

ORIGINAL ARTICLE

Prevalence and Natural History of Colonization With Fluoroquinolone-Resistant Gram-Negative Bacilli in Community-Dwelling People With Spinal Cord Dysfunction

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ABSTRACT. Roghmann M-C, Wallin MT, Gorman PH, Johnson JA. Prevalence and natural history of colonization with fluoroquinolone-resistant gram-negative bacilli in community-dwelling people with spinal cord dysfunction. *Arch Phys Med Rehabil* 2006;87:1305-9.

Objectives: To estimate the prevalence of colonization with fluoroquinolone-resistant gram-negative bacilli (GNB) and to assess risk factors for and define the natural history of colonization.

Design: Cross-sectional study with follow-up of up to 1 year.

Setting: Multiple outpatient sites.

Participants: Eighty-four community-dwelling adults with spinal cord dysfunction.

Interventions: Not applicable.

Main Outcome Measure: Colonization of perineum with fluoroquinolone-resistant GNB.

Results: Overall, 24% of this community-dwelling cohort was colonized with fluoroquinolone-resistant GNB with resistance to both levofloxacin and gatifloxacin. The use of any antibiotic in the last 90 days was most strongly associated with an increased risk of colonization with fluoroquinolone-resistant GNB (relative risk, 2.3; 95% confidence interval, 1.1–4.8; $P=.05$). Incontinence was significantly more common among those with fluoroquinolone-resistant GNB colonization. Among the participants with incontinence ($n=42$), the use of intermittent catheterization (vs suprapubic, urethral, or condom catheters or overflow incontinence) was significantly protective. Colonization was not associated with an increase in urinary tract infection and was often transient.

Conclusions: Fluoroquinolone resistance among GNB colonizing community-dwelling people with spinal cord dysfunction is common. Colonization is more common among those receiving antibiotics and less common among those continent of urine. Among those with incontinence, those using intermittent catheterization have less colonization.

Key Words: Antibiotic resistance; Anti-infective agents, fluoroquinolone; Cross-sectional study; Multiple sclerosis; Rehabilitation; Spinal cord injuries; Urinary tract infections.

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ANTIBIOTIC RESISTANCE IS A growing problem in gram-negative bacteria such as *Escherichia coli*, *Klebsiella* species, and *Pseudomonas aeruginosa*. Resistance to fluoroquinolone antibiotics in *P. aeruginosa* has increased by 37% in intensive care units with 33% of *P. aeruginosa* resistant to fluoroquinolones in 2002.¹ Resistance to fluoroquinolones in *E. coli* and *K. pneumoniae* has also been increasing in both inpatients and outpatients.²

Colonization and infection with antibiotic-resistant bacteria has long been a major problem for people with spinal cord injury (SCI) and disease (SCD)³⁻⁵; however, many of the studies in this population have been conducted in the inpatient setting.^{3,6,7} There have been a few reports of antibiotic resistance in a community setting. Waites et al⁸ reported resistance to 2 or more antibacterial agent categories in 33% of bacterial isolates from sterilely collected urine samples of outpatients with SCI returning for annual checkups. Hinkel et al⁴ reported an increasing number of fluoroquinolone-resistant gram-negative bacilli (GNB) obtained by aseptic catheterization among outpatients with SCI at their institution.⁴ GNB commonly cause urinary tract infections (UTIs), which are the most frequent infection in people with SCI.³ Antibiotic resistance can lead to inappropriate antibiotic selections, which can in turn lead to treatment failures.⁹ In addition, parenteral antibiotics are needed when UTIs are caused by bacteria resistant to all oral antibiotics.

Because most UTIs are caused by endogenous gastrointestinal flora, understanding the risk factors for colonization with antibiotic-resistant GNB in community-dwelling people with SCI or SCD can improve our care of these patients. We focused on resistance to fluoroquinolones because this class of antibiotics is typically the most active oral antibiotic class available for the treatment of UTIs. The objective of this study was to estimate the prevalence of colonization with fluoroquinolone-resistant GNB, to assess risk factors for colonization, and to define the natural history of colonization in a population of community-dwelling people with SCI or SCD.

METHODS

Study Design

This was a prospective study of community-dwelling adults with SCI or SCD (hereafter referred to collectively as SCD). We cultured the perineum of participants for fluoroquinolone-resistant GNB and assessed risk factors for colonization in a cross-sectional study. We then followed participants for up to

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1 year for antibiotic use and UTI. If participants were previously colonized, we repeated their cultures to determine if colonization was persistent.

Study Population

From April 2003 to June 2004, participants were recruited from multiple outpatient sites including a university-affiliated rehabilitation center (Kernan Orthopaedics and Rehabilitation Hospital, Baltimore, MD), 2 Veterans Affairs medical centers (VAMCs) (Baltimore, MD; Washington, DC), and a university-affiliated center for multiple sclerosis (MS) (Maryland Center for Multiple Sclerosis, Baltimore, MD). We used patient support groups (Paralyzed Veterans of America, Multiple Sclerosis Society) to increase study exposure during our recruitment period.

