bile is of key importance in primary gallstone formation. However, the degree of supersaturation in bile is not related to the presence of cholesterol crystals or to the time required for their nucleation. Therefore, nucleation-promoting factors in lithogenic bile have been postulated.

Groen et al. have isolated by concanavaline A-Sepharose chromatography of gallbladder bile a glucose-/mannose-containing 130-kD glycoprotein with strong cholesterol nucleation-promoting activity of model biles. The activity was found in the majority of gallbladder biles investigated and high nucleation-promoting activity titers were observed in biles from patients with multiple cholesterol stones. The activity titer in bile was not correlated to total protein content, cholesterol saturation index and total lipid concentration. Furthermore and more important, according to a prior publication of the authors (Clin Chim Acta 1987;165:292–302), no correlation between the nucleating promoting activity titer and the cholesterol nucleation time has been observed. The data of Groen et al. are of particular interest and the relationship between the 130-kD glycoprotein and the pathogenesis of multiple cholesterol gallstones seems to be evident.

The low nucleation-promoting activity titer in biles from patients with solitary cholesterol stones, indistinguishable from the titers in biles of patients with pigment stones or no stones, is surprising and difficult to explain. It points to an exclusive role of the isolated glycoprotein in the pathogenesis of multiple cholesterol gallstones.

However, the finding of low-activity titers in biles of patients with solitary cholesterol gallstones

and the missing correlation between activity titer and cholesterol nucleation time clearly shows that the 130-kD glycoprotein could not be the sole nucleation-promoting factor. This underscores the multifactorial etiology of cholesterol gallstone disease and should stimulate further investigation of the pathophysiology of cholesterol gallstone formation.

Dieter Jüngst, M.D.
Munich, Federal Republic of Germany

Biliary Literature Survey

Albert MB, Fromm H, Borstelmann R, et al. Successful outpatient treatment of gallstones with piezoelectric lithotripsy. Ann Intern Med 1990;113:164–166.

Aoki Y, Tanimura H, Kawashima H, et al. Cholescintigraphic observation of the sphincter of Oddi motor activity in patients with gallstone. Nippon Geka Hokan 1989;58:289–298.

Baillie J, Cairns SR, Putman WS, et al. Endoscopic management of choledocholithiasis during pregnancy. Surg Gynecol Obstet 1990;171:1–4.

Braver JM, Clarke PD. Cholecystoduodenal fistula with impending gallstone ileus. Invest Radiol 1990;25:757–758.

Brink JA, Simeone JF, Saini S, et al. Simulation of gallstone fragments by cavitation bubbles during extracorporeal shock wave lithotripsy: physical basis and in vitro demonstration. Radiology 1990;174:787–791.

Buiumsohn A, Albu E, Gerst PH, et al. Cholelithiasis and teenage mothers. J Adolesc Health Care 1990; 11:339–342.

Burch JM, Feliciano DV, Mattox KL, et al. Gallstone pancreatitis. The question of time. Arch Surg 1990;125:853–860.

Burnett DA, Greenberger NJ. Restraint urged for biliary lithotripsy: reply. Dig Dis Sci 1990;35:917.

Carr Locke DL. Acute gallstone pancreatitis and endoscopic therapy. Endoscopy 1990;22:180–183.

Chen MF, Jan YY. Percutaneous transhepatic cholangioscopic lithotripsy. Br J Surg 1990;77:530–532.

Clavien PA, Richon J, Burgan S, et al. Gallstone ileus. Br J Surg 1990;77:737–742.

Cometta A, Gallot-Lavallee-Villars S, Iten A, et al. Incidence of gallbladder lithiasis after ceftriaxone treatment. J Antimicrob Chemother 1990;25:689–695.

Connelly NR, Weinstock AD. Continuous alfentanil infusion for extracorporeal shock wave lithotripsy of gallbladder stones. Anesth Analg 1990;70:299–302.

Cope C, Burke DR, Meranze SG. Percutaneous extraction of gallstones in 20 patients. Radiology 1990;176:19–24.

Cucchiaro G, Rossitch JC, Bowie J, et al. Clinical significance of ultrasonographically detected coincidental gallstones. Dig Dis Sci 1990;35:417–421.

