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Urinary tract infections in inpatients: that challenge

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ABSTRACT

Urinary tract infection (UTI) is one of the major nosocomial infections. In more than 80% of cases it is related to the use of urological devices, especially linked to the misuse of urinary catheters. Empirical treatment should be based on local epidemiology, severity criteria and risk of multiresistant bacteria. This review shows the most important aspects of nosocomial UTI, as well as the recommendations for correct treatment adjustment; both empirical and definitive, that is the great challenge to avoid multiresistance, as well as to avoid unnecessary treatments.

Key words: Urinary Tract Infections, Nosocomial Infections, Antimicrobial Treatment.

Las infecciones del tracto urinario en el paciente ingresado: ese reto

RESUMEN

La infección del tracto urinario (ITU) es una de las principales infecciones nosocomiales. En más del 80% de los casos está relacionada con el empleo de dispositivos urológicos, sobre todo, con el mal uso de las sondas vesicales. El tratamiento empírico debe estar basado en la epidemiología local, criterios de gravedad y riesgo de bacterias multirresistentes. Esta revisión muestra los aspectos más importantes de la ITU nosocomial, así como las recomendaciones para el correcto ajuste del tratamiento; tanto empírico, como dirigido, ese es el gran reto para evitar la multirresistencia, así como evitar los tratamientos innecesarios.

Palabras clave: Infecciones del Tracto Urinario, Infección Nosocomial, Tratamiento Antibiótico.

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IMPORTANCE

Urinary tract infections (UTI) are a well-known cause of nosocomial infection. They are the third most common infection occurring in admitted patients after surgical site and respiratory infections in our country. Urinary catheters (UC) are the most important contributors to nosocomial UTI. According to the *Estudio de la Prevalencia de la Infección Nosocomial en España* (EPINE)[1], 19.0% of inpatients from Spanish hospitals have an indwelling UC. It also shows that 60.2% of nosocomial UTI were associated to UC carriage; and that 7.1% of nosocomial bloodstream infections (BSI) are secondary to nosocomial UTI. As a result, nosocomial UTI not only derives in worse outcomes but also in higher economic costs[2] and antibiotics abuse. Nevertheless, a decrease in the incidence of UTI has occurred during the last years as a result of closed urinary drainage systems.

PATHOGENESIS AND AETIOLOGY

Pathogenesis of UTI is well-known nowadays and two pathways have been described. The first one, the extraluminal pathway, describes a passage of bacteria colonizing the periurethral zone towards the bladder. The intraluminal pathway, on the other side, comprises the introduction of bacteria colonizing the drainage bag or the UC towards the urinary tract. Formation of biofilm facilitates this bacterial progression.

Regarding the aetiology, multiple studies have addressed this issue. Results by Andreu et al[3] show *Escherichia coli* is the most common causal agent of non-complicated cystitis (86%) and up to 90% of non-complicated pyelonephritis. However, complicated UTI have a more varied aetiology. *E. coli* remains the main causal pathogen but other Gram-negative bacilli like *Klebsiella*, *Citrobacter* and *Enterobacter* spp. cause 11%; and *Pseudomonas aeruginosa*, 8%. Gram-positive bacteria also have a role in urinary catheter-associated urinary tract infections (CAUTI) with D-group *Streptococci* causing 19% of them,

and *Staphylococcus aureus*, 4%. Polymicrobial UTI cases represent 30%. Other microorganisms such as yeasts cause 18% of UTI.

Horcajada et al[4] published in 2013 the different aetiology in bacteraemia secondary to UTI in hospitalized patients comparing community, nosocomial and healthcare-associated acquisition, being significant the appearance of *P. aeruginosa* in those of nosocomial origin and extended-spectrum beta-lactamase (ESBL) as well as quinolone-resistant Enterobacteriaceae in those having healthcare-associated acquisition.

DIAGNOSIS

Diagnosis of CAUTI requires the isolation of no more than two species of organisms, at least one of which is a bacterium of $\geq 10^5$ CFU/ml from urine cultures. Present symptoms or signs must include at least one of the following: fever, hypothermia, suprapubic tenderness, or systemic signs without another explanation, like mental status alteration or systemic response inflammatory syndrome. Neither dysuria nor altered urinary frequency nor urinary urgency are valid for this diagnosis. Patients must have had an indwelling UC for more than 2 days on the date of event or a UC that was removed the day before the date of event to be considered as catheter-associated[5].

Asymptomatic bacteriuria, on the other hand, is the growth of more than 10^5 CFU/ml of one usual urinary tract pathogen without any symptoms.

Urine sediments have a high negative predictive value when there is absence of pyuria. Blood cultures are positive only in 30-40% of pyelonephritis. New tools are emerging such as polymerase chain reaction (PCR), matrix-assisted laser desorption/ionization-time-of-flight (MALDI-TOF) or an old tool such as performing a direct antibiogram from the urine. They can also be useful when a multidrug resistant (MDR) microorganism is suspected to establish an optimal empirical treatment. For UTI complications, imaging like computed tomography and echography have been proven as useful.

