So-called Urinary Tract Infection in the Era of COVID-19

To the Editor: When a frail older adult with incident delirium is found to have bacteria in the urine, doctors often assume the bacteriuria represents a urinary tract infection (UTI), and that the so-called UTI is causing delirium, but bacteriuria is common in older adults who are otherwise clinically stable. Accordingly, guidelines from the Infectious Diseases Society of America (IDSA) include a strong recommendation against antibiotic treatment when a frail older adult develops delirium and is found to have asymptomatic bacteriuria (ASB) (Table 1). "In older patients with functional and/or cognitive impairment with bacteriuria and delirium and without local genitourinary symptoms or other systemic signs of infection (e.g., fever or hemodynamic instability), we recommend assessment for other causes and careful observation rather than antimicrobial treatment (strong recommendation, very low-quality evidence)."[1] No randomized trials have studied this question. Before 2019 coronavirus disease (COVID-19), Dasgupta et al.[2] reported a prospective cohort study of delirious patients with ASB. The group that received antibiotics had worse functional recovery 3 months after discharge than the group that did not (relative risk = 1.34; 95% confidence interval = 1.08–1.66). No trials have shown that delirium outcomes are improved with the treatment of ASB.

ASB is defined as "the presence of 1 or more species of bacteria growing in the urine at specified quantitative counts ($\geq 10^5$ colony-forming units [CFU]/mL or ≥108 CFU/L), irrespective of the presence of pyuria, in the absence of signs or symptoms attributable to urinary tract infection."[1] Taken together, the recommendation and the definition imply that delirium is not itself attributable to UTI. Nonetheless, inappropriate antibiotic treatment remains common in this situation.

When a patient is seriously ill with COVID-19, has become delirious, and is discovered to have bacteriuria, the decision about antibiotic treatment is complex and challenging. Favoring treatment, the IDSA guideline against antibiotic treatment is not applicable because the patient does have "systemic signs of infection."

Favoring nontreatment (with careful observation) is the very low pretest likelihood that so-called UTI is causing delirium because delirium is so highly prevalent in patients with COVID-19 for reasons unrelated to the urinary tract. Delirium might be a direct effect of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that may bind to angiotensin-converting enzyme (ACE)-2 receptors.[3] Alkeridy et al.[4] reported a cognitively intact person who developed delirium as the sole manifestation of COVID-19. Delirium could also be explained by the massive social disruption caused by the pandemic that has destroyed comforting routines and group activities, isolated patients, separated close relatives and caregivers, dramatically altered the appearance of all human visitors (now wearing extensive personal protective equipment [PPE]). and redeployed unfamiliar healthcare staff to care for these patients. Delirium in COVID-19 is common enough that the World Health Organization included "Altered Consciousness/Confusion" in their Case Record Form among the routinely collected symptoms.[5]

Table 1 2019 IDSA Guidelines Update for Treatment of Asymptomatic Bacteriuria in Older Adults[1]

"In older, community-dwelling persons who are functionally impaired, we recommend against screening for or treating ASB (strong recommendation, low-quality evidence)."
"In older persons resident in long-term care facilities, we recommend against screening for or treating ASB (strong recommendation, moderate-quality evidence)."
"In older patients with functional and/or cognitive impairment with bacteriuria and delirium and without local genitourinary symptoms or other systemic signs of infection (eg, fever or hemodynamic instability), we recommend assessment for other causes and careful observation rather than antimicrobial treatment (strong recommendation, very low-quality evidence)."

Abbreviations: ASB, asymptomatic bacteriuria; IDSA, Infectious Diseases Society of America.

Therefore, for a patient with COVID-19, delirium, signs of systemic illness, and bacteriuria, clinicians face an evidence-free zone of decision making in the early months of an outbreak with a novel pathogen. The potential harm of antibiotic overtreatment is not diminished by COVID-19. Yet if we want to ensure that no patient with COVID-19 dies for lack of antibiotics, then all patients with COVID who are seriously ill should be treated with antibiotics.

We suggest that if a patient has severe COVID-19 and develops delirium, the finding of ASB should not trigger antibiotic treatment. We echo the IDSA recommendation of "assessment for other causes and careful observation rather than antimicrobial treatment."[1] If the patient has urinary tract symptoms as well, antibiotics directed to urinary pathogens should be considered. If a UTI is suspected, urine cultures should be drawn. If the urine culture is negative, antibiotics should be withheld or discontinued. The absence of pyuria suggests against antibiotic treatment (the presence of pyuria does not provide support for treatment).[1,6]

In conclusion, risks from antibiotic overtreatment are not reduced by the presence of COVID-19. No studies have shown benefit from antibiotic treatment for so-called UTI in vulnerable older adults who become delirious and are found to have bacteriuria. The costs, bacterial resistance, destabilization of the generally beneficial microbiome, and adverse drug effects including fatal diarrhea may be harmful to patients with COVID-19. Dasgupta and colleagues observed a further functional loss in patients who received antibiotics compared with those who did not in a pre–COVID-19 study. Meticulous ongoing evaluation in a delirious COVID-19 patient should allow a less harmful approach than antibiotic treatment of ASB.

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