Dig Dis Sci (2017) 62:2961–2963
DOI 10.1007/s10620-017-4761-1

EDITORIAL

Eliminating Duodenoscope-Associated Transmission of Carbapenem-Resistant Enterobacteriaceae (CRE): In Search of an Optimal Strategy

Divyanshoo R. Kohli[1] · Thomas E. Grys[2] · Rahul Pannala[1]

Published online: 20 September 2017

A much feared and increasingly commonplace complication of gastrointestinal endoscopic procedures is endoscope-to-patient transmission of bacterial pathogens resistant to multiple antibiotics, known as multi-drug-resistant organisms (MDRO). Multiple outbreaks of duodenoscope-associated infections with MDRO, including carbapenem-resistant Enterobacteriaceae (CRE), have been reported in the USA and in Europe [1, 2]. The presence of an elevator mechanism in duodenoscopes used in endoscopic retrograde cholangiopancreatography (ERCP) impedes effective decontamination and has been implicated in the risk of persistent bacterial contamination [3]. Several strategies have been proposed to mitigate the risk of transmission, including strict adherence to manufacturer-recommended high-level disinfection (HLD), universal ethylene oxide (EtO) sterilization, the culturing and sequestering of endoscopes, and patient screening with polymerase chain reaction (PCR)-based tests. Nevertheless, there is substantial variability in the strategies being utilized across institutions, and outcomes data for these approaches are limited.

In a study published in this issue of *Digestive Diseases and Sciences*, Smith et al. [4], present the outcomes of a novel protocol that was initiated after an outbreak of duodenoscope-associated CRE at their institution. This strategy obviates the need for routine endoscope culturing but involves the PCR test on rectal swabs in all patients, a preprocedure questionnaire to risk stratify patients, an on-demand EtO sterilization process for procedures determined by the endoscopist as having an increased infectious burden, and a rotational weekly sterilization of a selected number of endoscopes. The authors report that this process was initiated based on the multi-disciplinary recommendations of the stakeholders at their institution. During this 8-month long study, 612 endoscopic procedures were performed with elevator-containing endoscopes. HLD was performed for every endoscope, and subsequent EtO sterilization was performed in 46 cases based on the protocol. There were no new cases of endoscope-related patient-to-patient CRE transmission throughout the institution. Importantly, the authors did not notice any damage to or change in the performance of the endoscopes after EtO sterilization.

There is no consensus regarding an effective surveillance strategy including the culturing of endoscopes or routine patient screening. The US Food and Drug Administration (FDA) recommends adherence to the multi-society guidelines on flexible endoscope reprocessing to minimize the chances of transmission [5–9]. It has also recommended microbiological culturing, EtO sterilization, use of a liquid chemical disinfectant, or repeated HLD [10]. The Centers for Disease Control and Prevention (CDC) have published interim protocols for surveillance which recommend careful inspection, cleaning and drying of the endoscopes and the elevator mechanism, and performing surveillance cultures from the instrument channel as well as the distal end of the endoscope, combined with tracking the results of the interventions [7]. The multi-society guidelines published by the American Society for Gastrointestinal Endoscopy (ASGE) have also recommended liquid HLD, followed by rinsing the endoscope and its

✉ Rahul Pannala
Pannala.rahul@mayo.edu

[1] Division of Gastroenterology and Hepatology, Departments of Medicine, Mayo Clinic, 13400 E Shea Blvd, Scottsdale, AZ 85259, USA

[2] Laboratory Medicine, Mayo Clinic, 13400 E Shea Blvd, Scottsdale, AZ 85259, USA

channels, flushing of channels with alcohol, and drying the endoscope with filtered forced air [9]. The American Gastroenterological Association (AGA) has recommended periodic culture of all elevator channel endoscopes [6]. In a 16-month study of 285 linear-array echoendoscopes and duodenoscopes, Ma et al. [11] performed weekly culture of 25% of all elevator-containing endoscopes. They noted that only 1.1% of the cultures displayed bacterial growth from oral and skin contaminants. Nonetheless, endoscope sampling for culturing as the sole measure of surveillance was noted to lack sensitivity, and may even increase risk of contamination of the sampling fluid [12].

Implementation of any of the above-mentioned strategies is challenging, necessitating substantial costs engendered by the purchase of instruments, reagents, and excess labor. The 'culture and quarantine' approach involves culturing the duodenoscopes and sequestering them for variable amounts of time until negative cultures are obtained [13]. This method, however, requires capital expenditure for acquiring new endoscopes and may disrupt workflow processes [14]. For the other strategies, the costs associated with upgrading endoscope reprocessing facilities, EtO installation, and purchasing additional endoscopes are substantial. Similarly, some institutions may not have ready access to reference laboratories which are able to rapidly perform PCR-based tests for CRE. Indeed, the authors of the current study [4] undertook the renovation of the reprocessing area and modified the staff training procedures for HLD. Such interventions may not be economically viable for smaller practices with relatively low procedure volumes. The study highlights that strategies to address this issue are dependent on local resources and the prevalence of CRE and other MDROs in their population. The success was a result of a risk-based approach along with multi-disciplinary input from equipment manufacturers, hospital leadership, clinical staff and facilities management.

Currently, there is no single, well-defined, well-studied, cost-effective intervention that can be applied to eliminate the risk of duodenoscope-associated MDRO transmission. As noted in multiple previous studies, the overall incidence of CRE is extremely low (0.5–1.1%) [11]. In the study by Smith et al. [4], no CRE infections were noted throughout the institution during the study period. While the prevalence and types of MDROs varies by geography and patient population, the risk of transmission of MDROs through these procedures is not established. Therefore, strategies to mitigate transmission should be developed through a risk-based approach, incorporating input from all stakeholders, as was done in the study by Smith et al. In a cost-effectiveness analysis, Almario et al. [15] compared different strategies of reprocessing duodenoscopes after ERCP. HLD of endoscopes, as per the recommendations of the US Food and Drug Administration (FDA), was the most cost-effective strategy, as compared to EtO sterilization, culturing and sequestering endoscopes, or not performing ERCP and opting for surgical interventions instead. Indeed, the study suggests that 'culture and quarantine' strategy would be cost-effective only if the pretest probability of CRE infection exceeded 24%.

