Transmission of carbapenem-resistant *Enterobacteriaceae* during ERCP: time to revisit the current reprocessing guidelines

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BACKGROUND

The emergence of antimicrobial-resistant organisms continues to be a serious concern both in the United States and globally. Carbapenem-resistant *Enterobacteriaceae* (CRE) such as *Klebsiella pneumoniae* and *Escherichia coli* have been increasingly recognized since the early 1990s.[1] The high mortality associated with CRE infections, combined with the limited therapeutic options, makes this an issue of significant epidemiologic importance.[1-3] A novel CRE subtype, New Delhi metallo-β-lactamase (NDM-1), producing *K pneumoniae*, was first described in 2009 in a Swedish patient who had undergone medical care in India where this strain is frequently recovered.[4] NDM-1–producing CRE demonstrate broad antibiotic resistance that is typically susceptible only to tigecycline and colistin. Currently, NDM-1–producing CRE have been isolated and reported in 15 states in the United States.[5]

Previous reports describe the transmission of CRE during endoscopy. A systematic review from 2013 identified 6 separate outbreaks of *K pneumoniae* carbapenemase worldwide.[6] To our knowledge, there are 3 reports of outbreaks of CRE in the United States associated with endoscopy, specifically ERCP.[7-9] One series that was presented as an abstract described an epidemiological investigation into an observed increased prevalence of CRE in abdominal solid-organ transplant patients at a tertiary academic medical center in Pennsylvania, many of whom had undergone GI endoscopy.[7] The investigators ultimately cultured carbapenem-resistant *K pneumoniae* from a single duodenoscope. Eighteen patients were positive for this organism, and of those, 9 had undergone ERCP with the implicated duodenoscope. Strains in each patient were confirmed to be the same as the cultured organism via pulsed-field gel electrophoresis. Another report described an outbreak in 7 patients in Florida with infections related to *K pneumoniae* carbapenemase, all of whom underwent ERCP at the same facility within the preceding 60 days.[8] In 2013, the first U.S. outbreak of NDM-1–producing *E coli* from a contaminated duodenoscope was reported.[9] Infections in 9 patients were documented in northeastern Illinois, and 6 (66.7%) of these had undergone ERCP at the same hospital. In all, 156 patients were notified of potential exposure, and 39 additional cases of CRE were discovered after screening. In all 3 of these outbreaks, the implicated organism was positively cultured from the elevator wire channel of the duodenoscope and matched the isolates to the index case.

Abbreviations: AER, Automated endoscope reprocessor; CRE, carbapenem-resistant Enterobacteriaceae*; EtO, ethylene oxide; HLD, high-level disinfection; NDM-1, New Delhi metallo-β-lactamase.*

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METHODS

From May 2013 to November 2013, 3 patients at our institution were identified as having a clinical infection related to an identical strain of NDM-1 *E coli*. After a careful chart review and epidemiological evaluation, it was discovered that all 3 patients had undergone ERCP with the same duodenoscope in May 2013. This discovery prompted a thorough evaluation of endoscopic reprocessing methods, extensive evaluation and culture of the endoscope in question, and identification of all potential patients who may have been exposed to the organism.

Institutional review board approval was obtained on May 13, 2014, to perform this review.

Evaluation of the implicated duodenoscope

The duodenoscope in question was immediately taken out of clinical use when the third CRE infection was identified in November 2013. The distal tip was sonicated in an effort to disrupt any organism from a potential biofilm. Three cultures from the endoscope were obtained: 1 sonication culture, 1 brush culture with the elevator wire channel open, and 1 brush culture with the elevator wire channel closed. Despite these measures, NDM-1 *E coli* was not cultured from the instrument. All duodenoscopes, including the implicated instrument, were ultimately

sterilized with ethylene oxide (EtO) and placed back into routine clinical use.