DeSantis A, Paganelli R, Stefanoni R, et al. Prevalence of gallstones in patients with primary immunoglobulin deficiency. Evidence for lack of association. Dig Dis Sci 1990;35:716–720.

Dickerman JL. Gallstone formation associated with weight reduction. J Am Osteopath Assoc 1990; 90:456–458.

Diehl AK, Sugarek NJ, Todd KH. Clinical evaluation for gallstone disease: usefulness of symptoms and signs in diagnosis. Am J Med 1990;89:29–33.

Ditzel H, Schaffalitzky-de-Muckadell OB. Endoscopic sphincterotomy in acute cholangitis due to choledocholithiasis. Hepatogastroenterology 1990;37:204–207.

Duane WC. Pathogenesis of gallstones: implications for management. Hosp Pract 1990;25:65–72.

Ericsson S, Eriksson M, Angelin B. Biliary lipids in familial combined hyperlipidaemia: effects of acipimox therapy. Eur J Clin Invest 1990;20:261–265.

Feldman RK, Freeny PC, Kozarek RA. Pancreatic and biliary calculi: percutaneous treatment with tunable dye laser lithotripsy. Radiology 1990;174:793–795.

Finch PJ, Haddock J, Grundy A. Duodenal pseudotumour: a silent impacted common bile duct calculus. Postgrad Med J 1989;65:794–796.

Flick AL. Restraint urged for biliary lithotripsy. Dig Dis Sci 1990;35:916–918.

Floyd JB Jr. Risk factors that would improve the course and outcome of acute gallstone pancreatitis. Am J Surg 1990;159:270.

Garcia-Ontiveros A, Cantero-Hinojosa J, Gil-Eextremera B, et al. Differences in gallstone structure in primary common bile duct lithiasis and gallbladder lithiasis. Klin Wochenschr 1990;68:496–502.

Gibney EJ. Asymptomatic gallstones. Br J Surg 1990;77:368–372.

Gleeson D, Ruppin DC, Saunders A, et al. Final outcome of ursodeoxycholic acid treatment in 126 patients with radiolucent gallstones. Q J Med 1990;76:711–730.

Haapiainen RK, Lindell OI, Schroder TM. Intraoperative removal of pancreatic duct calculus with a rigid ureterorenoscope and ultrasonic lithotripsy. Surgery 1990;107:353–355.

Hall RI, Ingoldby CJ, Denyer ME. Periampullary diverticula predispose to primary rather than secondary stones in the common bile duct. Endoscopy 1990;22:127–128.

Ho YD, Ho KJ. Biliary D-glucaric acid: its quantitation and preventive role in gallstone formation. Scand J Gastroenterol 1990;25:631–640.

Hore PJ, Silbert BS, Cook R-J, et al. A double-blind assessment of segmental sensory changes with epidural fentanyl versus epidural saline in patients undergoing extracorporeal shock-wave lithotripsy. Anesthesiology 1990;2:603–606.

Ingber S, Jacobson IM. Biliary and pancreatic disease in the elderly. Gastroenterol Clin North Am 1990;19:433–457.

