levels in all parts of the water distribution system. As a consequence of the establishment and maintenance of adequate chlorine levels at distal sites in the water distribution system, corrosion of pipes often occurs at sites closest to the chlorine source. The authors further emphasize that heat shock or hot water flush is only transiently effective in the remediation of biofilm, which serves as the repository for sustained release of Legionella species. Furthermore, despite the fact that diligence can be applied to the maintenance of effective copper-silver ionization programs through aggressive monitoring, this in and of itself does not guarantee that such equipment cannot malfunction and, in turn, lead to outbreaks of Legionella infection. The major lesson learned from this valuable report is that HALD may still occur, even in the face of our best efforts and the considerable cost associated with implementing and maintaining systemic disinfection strategies.

Recently, however, point-of-use water filtration has become available in the United States. This may provide a cost-effective complementary strategy to reduce HALD and other health care-associated infections. The Centers for Disease Control and Prevention acknowledges that 0.2-μm filters are more effective than are filters with larger pore sizes [2]. Such filters have been used to replace the aerators of faucet taps and shower heads, and they are easily replaced, because they are fitted with quick-connect and quick-disconnect fittings. Their performance has been characterized in a laboratory setting, and they have been shown to prevent the passage of surrogate test bacteria that are smaller than Legionella organisms [3]. In a study in which filters were used in 3 intensive care units, a total of 767 water samples were obtained, and the resulting data revealed that the presence of legionellae was reduced from 30 of 32 unfiltered samples to 1 of 256 of filtered samples [4]. In addition, this study reported that, before filtration, the concentration of legionellae in Legionella-positive samples ranged from 1 to 106 CFU/mL. It should be noted that the concentration in that single Legionella-positive postfiltration sample was only 1 CFU/mL.

The successful application of water filtration to reduce health care-associated infections has been well documented. A pediatric nephrology unit that was experiencing difficulty with Legionella pneumophila serotype 6 was able to implement point-of-use water filtration in their unit in a manner that was cost permissive [5]. Another study revealed that Legionella serogroup 1 was refractory to systemic disinfection regimens in a heart transplant unit. However, after implementation of point-of-use water filters, urinary antigen screening results suggested a reduction in infection rates from 23% to 15% [6].

Despite the simplistic perception of filtration technology, not all filters are alike [7], and confidence in their use should be based on performance claims and actual clinical use experience. Nonetheless, there are some filters that are suitable for application in the health care setting, particularly when limited to areas of the hospital where patients are known to be at the highest risk of infection, where evidence has demonstrated that their effects are immediate, and where they can be applied in a cost-effective manner.

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References


Diffuse Cutaneous Hyperpigmentation Due to Tigecycline or Polymyxin B

To the Editor—Hyperpigmentation has been described in association with the use of several medications, including quinidine [1], terbinafine [2], and the tetracyclines [3]. Minocycline hyperpigmentation has been noted to occur at various sites, including the skin [4, 5], thyroid gland [6, 7], and sclera [8]. In cases of skin hyperpigmentation, the areas of pigmentation have typically been focal in distribution [4, 5]. Tigecycline, the first of a new class of antibiotics known as glycyclines, is a semisynthetic derivative of minocycline. To date, there have been no published reports of hyperpigmentation attributed to tigecycline use. We describe 2 patients who developed diffuse cutaneous hyperpigmentation while receiving treatment with tigecycline.

A 46-year-old Hispanic man with a myocardial infarction was admitted to the hospital for coronary bypass surgery. He subsequently developed pneumonia, and carbapenem-resistant Klebsiella pneumoniae was recovered from a tracheal aspirate specimen. The patient started receiving a regimen of tigecycline...
revealed highly drug-resistant K. pneumoniae, underlined with prior hemodialysis. Blood cultures revealed kidney disease was admitted to an outside hospital with fever and chills after he had undergone hemodialysis. Blood cultures revealed highly drug-resistant K. pneumoniae, and the patient initiated a regimen of polymyxin B. Seven days later, he was transferred to our hospital for additional treatment, at which time tigecycline (50 mg intravenously every 12 h after an initial 100-mg loading dose) was added to the treatment regimen. Tigecycline and polymyxin B were discontinued after 16 days from the first sterile blood cultures (after a total of 22 days of antibiotic therapy). Just before the patient completed the course of antibiotics, the patient’s family noticed significant darkening of the patient’s face, ears, neck, and upper chest that progressed over the next several days. Other medications that the patient used before the onset of hyperpigmentation included metronidazole, rifampin, oral vancomycin, simvastatin, metoclopramide, amiodarone, linsopril, metoprolol, phenytoin, clonazepam, furosemide, methylphenidate, intravenous heparin, intravenous norepinephrine, lorazepam, hydromorphone, fentanyl, esomeprazole, asprin, and epoetin. Over the next 3 months, the patient reported a gradual decrease in skin pigmentation, although it still had not returned to its original appearance.

An 80-year-old Hispanic man with a history of diabetes mellitus and end-stage renal disease was admitted to an outside hospital with fever and chills after he had undergone hemodialysis. Blood cultures revealed highly drug-resistant K. pneumoniae, and the patient initiated a regimen of polymyxin B. Seven days later, he was transferred to our hospital for additional treatment, at which time tigecycline (50 mg intravenously every 12 h after an initial 100-mg loading dose) was added to the treatment regimen. Tigecycline and polymyxin B were discontinued after 16 days from the first sterile blood cultures (after a total of 22 days of tigecycline treatment and 30 days of polymyxin B treatment). Two days after the patient stopping taking both antibiotics, he developed darkening of the skin that primarily involved his face. Other medications that the patient had used before the onset of hyperpigmentation included insulin aspart and esomeprazole. His hyperpigmentation subsequently decreased but did not completely resolve, even after 5 months of therapy.

