Significance of the Presence of Conjugated Iopanoic Acid in the Bowel of Patients with Abnormal Oral Cholecystogram

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Abstract
The significance of the presence of conjugated iopanoic acid in the bowel in patients with faint or non-visualized gall bladder was evaluated in predicting gall bladder (GB) pathology. Of the 60 patients with oral cholecystography (OCG) performed using 3 g of iopanoic acid, 45 had either faintly visualized or non-visualized gall bladder and were reviewed for the presence of conjugated contrast material in the bowel. All these underwent a second OCG; three showed normal opacification of GB while 42 showed faintly visualized (3) or non-visualized (39) gall bladder with conjugated contrast material in the bowel. These 42 patients were then subjected to surgery (25), ultrasound (10) or ERCP (7), and all showed evidence of gall bladder pathology. It is concluded that the presence of conjugated iopanoic acid in the bowel in patients showing faintly or non-visualized gall bladder is a strong evidence of gall bladder disease, with a specificity rate of 92%.

Key words: Oral cholecystogram, poor or non-visualization of gall bladder, iopanoic acid in the bowel.

Introduction
Oral cholecystogram (OCG) as a method of investigating gall bladder (GB) disease was first introduced in 1924 by Graham and Cole and until recently remained unchallenged in this respect. The introduction of newer techniques such as ultrasound, endoscopic retrograde cholangiopancreatography (ERCP) and HIDA scan has somewhat decreased the enthusiasm for this procedure. However, the ease of performance, safety and universal applicability of OCG makes it an ideal investigation in developing countries such as India, provided the results obtained are accurate.

Non-visualization or faint visualization of the GB after a single or double dose of an oral cholecystographic agent is considered diagnostic of either an abnormal GB or cystic duct obstruction, provided extrinsic causes for non-visualization can be excluded and liver functions are normal. Furthermore the recognition of conjugated iopanoic acid in the bowel and/or the opacification of the common bile duct in patients with faint or non-visualized GB excludes extra-biliary causes for non-visualization of the GB and allows the presumptive diagnosis of an obstructed cystic duct or gall bladder pathology.

The aim of the present study was to determine the accuracy of OCG in diagnosing GB disease and for this purpose we have assessed the significance of the presence of conjugated iopanoic acid in the bowel in patients with faint or non-visualized GB.

Material and Methods

Control Group
Twenty healthy subjects apparently free from any gastrointestinal disorder served as the controls. After suitable preparation, plain abdominal skigrams including the lower pelvis were obtained in ten of these subjects in order to assess the relative soft tissue densities of psoas muscles and the gas filled colon. In the remaining ten subjects the normal course of the absorption and excretion of iopanoic acid over a 14-hour period was observed. Iopanoic acid (6 tablets of Telepaque—3 g) was administered at 6 AM and serial full abdominal skigrams were obtained at 2 hourly intervals until 8 PM.

Patient Group
Sixty patients with suspected gall bladder disease were included in the study. Patients were instructed to take 50 g of batter at lunch on the day prior to the examination followed by a light fat-free evening meal. At 8 PM they were advised to swallow 6 Telepaque tablets one at a time with water. The following morning, at 10 AM, abdominal radiographs using 66-70 KVP were obtained with the patient in the supine position. Special emphasis was placed on including the entire pelvis in the radiographs in order to study the presence of conjugated or unconjugated contrast material in the bowel lumen. If the pelvis could not be included in the abdominal radiograph a separate skigram of the pelvis was obtained.

Patients showing a faint or non-visualized GB were re-examined within seven days of the first test, 35 with 3 g of iopanoic acid and the remaining ten with a double dose of Telepaque tablets.

All roentgenograms were read and analyzed independently by two gastroenterologists and two radiologists who were well acquainted with the appearances of conjugated contrast material.

Results

Control Group
There were 13 males and 7 females with a mean ± SD age of 31.9±11.06 years (range 18-56 years). Plain abdominal skigrams showed that the psoas muscles were more radio-dense compared to the gas in the right colon. However, in the presence of conjugated
contrast material, the colon appeared denser than the psoas muscles (Fig 1).

Radiographs taken at 2 h, 4 h, and 6 h after ingestion of iopanoic acid showed (unabsorbed) granular contrast material in the stomach (8/10), proximal small bowel (7/10), and distal small bowel (8/10) respectively (Fig 2). In two subjects, unabsorbed contrast material was seen in the colon at 6 hours.

