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Original article

Prevention of urinary tract infections by antibiotic cycling in spinal cord injury patients and low emergence of multidrug resistant bacteria

Prévention des infections urinaires par antibiothérapie cyclique chez les patients blessés médullaires et faible émergence de résistances

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Abstract

Background. – Urinary tract infections (UTIs) are a major recurrent problem for spinal cord injury (SCI) patients. Repeated antibiotic treatments contribute to the emergence of multidrug-resistant bacteria (MDRB). We evaluated the use of weekly oral cycling antibiotics (WOCA) in the prevention of UTIs over a mean follow-up period of 53 months (median follow-up period: 57 months) and analyzed the risk of MDRB emergence.

Methods. – We conducted a cross-sectional study of adult SCI patients with neurogenic bladder who were receiving the WOCA regimen.

Results. – We included 50 patients, mainly men (60%), with a mean age of 51 ± 13.5 years. Overall, 66% of patients had been paraplegic or tetraplegic for 19.4 ± 14.3 years; 92% underwent intermittent catheterization; and 36% had no postvoid residual. The number of febrile and non-febrile UTIs significantly reduced after WOCA initiation (9.45 non-febrile UTIs before WOCA initiation *vs*. 1.57 after; 2.25 febrile UTIs before WOCA initiation *vs*. 0.18 after; $P = 0.0001$). Only one adverse event was reported during the follow-up period. The number of MDRB-colonized patients decreased from 9/50 to 4/50 during the follow-up period.

Conclusion. – WOCA is an effective and safe strategy to prevent UTIs in SCI patients with neurogenic bladder. WOCA does not lead to the emergence of MDRB resistance and even seems to reduce MDRB carriage.

Keywords: Urinary tract infection; Antibiotic cycling; Spinal cord injury; Multidrug resistant bacteria

Résumé

Contexte. – Les infections urinaires (UI) représentent un problème récurrent chez les patients blessés médullaires. La prescription répétée d'antibiotiques participe à l'émergence de bactéries multirésistantes (BMR). Nous avons évalué, sur une longue période de suivi (53 mois en moyenne, avec une médiane de 57 mois), l'intérêt d'une antibioprophylaxie cyclique dans la prévention des infections urinaires (stratégie WOCA) et analysé le risque d'émergence de résistance induite.

Matériel et méthodes. – Nous avons réalisé une étude transversale portant sur des patients blessés médullaires avec vessie neurologique sous WOCA.

Résultats. – L'étude portait sur 50 patients, principalement des hommes (60 %), d'une moyenne d'âge de 51 ± 13,5 ans. Au total, 66 % étaient paraplégiques ou tétraplégiques depuis 19,4 ± 14,3 années en moyenne ; 92 % bénéficiaient d'un sondage intermittent ; et 36 % présentaient une vessie sans résidu postmictionnel. Le nombre d'infections urinaires fébriles et non fébriles a significativement diminué après la mise en place de l'antibioprophylaxie cyclique (9,45 infections urinaires non fébriles en moyenne avant WOCA versus 1,57 après WOCA ; 2,25 infections urinaires fébriles en moyenne avant WOCA versus 0,18 après WOCA, $p = 0{,}0001$). Un seul évènement indésirable a été rapporté au cours du suivi. Le nombre de patients colonisés à BMR a diminué au cours du suivi (9/50 à 4/50).

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Conclusion. – L'antibioprophylaxie cyclique est une stratégie efficace dans la prévention des IU chez les patients blessés médullaires avec vessie neurologique et n'induit pas l'émergence de résistance bactérienne, voire en diminue le portage.