Josephs LG, Birkett DH. Electrohydraulic lithotripsy

(EHL) for the treatment of large retained common duct stones. Am Surg 1990;56:232–234.
Kelly TR, Elliott DW. Proper timing of surgery for gallstone pancreatitis. Am J Surg 1990;159:361–362.
Kopecky KK, Hawes RH, Bogan ML, et al. Percutaneous pulsed-dye laser lithotripsy of gallbladder stones in swine. Invest Radiol 1990;25:627–630.
Kowak A, Nowakowska-Dutawa E, Rybicka J. Patency of the Santorini duct and acute biliary pancreatitis. A prospective ERCP study. Endoscopy 1990;22:124–126.
Landreneau RJ, McClelland RN. Impaction of the endoscopic basket. An important consideration in the trans-sphincteric management of choledocholithiasis. Am Surg 1990;56:388–393.
Levin DC, Matteucci T. "Turf battles" over imaging and interventional procedures in community hospitals: survey results. Radiology 1990;176:321–324.
Lorusso D, Misciagna G, Mangini V, et al. Duodenogastric reflux of bile acids, gastrin and parietal cells, and gastric acid secretion before and 6 months after cholecystectomy. Am J Surg 1990;159:575–578.
Lu DS, Ho CS, Allen L-C. Gallstone dissolution in methyl tert-butyl ether after mechanical fragmentation: in vitro study. Am J Roentgenol 1990;155:67–72.
MacFadyen BV Jr, Sandler CM. Percutaneous cholecystostomy and lithotripsy of gallstones. Am Surg 1990;56:226–231.
Magnuson TH, Lillemoe KD, Scheeres DE, et al. Altered bile composition during cholesterol gallstone formation: cause or effect? J Surg Res 1990;48:584–589.
Marteau C, Sastre B, Iconomidis N, et al. pH regulation in human gallbladder bile: study in patients with and without gallstones. Hepatology 1990;11:997–1002.
McGrath FP, Lee SH, Gibney RG, et al. Hepatic subcapsular hematoma: an unusual complication of biliary lithotripsy. AJR 1990;154:1015–1016.
Morgentaler A, Kourman CN. Treatment of an impacted fecalith with electrohydraulic lithotripsy. N Engl J Med 1990;322:855–856.
Nowak A, Nowakowska-Dutawa E, Rybicka J. Patency of the Santorini duct and acute biliary pancreatitis. A prospective ERCP study. Endoscopy 1990;22:124–126.
Ohara N, Schaefer J. Clinical significance of biliary sludge. J Clin Gastroenterol 1990;12:291–294.
Ransohoff DF, Gracie WA. Management of patients with symptomatic gallstones: a quantitative analysis. Am J Med 1990;88:154–160.
Rawat B, Burhenne HJ. Extracorporeal shock wave lithotripsy of calcified gallstones. Work in progress. Radiology 1990;175:667–670.
Rege RV, Dawes LG, Moore EW. Biliary calcium secretion in the dog occurs primarily by passive convection and diffusion and is linked to bile flow. J Lab Clin Med 1990;115:593–602.
Reihner E, Rudling M, Stahlberg D, et al. Influence of pravastatin, a specific inhibitor of HMG-CoA reductase, on hepatic metabolism of cholesterol. N Engl J Med 1990;323:224–228.
Rothschild JG, Holbrook RF, Reinhold RB. Gallstone lithotripsy vs cholecystectomy. A preliminary cost-benefit analysis. Arch Surg 1990;125:710–714.
Sanden HV, Schmitt W, Ottenjann R. Single-step percutaneous transhepatic cholecystoscopy. Endoscopy 1990;22:149–150.
Scheeres DE, Magnuson TH, Pitt HA, et al. The effect of calcium on gallbladder absorption. J Surg Res 1990;48:547–551.
Senior JR, Johnson MF, DeTurck DM, et al. In vivo kinetics of radiolucent gallstone dissolution by oral dihydroxy bile acids. Gastroenterology 1990;99:243–251.
Smith BF. Effect of laser fragmentation of cholesterol and mixed gallstones on in vitro dissolution in methyl tert-butyl ether. Dig Dis Sci 1990;35:236–241.
Soehendra N, Schulz H, Nam VC, et al. ESWL and gallstone dissolution with MTBE via a naso-vesicular catheter. Endoscopy 1990;22:176–179.
Tandon RK, Anand AC. Dietary factors in the pathogenesis and management of gallstones. J Assoc Physicians India 1989;37:337–340.
Tung GA, Mueller PR, Brink JA, et al. Gallstone fragmentation with contact electrohydraulic lithotripsy: in vitro study of physical and technical factors. Radiology 1990;174:781–785.
Weingarten MA, Eilat-Zanani Z, Hart J. Frequency of clinical gallstone disease among Yemenite Jews in Israel. Isr J Med Sci 1990;26:200–204.
Weinstein MC, Coley CM, Richter JM. Medical management of gallstones: a cost-effectiveness analysis. J Gen Intern Med 1990;5:277–284.
Westlake PJ, Hershfield NB, Kelly JK, et al. Chronic right upper quadrant pain without gallstones: does HIDA scan predict outcome after cholecystectomy? Am J Gastroenterol 1990;85:986–990.
Yee AC, Ho CS. Percutaneous transhepatic biliary drainage: a review. Crit Rev Diagn Imaging 1990;30:247–279.
Zeman RK, Davros WJ, Garra BS, et al. Relationship between stone motion, targeting, and fragmentation during experimental biliary lithotripsy. Radiology 1990;176:125–128.