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patients with nondiagnostic transabdominal ultrasound findings underwent endoscopic retrograde cholangiography (ERC) and successful ES after bile duct cannulation using a double-lumen papillotome over a guidewire in combination with a Dormia basket (FG 22Q, Olympus, Tokyo, Japan) exploration of the extrahepatic bile duct system. The Dormia basket was passed at least twice to look for any stones, or sludge, which was defined as the presence of granular material within the bile without evidence of stones. Six patients showed clear pathology on ERC (papillary adenoma in one and visible common bile duct stones in five) necessitating endoscopic sphincterotomy and were excluded from the analysis.

The remaining group of 29 patients consisted of 11 men and 18 women with a median age of 57 yr. The median duration of symptoms was 12 months (range = 1–130). Diagnostic ERC showed a median common bile duct diameter of 8 mm (range = 4–11). Twenty patients (69%) revealed macroscopic or microscopic evidence of lithogenic bile after Dormia exploration. The four patients with elevations of pancreatic enzymes before treatment showed either a small stone ($n = 1$), sludge ($n = 2$), or cholesterol crystals ($n = 1$). Four of the eight postcholecystectomy patients showed either stones ($n = 2$) or sludge ($n = 2$). The sensitivity of diagnostic ERC for detection of biliary pathology was 23% (6/26) and the negative predictive value was 35% (9/26) in this selected group of patients.

A total of 21 patients (72%) became pain free after 1 wk and 26 (90%) after 12 wk, with 93% (26/28) remaining asymptomatic over a median follow-up period of 19 months. One patient died of an unrelated cause, whereas two patients continued to have vague pain; however, one became pain free after therapy for a musculoskeletal disorder. After 12 wk, 22 patients (76%) had complete normalization of all laboratory parameters. Serum bilirubin levels normalized in 15 of 18 patients. Significant hyperamylasemia occurred in only one patient after ERC, and this patient made an uneventful recovery. No other complications occurred.

Although the results of this study suggest a favorable long term outcome of performing ES in a highly preselected group of patients with biliary-type pain, the lack of a control group (sham ES) makes the conclusions less convincing. The authors' contention that the typical clinical presentation (*i.e.*, patient selection) was key to obtaining clinical improvement and to providing evidence of stone disease—as 69% had evidence of altered bile—seems well founded. The lower (<5%) incidence of post-ERC pancreatitis seen in this cohort is at variance with previously reported values of up to 30% (9) and is more in keeping with stone disease than a functional (dyskinesia) disturbance. All procedures were performed by expert endoscopists. The sensitivity of ERC in diagnosing biliary pathology (stone disease) in this study is surprisingly low—again, possibly related to patient preselection; also, routine common duct sweeping with a Dormia basket as utilized in this trial is not universally practiced. Unfortunately, the characteristics (clinical/outcome) of each patient were not revealed by the authors.

In conclusion, this article seemingly extends the indication for ES in patients with suspected biliary or papillary pain—when performed by expert endoscopists in a highly preselected group of patients. Further prospective trials employing biliary manometry before ES and longer follow-up would help in clarifying this issue.

Colm O'Loughlin, M.D., M.R.C.P.

Umappasanna S. Karnam, M.D.

Arvey I. Rogers, M.D., F.A.C.P., M.A.C.G.

University of Miami School of Medicine

Miami, Florida

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Stool Cultures for Nosocomial Diarrhea: Money Down the Drain?

Bauer TM, Lalvani A, Fehrenbach J, et al.

Derivation and Validation of Guidelines for Stool Cultures for Enteropathogenic Bacteria Other Than Clostridium difficile in Hospitalized Adults

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ABSTRACT

The authors report on a modified “3-day rule” for limiting low-yield stool cultures obtained from hospitalized patients

with nosocomial diarrhea. The modified rule addresses the two known weaknesses of the strict 3-day rule: immune-suppressed patients and nosocomial outbreaks of bacterial gastroenteritis. In addition, the modified rule addresses a third group of previously unidentified patients at risk of non-*Clostridium difficile* bacterial nosocomial diarrhea: patients older than 65 with comorbidity. The modified rule would decrease the number of stool cultures by half without missing any clinically significant cases. The authors recommend the modified 3-day rule as a way to “greatly reduce the laboratory burden of stool culture, yet provide rapid diagnosis for patients at increased risk of nosocomial bacterial gastroenteritis.” (Am J Gastroenterol 2002;97:1054–1056. © 2002 by Am. Coll. of Gastroenterology)

