Clinical characteristics predicting early clinical failure after 72 h of antibiotic treatment in women with community-onset acute pyelonephritis: a prospective multicentre study

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Abstract

In patients with community-onset acute pyelonephritis (CO-APN), assessing the risk factors for poor clinical response after 72 h of antibiotic treatment (early clinical failure) is important. The objectives of this study were to define those risk factors, and to assess whether early clinical failure influences mortality and treatment outcomes. We prospectively collected the clinical and microbiological data of women with CO-APN in South Korea from March 2010 to February 2012. The numbers of cases in the early clinical success and early clinical failure groups were 840 (79.1%) and 222 (20.9%), respectively. Final clinical failure and mortality were higher in the early clinical failure group than in the early clinical success group (14.9% vs 2.3%, p <0.001; 6.8% vs 0.1%, p 0.001, respectively). In a multiple logistic regression model, the risk factors for early clinical failure among the total 1062 patients were diabetes mellitus (OR 1.5; 95% CI 1.1–2.1), chronic liver diseases (OR 3.3; 95% CI 1.6–6.7), malignancy (OR 2.2; 95% CI 1.1–4.4), Pitt score ≥2 (OR 2.5; 95% CI 1.6–3.8), presence of azotaemia (OR 1.8; 95% CI 1.2–2.7), white blood cell count ≥20 000/mm^3 (OR 2.5; 95% CI 1.6–4.0), serum C-reactive protein level ≥20 mg/dL (OR 1.7; 95% CI 1.2–2.4), and history of antibiotic usage within the previous year (OR 1.5; 95% CI 1.1–2.2). Analysing the subgroup of 743 patients with CO-APN due to Enterobacteriaceae, fluoroquinolone resistance of the uropathogen was another factor associated with early clinical failure (OR 1.7; 95% CI 1.1–2.5). Simple variables of underlying diseases, previous antibiotic usage and initial laboratory test outcomes can be used to decide on the direction of treatment in CO-APN.

Keywords: acute pyelonephritis, early clinical failure, risk factor
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Introduction

Acute pyelonephritis (APN) is an upper urinary tract infection characterized by inflammation of the renal parenchyma and renal pelvis typically due to a bacterial infection ascending from the bladder. It is a common bacterial infection in the community, especially in otherwise healthy women. It has been estimated that women are almost five times as likely as

men to be hospitalized for APN (11.7/10 000 vs 2.4/10 000) [1,2]. In South Korea, the annual incidence of APN is 35.7 per 10 000 people, with the rate of hospitalization for APN being 9.96 per 10 000 women and 1.18 per 10 000 men [3]. Several factors such as frequency of sexual intercourse in the previous 30 days, diabetes mellitus, urinary incontinence and a family history of urinary tract infections have been shown to increase the risk of APN [4,5].

Although APN is a common disease and is usually treated successfully with antimicrobial agents, it often requires hospitalization, and when accompanied by bacteraemia has a mortality rate of 5–20% [6–8]. In a retrospective study, factors associated with death among men and women with APN included age >65 years, septic shock and bedridden status; immunosuppression was a risk factor for death among men only and recent antibiotic use was a risk factor among women only [9]. Another study analysing uncomplicated APN in women showed that hospitalization at baseline, the presence of a resistant infecting organism, diabetes mellitus and a history of kidney stones were significant risk factors for a poor clinical response [10]. Patients with APN who have a risk of death or of a poor clinical response need hospitalization and close observation.

In clinical practice, if patients with APN do not show a clinical response after 72 h of antibiotic treatment (early clinical failure), radiological imaging of the urinary tract, investigation of other complicating factors or modification of the initial antimicrobial regimen in line with antibiotic susceptibility results are usually required [11]. Objective assessment of the risk factors for a poor clinical response after 72 h of treatment would help physicians to determine at the initial presentation whether hospitalization is needed. Furthermore, the increase of antimicrobial resistance among urinary pathogens in community-onset APN (CO-APN) makes the assessment of antibiotic resistance even more necessary [11]. We anticipate that demographic and clinical factors such as age, menopausal status, diabetes mellitus or other underlying diseases, simple laboratory test results that can be obtained in a short time in most hospitals and risk factors for antimicrobial resistance could be used to predict which APN patients are likely to suffer early clinical failure.

The objectives of our study were to define and characterize the risk factors for early clinical failure in CO-APN patients, and to establish whether early clinical failure has an effect on mortality and final treatment outcomes. To this end, we prospectively collected and analysed the clinical and microbiological data of women with CO-APN who visited 11 hospitals in South Korea from March 2010 to February 2012.

Materials and Methods

Study design

This study was a prospective, observational, multicentre cohort study of women with CO-APN in South Korea performed from 1 March 2010 to 28 February 2012. The study was conducted in 11 South Korean university hospitals with between 582 and ~1250 beds each. The hospitals that participated in this study were located throughout the Korean peninsula (three in Seoul, three in Gyeonggi-do, two in Incheon, two in Daegu and one in Busan), and ten were academic hospitals. The study protocol was approved by the institutional review boards of each participating centre. The institutional review boards waived the requirement for written informed consent from patients. All the data collected for this study were kept confidential.

Patient population

All patients admitted to the participating hospitals for CO-APN from March 2010 to February 2012 were enrolled consecutively in the study. APN was defined as fever ≥37.8°C, and presence of at least three of the followings: (i) pain in the flanks; (ii) costovertebral angle tenderness on examination; (iii) symptoms of lower urinary tract infection (dysuria, urgency, frequency, pain in the suprapubic region); (iv) pyuria (≥5–9 leucocytes/high-power field); and (v) leucocytosis (peripheral white blood cell (WBC) count >11 600/mm^3 or polymorphonuclear cells plus bands >65%) [12,13]. CO-APN was defined as a case presenting to the emergency department or an outpatient clinic from the community with the signs of APN just described. Any patient who was diagnosed with APN >48 h after admission or with a urinary-catheter-related infection was excluded from the study. Patients under 15 years, of male gender, those with other reasons for pyuria and fever and those with insufficient data were also excluded. Cases of CO-APN were enrolled at admission by an infectious diseases specialist.

Data collection and definitions

The clinical characteristics of all the eligible patients were collected prospectively using a web-based medical records system. Variables included demographic features (age, menopause status), clinical features and treatment outcomes. Treatment outcome was assessed in terms of early clinical response after 72 h of treatment, final clinical outcome (clinical cure or failure), microbiological outcome (microbiological eradication or failure), hospitalization days, and febrile days. Early clinical success was defined if the following criteria were met at 72 h after the start of empirical antimicrobial