The Journal of
Lithotripsy & Stone Disease

JULY 1991
VOLUME 3 NUMBER 3

CONTENTS

BILIARY CLASSIC ARTICLE

UROLOGICAL CLASSIC ARTICLE

Abstracts

ALTERED BILE COMPOSITION DURING GALLSTONE FORMATION: CAUSE OR EFFECT? *Magnuson TH, Lillemoe KD, Scheeres DE, et al. J Surg Res 1990;48:584–589.*

Gallbladder stasis, increased absorption, and elevated levels of calcium, hydrogen ion, and bilirubin have been implicated as factors potentially critical to cholesterol crystal precipitation. Previous studies, however, have analyzed bile only when crystal or gallstones have already formed. Therefore, we

tested the hypothesis that changes in bile are a late effect, occurring only after crystal formation. Adult male prairie dogs were fed a standard nonlithogenic control diet (n = 7) or a lithogenic 1.2% cholesterol diet for 5, 9, or 14 days to cause cholesterol saturation (n = 7), cholesterol monohydrate crystals (n = 7), or gallstones (n = 7). Gallbladder bile was examined microscopically for crystals, and analyzed for ionized calcium, bilirubin, pH, total protein, biliary protein, and biliary lipids. The ratio of gallbladder to hepatic bile radiolabeled cholic acid specific activity (R) was calculated as an index of gallbladder stasis. Cholesterol saturation index was calculated. The results demonstrate that increased gallbladder bile cholesterol saturation and total protein concentrations precede cholesterol monohydrate crystal precipitation. However, changes in gallbladder ionized calcium, unconjugated bilirubin, pH, stasis, and absorption were noted only after crystals and gallstones had already formed. These data indicate that alterations in gallbladder bile calcium, bilirubin, pH, stasis, and absorption are not early changes but occur simultaneously with or after crystal formation. Increased biliary protein, however, which was elevated prior to nucleation, may be an important mediator of cholesterol precipitation in cholesterol-supersaturated bile.

Comment

In view of the sometimes high recurrence rates after successful nonsurgical treatment of gallstones, there is an urgent need for an appropriate treatment to prevent the formation of cholesterol crystals. Factors critical to cholesterol precipitation in bile are usually assessed in gallstone-containing bile. It is, therefore, unclear which of the observed alterations in bile precede crystal formation and which are secondary to gallstone formation. In the well designed and carefully performed study of Magnuson et al. the authors seek a better understanding of the sequence of events leading to cholesterol gallstone formation. Using prairie dogs fed with a lithogenic cholesterol-rich diet as a model of cholesterol crystal formation, the authors were able to analyze bile composition before, during, and after crystal formation. While increased levels of bilirubin, ionized calcium, and pH changes only occurred after gallstone formation, total protein concentrations were increased before cholesterol precipitation. This points toward a central role of increases in total biliary protein in the pathogenesis of cholesterol crystals formation in bile.

The presented data only allow us to speculate about the mechanisms that lead to increases in biliary protein. Mucin glycoproteins (unfortunately not determined in the study) may be one source. However, since the protein content of mucins is only 15%–30% it is unlikely that an increase in mucus secretion alone accounts for the more than fivefold increase in total biliary protein. Diffusion of plasma proteins through a damaged mucosa may be an alternative or additional source. Inflammatory reactions of the gallbladder mucosa triggered by for example high lysolecithin concentrations in the cholesterin-supersaturated bile may increase mucus secretion and cause an increased permeability of the gallbladder mucosa with subsequent "leakage" of plasma proteins into the bile. An increased concentration of total biliary protein may, therefore, reflect mucosal inflammation of the gallbladder and it is conceivable that high biliary protein concentrations are only one aspect of inflammation-induced changes in bile, which together favor cholesterol crystal formation. Further experiments along the line of the study of Magnuson et al. are needed to clarify this point and provide a better understanding of factors predisposing to gallstone disease.

C. von Ritter, M.D., PH.D.
D. Jüngst, M.D.
G. Paumgartner, M.D.
Munich, Germany