Mots clés : Infection urinaire ; Antibiothérapie cyclique ; Blessés médullaires ; Bactéries multirésistantes

1. Introduction

A recent report published by the World Health Organization (WHO) revealed the extent of the public health threat posed by antimicrobial resistance [1]. Antibiotic therapy is now lacking therapeutic options and a steady increase in worldwide antimicrobial consumption is observed. This is leading to a constant increase in antimicrobial resistance [2]. The lack of new antimicrobial agents is not helping. Physicians sometimes have no choice but to expose patients to repeated antibiotic therapies such as patients presenting with recurrent urinary tract infection (UTI) or recurrent pneumonia due to chronic obstructive pulmonary disease. Patients with spinal cord injury (SCI) are of particular interest as they frequently present with recurrent UTIs and are thus particularly exposed to antibiotic therapy. The proportion of multidrug-resistant bacteria (MDRB)-colonized and -infected patients is higher in this population than in the general population [3]. UTI is also the primary cause of mortality and hospitalization in SCI patients and the main reason for antibiotic exposure [4,6]. Preventing UTIs is therefore a key priority in the management of SCI patients. Non-pharmacological interventions (intermittent catheterization, correct voiding and good bladder control, low vesical pressure) are effective but insufficient to prevent all UTIs in this population [7,8]. Effective strategies such as continuous antibiotic prophylaxis have been developed. However, they are associated with a high MDRB emergence, mainly because they disturb the intestinal microbiota [5,9,10]. Antibiotics have two main effects on the intestinal microbiota: they reduce bacterial diversity and result in an increased density and prevalence of resistant bacteria. The emergence of resistance in the commensal flora is the main driving force of bacterial resistance spreading to pathogenic bacteria with a high risk of patient-to-patient transmission [11]. These findings led to developing the Weekly oral cycling antibiotic (WOCA) program, which consists of the alternate weekly administration of an antibiotic to prevent the occurrence of UTIs. The efficacy of the WOCA regimen in preventing UTIs in SCI patients has already been proven [12]. Using various antibiotics administered in cycles may prevent the emergence of MDRB. However, the study was based on a two-year follow-up period and only included traumatic SCI patients with intermittent self-catheterization and without postvoid residual. Our aim was to analyze the efficacy of the WOCA strategy and to measure the incidence of MDRB emergence after a prolonged exposure (mean exposure of 63 months and median exposure of 57 months) in a large cohort study of SCI patients presenting with recurrent UTIs.

2. Methods

2.1. Study design

We conducted a cross-sectional single-center study in our teaching hospital. The hospital is a tertiary care hospital with expertise in the management of SCI patients.

2.2. Patients

We included SCI patients presenting with neurogenic bladder and recurrent UTIs. Prior to WOCA, all patients had experienced > 4 UTIs per year. Patients were followed for at least two years after inclusion in the study.

2.3. Definition of UTI

UTI was defined as followed:

- recent (< 48 h) onset of one or more of the following clinical symptoms: fever or shivers; altered mental status; malaise or lethargy with no other identifiable cause; flank pain, costovertebral angle tenderness; acute hematuria; pelvic discomfort; discomfort or pain in the kidney or bladder or during urination; urinary incontinence-onset or deterioration of urinary incontinence; increased frequency of catheterization/voiding; increased spasticity; autonomic dysreflexia;
- AND a bacteriuria ≥ 105 colony forming units (CFU)/mL of at least one bacterial species [13].

2.4. Data collection

Data was collected with a standardized questionnaire and included site of SCI, date and cause of injury, history of UTIs, allergies, immunosuppression, UTI risk factors, number of bladder catheterizations per day, voiding practice, number of related hospitalizations, number of UTIs before and with WOCA, duration of WOCA (at least two years), antibiotic treatment, discontinuation or switch of antibiotic regimen, adverse effects related to treatment, compliance, and UTI (febrile or non-febrile). Adverse events were recorded using the international Common Terminology Criteria [14]. Compliance was recorded using the Compliance Evaluation Test (CET), which contained six previously-validated questions assessing factors that could affect adherence to treatment [15]. We defined patients as "highly compliant" when "No" was answered to the six items and as "moderately compliant" in other cases.