Many recommendations include extensive microbiological culturing, a process that is unable to provide real-time results of time-sensitive data. A low-cost protocol with high sensitivity, such as screening patients by PCR, may be a more reasonable alternative compared to universal culturing. Another option is to identify patients at higher risk of MDRO transmission, limiting interventions to this high-risk cohort. In a single-center case–control study from the University of California, Los Angeles, investigators proposed that placement of a biliary stent, diagnosis of cholangiocarcinoma, and inpatient status independently increased the risk of CRE transmission [16]. In view of the prohibitive costs associated with 'culturing and quarantining' all endoscopes with elevator mechanisms, point-of-care testing of endoscopes or patients, and risk stratifying patients may be alternatives that need to be explored in well-designed prospective trials.

In the absence of robust clinical data and established evidence-based guidelines, it would be prudent for hospitals and practices to review and enforce the best practices of endoscope reprocessing, perform frequent audits of endoscopes, and invest in staff training [14]. The FDA recommends that physicians should discuss the risks and clinical presentation of MDRO transmission with patients undergoing procedures requiring the use of endoscopes with elevators [3]. In the long term, mitigating the risk of MDRO transmission may require redesigning the elevator mechanism or the endoscope itself. In the interim, further outcomes studies, such as the one highlighted in this issue [4], are important to conduct to define an optimal mitigation strategy for MDRO transmission.

References

1. Wendorf KA, Kay M, Baliga C, et al. Endoscopic retrograde cholangiopancreatography-associated AmpC *Escherichia coli* outbreak. *Infect Control Hosp Epidemiol*. 2015;36:634–642.
2. O'Horo JC, Farrell A, Sohail MR, Safdar N. Carbapenem-resistant enterobacteriaceae and endoscopy: an evolving threat. *Am J Infect Control*. 2016;44:1032–1036.
3. US Food and Drug Administration. Safety communications—design of endoscopic retrograde cholangiopancreatography (ERCP) duodenoscopes may impede effective cleaning: FDA safety communication [Internet]. https://www.fda.gov/medicaldevices/safety/alertsandnotices/ucm434871.htm. [cited 2017 Jul 19].

4. Smith ZL, Dua A, Saeian K, Ledeboer NA, Graham MB, Aburajab M, et al. A novel protocol obviates endoscope sampling for carbapenem-resistant enterobacteriaceae: experience of a center with a prior outbreak. *Dig Dis Sci*. (Epub ahead of print). doi: 10.1007/s10620-017-4669-9.
5. Transmission of CRE bacteria through Endoscopic retrograde cholangiopancreatography (ERCP) [Internet]. https://www.asge.org/docs/default-source/ImportFiles/Publications_and_Products/ASGE_InterimGuidance_CRE_03172015.pdf.
6. How to stop duodenoscope infections [Internet]. http://www.gastro.org/press_releases/2015/3/23/how-to-stop-duodenoscope-infections. [cited 2017 Jul 16].
7. Interim Duodenoscope Surveillance Protocol | HAI | CDC [Internet]. https://www.cdc.gov/hai/organisms/cre/cre-duodenoscope-surveillance-protocol.html. [cited 2017 Aug 6].
8. US Food and Drug Administration. Reprocessing of reusable medical devices—infections associated with reprocessed duodenoscopes [Internet]. https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ReprocessingofReusableMedicalDevices/ucm454630.htm. [cited 2017 Aug 6].
9. Reprocessing Guideline Task Force, Petersen BT, Cohen J, et al. Multisociety guideline on reprocessing flexible GI endoscopes: 2016 update. *Gastrointest Endosc*. 2017;85:282–294.
10. US Food and Drug Administration. Safety communications—supplemental measures to enhance duodenoscope reprocessing: FDA safety communication [Internet]. https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm454766.htm. [cited 2017 Aug 6].
11. Ma GK, Pegues DA, Kochman ML, et al. Implementation of a systematic culturing program to monitor the efficacy of endoscope reprocessing: outcomes and costs. *Gastrointest Endosc*. 2017. doi:10.1016/j.gie.2017.05.001.
12. Gazdik MA, Coombs J, Burke JP, Lopansri BK. Comparison of two culture methods for use in assessing microbial contamination of duodenoscopes. *J Clin Microbiol*. 2016;54:312–316.
13. Ross AS, Baliga C, Verma P, Duchin J, Gluck M. A quarantine process for the resolution of duodenoscope-associated transmission of multidrug-resistant *Escherichia coli*. *Gastrointest Endosc*. 2015;82:477–483.
14. Rutala WA, Weber DJ. Outbreaks of carbapenem-resistant enterobacteriaceae infections associated with duodenoscopes: what can we do to prevent infections? *Am J Infect Control*. 2016;44:e47–e51.
15. Almario CV, May FP, Shaheen NJ, et al. Cost utility of competing strategies to prevent endoscopic transmission of carbapenem-resistant enterobacteriaceae. *Am J Gastroenterol*. 2015;110:1666–1674.
16. Kim S, Russell D, Mohamadnejad M, et al. Risk factors associated with the transmission of carbapenem-resistant enterobacteriaceae via contaminated duodenoscopes. *Gastrointest Endosc*. 2016;83:1121–1129.