Percutaneous dissolution of gallstones using methyl tert-butyl ether

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ABSTRACT: Radiolucent cholesterol gallstones can be dissolved rapidly by methyl tert-butyl ether (MTBE) introduced directly into the gallbladder. Percutaneous transhepatic catheter placement is a well established interventional radiology procedure and is the preferred route for MTBE administration. A small number of patients have been treated using nasobiliary placement of a gallbladder catheter. Rapid stirring automatic pump systems allow dissolution of most cholesterol stones, but some may require extracorporeal shock wave lithotripsy to achieve complete dissolution and aspiration of debris. Large bore percutaneous fragmentation and extraction methods require general anesthesia but are applicable to pigment stones. *Can J Gastroenterol* 1990;4(9):624-627

Key Words: Direct contact dissolution, Gallstones, MTBE

La dissolution percutanée des lithiases biliaires par instillation de méthyl tert-butyl éther

RESUME: Les lithiases cholestéroliques radiotransparentes sont aisément dissoutes par instillation directe de méthyl tert-butyl éther (MTBE) dans la vésicule biliaire. La mise en place d’un cathéter transhépatique percutané est une intervention radiologique bien établie et représente la voie préférée pour l’administration du MTBE. Un petit nombre de patients ont été traités par drainage nasobiliaire. Les pompes rotatives rapides viennent à bout de la plupart des calculs cholestéroliques mais pour parvenir à la dissolution et à l’aspiration complètes des débris, il est parfois nécessaire de recourir à une lithotrite extracorporelle par ondes de choc (LEOC). Une anesthésie générale est nécessaire à la fragmentation et à l’extraction des gros calculs, méthodes qui s’appliquent également aux calculs pigmentaires.

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RADIOLUCENT CHOLESTEROL GALLSTONES can be rapidly dissolved in vitro by methyl tert-butyl ether (MTBE) (1). This rapidly effective cholesterol solvent is an alkyl ether liquid at body temperature (boiling point 55°C) and will dissolve even large cholesterol stones (4 to 6 cm in diameter) within hours (2). Animal and human studies have demonstrated little toxicity when MTBE is retained in the gallbladder (2,3). Continuous infusion into the duodenum may produce duodenitis and extensive systemic absorption can induce intravascular hemolysis. Both of these side effects can easily be avoided by retrieval of most of the administered MTBE. This solvent remains investigational for human use in the United States.

PERCUTANEOUS TRANSHEPATIC CATHETER PLACEMENT

Introduction of a 5F (1.7 mm) pigtail catheter through the hepatic-gallbladder attachment into the gallbladder can be performed using either fluoroscopic or ultrasound targeting for initial entr...
into the gallbladder (Figure 1). Mayo Clinic interventional radiologists have successfully placed catheters in 130 consecutive patients regardless of gallbladder anatomy, extent of hepatic attachment or gallbladder wall thickness. Discomfort has been managed using local anesthesia and intravenous fentanyl and diazepam. Anticholinergic premedication decreases the risk of vagal bradycardia and hypotension.

When gallbladder capacity permits, one or two loops of the pigtail catheter (Cook Inc, Bloomington, Indiana) are placed in the gallbladder with the pigtail preferably in the fundus. This minimizes the potential for migration of the catheter out of the gallbladder. The small diameter catheter and transhepatic tract allow removal of the catheter as soon as stone dissolution is complete, providing there is not extravasation at the gallbladder wall entry site when the gallbladder and ducts are filled with contrast. The potential for bile leakage after catheter removal can be minimized by leaving the catheter in place for several days, and this is prudent if substantial extravasation is apparent or if little or no gallbladder attachment to the liver is present. Gelfoam (UpJohn, Michigan) may be placed in the transhepatic tract to decrease the risk of bile leak via this route.

**NASOBILIARY CATHETER PLACEMENT**

Endoscopic retrograde catheterization of the cystic duct can be achieved in most patients. The present authors and others have placed nasobiliary catheters into the gallbladder for gallstone dissolution in a small number of patients but experience, especially in patients without dilated cystic ducts, is insufficient to predict an incidence of success (4,5). Stone dissolution by nasobiliary catheter presents potential...
This compressed air
mins. The authors have recen­
scone debris with each aspiration four to
during which the gallbladder is com­
is
multicentre trials of this pump
system are expected to begin in the
United States and other countries in
1990.