Adults with an SCD who have lived in the community more than 90% of the past 3 months were eligible to participate. SCD was defined as chronic (>3mo) complete or incomplete motor or sensory dysfunction because of either a posttraumatic or a medical disorder of the spinal cord. SCD from nontraumatic SCDs could include but were not limited to MS, spondylotic myelopathy, syringomyelia, epidural abscess or hemorrhage, spinal cord tumor, virus-related transverse myelitis, spinal cord infarction, or other familial or degenerative spinal cord disease. People with MS and associated urinary dysfunction were eligible to participate. Urinary dysfunction in people with MS was defined as any or all of the following urinary tract symptoms in the last 12 months: frequency, nocturia, hesitancy, retention, urgency, incontinence, dysuria, or change in urine color or odor.¹⁰

Participants provided informed consent and were followed longitudinally for up to 1 year. The institutional review boards of the University of Maryland, Baltimore, and the Washington, DC, VAMC approved the study protocol. Implementation of this study conformed to the approved protocol, as well as the ethical and humane principles of research.

Study Variables

We collected the following at enrollment from participants and their medical records: age, sex, ethnic background, etiology of SCD, years since onset of SCD, level of disability as measured by the Eastern Cooperative Oncology Group (ECOG),¹¹ presence of decubiti, method of emptying bladder, and previous hospitalizations and antibiotics within the last 90 days. If participants had MS, we classified them by subtype.¹² If participants had SCI because of trauma, we collected their American Spinal Injury Association (ASIA) Impairment Scale score.¹³ We chose to categorize the 6-point ECOG score as 0 to 2 and 3 to 5. People with an ECOG score of 0 to 2 are capable of all self-care. People with an ECOG score of 3 to 5 are capable of only limited self-care or completely disabled.

We obtained cultures of the perineal skin on enrollment and then quarterly. Cultures were plated on MacConkey agar and MacConkey agar with 4 µg/mL of ciprofloxacin to screen for the presence of fluoroquinolone-resistant GNB in a research microbiology laboratory. Ciprofloxacin-resistant bacteria were identified by using Vitek GNI cards or API20E.⁹ We used Etest assays^b to determine susceptibility to trimethoprim-sulfamethoxazole, gatifloxacin, levofloxacin, ertapenem, imipenem, ampicillin and sulbactam, piperacillin and tazobactam, and ceftazidime per Clinical and Laboratory Standards Institute standards.¹⁴ We collected data on antibiotic use including days on intravenous and oral (as applicable) antibiotics during the time in which the patients were being followed from their medical records. All patients were followed for at least 3 months.

In addition, we determined whether the antibiotic was prescribed for a UTI.

Urine for culture was collected via sterile intermittent catheterization when clinically indicated. UTIs were defined as 1 of the following: a urine culture of 10⁵ colony-forming units (cfu) per milliliter or more in a patient with at least 1 symptom of UTI or at least 2 urine cultures of 10³ cfu/mL or more in a patient with at least 2 of the common symptoms of UTI. Common symptoms of UTI included the following: fever (>38°C), urgency, frequency, dysuria, and suprapubic tenderness. Autonomic dysreflexia (hypertension, headache, visual changes, altered heart rate, flushing, diaphoresis, and/or nasal congestion) was also considered a symptom of UTI in our SCI participants. Worsening of MS symptoms was also considered a symptom of a UTI in patients with MS. The clinical microbiology laboratories for these outpatient sites worked up urine cultures from patients with SCI for 1 or more bacteria at concentrations of 10³ cfu/mL or more.

Study Analysis

Summary statistics included means and standard deviations for continuous variables and proportions for categorical variables. Group means were compared by using the *t* test or 1-way analysis of variance and proportions by the Pearson chi-square test or Fisher exact test, as appropriate. All statistical analyses were performed by using SPSS^c statistical software.

RESULTS

Table 1 gives a description of our participants. Of note, 83% were men. Fifty-two percent had MS, and 46% had trauma as a cause of their SCD. Of the 44 participants with MS, 20 were classified as relapsing remitting, 19 as secondary progressive, 3 as primary progressive, and 2 were not specified. Of the 36 participants with SCI because of trauma, 21 were ASIA grade A, 4 were B, 7 were C, and 4 were D. Of the remaining 4 participants, 1 had Brown-Sequard syndrome, 2 had central cord syndrome, and 1 had cauda equine syndrome.

Half of the cohort was continent, 43% used some type of urinary catheter, and 7% had overflow incontinence. Twenty-seven percent had used antibiotics in the 90 days before study enrollment, and 6% were hospitalized in the 90 days before enrollment.

Overall, 24% of this community-dwelling cohort was colonized with fluoroquinolone-resistant GNB with resistance to both levofloxacin and gatifloxacin. All levofloxacin-resistant isolates were also gatifloxacin resistant and vice versa. *Pseudomonas* species were the most common fluoroquinolone-resistant GNB (8/20), followed by *Acinetobacter* species (3/20), *Enterobacter* species (3/20), and *Citrobacter*, *Serratia*, *Proteus*, *S. maltophilia*, *E. coli*, and *E. fergusonii* (1 each). Fluoroquinolone-resistant GNB were also likely to be resistant to other antibiotics. Eighty percent were resistant to trimethoprim and sulfamethoxazole, 75% to ampicillin and sulbactam, 55% to ceftazidime, 25% to piperacillin and tazobactam, and 20% to imipenem.

Table 2 shows characteristics associated with fluoroquinolone-resistant GNB colonization. The use of any antibiotic in the last 90 days was most strongly associated with an increased risk of colonization with fluoroquinolone-resistant GNB (relative risk [RR], 2.3; 95% confidence interval [CI], 1.1–4.8; *P* = .05). Fluoroquinolone use alone did not increase the risk of colonization with fluoroquinolone-resistant GNB in a statistically significant degree (RR = 1.31; 95% CI, 0.46–3.67; *P* = .56).

Method of emptying the bladder was associated with colonization with fluoroquinolone-resistant GNB. Incontinence was

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