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Mini review

Urinary Tract Infections in End-Stage Renal Disease Patients -A Practice Conundrum

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Abstract

Patients with end-stage renal disease have a markedly abnormal genitourinary system marked by loss of function, atrophy, and inflammation. This poses a unique diagnostic and management challenge when being evaluated and treated for concurrent infections. Many of the diagnostic and treatment strategies have not been properly studied in dialysis patients. Clinical guidelines are also not well-defined given the paucity of evidence. This review article aims to shed more light on management consideration of urinary tract infections in patients with ESKD.

Keywords: Genitourinary infections; urinary tract infections; chronic kidney disease; end-stage renal disease; pyuria; bacteriuria

Abbreviations

ESKD: End-stage kidney disease

ESRD: End-stage renal disease

WBC: White blood cell

HPF: High power field

Introduction

Patients with end stage renal disease are predisposed to microbial infections due to combination of immunosuppressed status, frequent comorbidities, and often advanced age. However, diagnoses of infections are not straightforward since such patients do not have robust immunologic response to infections. Moreover, such patients have frequent presentations due to fluid and electrolyte imbalances, blood pressure abnormalities and polypharmacy which may mimic an infectious disorder. Resultantly, such patients frequently undergo infectious workup when seen in emergency rooms, and this often includes urinalysis and reflex culture. The diagnostic approach to investigating genitourinary infections in ESKD patients remains a conundrum since patients who have end-stage kidney disease are frequently oliguric and urine specimen results may be markedly abnormal even without any acute illness. Moreover, there may be anatomical variations like prior ureteral stents, polycystic kidneys, vesicoureteral reflex which are associated with recurrent infections. There is a paucity of guidelines regarding infectious evaluation and treatment of patients with end-stage kidney disease and this review aims to address issues relating to genitourinary infections in this population.

Discussion

Urinary symptoms of UTI can be variable and generally vague in patients with ESKD due to low urine volume. A significant number of patients suffer from chronic bladder symptoms at baseline, in-

cluding bladder pain/spasms, cloudy or pus-laden urine at baseline and such symptoms may mask development of new UTI. Hence, it is important to obtain history about both baseline urinary habits and symptoms and any new symptomology. Nevertheless, a high index of suspicion is necessary due to the substantial burden of disease. Keane et al reported in their case series that close to 20% of non-access related bacteremia in hemodialysis patients were attributable to genitourinary system [1]. Initial evaluation frequently includes urinary WBC count. Prevalence of pyuria increases linearly with stage of CKD in healthy state, with a recent analysis revealing close to half of patients on chronic hemodialysis have asymptomatic pyuria [2]. Prevalence was almost twice as high in women (68%) than in men (36%). Other series have found prevalence between 28-45% [3,4], though this number is highly variable.

Pyuria in kidney disease can reflect noninfectious entities including inflammation as is seen in patients with acute glomerulonephritis and interstitial nephritis. Hence, only a variable minority of patients with pyuria have presence of UTI: in the same series, 11% of ESKD patients who had asymptomatic pyuria had positive urine culture. While correlation between pyuria and bacteriuria remains a weak one, a negative result of urine WBC correlates strongly with absence of bacterial growth (high negative predictive value), and hence can be useful in ruling out urinary tract infection. Most employed method of detecting pyuria is using automated cell count analyzer on sedimented urine, with common cut-off being at <5 cells/hpf. A higher cut-off value for >20 cells/HPF correlated with presence of UTI with an improved specificity of 70%, while still maintaining a high sensitivity of close to 80%. In a retrospective analysis of matching urinalysis, dipstick, and culture results on 134 hemodialysis patients, the presence of urinary nitrites on dipstick was found to be a highly specific marker of urinary tract infection (sensitivity 14-20%; specificity 94%) [5].