COMMENT

Nosocomial diarrhea (ND; the onset of two or more loose or watery stools per day for more than 2 days, at least 72 h after hospital admission) is increasingly recognized as a serious medical condition. Multiple etiologies have been linked to ND, including medication intolerance or abuse, antibiotic-associated disease, medical procedures, hyperalimentation, diarrhea associated with other medical conditions (diabetic neuropathy, uremia, etc), or acquisition of a nosocomial pathogen (1). The National Nosocomial Infections Study reported an overall rate of ND of 1.3/10,000 hospital discharges (2) from 1980 to 1984. In the 1990s, rates of ND in adults and elderly patients of 3.2–31.3 per 100 hospital admissions (3–7) were reported.

Multiple risk factors have been linked to ND, including age, length of stay, hospital roommates, and antibiotic use (especially broad spectrum antibiotics and third generation cephalosporins). For infectious ND, the most common etiological agent in the United States is *Clostridium difficile* (21–52%), followed by salmonellae (3–11.8%). Immune-compromised patients, especially after transplant procedures, and HIV-infected patients can have a variety of pathogens including bacteria (*C. difficile*, *Salmonella*, and enteropathogenic *Escherichia coli*), viruses (rotavirus, cytomegalovirus, adenovirus, coronavirus, coxsackievirus, etc), protozoa (*Cryptosporidium* and *Microsporidia*), and fungi (*Candida*) (1).

A different set of pathogens is usually implicated in community-acquired diarrhea (occurring in outpatients and hospitalized patients within the first 72 h after admission), including *C. perfringens*, *C. botulinum*, *Staphylococcus aureus*, *Bacillus cereus*, *Salmonella*, *Vibrio*, and *Shigella*. These are usually identified through stool cultures. Because they rarely cause ND, very few stool cultures ordered after 72 h of hospitalization are positive (0.6%) relative to community-acquired diarrhea (2.6–6.4%) (8–10). The extremely low rate of positive cultures has led to an estimated cumulative cost per positive stool culture of \$1300 (9). This has not gone unnoticed in these cost conscious times, and multiple strategies have been devised and studied to address this issue.

In 1990, Siegel *et al.*, after a retrospective study of positive stool cultures at the University of Pennsylvania, suggested the “3-day rule” of limiting stool cultures and ova and parasite examination of stools to patients who develop diarrhea within the first 3 days of admission to the hospital. They estimated that this would decrease the number of stool exams by 30–50% without negatively affecting quality of care, and resulting in savings to the health care system of \$20–30 million a year in 1990 dollars. They recognized, however, certain circumstances where the strict enforcement of this rule would negatively impact quality of care—namely, diarrhea in immune-compromised patients and during nosocomial outbreaks.

In 1993, Fan *et al.* (9) published data from a prospective study at the Duke University Medical Center supporting the 3-day rule. In the first part of their study, they analyzed data for all stool cultures ordered. Fifty-three percent (567/1097) of adult stool cultures were ordered on patients hospitalized for longer than 3 days. None of those cultures were positive. They estimated that the cost per positive culture would drop from \$1276 to \$670 if cultures after the 3rd hospital day were rejected. In the second part of their trial, they instituted an intervention comprised of rejection of all stool cultures ordered past the 3rd hospital day, a circular to the medical staff justifying this rule, and the option for the clinician to contact the on-call fellow to override the rejection for clinical reasons. Their intervention resulted in a decrease of the percentage of stool cultures ordered past the 3rd hospital day from 53% to 30%. Three hundred sixty-eight cultures were rejected under the new rule. Clinical override was granted for 23 specimens, none of which turned out positive. They found stool leukocytes to be unhelpful as a screening test before culturing.

In 1996, Valenstein *et al.* (8) published the College of Pathologists Q-Probes Study of 601 Institutions. One hundred stool cultures from each of 601 participating institutions were analyzed. Of 59,500 specimens analyzed, 51.5% were from inpatients and 39.3% were from patients hospitalized for more than 3 days. Only 0.56% of cultures obtained after the 3rd hospital day were positive, compared to 3.1% of those obtained within the first 3 days. A recommendation was made to reject stool cultures submitted after the 3rd hospital day.