Tigecycline is a new antibiotic with activity against a variety of gram-positive, gram-negative, anaerobic, and atypical organisms, including drug-resistant, gram-negative Enterobacteriaceae, such as K. pneumoniae [9–12]. As tigecycline use becomes more prevalent, additional adverse effects are likely to be reported. Although, to our knowledge, tigecycline hyperpigmentation has not yet been reported elsewhere, significant literature exists describing various pigmentation abnormalities associated with minocycline, which is structurally similar to tigecycline. It is unclear whether the aforementioned skin changes imply that tigecycline (alone or in combination with polymyxin B) can cause these skin manifestations. Although both patients were receiving polymyxin B, it is unlikely that this agent was responsible for the skin pigmentation, given our institution’s extensive use of polymyxin B without prior skin changes having been observed. Of the medicines listed above that were given to our patients, it has been documented in the literature that rifampin [13, 14], amiodarone [15, 16], and phenytoin [17, 18] have caused cutaneous hyperpigmentation, although none of the documented cases had patterns similar to those seen in our patients. We cannot exclude the possibility that one of these other medications was responsible for the skin changes. However, tigecycline, polymyxin B, and esomeprazole were the only medications that were administered to both patients, and esomeprazole has not been reported to cause hyperpigmentation. Furthermore, both cases involved diffuse hyperpigmentation that predominantly affected the face, suggesting a similar etiology. We recommend that patients receiving tigecycline, either alone or in combination with polymyxin B, be monitored for hyperpigmentation.

Acknowledgments


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References

Diagnosing Catheter-Related Bloodstream Infection without Catheter Removal? Not so Fast!

To the Editor—I want to congratulate Bouza et al. [1] for their effort to solve part of the puzzle regarding the diagnosis of catheter-related bloodstream infection without catheter removal in critically ill patients [1]. I would like to make 2 comments to place the results in a broader perspective.

The authors excluded arterial and Swan-Ganz catheters from the analysis, notwithstanding the fact that probably >50% of critically ill patients have more than just the central venous catheter in place. What happened with these other catheters? Were they removed in all cases, to exclude or identify the arterial line as a source of non–central venous catheter–related bloodstream infection? If these other catheters were removed per protocol, then the conclusion of the authors should be that the evaluated techniques for the diagnosis of catheter-related bloodstream infection are useful when all other intravascular catheters are removed. If they were not removed, then the authors cannot exclude the possibility that other catheters were the source of the so-called non–catheter-related bloodstream infection.

Furthermore, even if these diagnostic techniques are truly accurate in differentiating catheter-related bloodstream infection from other bloodstream infections, the problem remains that, in the large majority of cases in this study, the indication for catheter removal was fever or some other symptom in a patient with negative blood culture results. A total of 159 of the 204 patients included in the study reported by Bouza et al. [1] did not have bloodstream infection. None of the evaluated diagnostic techniques will overcome this problem of clinical over-diagnosis of catheter-related infection, because the techniques can only be used to differentiate between sources of bloodstream infection.

I think that the only correct conclusion that can be drawn from this study is that, in the small subset of patients with suspected catheter-related infection who turn out to have bacteremia (45 of the 204 patients included in the study [1]), techniques exist to differentiate catheter-related bloodstream infection from other bloodstream infections. Future studies should evaluate the safety of protocols that try to avoid catheter removal in patients in whom bloodstream infection is suspected but unconfirmed [2]. If this policy is proven to be safe, we will be able to avoid unnecessary catheter removal in patients with unexplained fever.

Acknowledgments


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References


Reply to Rijnders

To the Editor—We thank Dr. Rijnders for his comments [1] regarding our recent article in Clinical Infectious Diseases [2]. The objective of the study was to compare the yield of 3 microbiological procedures (semiquantitative cultures from hub and skin samples, differential quantitative blood cultures, and differential time to positivity between cultures of blood samples obtained from catheter hubs and peripheral blood samples) to assess the presence or absence of catheter-related bloodstream infection without catheter removal. This was, to our knowledge, the first study to compare the 3 methods in nonneutropenic patients with critical conditions who had short-term central venous catheters and clinical suspicion of bacteremia. We identified 55 patients with bloodstream infection among the 204 episodes of clinical suspicion of sepsis included in the study. According to standard definitions, 28 cases were classified as catheter-related bloodstream infection, and 27 cases were classified as non–catheter-related bloodstream infection. Dr. Rijnders raises the possibility that these cases could actually be attributed to bacteremia related to catheters other than the studied central venous catheter that might potentially be present. In addition to the studied central venous catheter, these 27 patients carried the following intravenous lines: Swan-Ganz catheters (0 patients), subcutaneous reservoirs (0 patients), arterial lines (19 patients), and other catheters (e.g., hemodialysis catheter, 13 patients).

First, we would like to clarify that we did not perform a complete catheter study involving all of these lines, because it would have been clinically and ethically impossible to do so. According to our protocol, the study of a 3-lumen catheter required the withdrawal of 80–100 mL of blood per study; therefore, an excessive quantity of blood would have been re-

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