PREVENTION

Numerous guidelines to prevent CAUTI have been published in the two last decades. Most of them highlight the importance of educational measures for all healthcare professionals[6]. Hand hygiene is the most important one. Once a patient is found to be either colonized or infected, contact precautions are needed, as well as performing a good environmental cleaning to avoid the MDR transmission.

Limiting unnecessary catheter insertion and reducing catheterization duration are relevant prevention strategies[7]. In a prospective study that described 202 hospitalized patients with urinary catheter, the initial indication was judged to be inappropriate in 21%, and continued catheterization was judged to be inappropriate for almost one-half of catheter-days[8]. Surveillance of an indwelling UC is important too. Saint et al[9] reported a nation-wide study where 56% of hospitals did not have a system for monitoring which patients had urinary catheters placed, and 74% did not monitor duration of catheterization. Furthermore, a French prospective intervention study, showed a reduction in the frequency of CAUTI from 10.6 to 1.1 episodes per 100 patients, when nurses and physicians were reminded daily to remove unnecessary urinary catheters four days after insertion[10]. It also decreased the incidence of CAUTI from 12.3 to 1.8 per 1000 catheter-days. Lately, alternative prevention strategies to consider after catheter insertion like antimicrobial-coated catheters, catheter irrigation with antimicrobials, antimicrobials in the drainage bag or prophylaxis with cranberry products have been proposed. However, data are insufficient to make a recommendation about whether to use them.

TREATMENT

First, asymptomatic bacteriuria should be treated only in certain cases[11] such as pregnant women, before transurethral resection of the prostate or any traumatic genitourinary procedures associated with mucosal bleeding, immunosuppressed patients, or after the first year of renal transplantation. We should consider treating non-pregnant women if there is asymptomatic bacteriuria in the first 48 hours after UC sample. In other cases, antibiotics only eliminate bacteriuria transitorily and their administration neither decreases the frequency of symptomatic infection nor prevents further episodes of asymptomatic bacteriuria. This may also select MDR microorganism.

For symptomatic bacteriuria, before initiation of antibiotics and take of a new urine sample, we must withdraw or replace the UC[12]. To choose an adequate empirical treatment, we should consider the underlying conditions and the local epidemiology (risk of MDR). Carbapenems should be used in patients with high risk of MDR microorganisms as empirical treatment. Quinolones have a resistance of up to 20% in our country. This is important to highlight as it is not recommended to administer empirical antimicrobial treatment with antibiotics having more than 20% of resistant strains for non-complicated UTI or 10% for complicated ones. Treatment must be adjusted once an antimicrobial susceptibility is ready. Other antimicrobial agents are used depending on the aetiology (yeasts or other bacterial species). If a yeast is suspected, fluconazole is the first line antifungal. Amphotericin B is recommended only when fluconazole resistance is suspected. Overall, optimal treatment duration has been classically 14 days, but this can be shortened up to 5 days if there is an adequate clinical response. Follow-up urine cultures are not needed except if there is no clinical improvement 72 hours after treatment start.

MDR microorganisms have emerged during the last years as potential threats to infection control and their treatment can become challenging. Piperacillin/tazobactam is not recommended in monotherapy as empirical treatment of CAUTI if a MDR microorganism is suspected. Carbapenems can be used in monotherapy instead, although higher dose regimens have been suggested. Other options include colistin and disodic

fosfomycin. Rodriguez-Baño et al[13] comparing carbapenems with β-lactams/β-lactamase inhibitor combinations (BLBIC) for treatment of bacteraemia due to ESBL *E. coli*; did not find any significant differences in urinary bacteraemia mortality between carbapenems and BLBIC administered as definitive or empirical treatment. For the treatment of carbapenemases (CBP) Enterobacteriaceae; Tumbarello et al[14] presented a multicentre cohort including 661 adults with bloodstream or non-bacteraemic infections like UTI caused by a CBP *Klebsiella pneumoniae*. They found combination therapy with at least two drugs displaying *in vitro* activity against the isolate was associated with lower mortality. Moreover, combinations that included meropenem were associated with significantly higher survival rates when the meropenem MIC was ≤8 mg/L.

Thus, for the treatment of UTI caused by MDR microorganisms, we suggest either monotherapy or bitherapy should be decided considering severity of underlying conditions, severity of infection, MIC values and clinical response. Monotherapy can be safely used when no severity signs are present. Quinolones and cotrimoxazole can be used safely in definitive treatment only if MIC is optimal given the high frequency of resistance. New drugs like ceftazidime/avibactam and ceftolozane/tazobactam have irrupted in the last year, their role in handling UTI caused by MDR bacteria needs further studies.

CONCLUSIONS

CAUTI still represents a challenging entity in the field of nosocomial infection control. Although improvements to prevent its expansion like closed urinary drainage systems have been made, unnecessary insertion or prolonged urinary catheter remain as important problems, healthcare professionals must be aware of. Treatment must be conducted following certain criteria such as risk factors of severity and MDR and local epidemiology. Of capital importance is not use antimicrobial treatment for all asymptomatic bacteriuria and considering adjustment of treatment once an aetiology and antimicrobial susceptibility has been found to avoid unnecessary antimicrobial treatment and prevent the multiresistant microorganisms.

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