An important confounder in dialysis population is urine production. Dialysis patients can range from being completely anuric to having more than 1liter daily urine production. When stratified based on urine volume, Hyodo et al reported progressively higher prevalence of pyuria and bacteriuria as urine volume declines in asymptomatic dialysis patients, with those making <100 ml of urine per day having 76% and 65% prevalence of pyuria and bacteriuria respectively [6]. Hence, clinicians must keep in mind urine volume at baseline and urine laboratory results. ESKD patients are also at risk for developing specific infectious complications of the genitourinary tract owing to anatomical and functional abnormalities. Purulent infection of the bladder content can develop owing to weakened immune system in the setting of poorly functioning bladder or following bladder diversion procedure (pyocystitis). This classically presents recurrent fevers in a hospitalized patient, and with bladder drainage following catheterization yielding grossly purulent urine of volume 300-500 ml [7].

Prompt bladder drainage, frequent irrigation, intravesical and parenteral antibiotics are mainstay of treatment. Patients with large ureteral stones and staghorn calculi can develop severe purulent infections like pyonephrosis upstream of obstruction [8], while patients with genetic and acquired polycystic kidney disease can develop perinephric abscess [9]. Hence, prior history of kidney stones, cysts and urological procedures remains important. Patients with ESKD are also not immune to development of other serious genitourinary infections despite having a nonfunctioning collecting system. Cases of emphysematous cystitis and pyelonephritis have been reported in diabetics with ESKD [10,11], as well as prostate abscess [12], perinephric abscess and severe relapsing bacterial infections requiring bilateral nephrectomies [13]. For patients who have asymptomatic bacteriuria, the efficacy of antimicrobial therapy to eradicate bacterial colonization or prevent recurrence is not established. Recurrent UTI is thought to occur due to bacterial regrowth from colonies protected by biofilm and colonizing deeply within renal parenchymal and urothelial tissue [14].

In a retrospective review of 68 hemodialysis patients who had bacteriuria during hospital admission, there was no statistical difference between bacteriuria recurrence between patients who received antibiotics to those who did not [15]. Therefore, while such patients are at risk for developing complications, asymptomatic bacterial colonization may not require antibiotic treatment. A review of prior microbial cultures and antimicrobial therapy should be conducted, and infectious disease consultation can be considered when appropriate to reduce unnecessary use of antibiotics. Optimal antibiotic dosing is another understudied aspect of management of UTI in such patients. Mainstay of treatment for uncomplicated cystitis/UTI's are antibiotics that achieve significant urinary concentration [16]. Most used antibiotics are sufficiently excreted in the urine to maintain high urinary concentrations even in patients with reduced renal function (except nitrofurantoin and trimethoprim-sulfamethoxazole). Pharmacokinetics of commonly used antibiotics in severely oliguric patients, however, remain unknown. Nekidy et al conducted a retrospective review of 56 ESKD patients treated for urinary tract infections and reported >90% cure rate with use of various antibiotics including penicillin's, cephalosporins and carbapenems [17].

Conclusion

In summary, the diagnostic evaluation and management of suspected urinary tract infection in dialysis patients is fraught with challenges. Clearly, more research needs to be done to provide an evidence-based approach to this vexing problem. Though practice guidelines lag, the following key summary points of existing literature can be relevant to clinician:

a) Potential genitourinary tract infections should not be discounted in ESKD patients even when they are anuric.

b) History should include prior nephrological and urologic history including cystic kidney disease, interstitial and glomerular kidney disease, acute kidney injury and genitourinary procedures. A review of prior microbiology results and antimicrobial therapy should also be conducted to identify asymptomatic colonizer, recurrent infection, and infections by drug resistant organisms.

c) High urine leukocyte count may or may not indicate bacteriuria and should reflect urine culture. Absence of pyuria (esp. less than 5/hpf) is strongly predictive of absence of uri-

nary tract infection. Sterile pyuria is found more commonly in patients with markedly reduced urine volume.

d) Presence of urinary nitrites on dipstick have high specificity for presence of UTI.

e) Patients with poorly draining bladder and obstructive uropathy are at risk for developing severe purulent infections of genitourinary system.

f) Asymptomatic bacteriuria in the absence of other causes of immunosuppression, genitourinary functional and anatomical risk factors should probably not be treated, though clear evidence is lacking.

g) Most antibiotic classes appear to be effective in eradicating urinary tract infections in ESKD patients despite lack of urinary concentrations as in anuric patients.

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Conflict of interest

The author has no conflicting interest to disclose.

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