PATIENT SELECTION
Only patients with specific biliary
stones should be considered for
therapeutic intervention, except
under unusual circumstances. If
cystic or common bile duct stones are present,
treatment may be successful, but
dissolution or extraction of duct stones
adds to the difficulty and length of the
procedure. Success is not as predictable
as with stones in the gallbladder only. If
cystic duct obstruction because of
fibrosis is present, the patient will be left
with hydrodrops and the potential for em­
pyema in the future. Methods for ablating
the gallbladder have not yet been
shown to be safe and effective (8).

Cholesterol stones radiolucent on
computed tomography scan will dis­
solve within one to three days leaving
no or very minimal residual debris with
rare exceptions (2). Based on in vitro
data, many stones which are radio­
lucent by abdominal plain film but con­
taining diffuse or rim calcium
measurable by computed tomography
scan may be dissolved with MTBE using
the automatic pump system (9). Stones
with more extensive calcification may
be more efficiently treated nonsurgical­
ly by predissolution fragmentation
using extracorporeal shock wave
lithotripsy (10). If stones are radio­
lucent on computed tomography scan,
however, solitary stones as large as 4 cm
may be completely dissolved within 2 or
3 h without fragmentation. Indeed,
fragmentation might scatter debris
throughout the gallbladder or even the
cystic duct, whereas a solitary stone will
remain within the pigtail zone until
completely dissolved.

The presence of irreversible coagu­
lopathy, hepatic abscess or heman­
gioma in the potential transhepatic
catheter path are contraindications to
this procedure. Patients with acute
cholecystitis who have a substantially
increased risk for surgery can have
catheter cholecystostomy performed
and then dissolution therapy after reso­
lution of the acute inflammation. The
most ideal candidates for MTBE treat­
ment are patients with increased risk for
surgery and with cholesterol stones
having little or no calcium apparent on
computed tomography scan. A variety
of other patients may also be candidates
for this treatment if nonsurgical therapy
is preferred. Cholesterol stones retained
in the duct system can be dissolved
rapidly with MTBE but additional
methods for retention and retrieval of
MTBE must be incorporated.

RESULTS
Treatment with MTBE has been
well tolerated in 130 consecutive
patients including two with duct stones,
three with cholecystostomies, and eight
treated with sequential extracorporeal
shock wave lithotripsy followed by
MTBE fragment dissolution. In four
patients, having one, two, three and
four stones, respectively, all less than or
equal to 5 mm in diameter, although
stone calcification was not apparent by
computed tomography scan, the stones
were insoluble in MTBE. All of
the other patients with little or no calcifica­
tion apparent on computed tomog­
raphy scan have had either no residue
or small amounts of residue 5 mm
or less in diameter. Only five patients
have had debris apparent fluoroscop­
ically but most of the others have had
one or more tiny echogenic densities
with or without acoustic shadowing
detectable by ultrasonogram. This
slight residue has not caused duct
obstruction, pancreatitis or chole­
cystitis. Solitary stones up to 6 cm in
maximum diameter have usually been
dissolved within one or two
two days, but multiple large mixed
cholesterol-pigment stones usually re­
quire two to four days of treatment using
the manual method. The 5F catheter
is very well tolerated in almost all patients
and is connected to sterile bile bag
drainage overnight.

SIDE EFFECTS
Both catheter placement and MTBE
treatment have been well tolerated.
When pain has occurred from extra
OVERVIEW
As experience and technology evolve, most patients' stones should be completely dissolved within one or two days with MTBE with minimal morbidity and almost immediate return to work. This methodology should be applicable to other solvents for cholesterol and noncholesterol stone components which may also be found to be safe and effective. Rapid dissolution of stone fragments using MTBE after extracorporeal lithotripsy would avoid complications from fragment passage and provide much more rapid and complete stone clearance than oral bile acid dissolution therapy.

The cost of materials and equipment for MTBE treatment is low, but the procedure usually requires at least 2 h from both an interventional radiologist and gastroenterologist as well as about 6 h a day of a paramedical assistant's time. The automatic pump system, however, should shorten dissolution time and allow two or three patients to be supervised by one paramedical assistant. As this and other nonsurgical or minor surgical alternatives to standard cholecystectomy evolve, their cost and ultimate outcome must be assessed and compared. The development of effective, safe and economical methods for prevention of stone recurrence will considerably expand the population of patients for whom nonsurgical treatments will be the therapy of choice.

REFERENCES
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