In 1997, Rohner *et al.* (10) retrospectively analyzed 13,965 stool cultures at the University Hospital of Geneva, Switzerland. Of 5,167 cultures from patients hospitalized for less than 3 days, 12.6% were positive, compared to 1.4% of 7,942 cultures obtained from patients hospitalized for more than 3 days. After a subanalysis of the positive cultures in patients hospitalized for more than 3 days, they endorsed the 3-day rule but recommended that follow-up samples, specimens for immune-compromised patients, specimens for culture negative first sample, and samples obtained during nosocomial food-borne diarrhea outbreaks should be exempt.

The authors of the article that is the focus of this literature

review propose a modified 3-day rule that exempts three groups of patients with ND: HIV-infected patients, chemotherapy-associated neutropenia patients (neutrophil count < 500/ml), and patients 65 and older with preexisting comorbidity (any preexisting disease that results in permanent alteration of organ function—e.g., insulin-dependent diabetes mellitus with secondary complication, cirrhosis, chronic renal failure, chronic obstructive pulmonary disease, leukemia, hemiparesis due to cerebrovascular accident).

Using a 10-yr review of all positive stool cultures at their institution, the authors derived the modified 3-day rule that would have allowed stool cultures in all of those cases. In a retrospective sample of 1,025 stool cultures, the modified rule would have prevented 52% of cultures without missing any clinically significant cases (one case of *Yersinia enterocolitica* biovar 1 without virulence plasmid pYV would have been missed). The modified 3-day rule was then retrospectively tested at three other institutions using 14 yr worth of data amounting to 27,000 stool cultures. The modified rule would have missed two of 65 positive cultures obtained from patients after their 3rd hospital day; neither of them required antibiotic treatment. The unmodified 3-day rule would have missed 52 positive cultures, 28 of which required antibiotic treatment. The modified 3-day rule would also have significantly limited the delay in recognizing two outbreaks of nosocomial bacterial enteritis, a delay that would have occurred with the unmodified 3-day rule.

Prospective data were collected during the trial, but no correlation of clinical findings (nausea or vomiting, eight or more bowel movements a day, temperature exceeding 38°C, or abdominal pain or tenderness) was found with positive stool cultures for enteropathogenic bacteria other than *C. difficile*.

In a survey of 67 microbiology laboratories, Morris *et al.* (11) found 25% of them rejected stool cultures obtained past the 3rd hospital day. This trial can provide these laboratories with the means to fine tune their strategy to minimize the risk to patients' well-being while maintaining significant cost benefits. Laboratories that have not yet implemented strategies to limit wasteful stool cultures for ND can find in this modified rule a relatively safe and effective way to achieve better yields. Even in the absence of laboratory strategies, physicians can use this modified rule to increase their effectiveness in ordering stool cultures and shift their focus to other causes of ND in patients who do not fit these criteria. It is important to reiterate that, in contrast to stool cultures, tests for *C. difficile* toxin are positive in 20–25% of cases and should continue to be a routine component of the evaluation of ND.

Sameh A. Basta, M.D.

Edward C. Oldfield, M.D., F.A.C.P., F.A.C.G.

Division of Infectious Diseases

Department of Medicine

Eastern Virginia School of Medicine

Norfolk, Virginia

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Prefundoplication Testing: Is Manometry Needed?

Fibbe C, Layer P, Keller J, et al.

Esophageal Motility in Reflux Disease Before and After Fundoplication: A Prospective, Randomized, Clinical and Manometric Study

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ABSTRACT

A prospective, randomized study was conducted to determine whether preoperative esophageal dysmotility affects clinical outcome of gastroesophageal reflux disease (GERD) after laparoscopic fundoplication and whether esophageal motor function changes postoperatively. Two hundred patients with chronic GERD referred for laparoscopic fundoplication underwent clinical assessment, esophagogastroduodenoscopy, esophageal manometry, and 24-h pH monitoring. Patients were stratified according to presence or absence of esophageal dysmotility (100 in each group) and randomized to either a 360° (Nissen) or a 270° (Toupet) fundoplication. This resulted in 50 patients with normal motility and 50 patients with dysmotility undergoing Nissen fundoplications and Toupet fundoplications, respectively.