Index patient

The index patient was a 57-year-old man originally from India who was admitted to the hospital in May 2013 with ascending cholangitis and underwent ERCP at that time with extraction of an impacted gallstone and biliary sphincterotomy. This patient had a history of non-Hodgkin's lymphoma and had undergone autologous peripheral stem cell transplantation 1 month earlier. Shortly after undergoing the transplantation and before the ERCP, he was admitted with febrile neutropenia and found to have blood cultures positive for NDM-1 *E coli.* The suspected source of the organism at that time was the GI tract as there were findings suggestive of typhlitis on a CT scan. Biliary cultures obtained during the ERCP grew the same isolate of NDM-1 *E coli* that was cultured from his blood 1 month earlier.

Patient notification

After identification of the index patient and the endoscope used during ERCP, 27 patients who underwent ERCP or EGD with the same instrument from May 19, 2013, to August 13, 2013, were identified and contacted. All patients were offered rectal surveillance culture for CRE. The presence of the NDM-1 enzyme was confirmed with mass spectrometry.

RESULTS

Patient outcomes

Details regarding patient characteristics, indications for endoscopy, and results of infection testing can be found in Table 1. The 3 patients with a diagnosis of clinical infection with NDM-1 *E coli* were as follows: a 72-year-old woman with pancreatic cancer in whom urinary sepsis developed 2 months after ERCP, a 23-year-old man with primary sclerosing cholangitis and cholangiocarcinoma who presented with ascending cholangitis and positive biliary cultures 6 months after ERCP for biliary stenting, and a 73-year-old woman with pancreatic cancer who presented with bacteremia and sepsis 10 months after ERCP with stenting of a malignant biliary stricture. The latter patient had undergone rectal surveillance culture 2 months earlier that was positive for NDM-1 *E coli*. A fourth patient, a 79-year-old man who underwent ERCP for obstructive jaundice due to metastatic esophageal cancer, tested positive for NDM-1 *E coli* on a rectal surveillance culture but a clinical infection related to the organism did not develop before his death. Thirteen patients agreed to undergo screening for CRE and tested negative. Three patients who were offered screening refused. The remaining 6 patients who were potentially exposed to NDM-1 *E coli* were not contacted because they had either died or were in hospice care. After EtO sterilization of all duodenoscopes, no additional cases of CRE infection were diagnosed.

DISCUSSION

Since the institution of protocol-driven high-level disinfection (HLD), the risk of infection transmission during endoscopy was initially estimated to be 1 per 1.8 million cases.[10] However, this figure may be an underestimate because it was only based on infections reported in the peer-reviewed literature.[11] The Centers for Disease Control and Prevention are collecting data on the prevalence of CRE from the Emerging Infections Program and the National Healthcare Safety Network; infections caused by various subtypes of CRE have now been reported in 47 states in the United States along with the District of Columbia and Puerto Rico.[5] We describe another outbreak of CRE from endoscopic transmission, and this is the second to our knowledge that was associated with NDM-1–producing *E coli*. Despite not culturing the organism from the instrument itself, the epidemiologic evidence was strong enough to implicate the duodenoscope as the mode of transmission. It has been suggested previously that antibiotic exposure in the past 30 days may be associated with an increased risk of CRE transmission[9] and indeed 3 of the 4 patients with clinical CRE infection in this series received at least 1 dose of antibiotics within 30 days of diagnosis. However, causality between antibiotic use and clinically significant CRE infection cannot be definitively proven in our series given the multiple potential confounders including immunosuppression from chemotherapy, which all 4 patients received either before or after the diagnosis.

The most current multisociety guidelines from 2011 outline the process of HLD and the use of automated endoscope reprocessors (AERs).[11] The guidelines specifically point out the importance of manually cleaning intricate pieces such as the elevator wire channel of the duodenoscope. In our experience, as with the reported outbreaks in Illinois and Pennsylvania, a review of the disinfection procedure revealed that all standard recommendations and guidelines with regard to endoscope reprocessing were followed.[7,9]

It has long been recognized that the side-viewing duodenoscope used during ERCP is a challenging instrument to adequately reprocess because the elevator wire hinge is difficult to access and therefore not readily amenable to disinfection by using AERs.[10] This specific component of the endoscope has been implicated in numerous reports of bloodstream and biliary infections after ERCP[6-9,12-15] despite the continued emphasis on the manual disinfection of these areas. In addition, 1 study raised the possibility that current HLD protocols could be insufficient for standard endoscopes as well.[16] A 5-year prospective