At 8 hours, the density of the granular contrast material had decreased followed by progressive opacification of the GB. No homogenous opacity indicating conjugated contrast material was seen in any volunteer. The GB was well opacified in skigrams taken at 12 h and 14 h in all the 10 subjects. In addition unabsorbed (granular) contrast material was seen in the small bowel in some subjects.

Patient Group

Sixty patients consisting of 43 females and 17 males (age range 17-76 years, mean 34.6 ± 21.4 years) were studied. The first OCG showed faint or non-visualized GB in 45 of the 60 patients. All 45 patients were then subjected to a second OCG and on this occasion 42 showed faint (3) or non-visualized GB (39); the remaining 3 patients had a well visualized GB.

All patients with faint or non-visualized GB had conjugated contrast material in the bowel indicating normal absorption, conjugation and excretion of iopanoic acid by the liver. In most patients (39 of 42; 93%) the amount of conjugated contrast material in the bowel was greater after the second examination compared with the first.

All 42 patients were then subjected to another procedure for confirmation of GB disease. In all patients the diagnosis of chronic cholecystitis and/or cholecystitis was confirmed at surgery (25), ultrasound (10) or ERCP (7).

Discussion

The appearance of the oral cholecystographic contrast material in bile represents the final stage of a cycle of events commencing with absorption at the mucosal surface of the bowel, binding to serum protein and then conjugation with glucuronic acid in the hepatocytes. The final radiographic density of the glucuronide conjugate in the gall bladder is, therefore, dependent on a multiplicity of factors but the part played by the gall bladder itself in modifying the radiographic image is not well understood. It was thought that it merely served to concentrate the bile by removing water but this view was challenged by Lasser and Sounder, who
showed that poor or non-visualization correlated with reduced GB mucosal thickness and reduced number of fluorescent granules containing hydrolyzing enzymes in the basilar mucosal cells. They concluded that diminished vitality of the mucosal surface or a decrease in the number of cells in the absorbing surface could promote reabsorption of the conjugated contrast medium, resulting in non-visualization of the GB. Similarly, Berck and Lasser showed that conjugated medium (Telepaque) was absorbed in patients with chemical or gangrenous cholecystitis but not in those with normal GB. Moreover, hydrolysis of iopanoic acid glucuronide has not been demonstrated in in vitro experiments. 

Conjugated contrast material has a smooth homogeneous density in contrast to the granular particulate appearance of the unconjugated compound. The presence of the homogenous density of iopanoic acid in the small bowel or colon in the absence of granular or particulate material indicates that conjugation has occurred and that the contrast medium has passed through the liver and bile ducts. Failure of the contrast medium to opacify the GB in such situations would indicate a pathologic GB. For this purpose it is important to accurately differentiate the homogenous density of conjugated iopanoic acid from the granular particulate appearance of unabsorbed and unconjugated iopanoic acid. Normally, the density of the pons muscles is greater than that of the colon; however, in the presence of conjugated contrast material the bowel loops have a denser appearance.

In the present study, all the 10 control subjects showed good GB opacification in 12-14 hours and none had conjugated contrast material in the bowel. In contrast, all 42 patients who showed faint visualization or non-visualization of GB after the second OCG in the presence of conjugated iopanoic acid in the bowel had GB disease as assessed by other investigative techniques. On the basis of the present study, we believe that if the GB is not visualized and no conjugated contrast material is seen in the bowel, factors other than GB disease such as defective absorption, abnormality of liver functions or defect in the bile ducts are perhaps responsible. The decision to repeat the OCG or to utilize other diagnostic procedures in the evaluation of the GB will depend on this information.

It is interesting to note that three of 45 patients (7%) with faint or non-visualized GB after the first OCG showed normal opacification after the second test. Other workers have also obtained similar results and no satisfactory explanation is available for these findings. Similarly, it is not clear why the density of conjugated contrast material is greater after the second OCG in patients with non-visualized GB.

It is concluded that GB should be considered diseased if it fails to opacify after an OCG in the presence of conjugated contrast material in the small bowel or colon. We believe that if this observation is incorporated in the routine interpretation of saligrams, an OCG would become an extremely useful screening test for GB disease. This is of special importance where more sophisticated techniques such as ultrasound are not freely available.

References